

HCV inhibitory chemical compounds, pharmaceutical compositions and applications thereof

Technical Field

- 5 This invention relates to HCV inhibitory chemical compounds, pharmaceutical compositions and their applications.

Background Art

10 Hepatitis C virus (HCV) is the major pathogen that causes non-A non-B hepatitis. HCV infection may result in chronic liver diseases, such as hepatic cirrhosis and hepatic carcinoma. Since it is estimated that 3-5% of the world population have been infected with HCV, HCV infection is deemed an urgent human health problem (Lavanchy et al, *J. Viral Hepatitis*, **1999**, 6, 35-47; Alter et al, *J. Hepatology* **1999**, 31, 88-91; Alberti et al, *J. Hepatology* **1999**, 31, 17-24.).

15 HCV is a single strand RNA virus in the Flaviviridae family. It is comprised of a nucleocapsid protein (C), envelope proteins (E1 and E2), and some non-structural proteins (NS1, NS2, NS3, NS4a, NS5a and NS5b). A number of enzymes and protein domains of the virus can be the target of new drugs. NS5a of HCV is among the latest and most promising target. NS5A structurally consists of 3 independent characteristic fragments and
20 the functions of these fragments are still under investigation. At present, researches on the application of numerous NS5A inhibitors have been carried out by pharmaceutical companies rapidly and extensively.

It is found a group of chemical compounds can effectively inhibit the replication of HCV RNA by targeting at NS5A. Biological chemistry studies indicate that NS5A molecular
25 inhibitors can directly bind to NS5A polypeptide. This has been proven by the drug-resistant mutant in fragment I of NS5A polypeptide chain.

NS5A protein is a multifunctional protein in the forms of phosphorylated(p56) and hyperphosphorylated(p58) exposed groups. NS5A phosphorylation is involved a multiple aspects of the regulation of HCV replication. Even though the exact inhibitory mechanism
30 of these chemical compounds is still not clear, it has been confirmed that they can inhibit the hyperphosphorylation of NS5A. NS5A inhibitors break the hyperphosphorylation without affecting the fundamental phosphorylation at C-terminal region of NS5A. The activity of these inhibitors is independent of the characteristic fragments II and III of

NS5A and totally different from that of inhibitors that block the hyperphosphorylated kinases of NS5A; their activity is consistent with that of NS5A inhibitors whose binding site is the N-terminal region.

Moreover, NS5A inhibitors can promote the accumulation of intermediate polyproteins, suggesting that the binding of these inhibitors with NS5A has priority over polyprotein complex. Experiments demonstrated that NS5A inhibitors did change the subcellular localization, separation mode and biochemical fractionation result of NS5A proteins. NS5A inhibitors may affect the expression and regulation of HCV in many aspects. These findings may be helpful to the explanation of the special efficacy of these HCV replication complex inhibitors. Since the year 2000, many European and American research institutes and pharmaceutical companies have been extensively and thoroughly developing a variety of micromolecular HCV NS5A inhibitors, but so far non of these NS5A inhibitors has been approved to be marketed. All NS5A inhibitors currently in clinical stage suffer from a variety of shortcomings such as side effects of different degrees, therefore it is necessary to further develop new NS5A inhibitor of better therapeutic effect and lower side effects.

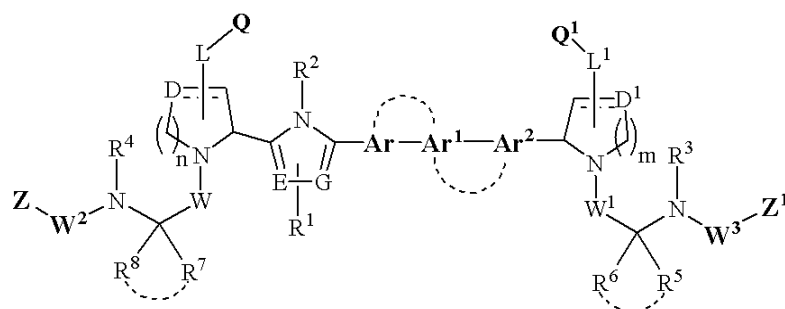
Summary of the invention

This invention, aiming to solve the existing technical problems and overcome the defect of the lack of effective HCV inhibiting drugs, proposes compounds, pharmaceutical compositions completely difference from existing ones and applications thereof. Capable of effectively inhibiting HCV NS5A, the compounds of this invention are used to prepare pharmaceutical drugs for the prevention and/or treatment of HCV-NS5A infection and showing a great market prospects.

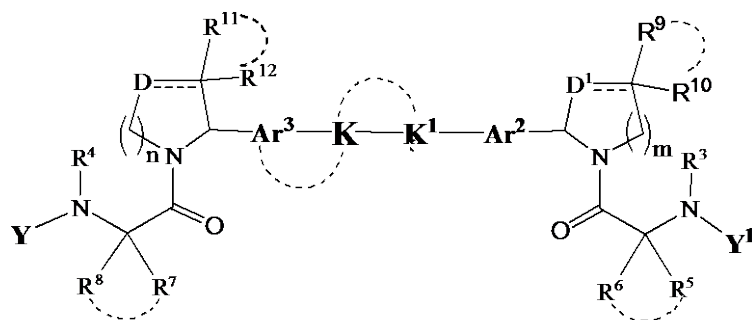
The present inventors have, through extensive R & D, designed and synthesized a group of chemical compounds which, being novel HCV-NS5A protein inhibitors, can be used to effectively inhibit HCV NS5A and treat HCV infections. It offers more and better options in the further optimization and clinical application of linear chain polypeptides polycyclic compounds for effective inhibition of HCV by introducing a variety of linear chain polypeptides based structures and structural optimization of the linear chain polypeptides polycyclic compounds for enhanced biological activities of the linear chain polypeptides heterocyclic compounds in inhibiting HCV NS5A.

This invention relates to compounds as represented by Formula Ia or Ib, their stereoisomers, tautomers, esterified or amidated prodrugs, pharmaceutically acceptable salts, or their isotopic substitutions in which the hydrogen, oxygen, nitrogen or sulfur

atom is replaced by its corresponding isotope,



Ia



Ib

5 Wherein, $n = 1, 2$ or 3 ; $m = 1, 2$ or 3 ;

“ ” is single bond or double bond;

When “ ” is a single bond, D and D^1 are each independently oxygen, sulfur,

$-\text{N}(\text{Ra})-$, $-\text{C}(\text{H}_2)-$, $-\text{C}(\text{OH})-$ or $-\text{C}(\text{Rb})(\text{Rc})-$; wherein, Ra is hydrogen, $\text{C}_1\text{-C}_{20}$ alkyl,

$\text{C}_3\text{-C}_{20}$ cycloalkyl, $\text{C}_6\text{-C}_{20}$ aryl, $\text{C}_2\text{-C}_{20}$ heterocyclic aryl, $\text{C}_1\text{-C}_{20}$ alkoxy carbonyl, $\text{C}_6\text{-C}_{20}$

10 aryloxycarbonyl, $\text{C}_2\text{-C}_{20}$ heterocyclic oxyl-carbonyl, $\text{C}_1\text{-C}_{20}$ alkylaminocarbonyl, $\text{C}_1\text{-C}_{20}$

cycloalkyl-oxy-carbonyl, $\text{C}_1\text{-C}_{20}$ alkyl sulfonyl, $\text{C}_3\text{-C}_{20}$ cycloalkyl sulfonyl, $\text{C}_1\text{-C}_{20}$

alkylamino sulfonyl, $\text{C}_2\text{-C}_{20}$ heterocyclic aminosulfonyl, or $\text{C}_6\text{-C}_{20}$ arylaminosulfonyl;

Rb and Rc are each independently hydrogen, halogen, hydroxy, nitrile, $\text{C}_1\text{-C}_{20}$ alkyl,

$\text{C}_3\text{-C}_{20}$ cycloalkyl, $\text{C}_2\text{-C}_{20}$ heterocyclic group, $\text{C}_6\text{-C}_{20}$ aryl, $\text{C}_1\text{-C}_{20}$ alkoxy, $\text{C}_1\text{-C}_{20}$ alkyl

15 sulphide, $\text{C}_1\text{-C}_{20}$ alkoxy carbonyl, $\text{C}_6\text{-C}_{20}$ aryloxy, $\text{C}_6\text{-C}_{20}$ heterocyclic aryloxy, $\text{C}_6\text{-C}_{20}$

fused aryloxy, $\text{C}_6\text{-C}_{20}$ fused cycloepoxy, $\text{C}_6\text{-C}_{20}$ aryloxycarbonyl, $\text{C}_2\text{-C}_{20}$ heterocyclic

oxy-carbonyl, $\text{C}_2\text{-C}_{20}$ heterocyclic aryl, $\text{C}_1\text{-C}_{20}$ alkylamino, $\text{C}_2\text{-C}_{20}$ heterocyclic amino,

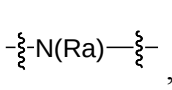
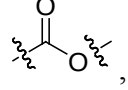
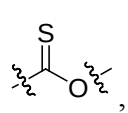
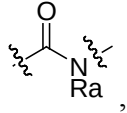
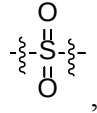
C₆-C₂₀ arylamino, C₁-C₂₀ alkylaminocarbonyl, C₁-C₂₀ alkylcarbonylamino, C₁-C₂₀ alkyl sulfonylamino, C₂-C₂₀ heterocyclic sulfonylamino, C₆-C₂₀ aryl sulfonylamino, C₁-C₂₀ alkylamino sulfonylamino; or Rb and Rc can be connected to become C₂-C₂₀ cycloalkenyl, C₂-C₂₀ cycloalkenyl, or C₂-C₂₀ cycloepoxy group;

- 5 When “ ” is a double bond, D and D¹ are each independently nitrogen, CH or C(Rb); wherein, Rb has the same definition with that of Rb in the defined D and D¹ when “ ” is a single bond;

- Ar, Ar¹, Ar² and Ar³ are each independently C₆-C₂₀ aryl, C₂-C₂₀ heterocyclic aryl, C₈-C₂₀ fused aryl, C₆-C₂₀ fused heterocyclic aryl; or, Ar and Ar¹ may be or Ar¹ and Ar² may be linked as shown by the dotted line to form C₁₀-C₂₀ fused alkylaryl, or C₈-C₂₀ fused aryl; if Ar¹ or Ar² does not exist, the groups on both sides of the absent Ar¹ or Ar² are linked directly; Ar³ is C₆-C₂₀ aryl, C₂-C₂₀ heterocyclic aryl, C₈-C₂₀ fused aryl group;

E and G are each independently nitrogen, CH or C(Rb); wherein, Rb has the same definition with that of Rb in the defined D and D¹ when “ ” is a single bond;

- 15 K and K¹ are each independently C₆-C₂₀ aryl, C₂-C₂₀ heterocyclic aryl, C₈-C₂₀ fused aryl, or C₄-C₂₀ fused heterocyclic aryl; wherein including heterocyclic aryl or non-aryl fused groups containing 2-4 fused rings;

L and L¹ are each independently oxygen, sulfur, , , , , , , or L and/or L¹ does not exist respectively; wherein, Ra has

- 20 the same definition with that of Ra in the defined D and D¹ when “ ” is a single bond;

Q and Q¹ are each independently C₁-C₂₀ alkyl, C₁-C₂₀ alkoxy, C₃-C₂₀ cycloalkyl, C₁-C₂₀ alkylamino, C₃-C₂₀ cycloalkylamino, C₆-C₂₀ aryl, C₃-C₂₀ fused aryl, C₃-C₂₀

heterocyclic aryl, or when L and/or L¹ does not exist respectively, Q and Q¹ connected by L and L¹ respectively do not exist either;

W and W¹ are each independently carbonyl, thiocarbonyl, C₁-C₂₀ alkyl, C₆-C₂₀ aryl or C₂-C₂₀ heterocyclic aryl group;

5 W² and W³ are each independently carbonyl, thiocarbonyl, sulfonyl, C₁-C₂₀ alkyl, C₂-C₂₀ heterocyclic group, C₆-C₂₀ aryl, C₂-C₂₀ heterocyclic aryl group;

Y and Y¹ are each independently hydrogen, C₁-C₂₀ alkyl, C₃-C₂₀ cycloalkyl, C₆-C₂₀ aryl, C₁-C₂₀ alkylcarbonyl, C₆-C₂₀ arylcarbonyl, C₁-C₂₀ alkoxy carbonyl, C₃-C₂₀ cycloalkoxy carbonyl, C₁-C₂₀ alkylaminocarbonyl, C₆-C₂₀ aryloxy carbonyl, C₃-C₂₀ heterocyclic aryloxy carbonyl, C₆-C₂₀ arylaminocarbonyl, C₁-C₂₀ alkylsulfonyl, C₃-C₂₀ cycloalkylsulfonyl, C₆-C₂₀ aryl sulfonyl, C₁-C₂₀ alkoxy sulfonyl, C₃-C₂₀ cycloalkyl-oxy-sulfonyl, or C₆-C₂₀ aryloxy sulfonyl group;

Z and Z¹ are each independently hydrogen, hydroxy, amino, C₁-C₂₀ alkyl, C₃-C₂₀ cycloalkyl, C₁-C₂₀ alkoxy, C₃-C₂₀ cycloalkoxy, C₁-C₂₀ alkylamino, C₃-C₂₀ cycloalkylamino, C₂-C₂₀ heterocyclic group, C₂-C₂₀ heterocyclic amino, C₆-C₂₀ aryl, C₆-C₂₀ aryloxy, C₆-C₂₀ arylamino, C₃-C₂₀ heterocyclic aryloxy, C₃-C₂₀ heterocyclic arylamino, C₁-C₂₀ alkyl sulfonylamino, C₃-C₂₀ cycloalkyl sulfonylamino, C₆-C₂₀ aryl sulfonylamino, C₁-C₂₀ alkoxy sulfonylamino, C₃-C₂₀ cycloalkoxy sulfonylamino, C₆-C₂₀ aryloxy sulfonylamino, C₁-C₂₀ alkylamino sulfonylamino, C₃-C₂₀ cycloalkylamino sulfonylamino, C₆-C₂₀ arylamino sulfonylamino group;

R¹, R², R³ and R⁴ are each independently hydrogen, C₁-C₂₀ alkyl, C₃-C₂₀ cycloalkyl, C₂-C₂₀ heterocyclic group, C₆-C₂₀ aryl, C₂-C₂₀ heterocyclic aryl, C₁-C₂₀ alkoxy carbonyl, C₆-C₂₀ aryloxy carbonyl, C₂-C₂₀ heterocyclic oxy-carbonyl, C₁-C₂₀ alkylaminocarbonyl, C₁-C₂₀ alkylaminosulfonyl, C₂-C₂₀ heterocyclic aminosulfonyl, or

C₆-C₂₀ arylaminosulfonyl group;

R⁵, R⁶, R⁷ and R⁸ are each independently hydrogen, halogen, hydroxy, nitrile, amino, C₁-C₂₀ alkyl, C₃-C₂₀ cycloalkyl, C₂-C₂₀ heterocyclic group, C₁-C₂₀ alkoxy, C₁-C₂₀ alkylamino, C₂-C₂₀ heterocyclic amino, C₆-C₂₀ aryl, C₆-C₂₀ arylamino, C₁-C₂₀ alkoxy carbonylamino, C₁-C₂₀ alkoxy carbonylamino, C₁-C₂₀ alkylsulfonylamino, C₂-C₂₀ heterocyclic sulfonylamino, C₆-C₂₀ arylsulfonylamino, C₁-C₂₀ alkylaminosulfonylamino, or cyclic structure formed by the linkage of R⁵ and R⁶, or cyclic structure formed by the linkage of R⁷ and R⁸;

R⁹, R¹⁰, R¹¹ and R¹² are each independently hydrogen, halogen, hydroxy, nitrile, amino, C₁-C₂₀ alkyl, C₃-C₂₀ cycloalkyl, C₁-C₂₀ alkoxy, C₁-C₂₀ alkylamino, C₂-C₂₀ heterocyclic amino, C₆-C₂₀ aryl, C₆-C₂₀ arylamino, or C₁-C₂₀ alkoxy carbonylamino; wherein, the R⁹ and R¹⁰ may be linked each other as a cyclic or spiral structure, the R¹¹ and R¹² may be linked each other as a cyclic or spiral structure.

The compounds as represented by Formula Ia or Ib mentioned in this invention, their stereoisomers, tautomers, esterified or amidated prodrugs, pharmaceutically acceptable salts, or their isotopic substitutions in which the hydrogen, oxygen, nitrogen or sulfur atom is replaced by its corresponding isotope, preferably, in Formula Ia or Ib,

Wherein, n = 1, 2 or 3; m = 1, 2 or 3;

“ ” is single bond or double bond;

When “ ” is a single bond, D and D¹ are each independently oxygen, sulfur,

$$-\overset{\cdot\cdot}{\underset{\cdot\cdot}{\text{N}}}(\text{Ra})-\overset{\cdot\cdot}{\underset{\cdot\cdot}{\text{C}}}^{\text{H}_2}, \quad -\overset{\cdot\cdot}{\underset{\cdot\cdot}{\text{C}}}^{\text{OH}}, \quad \text{or} \quad -\overset{\cdot\cdot}{\underset{\cdot\cdot}{\text{C}}}(\text{Rb})(\text{Rc})-\overset{\cdot\cdot}{\underset{\cdot\cdot}{\text{C}}}-$$
; wherein, Ra is hydrogen, C₁-C₁₅ alkyl, C₃-C₁₅ cycloalkyl, C₆-C₁₅ aryl, C₂-C₁₅ heterocyclic aryl, C₁-C₁₅ alkoxy carbonyl, C₆-C₁₅ aryloxy carbonyl, C₂-C₁₅ heterocyclic oxy-carbonyl, C₁-C₁₅ alkylaminocarbonyl, C₁-C₁₅ cycloalkyl-oxy-carbonyl, C₁-C₁₅ alkyl sulfonyl, C₃-C₁₅ cycloalkyl sulfonyl, C₁-C₁₅ alkylamino sulfonyl, C₂-C₁₅ heterocyclic aminosulfonyl, or C₆-C₁₅ arylaminosulfonyl; Rb and Rc are each independently hydrogen, halogen, hydroxy, nitrile, C₁-C₁₅ alkyl, C₃-C₁₅ cycloalkyl, C₂-C₁₅ heterocyclic group, C₆-C₁₅ aryl, C₁-C₁₅ alkoxy, C₁-C₁₅ alkyl sulphide, C₁-C₁₅ alkoxy carbonyl, C₆-C₁₅ aryloxy, C₆-C₁₅ heterocyclic aryloxy, C₆-C₁₅

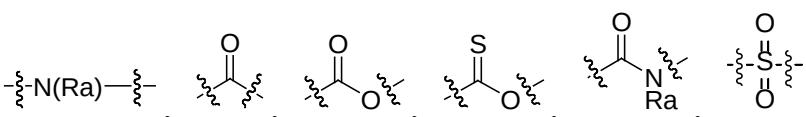
fused aryloxy, C₆-C₁₅ fused cycloepoxy, C₆-C₁₅ aryloxy-carbonyl, C₂-C₁₅ heterocyclic oxy-carbonyl, C₂-C₁₅ heterocyclic aryl, C₁-C₁₅ alkylamino, C₂-C₁₅ heterocyclic amino, C₆-C₁₅ arylamino, C₁-C₁₅ alkylaminocarbonyl, C₁-C₁₅ alkylcarbonylamino, C₁-C₁₅ alkyl sulfonylamino, C₂-C₁₅ heterocyclic sulfonylamino, C₆-C₁₅ aryl sulfonylamino,
 5 C₁-C₁₅ alkylamino sulfonylamino; or Rb and Rc can be connected to become C₂-C₁₅ cycloalkenyl, C₂-C₁₅ cycloalkenyl, or C₂-C₁₅ cycloepoxy group;

When “ ” is a double bond, D and D¹ are each independently nitrogen, CH or C(Rb); wherein, Rb has the same definition with that of Rb in the defined D and D¹ when “ ” is a single bond;

10 Ar, Ar¹, Ar² and Ar³ are each independently C₆-C₁₅ aryl, C₂-C₁₅ heterocyclic aryl, C₈-C₁₅ fused aryl, C₆-C₁₅ fused heterocyclic aryl; or, Ar and Ar¹ may be or Ar¹ and Ar² may be connected as shown by the dotted line to form C₁₀-C₁₅ fused alkylaryl, or C₈-C₁₅ fused aryl; if Ar¹ or Ar² does not exist, the groups on both sides of the absent Ar¹ or Ar² are linked directly; Ar³ is C₆-C₁₅ aryl, C₂-C₁₅ heterocyclic aryl, C₈-C₁₅ fused aryl group;

15 E and G are each independently nitrogen, CH or C(Rb); wherein, Rb has the same definition with that of Rb in the defined D and D¹ when “ ” is a single bond;

K and K¹ are each independently C₆-C₁₅ aryl, C₂-C₁₅ heterocyclic aryl, C₈-C₁₅ fused aryl, or C₄-C₁₅ fused heterocyclic aryl; wherein including heterocyclic aryl or non-aryl fused groups containing 2-4 fused rings; L and L¹ are each independently

20 oxygen, sulfur, , or L and/or L¹ does not exist respectively; wherein, Ra has the same definition with that of Ra in the defined D and D¹ when “ ” is a single bond;

Q and Q¹ are each independently C₁-C₁₅ alkyl, C₁-C₁₅ alkoxy, C₃-C₁₅ cycloalkyl,

C₁-C₁₅ alkylamino, C₃-C₁₅ cycloalkylamino, C₆-C₁₅ aryl, C₃-C₁₅ fused aryl, C₃-C₁₅ heterocyclic aryl, or when L and/or L¹ does not exist respectively, Q and Q¹ connected by L and L¹ respectively do not exist either;

W and W¹ are each independently carbonyl, thiocarbonyl, C₁-C₁₅ alkyl, C₆-C₁₅ aryl
5 or C₂-C₁₅ heterocyclic aryl group;

W² and W³ are each independently carbonyl, thiocarbonyl, sulfonyl, C₁-C₁₅ alkyl, C₂-C₁₅ heterocyclic group, C₆-C₁₅ aryl, C₂-C₁₅ heterocyclic aryl group;

Y and Y¹ are each independently hydrogen, C₁-C₁₅ alkyl, C₃-C₁₅ cycloalkyl, C₆-C₁₅ aryl, C₁-C₁₅ alkylcarbonyl, C₆-C₁₅ arylcarbonyl, C₁-C₁₅ alkoxy carbonyl, C₃-C₁₅
10 cycloalkyl-oxy-carbonyl, C₁-C₁₅ alkylaminocarbonyl, C₆-C₁₅ aryloxy carbonyl, C₃-C₁₅ heterocyclic aryloxy carbonyl, C₆-C₁₅ arylaminocarbonyl, C₁-C₁₅ alkylsulfonyl, C₃-C₁₅ cycloalkylsulfonyl, C₆-C₁₅ aryl sulfonyl, C₁-C₁₅ alkoxy sulfonyl, C₃-C₁₅ cycloalkoxy sulfonyl, or C₆-C₁₅ aryloxy sulfonyl group;

Z and Z¹ are each independently hydrogen, hydroxy, amino, C₁-C₁₅ alkyl, C₃-C₁₅
15 cycloalkyl, C₁-C₁₅ alkoxy, C₃-C₁₅ cycloalkoxy, C₁-C₁₅ alkylamino, C₃-C₁₅ cycloalkylamino, C₂-C₁₅ heterocyclic group, C₂-C₁₅ heterocyclic amino, C₆-C₁₅ aryl, C₆-C₁₅ aryloxy, C₆-C₁₅ arylamino, C₃-C₁₅ heterocyclic aryloxy, C₃-C₁₅ heterocyclic arylamino, C₁-C₁₅ alkyl sulfonylamino, C₃-C₁₅ cycloalkyl sulfonylamino, C₆-C₁₅ aryl sulfonylamino, C₁-C₁₅ alkoxy sulfonylamino, C₃-C₁₅ cycloalkoxy sulfonylamino,
20 C₆-C₁₅ aryloxy sulfonylamino, C₁-C₁₅ alkylamino sulfonylamino, C₃-C₁₅ cycloalkylamino sulfonylamino, C₆-C₁₅ arylamino sulfonylamino group; R¹, R², R³ and R⁴ are each independently hydrogen, C₁-C₁₅ alkyl, C₃-C₁₅ cycloalkyl, C₂-C₁₅ heterocyclic group, C₆-C₁₅ aryl, C₂-C₁₅ heterocyclic aryl, C₁-C₁₅ alkoxy carbonyl, C₆-C₁₅ aryloxy carbonyl, C₂-C₁₅ heterocyclic oxy-carbonyl, C₁-C₁₅ alkylaminocarbonyl,

C₁-C₁₅ alkylaminosulfonyl, C₂-C₁₅ heterocyclic aminosulfonyl, or C₆-C₁₅ arylaminosulfonyl group;

R⁵, R⁶, R⁷ and R⁸ are each independently hydrogen, halogen, hydroxy, nitrile, amino, C₁-C₁₅ alkyl, C₃-C₁₅ cycloalkyl, C₂-C₁₅ heterocyclic group, C₁-C₁₅ alkoxy, C₁-C₁₅ alkylamino, C₂-C₁₅ heterocyclic amino, C₆-C₁₅ aryl, C₆-C₁₅ arylamino, C₁-C₁₅ alkoxy carbonylamino, C₁-C₁₅ alkoxy carbonylamino, C₁-C₁₅ alkylsulfonylamino, C₂-C₁₅ heterocyclic sulfonylamino, C₆-C₁₅ arylsulfonylamino, C₁-C₁₅ alkylaminosulfonylamino, or cyclic structure formed by the linkage of R⁵ and R⁶, or cyclic structure formed by the linkage of R⁷ and R⁸;

R⁹, R¹⁰, R¹¹ and R¹² are each independently hydrogen, halogen, hydroxy, nitrile, amino, C₁-C₁₅ alkyl, C₃-C₁₅ cycloalkyl, C₁-C₁₅ alkoxy, C₁-C₁₅ alkylamino, C₂-C₁₅ heterocyclic amino, C₆-C₁₅ aryl, C₆-C₁₅ arylamino, or C₁-C₁₅ alkoxy carbonylamino; wherein, the R⁹ and R¹⁰ may be linked each other as a cyclic or spiral structure, the R¹¹ and R¹² may be linked each other as a cyclic or spiral structure.

The compounds as represented by Formula Ia or Ib mentioned in this invention, their stereoisomers, tautomers, esterified or amidated prodrugs, pharmaceutically acceptable salts, or their isotopic substitutions in which the hydrogen, oxygen, nitrogen or sulfur atom is replaced by its corresponding isotope, more preferably, in Formula Ia or Ib,

Wherein, n = 1, 2 or 3; m = 1, 2 or 3;

“ ” is single bond or double bond;

When “ ” is a single bond, D and D¹ are each independently oxygen, sulfur, $-\overset{\text{OH}}{\underset{\text{H}_2}{\text{C}}}-$, $-\overset{\text{OH}}{\underset{\text{H}}{\text{C}}}-$ or $-\text{C(Rb)(Rc)}-$; wherein, Ra is hydrogen, C₁-C₈ alkyl, C₃-C₈ cycloalkyl, C₆-C₁₂ aryl, C₂-C₁₂ heterocyclic aryl, C₁-C₈ alkoxy carbonyl, C₆-C₁₂ aryloxy carbonyl, C₂-C₈ heterocyclic oxy-carbonyl, C₁-C₈ alkylaminocarbonyl, C₁-C₈

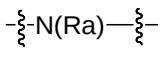
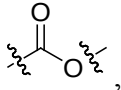
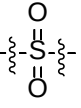
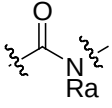
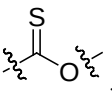
cycloalkyl-oxy-carbonyl, C₁-C₈ alkyl sulfonyl, C₃-C₈ cycloalkyl sulfonyl, C₁-C₈ alkylamino sulfonyl, C₂-C₈ heterocyclic aminosulfonyl, or C₆-C₁₂ arylaminosulfonyl; R_b and R_c are each independently hydrogen, halogen, hydroxy, nitrile, C₁-C₈ alkyl, C₃-C₈ cycloalkyl, C₂-C₈ heterocyclic group, C₆-C₁₂ aryl, C₁-C₈ alkoxy, C₁-C₈ alkyl sulphide, C₁-C₈ alkoxy carbonyl, C₆-C₁₂ aryloxy, C₆-C₁₂ heterocyclic aryloxy, C₆-C₁₂ fused aryloxy, C₆-C₁₂ fused cycloepoxy, C₆-C₁₂ aryloxycarbonyl, C₂-C₈ heterocyclic oxy-carbonyl, C₂-C₈ heterocyclic aryl, C₁-C₈ alkylamino, C₂-C₈ heterocyclic amino, C₆-C₁₂ arylamino, C₁-C₈ alkylaminocarbonyl, C₁-C₈ alkylcarbonylamino, C₁-C₈ alkyl sulfonylamino, C₂-C₈ heterocyclic sulfonylamino, C₆-C₁₂ aryl sulfonylamino, C₁-C₈ alkylamino sulfonylamino; or R_b and R_c can be connected to become C₂-C₈ cycloalkenyl, C₂-C₈ cycloalkenyl, or C₂-C₈ cycloepoxy group;

When “” is a double bond, D and D¹ are each independently nitrogen, CH or C(R_b); wherein, R_b has the same definition with that of R_b in the defined D and D¹ when “” is a single bond;

Ar, Ar¹, Ar² and Ar³ are each independently C₆-C₁₂ aryl, C₂-C₁₂ heterocyclic aryl, C₈-C₁₂ fused aryl, C₆-C₁₂ fused heterocyclic aryl; or, Ar and Ar¹ may be or Ar¹ and Ar² may be linked as shown by the dotted line to form C₁₀-C₁₅ fused alkylaryl, or C₈-C₁₅ fused aryl; if Ar¹ or Ar² does not exist, the groups on both sides of the absent Ar¹ or Ar² are linked directly;

E and G are each independently nitrogen, CH or C(R_b); wherein, R_b has the same definition with that of R_b in the defined D and D¹ when “” is a single bond;

K and K¹ are each independently C₆-C₁₂ aryl, C₂-C₁₂ heterocyclic aryl, C₈-C₁₂ fused aryl, or C₄-C₁₂ fused heterocyclic aryl; wherein including heterocyclic aryl or non-aryl fused groups containing 2-4 fused rings;

L and L¹ are each independently oxygen, sulfur, , , , , , , or L and/or L¹ does not exist respectively; wherein, Ra has the same definition with that of Ra in the defined D and D¹ when “” is a single bond;

5 Q and Q¹ are each independently C₁-C₈ alkyl, C₁-C₈ alkoxy, C₃-C₁₂ cycloalkyl, C₁-C₈ alkylamino, C₃-C₈ cycloalkylamino, C₆-C₁₂ aryl, C₃-C₁₅ fused aryl, C₃-C₁₂ heterocyclic aryl, or when L and/or L¹ does not exist respectively, Q and Q¹ connected by L and L¹ respectively do not exist either;

W and W¹ are each independently carbonyl, thiocarbonyl, C₁-C₈ alkyl, C₆-C₁₂ aryl
10 or C₂-C₁₂ heterocyclic aryl group;

W² and W³ are each independently carbonyl, thiocarbonyl, sulfonyl, C₁-C₈ alkyl, C₂-C₈ heterocyclic group, C₆-C₁₂ aryl, C₂-C₁₂ heterocyclic aryl group;

Y and Y¹ are each independently hydrogen, C₁-C₈ alkyl, C₃-C₈ cycloalkyl, C₆-C₁₂ aryl, C₁-C₈ alkylcarbonyl, C₆-C₁₂ arylcarbonyl, C₁-C₈ alkoxy carbonyl, C₃-C₈
15 cycloalkyl-oxy-carbonyl, C₁-C₈ alkylaminocarbonyl, C₆-C₁₂ aryloxy carbonyl, C₃-C₁₂ heterocyclic aryloxy carbonyl, C₆-C₁₂ arylaminocarbonyl, C₁-C₈ alkylsulfonyl, C₃-C₈ cycloalkylsulfonyl, C₆-C₁₂ aryl sulfonyl, C₁-C₈ alkoxy sulfonyl, C₃-C₈ cycloalkoxy sulfonyl, or C₆-C₁₂ aryloxy sulfonyl group;

Z and Z¹ are each independently hydrogen, hydroxy, amino, C₁-C₈ alkyl, C₃-C₈
20 cycloalkyl, C₁-C₈ alkoxy, C₃-C₈ cycloalkoxy, C₁-C₈ alkylamino, C₃-C₈ cycloalkylamino, C₂-C₈ heterocyclic group, C₂-C₈ heterocyclic amino, C₆-C₁₂ aryl, C₆-C₁₂ aryloxy, C₆-C₁₂ arylamino, C₃-C₁₂ heterocyclic aryloxy, C₃-C₈ heterocyclic arylamino, C₁-C₈ alkyl sulfonylamino, C₃-C₈ cycloalkyl sulfonylamino, C₆-C₁₂ aryl

sulfonylamino, C₁-C₈ alkoxy sulfonylamino, C₃-C₈ cycloalkoxy sulfonylamino, C₆-C₁₂ aryloxy sulfonylamino, C₁-C₈ alkylamino sulfonylamino, C₃-C₈ cycloalkylamino sulfonylamino, C₆-C₁₂ arylamino sulfonylamino group;

R¹, R², R³ and R⁴ are each independently hydrogen, C₁-C₈ alkyl, C₃-C₈ cycloalkyl, C₂-C₈ heterocyclic group, C₆-C₁₂ aryl, C₂-C₁₂ heterocyclic aryl, C₁-C₈ alkoxy carbonyl, C₆-C₁₂ aryloxy carbonyl, C₂-C₈ heterocyclic oxy-carbonyl, C₁-C₈ alkylaminocarbonyl, C₁-C₈ alkylaminosulfonyl, C₂-C₈ heterocyclic aminosulfonyl, or C₆-C₁₂ arylaminosulfonyl group;

R⁵, R⁶, R⁷ and R⁸ are each independently hydrogen, halogen, hydroxy, nitrile, amino, C₁-C₈ alkyl, C₃-C₈ cycloalkyl, C₂-C₈ heterocyclic group, C₁-C₈ alkoxy, C₁-C₈ alkylamino, C₂-C₈ heterocyclic amino, C₆-C₁₂ aryl, C₆-C₁₂ arylamino, C₁-C₈ alkoxy carbonylamino, C₁-C₈ alkoxy carbonylamino, C₁-C₈ alkylsulfonylamino, C₂-C₈ heterocyclic sulfonylamino, C₆-C₁₂ arylsulfonylamino, C₁-C₈ alkylaminosulfonylamino, or cyclic structure formed by the linkage of R⁵ and R⁶, or cyclic structure formed by the linkage of R⁷ and R⁸;

R⁹, R¹⁰, R¹¹ and R¹² are each independently hydrogen, halogen, hydroxy, nitrile, amino, C₁-C₈ alkyl, C₃-C₈ cycloalkyl, C₁-C₈ alkoxy, C₁-C₈ alkylamino, C₂-C₈ heterocyclic amino, C₆-C₁₂ aryl, C₆-C₁₂ arylamino, or C₁-C₈ alkoxy carbonylamino; wherein, the R⁹ and R¹⁰ may be linked each other as a cyclic or spiral structure, the R¹¹ and R¹² may be linked each other as a cyclic or spiral structure.

The compounds as represented by Formula Ia or Ib mentioned in this invention, their stereoisomers, tautomers, esterified or amidated prodrugs, pharmaceutically acceptable salts, or their isotopic substitutions in which the hydrogen, oxygen, nitrogen or sulfur atom is replaced by its corresponding isotope, more preferably, in Formula Ia or Ib,

Wherein, n = 1, 2 or 3; m = 1, 2 or 3;

“ ” is single bond or double bond;

When “ ” is a single bond, D and D¹ are each independently oxygen, $\begin{array}{c} \text{H}_2 \\ \vdots \\ \text{C} \\ \vdots \end{array}$,

$\begin{array}{c} \text{OH} \\ | \\ \text{---} \end{array}$, ---N(Ra)--- or ---C(Rb)(Rc)--- ; wherein, Ra is hydrogen, C₁-C₅ alkoxy carbonyl, C₁-C₅ alkyl sulfonyl, C₃-C₅ cycloalkyl sulfonyl; Rb is hydrogen; Rc is hydrogen, hydroxy, C₁-C₅ alkoxy, C₆-C₁₂ aryloxy, C₆-C₁₂ heterocyclic aryloxy, C₆-C₁₂ fused aryloxy, C₆-C₁₂ fused cycloepoxy; or Rb and Rc can be connected to become C₂-C₅ cycloalkenyl, or C₂-C₅ cycloepoxy group;

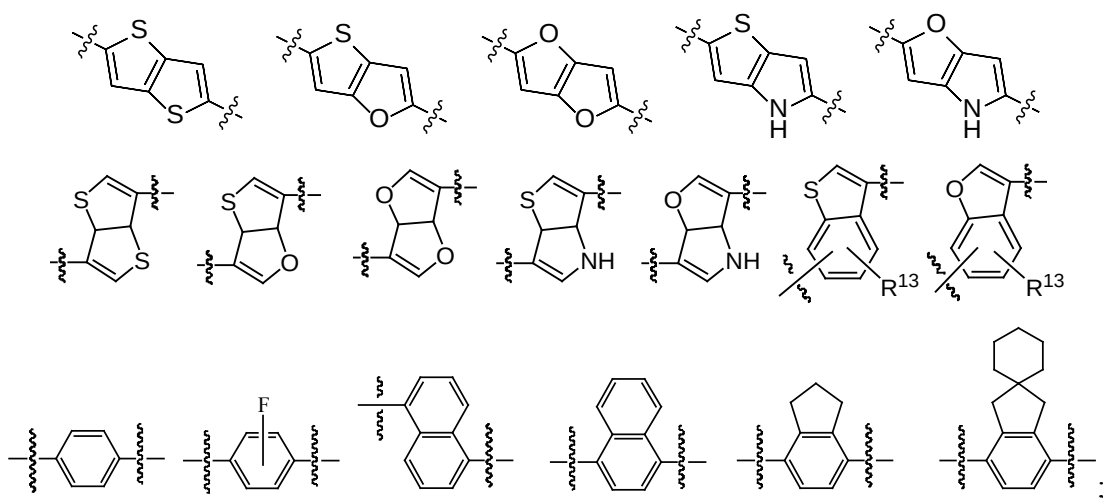
When “ --- ” is a double bond, D and D¹ are each independently CH;

Ar is C₆-C₈ aryl, C₁₀-C₁₅ fused aryl;

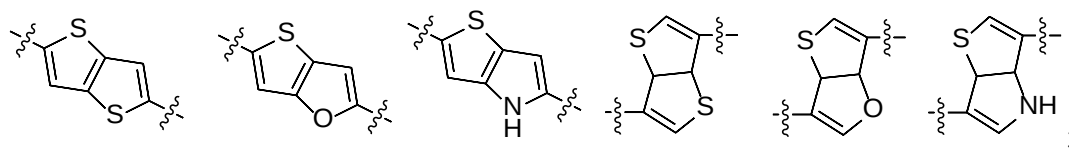
Ar¹, Ar² and Ar³ are each independently C₆-C₈ aryl, C₂-C₈ heterocyclic aryl, C₈-C₁₀ fused aryl, C₆-C₁₀ fused heterocyclic aryl, or Ar and Ar¹ may be or Ar¹ and Ar² may be linked as shown by the dotted line to form C₈-C₁₂ fused aryl; if Ar¹ or Ar² does not exist, the groups on both sides of the absent Ar¹ or Ar² are linked directly;

E is nitrogen; G is CH;

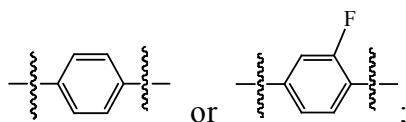
K and K¹ are each independently C₆-C₈ aryl, C₂-C₁₀ heterocyclic aryl, C₈-C₁₂ fused aryl, or C₄-C₁₂ fused heterocyclic aryl; wherein including the following heterocyclic aryl or non-aryl fused groups containing 2-4 fused rings;

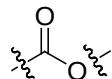


the described K is preferably



the described K^1 is preferably



L and L^1 are each independently oxygen, , , or L and/or L^1 does not
5 exist respectively;

Q and Q^1 are each independently C_1 - C_6 alkyl, C_1 - C_6 alkoxy, C_3 - C_6 cycloalkyl, C_3 - C_6 cycloalkylamino, C_6 - C_{12} aryl, C_3 - C_{12} fused aryl, or when L and/or L^1 does not exist respectively, the Q and Q^1 connected by L and L^1 respectively do not exist either;

W and W^1 are each independently carbonyl;

10 W^2 and W^3 are each independently carbonyl, thiocarbonyl, sulfonyl, C_1 - C_8 alkyl, C_2 - C_8 heterocyclic group, C_6 - C_{12} aryl, C_2 - C_{12} heterocyclic aryl group;

Y and Y^1 are each independently hydrogen, C_1 - C_6 alkylcarbonyl, C_6 - C_{10} arylcarbonyl, C_1 - C_6 alkoxy carbonyl, C_3 - C_6 cycloalkyl-oxy-carbonyl, C_1 - C_6 alkylaminocarbonyl, C_1 - C_6 alkylsulfonyl, C_3 - C_6 cycloalkylsulfonyl, or C_6 - C_{10} aryl
15 sulfonyl group;

Z and Z^1 are each independently C_1 - C_5 alkoxy, C_3 - C_5 cycloalkoxy, or C_1 - C_5 alkylamino group

R^1 and R^2 are each independently hydrogen; R^3 and R^4 are each independently hydrogen, C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, or C_6 - C_8 aryl group;

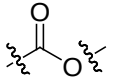
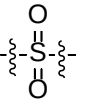
20 R^5 and R^7 are each independently hydrogen or C_1 - C_6 alkyl; R^6 and R^8 are each independently C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, or C_6 - C_8 aryl group; or a cyclic structure formed by the linkage of R^5 and R^6 , a cyclic structure formed by the linkage of R^7 and R^8 ;

Wherein, R^9 , R^{10} , R^{11} and R^{12} are each independently hydrogen, or C_1 - C_5 cyclic structure formed by the linkage of R^9 and R^{10} , C_1 - C_5 cyclic structure formed by the linkage of R^{11} and R^{12} ; R^{13} is hydrogen, halogen (e.g. fluorine, chlorine, bromine or iodine), C_1 - C_6 alkyl group (e.g. methyl, ethyl, propyl, isopropyl or tert-butyl group) or C_1 - C_6 alkoxy (e.g., methoxyl, ethoxyl, propoxyl, isopropoxyl or butoxyl group).

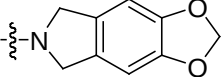
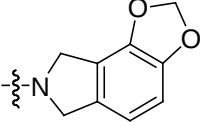
In this invention, the described compounds as represented by Formula Ia or Ib, their stereoisomers, tautomers, esterified or amidated prodrugs, pharmaceutically acceptable salts, or their isotopic substitutions in which the hydrogen, oxygen, nitrogen or sulfur atom is replaced by its corresponding isotope,

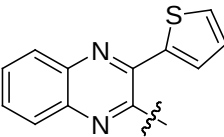
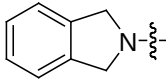
Wherein, $n = 1$, or 2 ; $m = 1$;

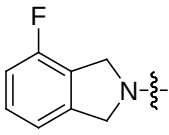
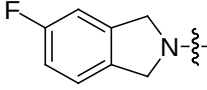
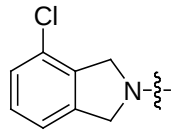
The D or D^1 are each independently oxygen, , , or ;

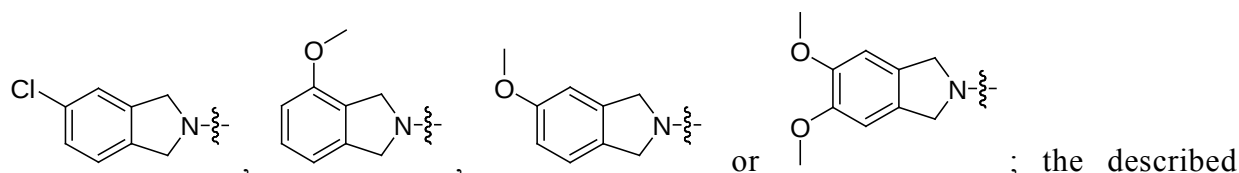
The described L or D^1 are each independently , , , or does not exist respectively;

the described Q or Q^1 is preferably C_1 - C_6 alkyl, C_1 - C_6 alkoxy, C_3 - C_6 cycloalkyl, or substituted or unsubstituted C_3 - C_{12} fused heterocyclic radical. the described C_1 - C_6 alkyl is preferably methyl, ethyl, propyl, isopropyl or tert-butyl; the described C_1 - C_6 alkoxy is preferably methoxyl, ethoxyl, propoxyl, isopropoxyl or butoxyl; the described C_3 - C_6 cycloalkyl is preferably cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl; the described substituted or unsubstituted C_3 - C_{12} fused heterocyclic radical is preferably substituted or unsubstituted C_3 - C_{12} fused aryl, in which the hetero-atom is oxygen, sulfur or nitrogen and the quantity of hetero-atom(s) is 1-3, more preferably, quinoxalyl, isoindolyl,

 or ; the described quinoxalyl is preferably

; the described isoindolyl is preferably , the described

substituted isoindolyl is preferably , , ,



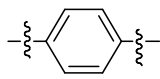
substitution in the described substituted or unsubstituted C₃-C₁₂ fused aryl is preferably by one or more halogen (preferably fluorine, chlorine or bromine), C₁-C₃ alkoxy (preferably methoxy) and C₄ heterocyclic aryl (preferably thiophene thiofuryl, more preferably 2-thiophene thiofuryl);

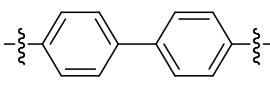
The described W、W¹、W² or W³ are  ;

The described E is nitrogen; G is CH;

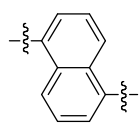
The described R³ or R⁴ is hydrogen;

The described Ar, Ar¹, Ar² or Ar³ is preferably substituted or unsubstituted C₆-C₁₂ aryl (preferably substituted or unsubstituted phenyl, or substituted or unsubstituted biphenyl);

the described unsubstituted phenyl is preferably  ; the described unsubstituted

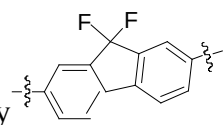
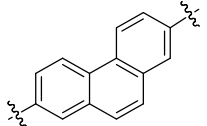
biphenyl is preferably ), the substituted or unsubstituted C₆-C₁₅

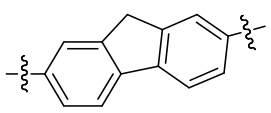
fused aryl (preferably substituted or unsubstituted naphthyl, substituted or unsubstituted anthryl, substituted or unsubstituted phenanthryl, substituted or unsubstituted fluorenyl, or substituted or unsubstituted C₆-C₁₂ fused aryl in which there are 1-3 hetero-atoms selected from oxygen, sulfur or nitrogen; the described unsubstituted naphthyl is preferably



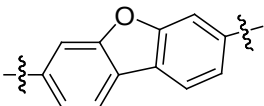
substituents selected from F, Cl and Br; the described fluorenyl with one or more substituents selected from F, Cl and Br is preferably fluorenyl substituted by one or more

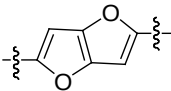
fluorine atoms, the described fluorenyl substituted by one or more fluorine atoms is

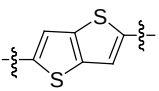
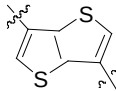
preferably  ; the described phenanthryl is preferably  ; the

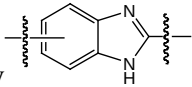
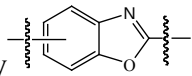
described unsubstituted fluorenyl is preferably  ; the described

unsubstituted C₆-C₁₂ fused aryl in which there are 1-3 hetero-atoms selected from oxygen,

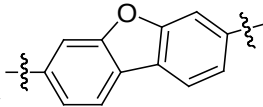
sulfur or nitrogen is preferably , furofuryl, thienothienyl or

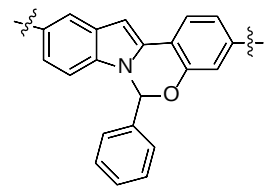
benzimidazolyl; the described furofuryl is preferably ; the described

thienothienyl is preferably  or ; the described benzimidazolyl is

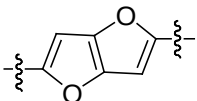
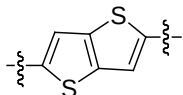
5 preferably ; the described benzoxazolyl is preferably ); wherein,

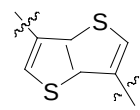
Ar and Ar¹ may be or Ar¹ and Ar² may be connected as shown by the dotted line to become substituted or unsubstituted C₆-C₁₅ fused aryl (preferably substituted or unsubstituted C₆-C₁₂ fused aryl in which there are 1-3 hetero-atoms selected from oxygen, sulfur or nitrogen, the described unsubstituted C₆-C₁₂ fused aryl in which there are 1-3

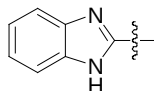
10 hetero-atoms selected from oxygen, sulfur or nitrogen is preferably ,



, furofuryl, thienothienyl or benzimidazolyl; the described furofuryl is

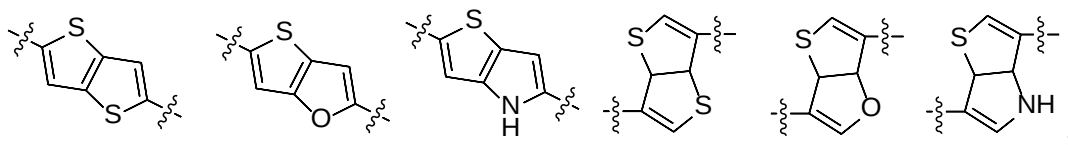
preferably ; the described thienothienyl is preferably  or



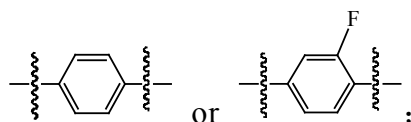
; the described benzimidazolyl is preferably ); the described

substituents in the described substituted or unsubstituted C₆-C₁₂ aryl, or substituted or unsubstituted C₆-C₁₅ fused aryl are preferably one or more substituents selected from F, Cl and Br; if Ar¹ or Ar² does not exist, the radicals on both side of the absent Ar¹ or Ar² are connected by chemical bonds directly; the described substituents in the described substituted or unsubstituted C₆-C₁₂ aryl, or substituted or unsubstituted C₆-C₁₅ fused aryl are one or more substituents selected from F, Cl and Br;

20 the described K is preferred selecting



the described K^1 is preferred selecting



the described R_5 or R_6 is preferably hydrogen, C_1 - C_5 alkyl (preferably C_1 - C_3 alkyl, more preferably isopropyl or tert-butyl), C_6 - C_{10} aryl (preferably phenyl; or C_3 - C_6 cycloalkyl or C_3 - C_6 heterocyclic radical formed by connecting R_5 and R_6 ;

the described R_7 or R_8 is preferably hydrogen, C_1 - C_5 alkyl (preferably C_1 - C_3 alkyl, more preferably isopropyl or tert-butyl), C_6 - C_{10} aryl (preferably phenyl); or C_3 - C_6 cycloalkyl (preferably cyclopropyl, cyclopentyl or cyclohexyl) or C_3 - C_6 heterocyclic radical formed by connecting R_7 and R_8 .

In this invention, the described compounds as represented by Formula Ia or Ib, their stereoisomers, tautomers, esterified or amidated prodrugs, pharmaceutically acceptable salts, or their isotopic substitutions in which the hydrogen, oxygen, nitrogen or sulfur atom is replaced by its corresponding isotope; when the described substituents in the described Q or Q^1 is substituted by halogens, the described halogens are selected from fluorine, chlorine or bromine;

When the described substituent Q or Q^1 is halogen, the described halogen is F, Cl, or Br;

When the described substituent Q or Q^1 is C_1 - C_3 alkoxy, the described C_1 - C_3 alkoxy is methoxy group;

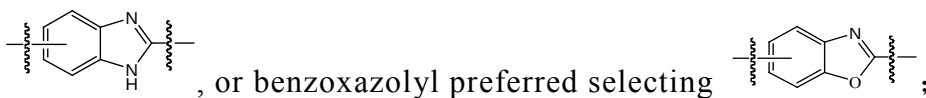
When the described substituent Q or Q^1 is C_4 heteroaryl, the described C_4 heteroaryl is thiophenyl;

When the described Ar, Ar^1 , Ar^2 or Ar^3 is substituted or unsubstituted C_6 - C_{12} aryl, the described substituted or unsubstituted C_6 - C_{12} aryl is substituted or unsubstituted phenyl, or substituted or unsubstituted biphenyl group;

When the described Ar, Ar^1 , Ar^2 or Ar^3 is substituted or unsubstituted C_6 - C_{15} fused aryl, the described substituted or unsubstituted C_6 - C_{15} fused aryl is substituted or unsubstituted naphthalenyl, substituted or unsubstituted anthracenyl, substituted or unsubstituted phenanthrenyl, substituted or unsubstituted fluorenyl, or substituted or

unsubstituted C₆-C₁₂ fused heteroaryl group with 1-3 of heteroatoms such as oxygen, sulfur, or nitrogen;

When the described Ar, Ar¹, Ar² or Ar³ is substituted or unsubstituted C₆-C₁₅ fused heterocyclic aryl, the described substituted or unsubstituted C₆-C₁₅ fused heterocyclic aryl is substituted or unsubstituted benzimidazolyl, which is preferred selecting



When the dotted line between both Ar and Ar¹ or both Ar² and Ar³ is linked each other to form the substituted or unsubstituted C₆-C₁₅ fused aryl group with heteroatom such as oxygen, sulfur, or nitrogen, or the substituted or unsubstituted C₆-C₁₂ fused aryl with 1-3 heteroatoms.

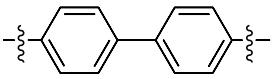
In this invention, the described compounds as represented by Formula Ia or Ib, their stereoisomers, tautomers, esterified or amidated prodrugs, pharmaceutically acceptable salts, or their isotopic substitutions in which the hydrogen, oxygen, nitrogen or sulfur atom is replaced by its corresponding isotope,

When the described Q or Q¹ is C₁-C₆ alkyl, the C₁-C₆ alkyl is methyl, ethyl, propyl, isopropyl, or t-butyl;

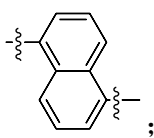
When the described Q or Q¹ is C₁-C₆ alkoxy, the C₁-C₆ alkoxy is methoxy, ethoxy, propoxy, isopropoxy, or t-butoxy;

When the described Q or Q¹ is C₃-C₆ cycloalkyl, the C₃-C₆ cycloalkyl is cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl;

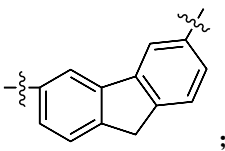
When the described Q or Q¹ is substituted or unsubstituted C₃-C₁₂ fused heterocyclic group, the substituted or unsubstituted C₃-C₁₂ fused heterocyclic group contains heteroatoms such as oxygen, sulfur, or nitrogen, or substituted or unsubstituted C₃-C₁₂ fused aryl with 1-3 of heteroatoms;

When the described Ar, Ar¹, Ar² or Ar³ is unsubstituted biphenyl, the unsubstituted biphenyl is  ;

When the described Ar, Ar¹, Ar² or Ar³ is unsubstituted naphthalenyl, the

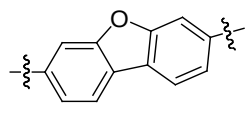
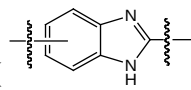
unsubstituted naphthalenyl is  ;

When the described Ar、Ar¹、Ar² or Ar³ is unsubstituted fluorenyl, the

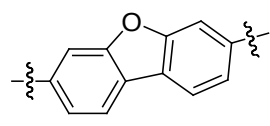
unsubstituted fluorenyl is  ;

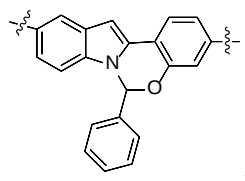
When the described Ar、Ar¹、Ar² or Ar³ is substituted fluorenyl, the substituted
5 fluorenyl has one or several of F, Cl, or Br substituents;

When the described Ar、Ar¹、Ar² or Ar³ is the substituted or unsubstituted C₆-C₁₂ fused heterocyclic aryl with 1-3 of heteroatoms such as oxygen, sulfur, or nitrogen, the corresponding unsubstituted C₆-C₁₂ fused heterocyclic aryl is

 , furo-furanyl, thienothiophenyl or benzimidazolyl () ;

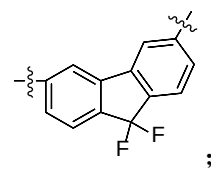
10 When the dotted line between both Ar and Ar¹ or both Ar² and Ar³ is linked each other to form the substituted or unsubstituted C₆-C₁₂ fused aryl group with 1-3 of heteroatoms such as oxygen, surfur, or nitrogen, the corresponding substituted or

unsubstituted C₆-C₁₂ fused aryl group with 1-3 of heteroatoms is  ,

 , furo-furanyl, thienothiophenyl or benzimidazolyl.

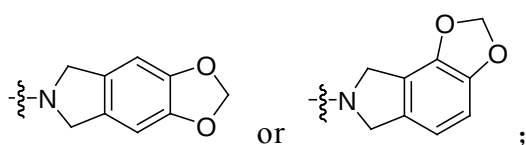
15 In this invention, the described compounds as represented by Formula Ia or Ib, their stereoisomers, tautomers, esterified or amidated prodrugs, pharmaceutically acceptable salts, or their isotopic substitutions in which the hydrogen, oxygen, nitrogen or sulfur atom is replaced by its corresponding isotope,

When the described Q or Q¹ is fluorenyl substituted with one or several of the

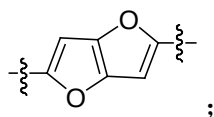
20 fluoro (F) atoms, the corresponding fluorenyl is  ;

When the described Q or Q¹ is the substituted or unsubstituted C₃-C₁₂ fused aryl group with 1-3 of heteroatoms such as oxygen, sulfur, or nitrogen, the corresponding

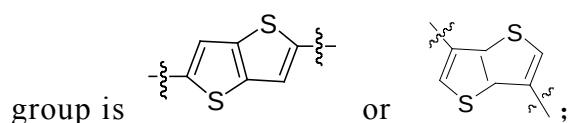
substituted or unsubstituted C₃-C₁₂ fused aryl is quinoxaliny, isoindolyl,



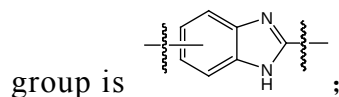
When the described Ar、Ar¹、Ar² or Ar³ is furo-furanyl, the furo-furanyl group is



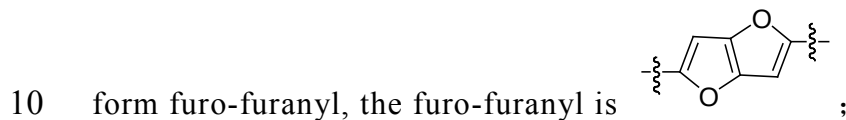
5 When the described Ar、Ar¹、Ar² or Ar³ is thienothiophenyl, the thienothiophenyl



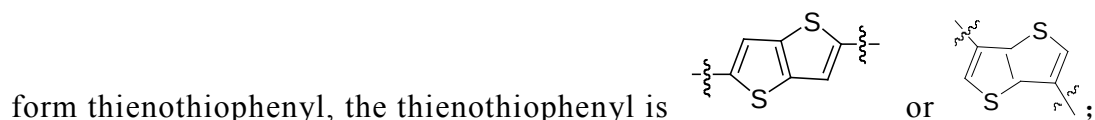
When the described Ar、Ar¹、Ar² or Ar³ is benzimidazolyl, the benzimidazolyl



When the dotted line between both Ar and Ar¹ or both Ar¹ and Ar² is linked to

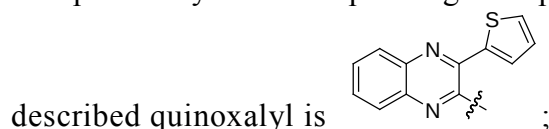


When the dotted line between both Ar and Ar¹ or both Ar¹ and Ar² is linked to



When the dotted line between both Ar and Ar¹ or both Ar¹ and Ar² is linked to form benzimidazolyl, the benzimidazolyl is

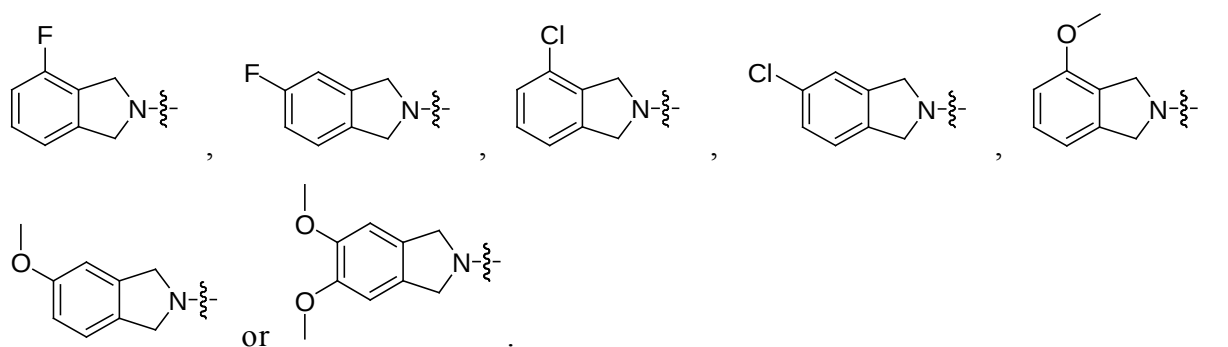
15 In this invention, the described compounds as represented by Formula Ia or Ib, their stereoisomers, tautomers, esterified or amidated prodrugs, pharmaceutically acceptable salts, or their isotopic substitutions in which the hydrogen, oxygen, nitrogen or sulfur atom is replaced by its corresponding isotope; when the described Q or Q¹ is quinoxalyl, the



20 When the described Q or Q¹ is isoindolyl, the isoindolyl is

When the described Q or Q¹ is the substituted isoindolyl, the substituted isoindolyl

is



The compounds as represented by Formula Ia or Ib mentioned in this invention, their stereoisomers, tautomers, isotope isomers, esterified or amidated prodrugs, pharmaceutically acceptable salts,

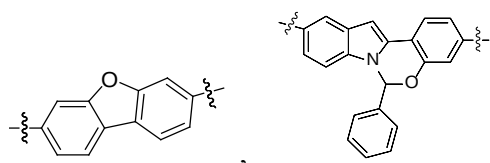
wherein, the described n is preferably 1 or 2; the described m is preferably 1; the described D or D¹ is preferably oxygen(O) or CH₂; the described L or L¹ is preferably absent; Q or Q¹ is preferably absent; the described W, W¹, W² or W³ is preferably ; the described E is preferably nitrogen; G is preferably CH; the described R³ or R⁴ is preferably hydrogen;

The described Ar, Ar¹, Ar² or Ar³ is preferably substituted or unsubstituted C₆-C₁₂ aryl (preferably substituted or unsubstituted phenyl, or substituted or unsubstituted biphenyl);

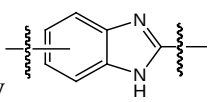
the described unsubstituted phenyl is preferably ; the described unsubstituted

biphenyl is preferably), substituted or unsubstituted C₆-C₁₅ fused aryl (the described substituted C₆-C₁₅ fused aryl is preferably C₆-C₁₅ fused aryl with F, Cl or Br substituent(s), or substituted or unsubstituted C₆-C₁₂ fused aryl in which there are 1-3 hetero-atom(s) selected from oxygen, sulfur or nitrogen, the described C₆-C₁₅ fused aryl with one or more F, Cl and Br substituents is preferably fluorenyl with one or more fluorine substituents, the described fluorenyl with one or more fluorine substituents is

preferably ; the described unsubstituted C₆-C₁₂ fused aryl is preferably



, furofuryl, thienothienyl or benzimidazolyl; the

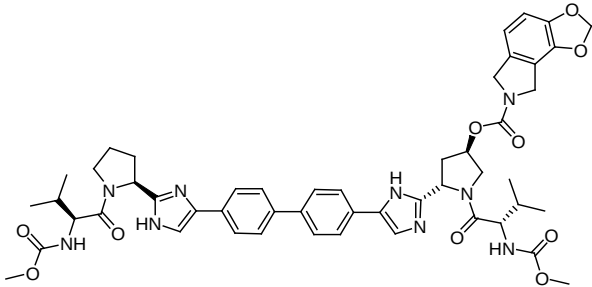
described benzimidazolyl is preferably );

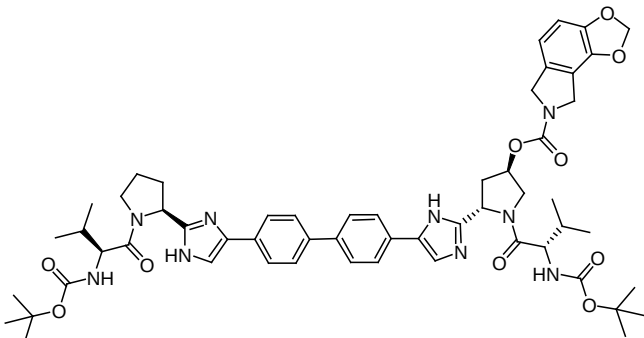
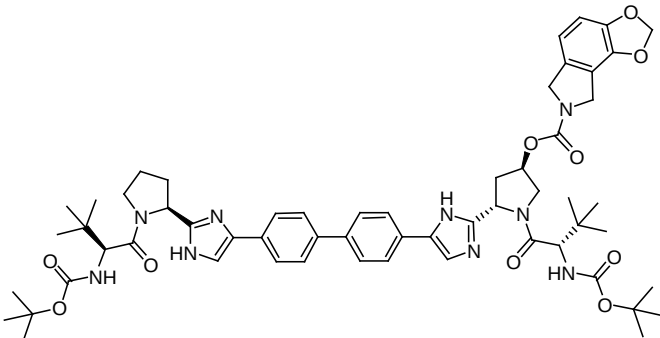
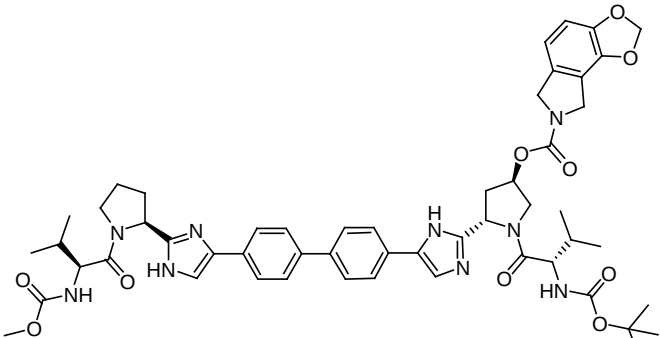
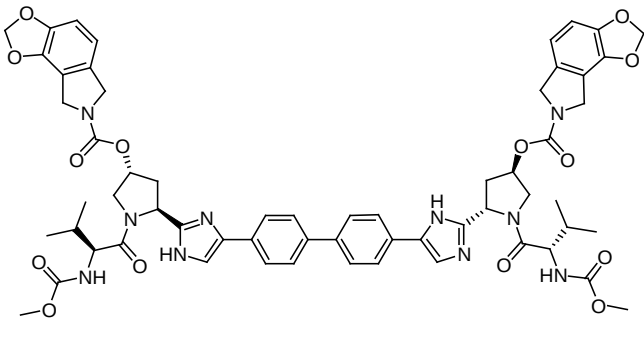
the described R⁵ or R⁶ is preferably hydrogen, C₁-C₅ alkyl (preferably C₁-C₃ alkyl, more preferably isopropyl or tert-butyl), C₆-C₁₀ aryl group (preferably substituted or unsubstituted phenyl); or C₃-C₆ cycloalkyl (preferably cyclopropyl, cyclopentyl or cyclohexyl) or C₃-C₆ aryl (preferably phenyl) formed by connecting R⁵ and R⁶, C₃-C₆ heterocyclic radical (preferably epoxyalkyl) formed by connecting R⁵ and R⁶; the described R⁷ or R⁸ is preferably hydrogen, C₁-C₅ alkyl (preferably C₁-C₃ alkyl, more preferably isopropyl or tert-butyl group), C₆-C₁₀ aryl (preferably substituted or unsubstituted phenyl); or C₃-C₆ cycloalkyl (preferably cyclopropyl, cyclopentyl or cyclohexyl) or C₃-C₆ heterocyclic radical (preferably epoxyalkyl) formed by connecting R⁷ and R⁸.

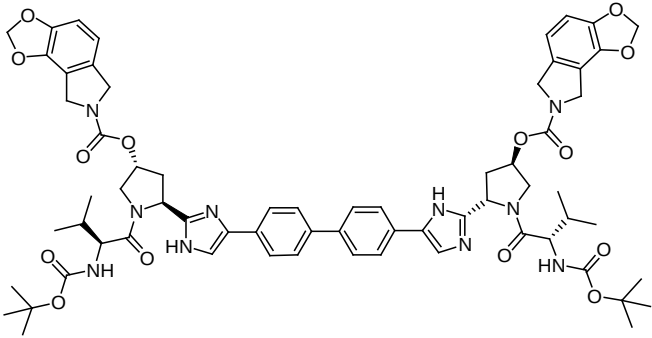
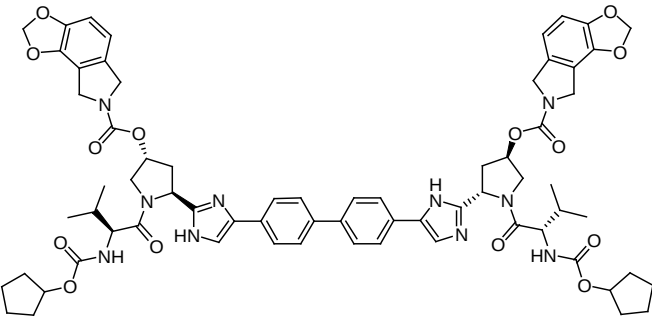
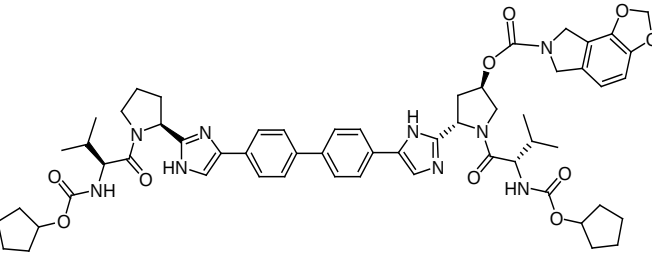
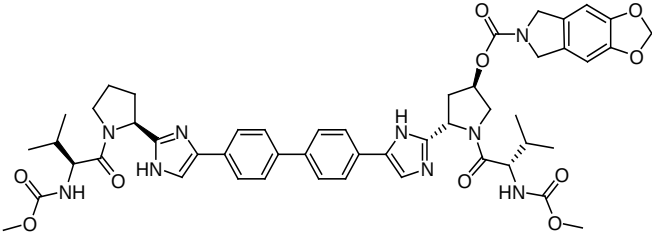
This invention also discloses mixtures of one or more components selected from the described compounds as represented by Formula **Ia** or **Ib**, their stereoisomers, tautomers, isotope isomers, esterified or amidated prodrugs and pharmaceutically acceptable salts.

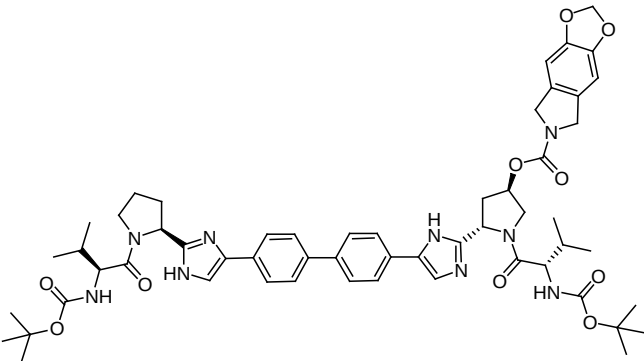
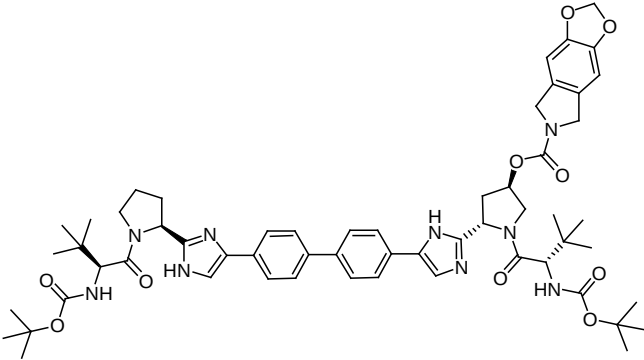
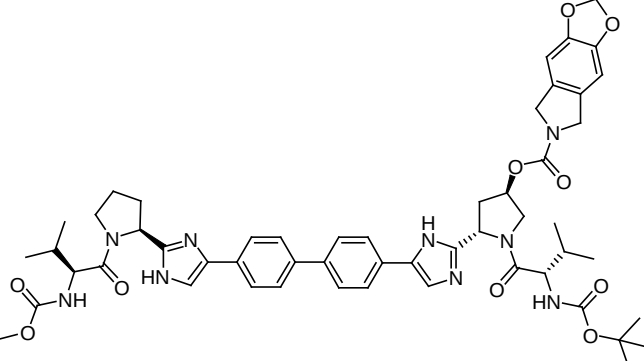
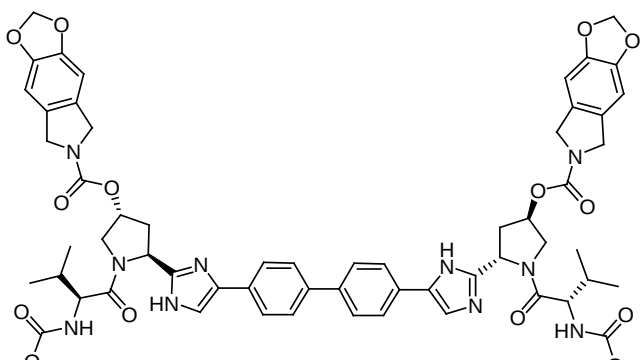
The compounds as represented by Formula **Ia** or **Ib** mentioned in this invention, their stereoisomers, tautomers, esterified or amidated prodrugs and pharmaceutically acceptable salts can be more preferably optimized to get any chemical compounds as shown below:

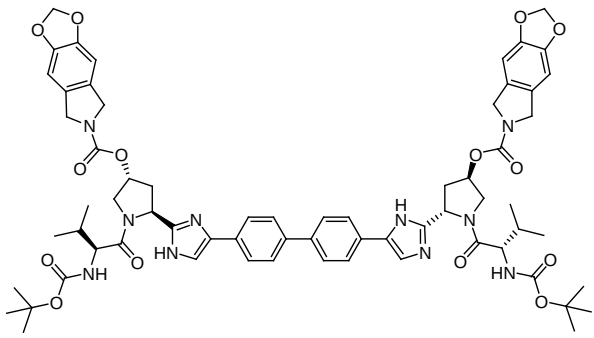
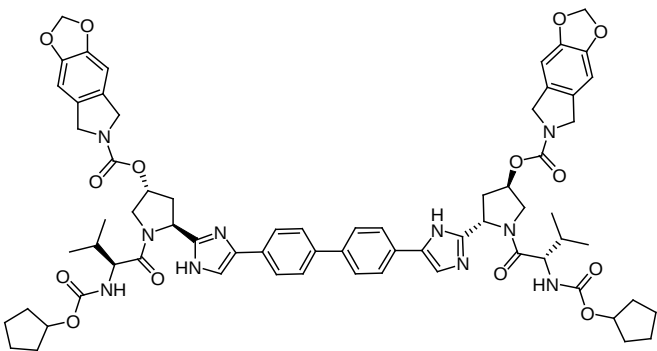
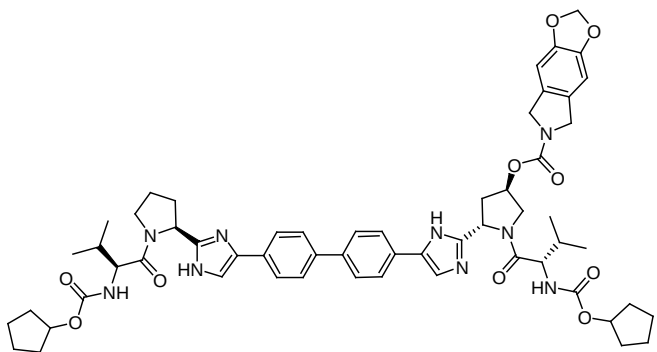
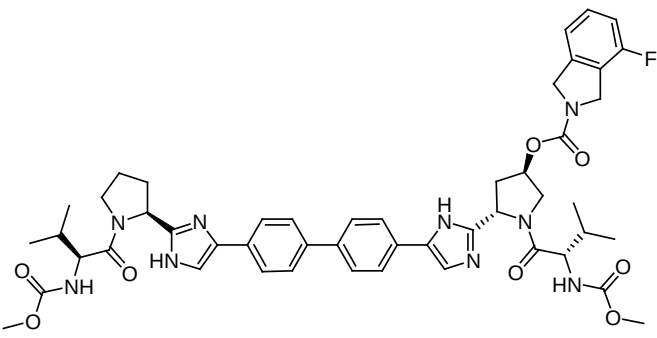
Compounds as represented by Formula **Ia** have a structural structure as shown below:

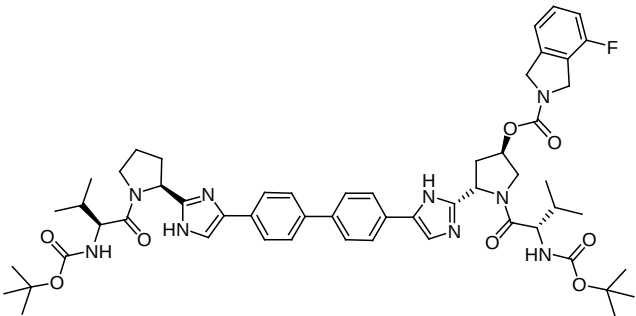
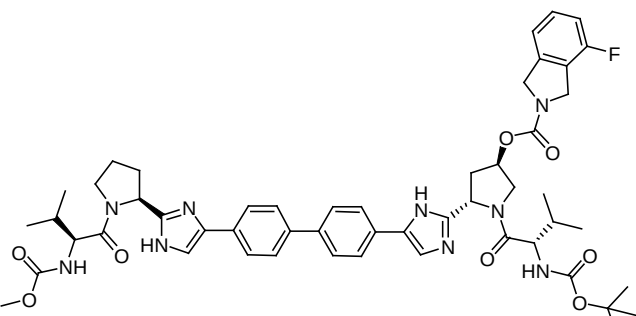
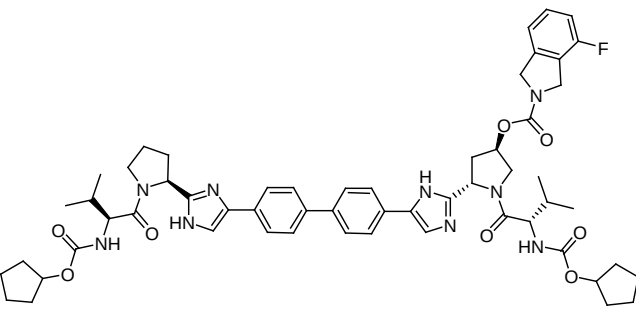
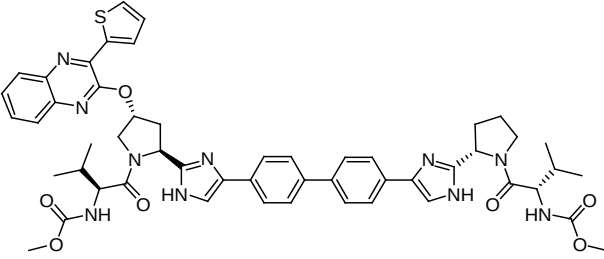
NO.	Compounds as represented by Formula Ia
Ia-1	 6a

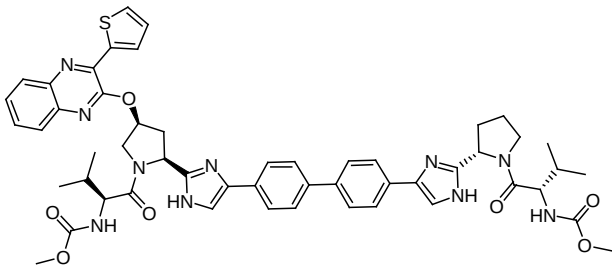
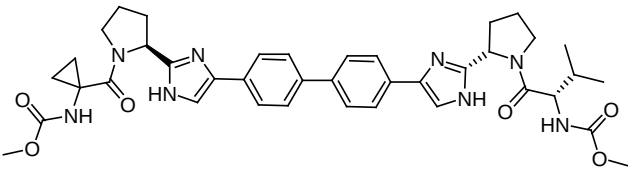
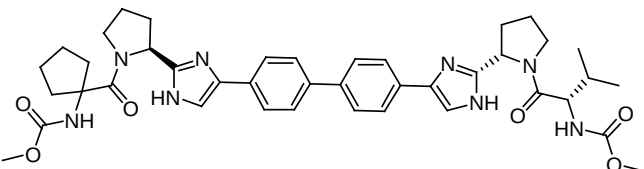
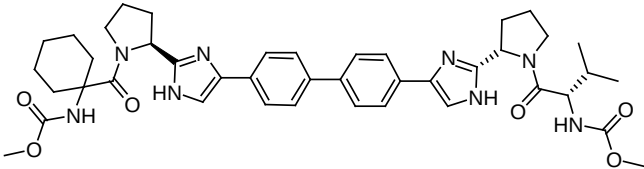
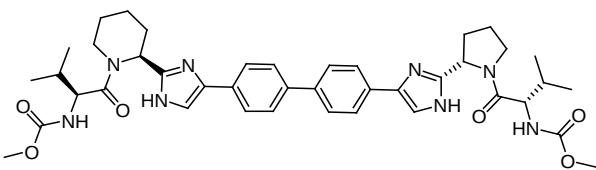
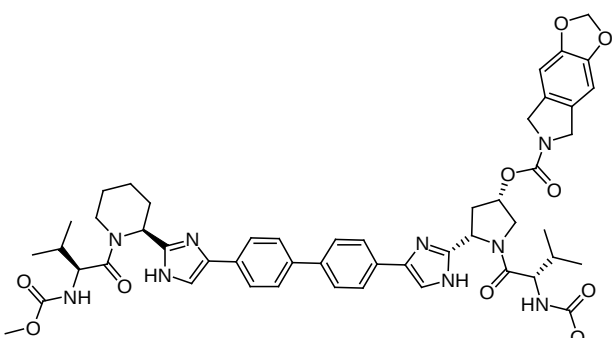
Ia-2	 6b
Ia-3	 6c
Ia-4	 6d
Ia-5	 6e

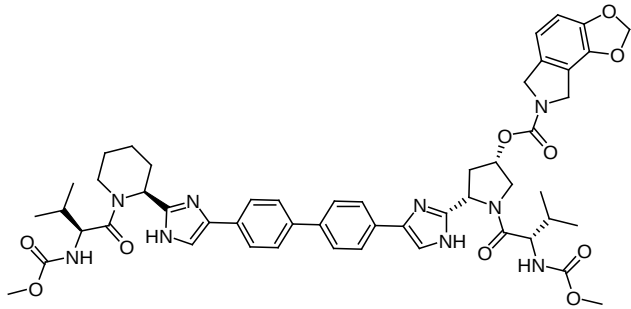
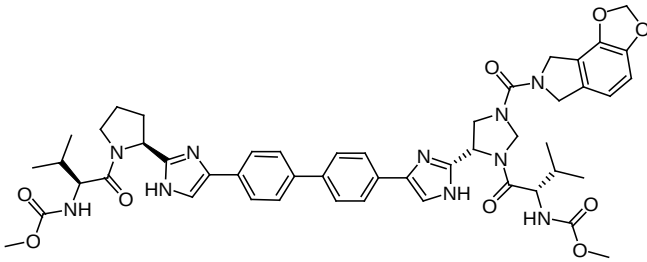
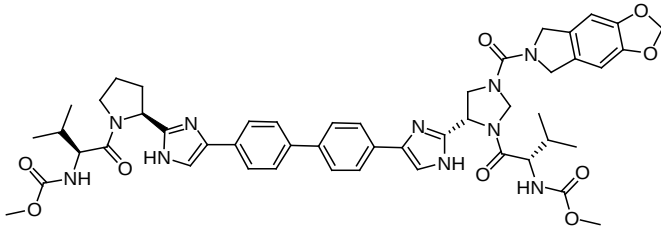
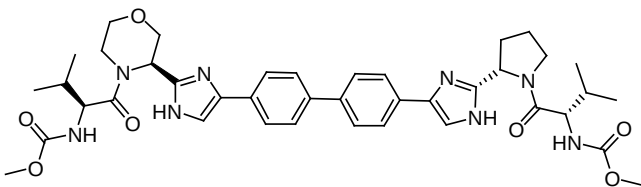
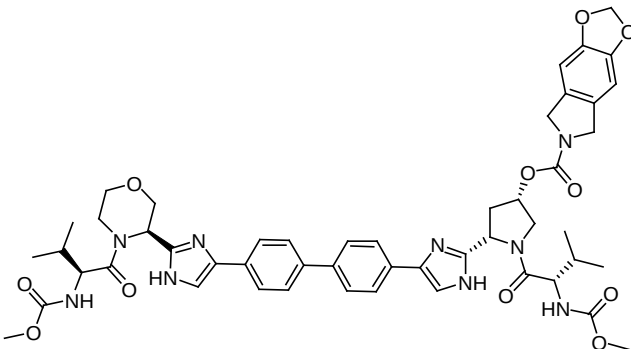
Ia-6	 6f
Ia-7	 6g
Ia-8	 6h
Ia-9	 6i

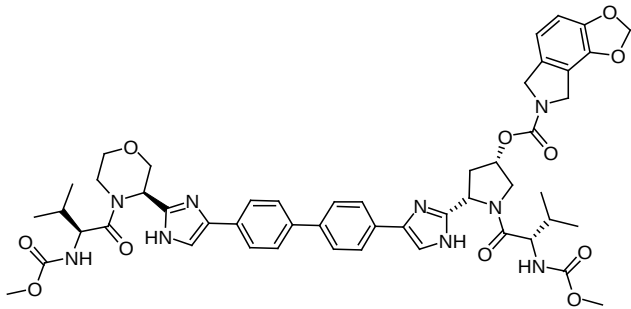
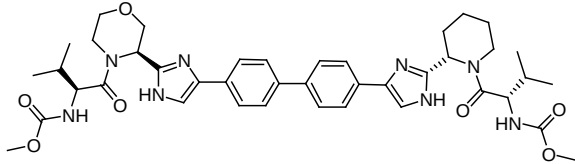
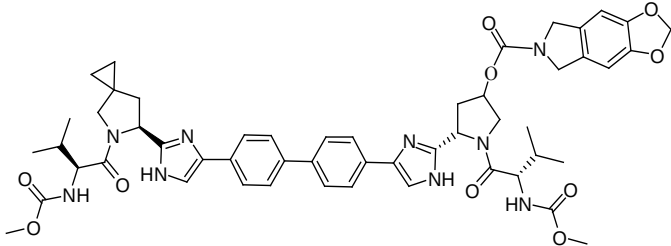
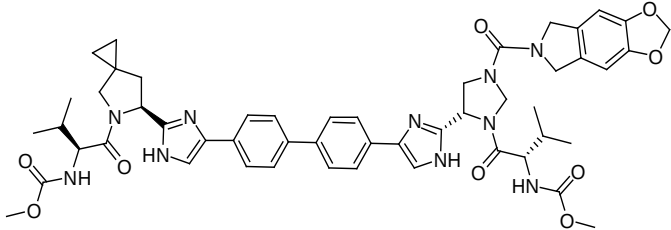
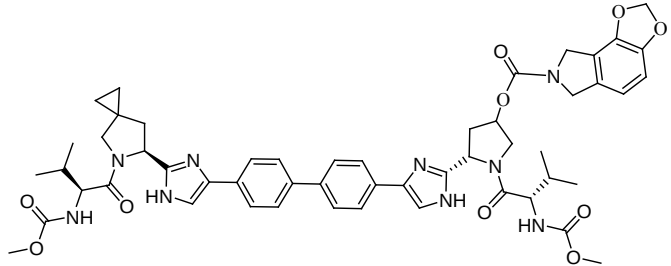
Ia-10	 6j
Ia-11	 6k
Ia-12	 6m
Ia-13	 6n

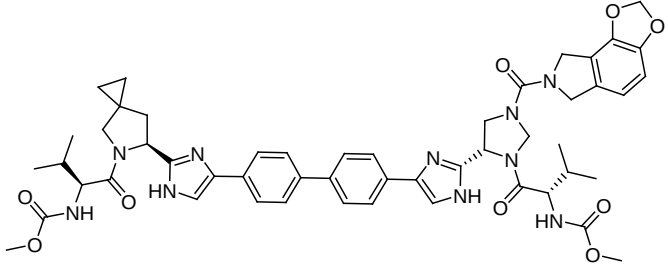
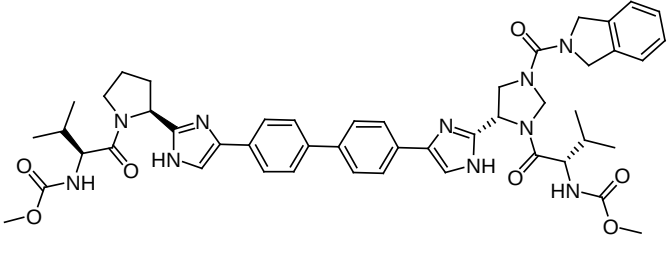
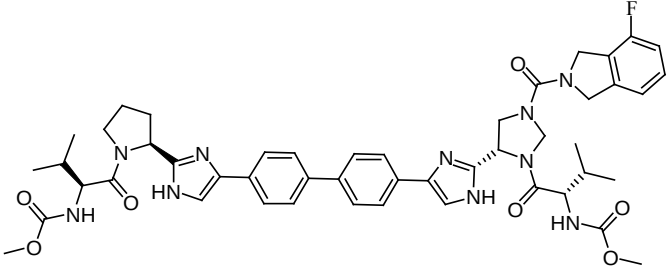
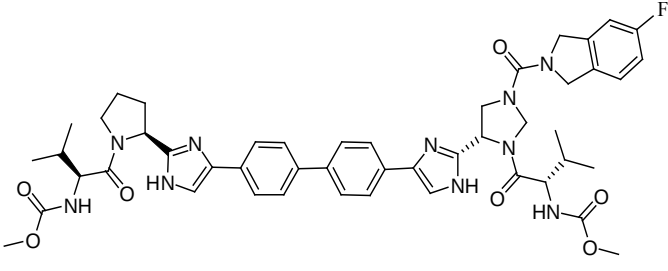
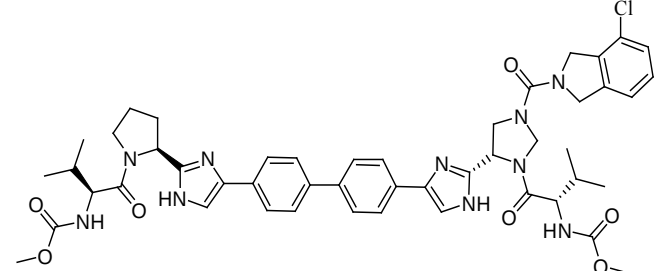
Ia-14	 6p
Ia-15	 6q
Ia-16	 6r
Ia-17	 6s

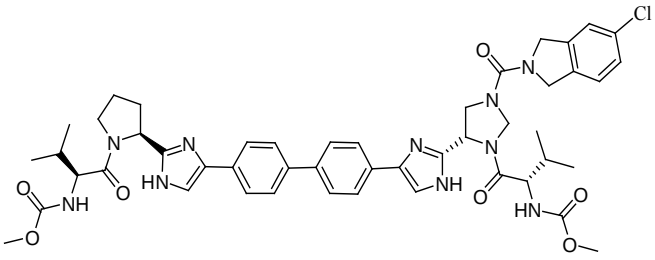
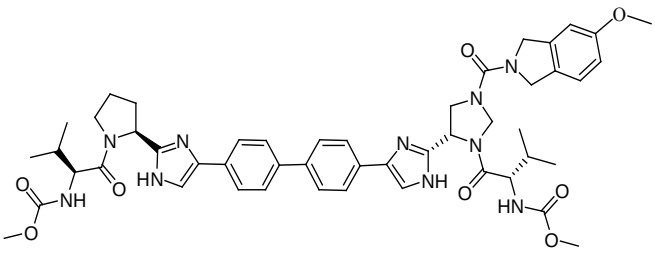
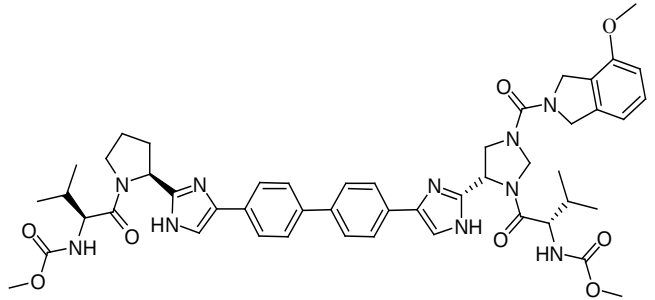
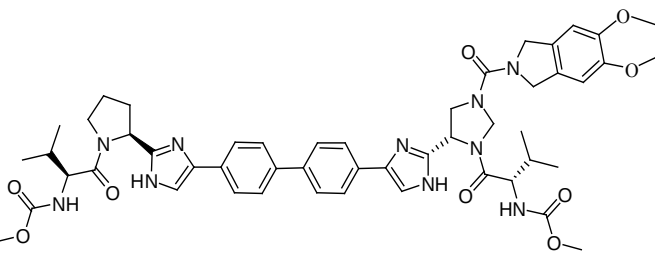
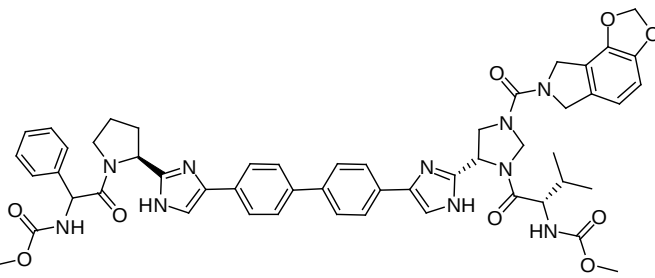
Ia-18	 6t
Ia-19	 6u
Ia-20	 6v
Ia-21	 6w

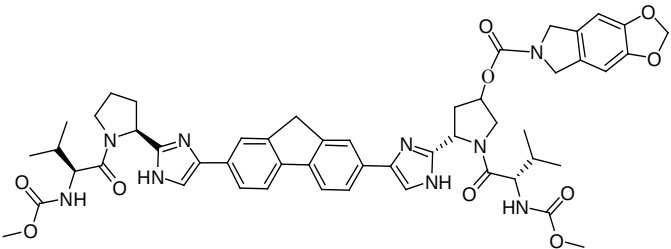
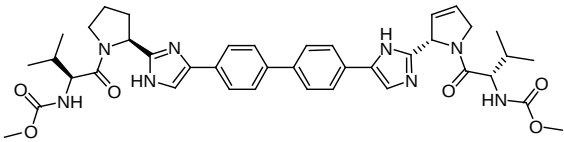
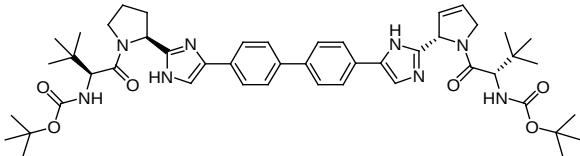
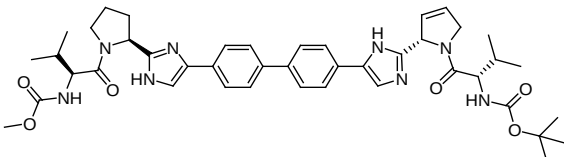
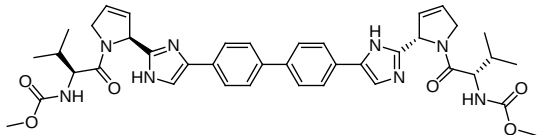
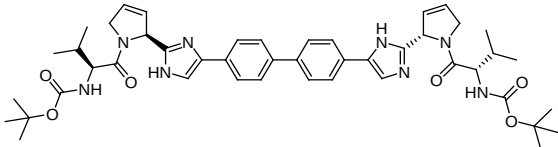
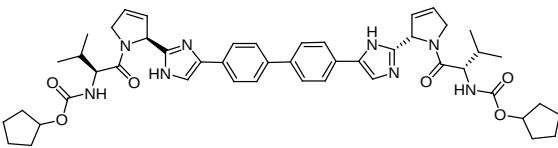
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Ia-27	

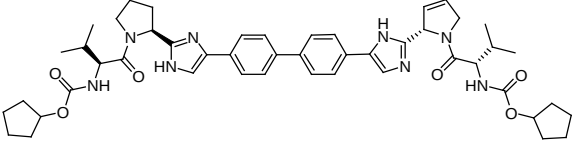
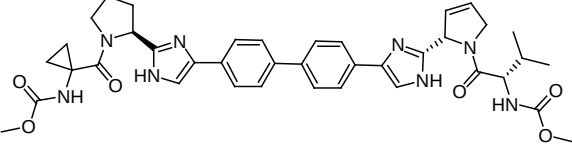
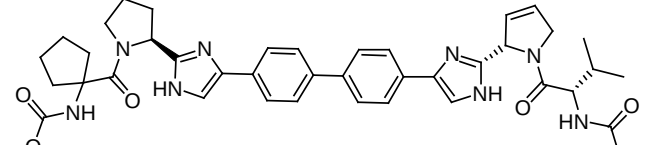
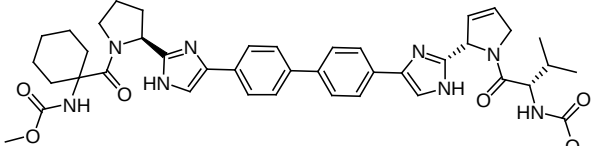
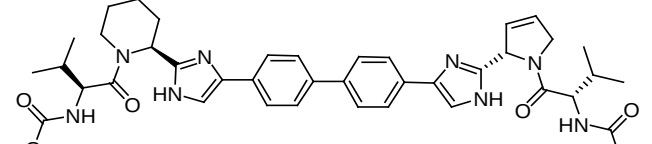
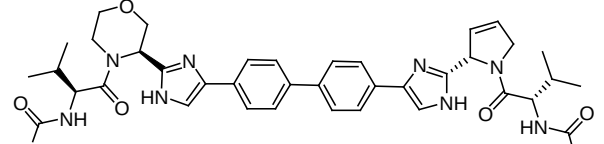
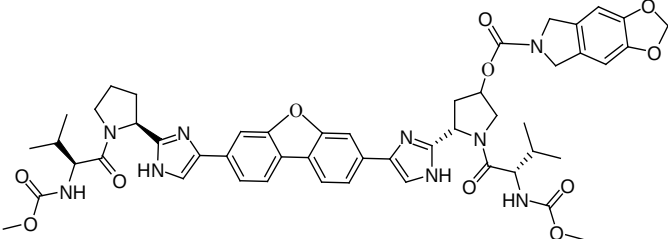
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Ia-32	

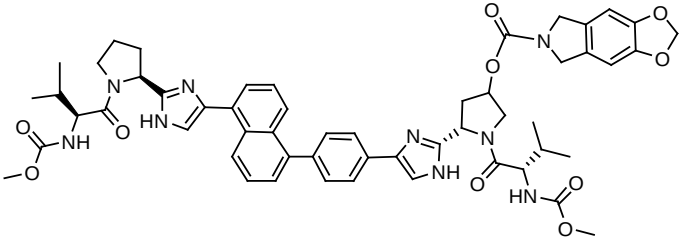
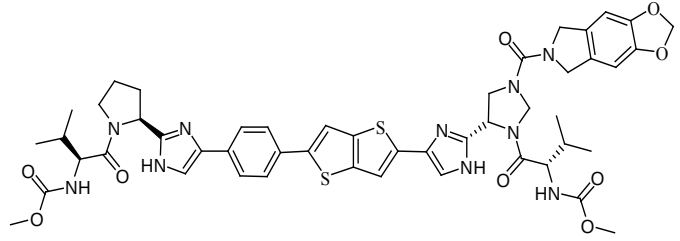
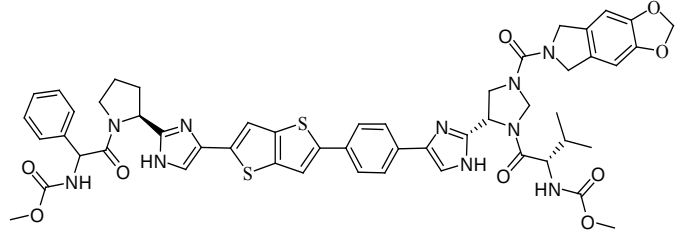
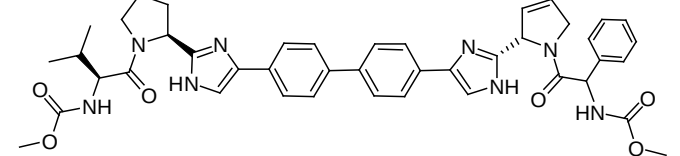
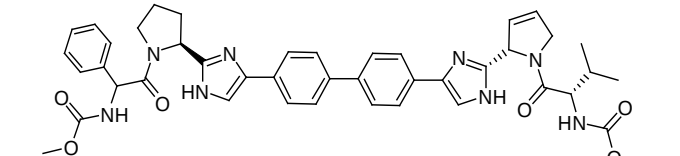
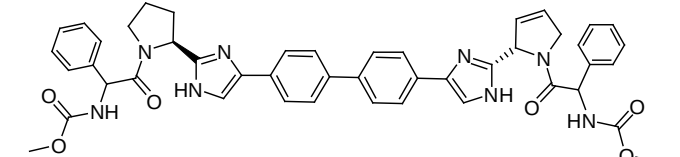
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Ia-37	6am 
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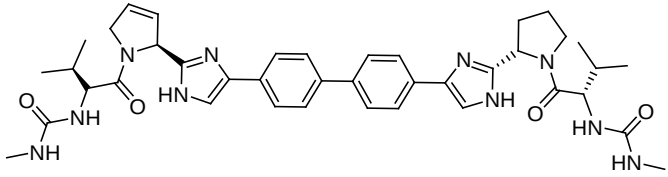
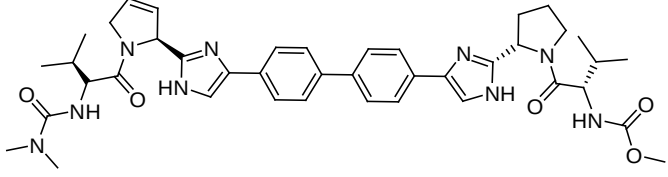
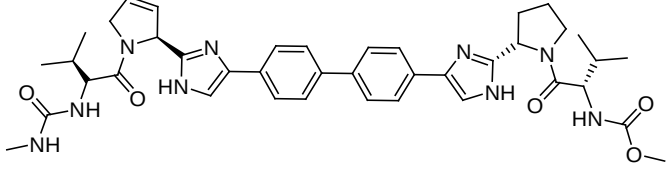
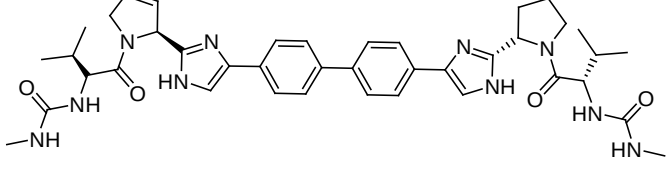
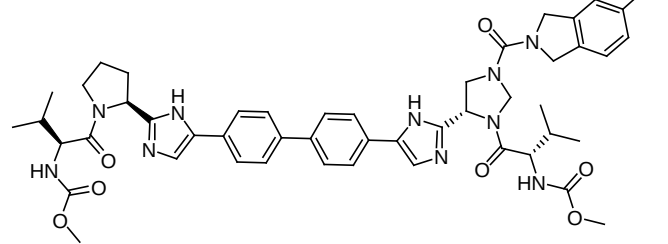
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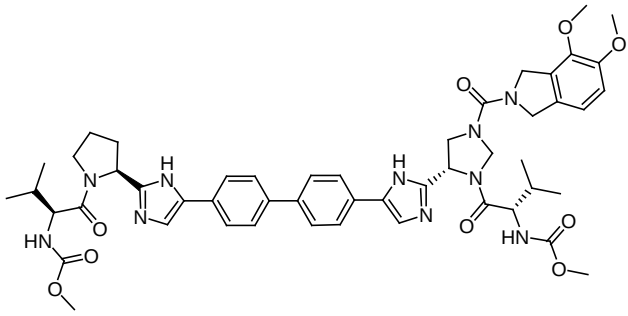
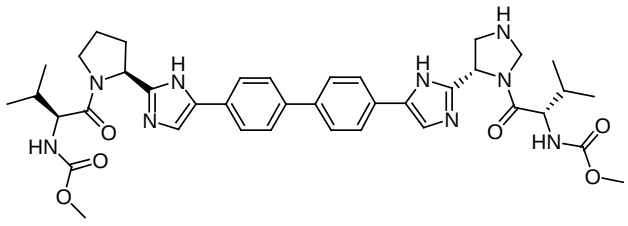
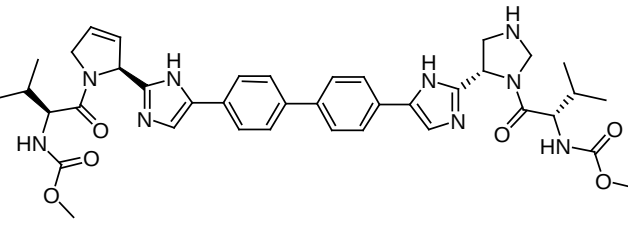
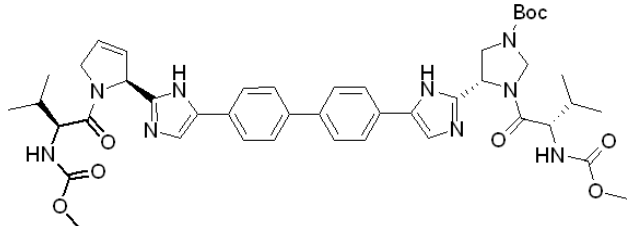
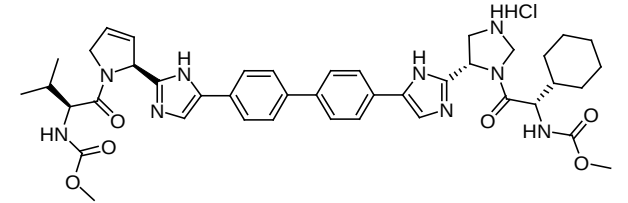
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Ia-45	 6aw
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Ia-47	 6ay

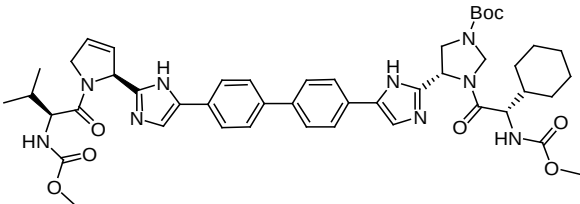
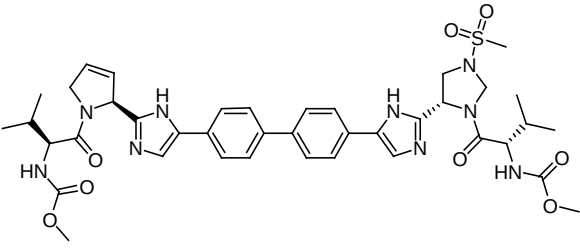
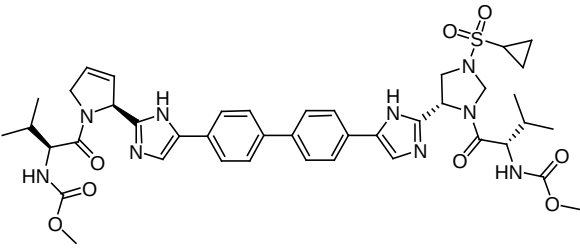
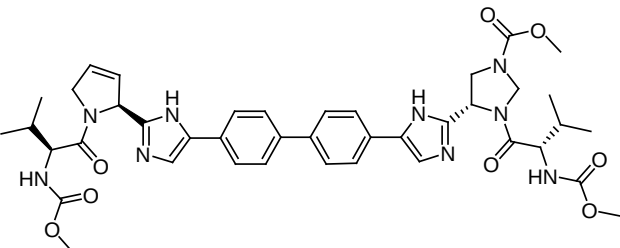
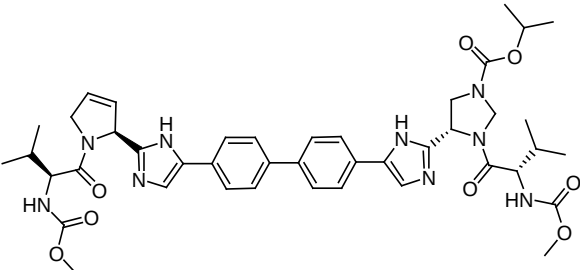
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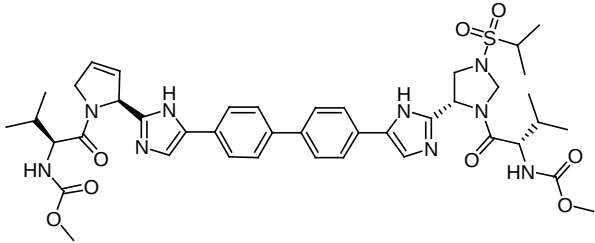
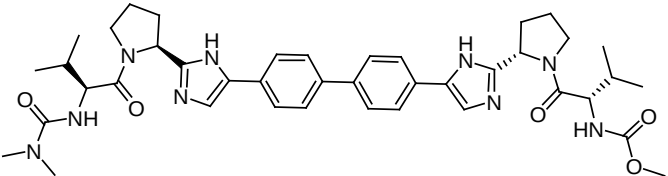
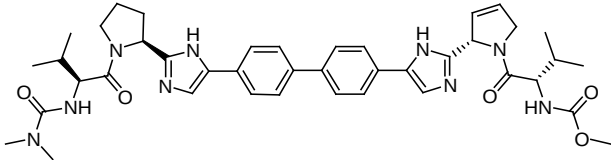
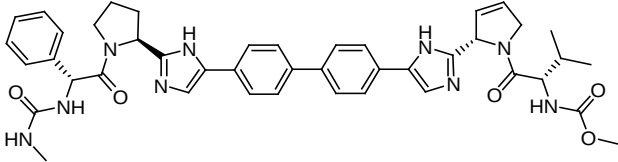
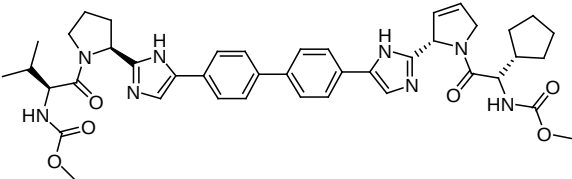
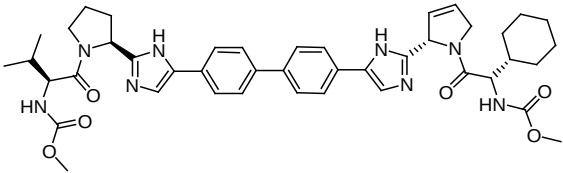
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Ia-59	 6bk
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Ia-61	

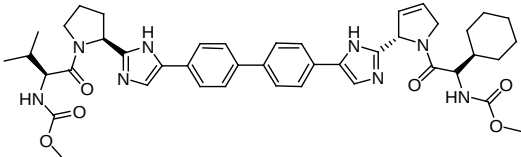
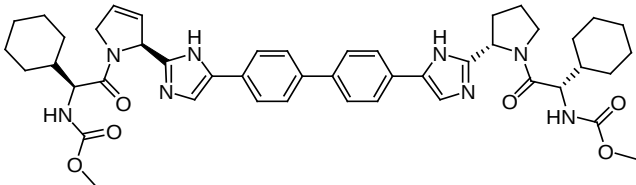
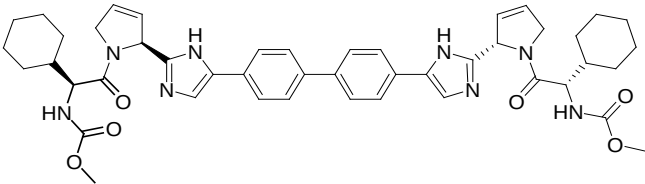
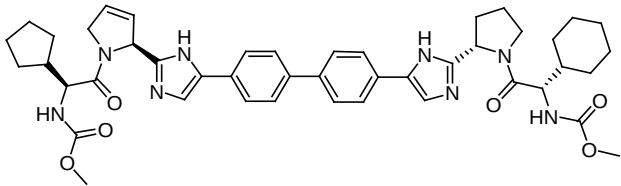
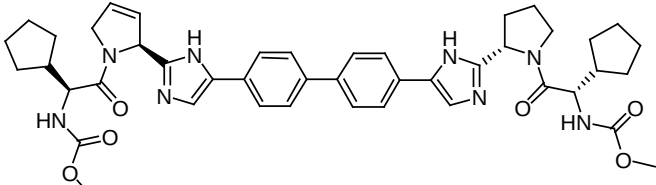
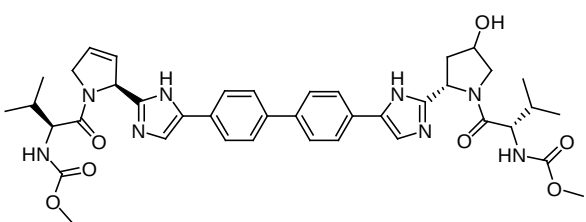
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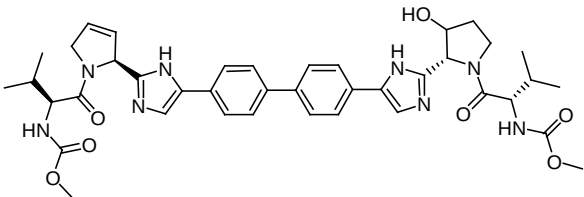
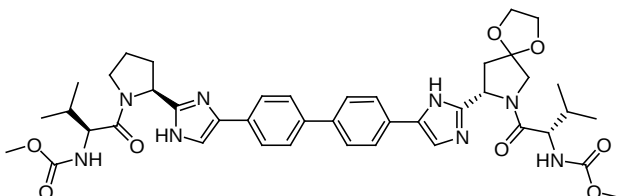
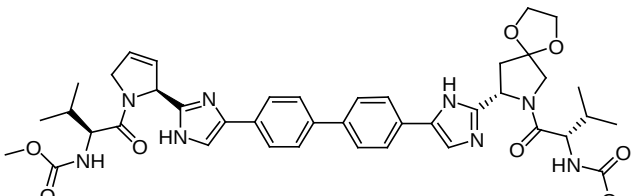
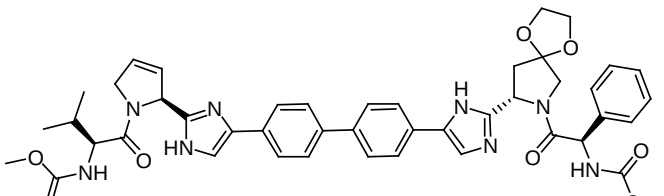
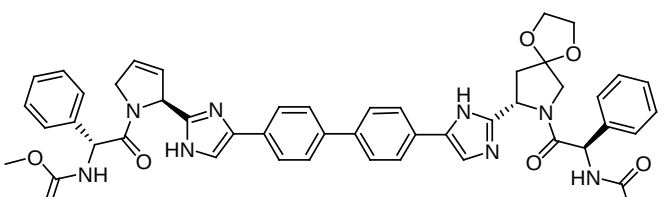
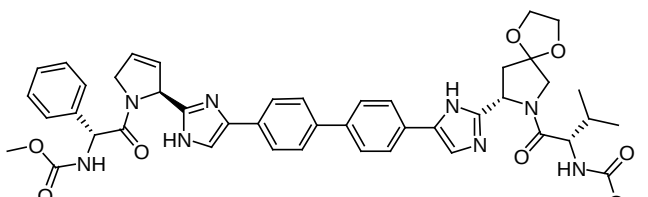
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Ia-81	
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Ia-84	
	6cm

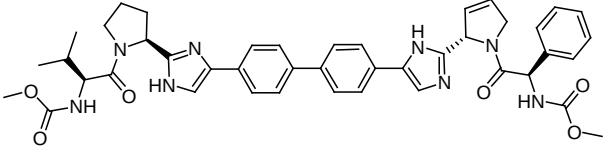
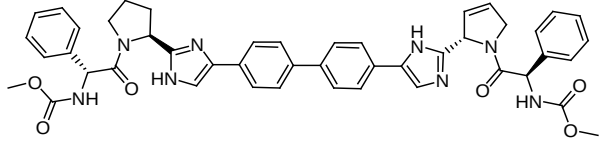
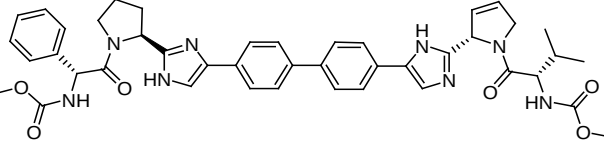
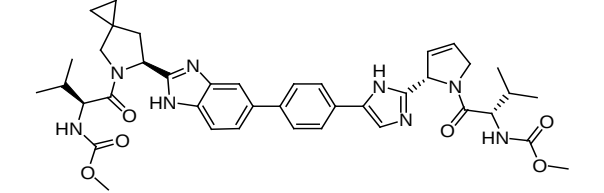
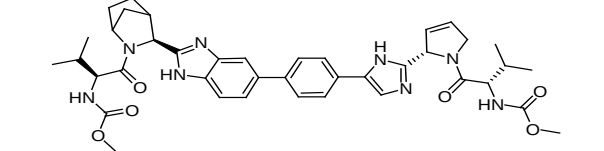
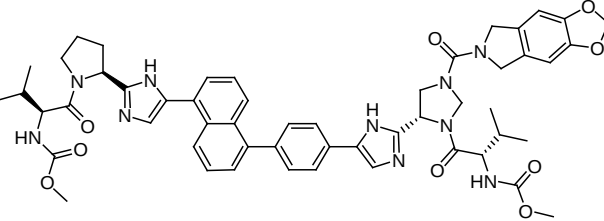
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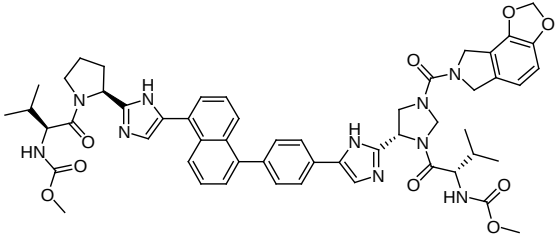
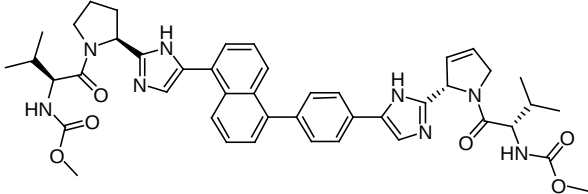
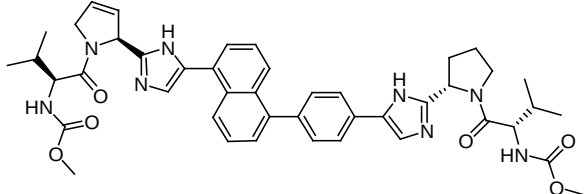
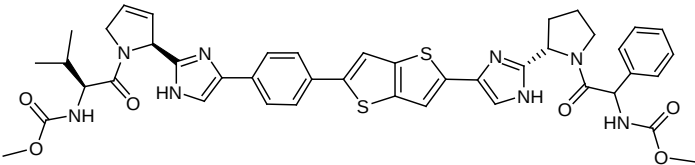
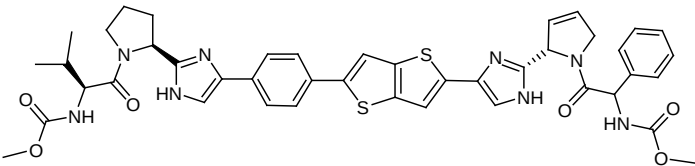
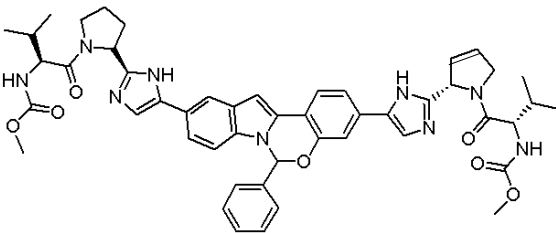
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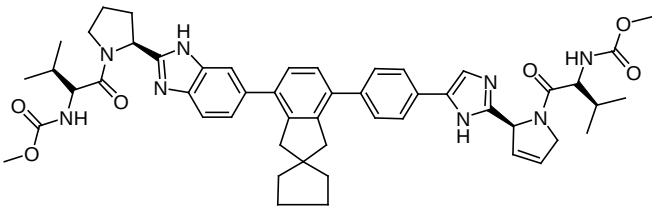
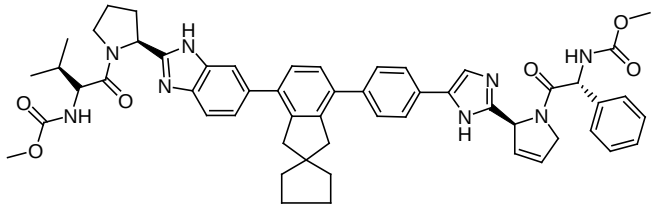
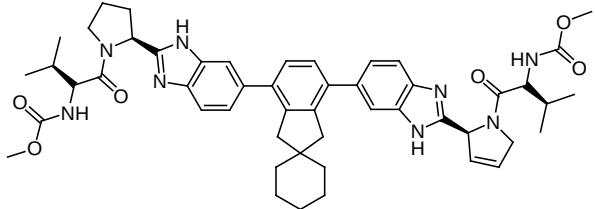
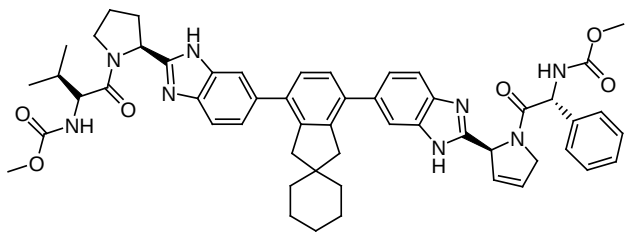
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Ia-99	 6dh
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Ia-106	 6dq

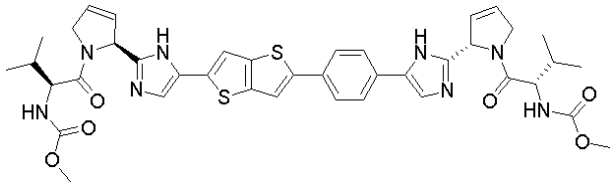
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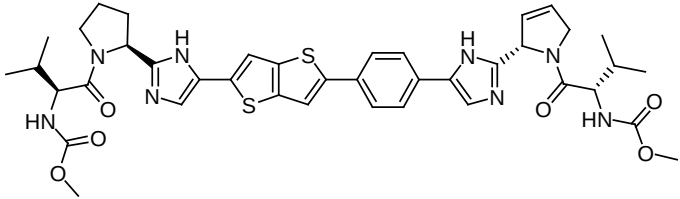
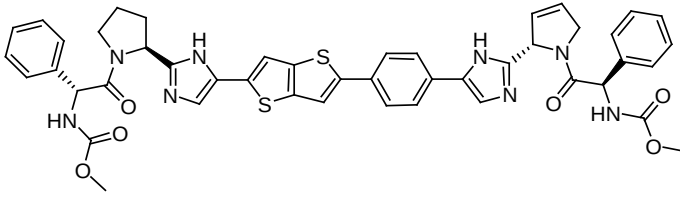
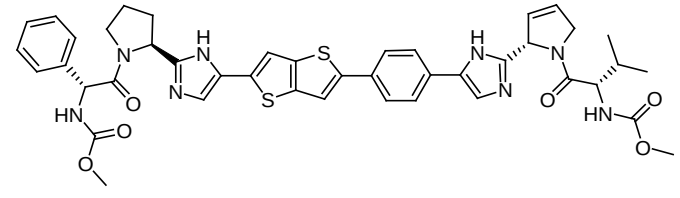
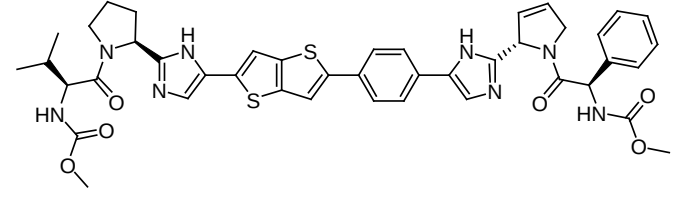
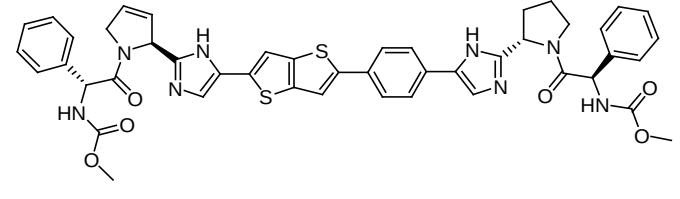
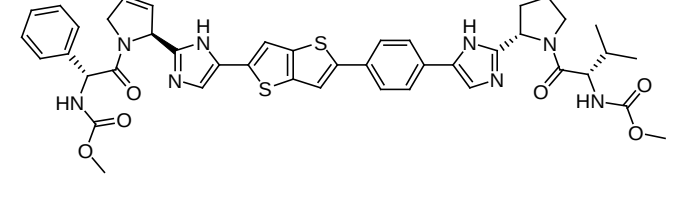
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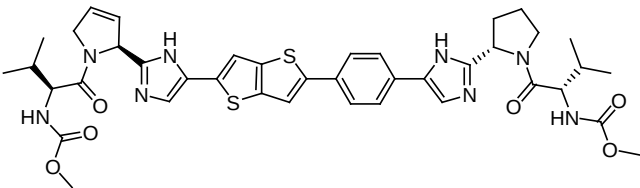
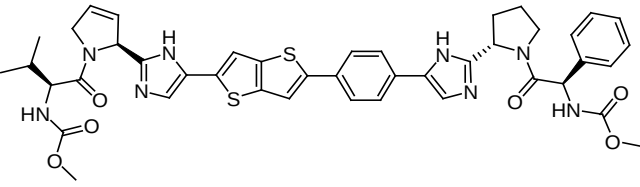
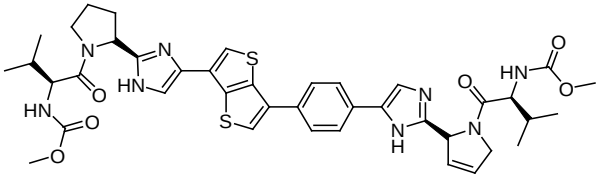
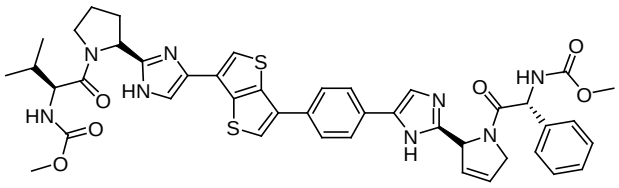
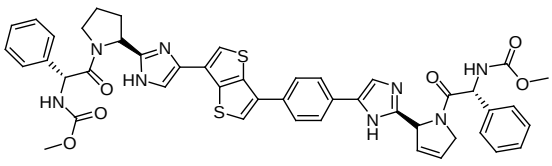
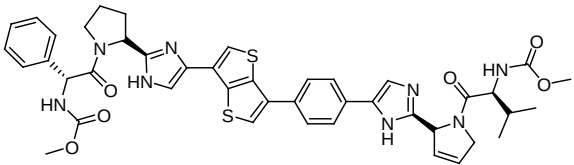
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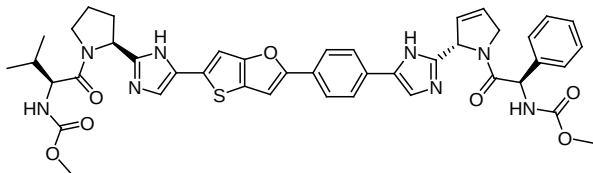
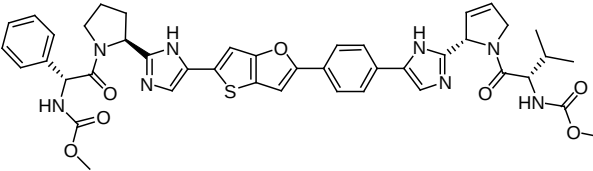
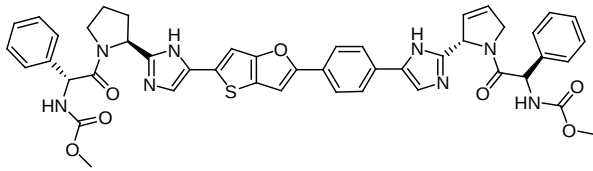
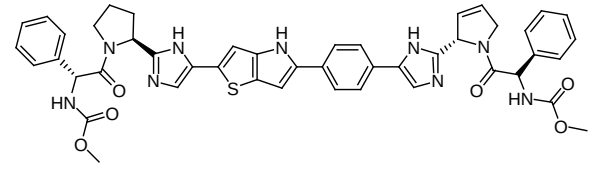
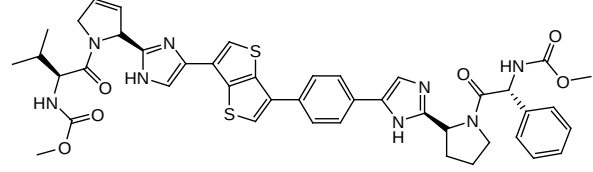
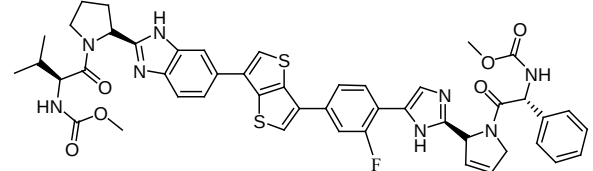
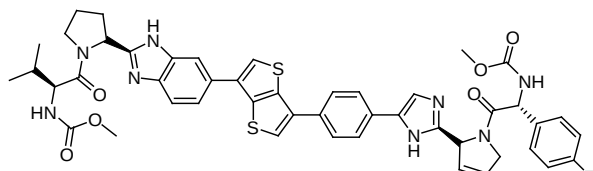
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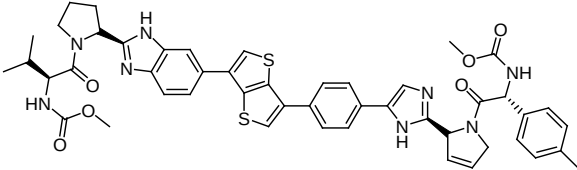
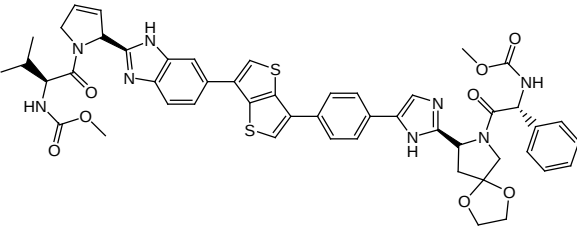
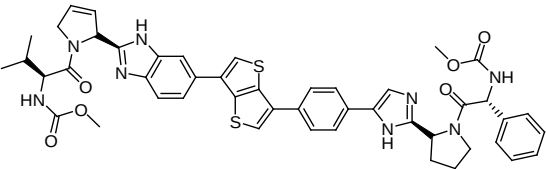
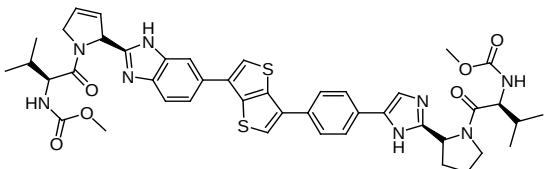
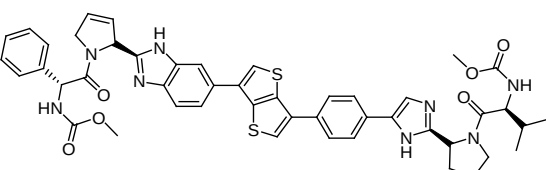
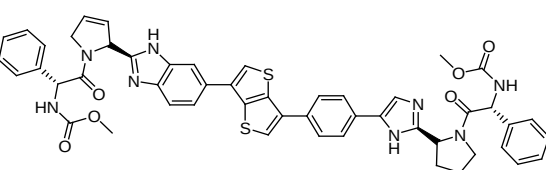
Compounds as represented by Formula **Ib** have a structural structure as follows:

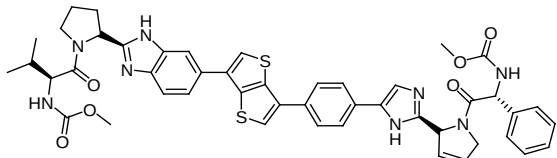
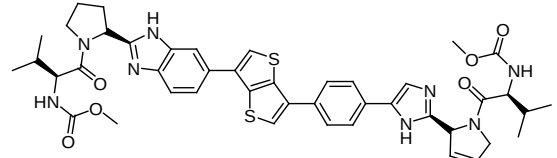
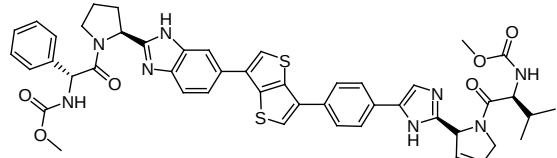
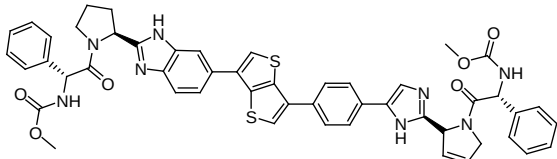
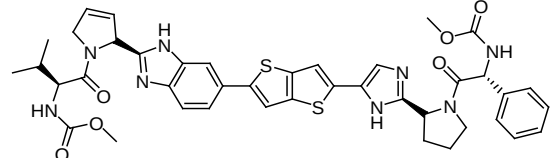
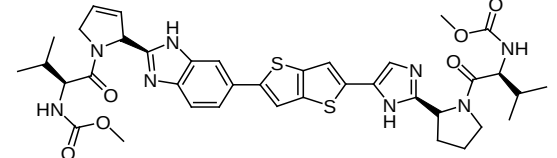
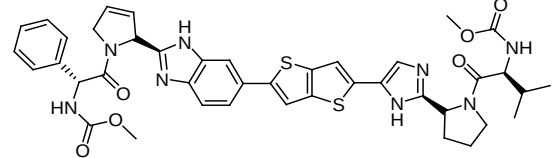
NO.	Compounds as represented by Formula Ib
Ib-1	 6fa

Ib-2	 6fb
Ib-3	 6fc
Ib-4	 6fd
Ib-5	 6fe
Ib-6	 6ff
Ib-7	 6fg

Ib-8	 6fh
Ib-9	 6fi
Ib-10	 6fj
Ib-11	 6fk
Ib-12	 6fm
Ib-13	 6fn

Ib-14	 6fp
Ib-15	 6fq
Ib-16	 6fr
Ib-17	 6fs
Ib-18	 6ft
Ib-19	 6fu
Ib-20	 6fu

	6fv
Ib-21	 Chemical structure of Ib-21: A complex molecule featuring a central benzothiazole core. The left side is substituted with a 1-methyl-2-((S)-1-methoxy-1-oxo-2-phenylethyl)pyrrolidine-3-carboxamide group. The right side is substituted with a 1-methyl-2-((S)-1-methoxy-1-oxo-2-phenylethyl)pyrrolidine-3-carboxamide group. The central benzothiazole is linked to a phenyl ring, which is further linked to a thiazole ring.
Ib-22	 Chemical structure of Ib-22: A complex molecule featuring a central benzothiazole core. The left side is substituted with a 1-methyl-2-((S)-1-methoxy-1-oxo-2-phenylethyl)pyrrolidine-3-carboxamide group. The right side is substituted with a 1-methyl-2-((S)-1-methoxy-1-oxo-2-phenylethyl)pyrrolidine-3-carboxamide group. The central benzothiazole is linked to a phenyl ring, which is further linked to a thiazole ring.
Ib-23	 Chemical structure of Ib-23: A complex molecule featuring a central benzothiazole core. The left side is substituted with a 1-methyl-2-((S)-1-methoxy-1-oxo-2-phenylethyl)pyrrolidine-3-carboxamide group. The right side is substituted with a 1-methyl-2-((S)-1-methoxy-1-oxo-2-phenylethyl)pyrrolidine-3-carboxamide group. The central benzothiazole is linked to a phenyl ring, which is further linked to a thiazole ring.
Ib-24	 Chemical structure of Ib-24: A complex molecule featuring a central benzothiazole core. The left side is substituted with a 1-methyl-2-((S)-1-methoxy-1-oxo-2-phenylethyl)pyrrolidine-3-carboxamide group. The right side is substituted with a 1-methyl-2-((S)-1-methoxy-1-oxo-2-phenylethyl)pyrrolidine-3-carboxamide group. The central benzothiazole is linked to a phenyl ring, which is further linked to a thiazole ring.
Ib-25	 Chemical structure of Ib-25: A complex molecule featuring a central benzothiazole core. The left side is substituted with a 1-methyl-2-((S)-1-methoxy-1-oxo-2-phenylethyl)pyrrolidine-3-carboxamide group. The right side is substituted with a 1-methyl-2-((S)-1-methoxy-1-oxo-2-phenylethyl)pyrrolidine-3-carboxamide group. The central benzothiazole is linked to a phenyl ring, which is further linked to a thiazole ring.
Ib-26	 Chemical structure of Ib-26: A complex molecule featuring a central benzothiazole core. The left side is substituted with a 1-methyl-2-((S)-1-methoxy-1-oxo-2-phenylethyl)pyrrolidine-3-carboxamide group. The right side is substituted with a 1-methyl-2-((S)-1-methoxy-1-oxo-2-phenylethyl)pyrrolidine-3-carboxamide group. The central benzothiazole is linked to a phenyl ring, which is further linked to a thiazole ring.

Ib-27	 6gc
Ib-28	 6gd
Ib-29	 6ge
Ib-30	 6gf
Ib-31	 6gg
Ib-32	 6gh
Ib-33	

	6gi
Ib-34	
Ib-35	
Ib-36	
Ib-37	
Ib-38	
Ib-39	

In this invention, heterocyclic compounds for inhibiting HCV are designed and synthesized, their inhibitory action against HCV activity further studied, the relation between novel heterocyclic compounds of various structures and their inhibitory action against HCV activity thoroughly explored, and the novel heterocyclic compounds and their preparation method are further developed and optimized for effective treatment of HCV infection.

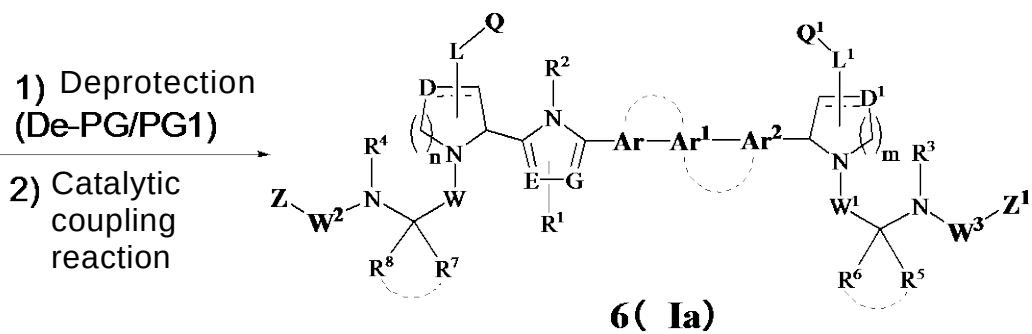
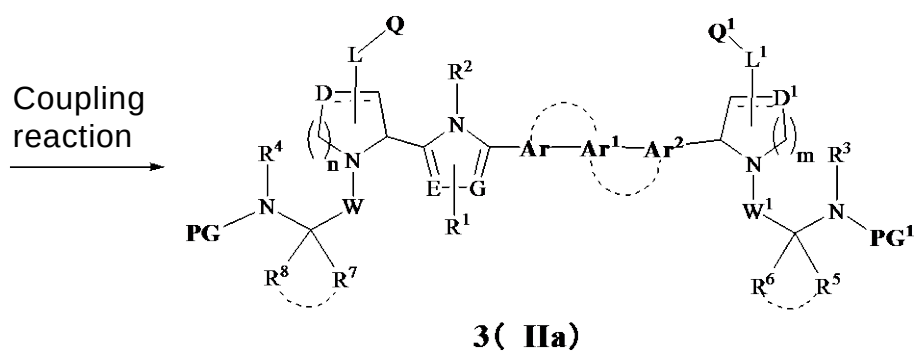
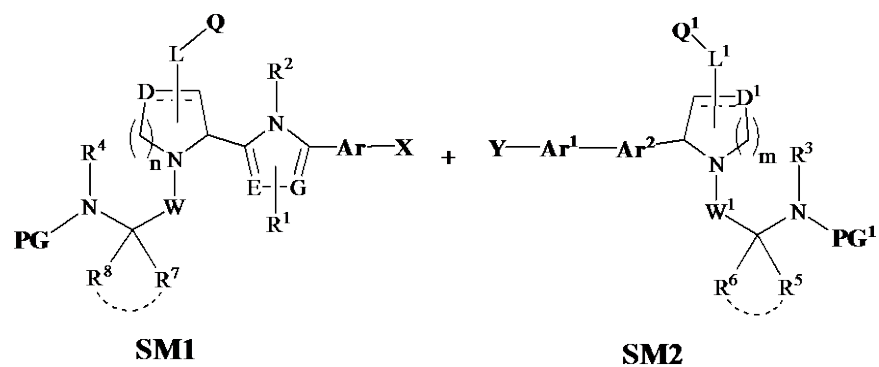
The key to abbreviations of the chemical reagents and solvents used in the synthesis of heterocyclic compounds in this invention is summarized in the explanations of apparatuses and raw materials section of embodiments.

It should be understood in the art that knowledge of the structure of the compounds of this invention can be used in conjunction with well-known methods, such as chemically synthetic methods or plant extraction methods, and well recognized raw materials, to get the compounds of this invention, and these methods have been included in this invention.

The key innovation point of this invention lies in the preparation of compound 6 (see structural formula series 3) through coupling reaction or amidation of intermediate **4 or 5**, obtained by deprotection (removal of PG and or PG1 group) of intermediate **3**, which is synthesized by amidation or coupling reaction of compound **SM1** of the structure formula series 1 and compound **SM2** of the structure formula series 2 as shown below. Methods for their preparation are shown in the following reaction schemes 1-3; wherein the "X" in compounds SM1 and SM3 in reaction schemes 1 and 2 is bromine (Br), "Y" in compounds SM2 and SM4 is boric acid or a borate.

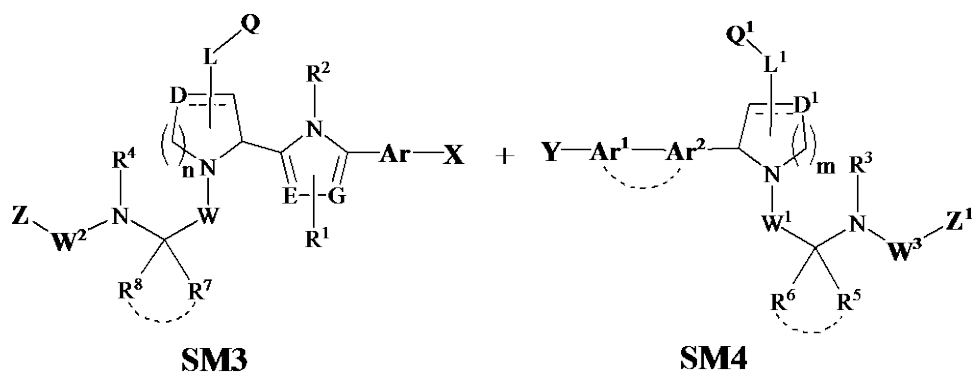
This invention also discloses the preparation of the described compounds as represented by Formula **Ia**, their stereoisomers, tautomers, esterified or amidated prodrugs, pharmaceutically acceptable salts, by any of the following methods (see embodiments for specific synthetic methods and reaction conditions):

Method1: Compound SM1 and compound SM2 were carried out by Suzuki catalytic coupling reaction in organic solvent to get compound 3 (**IIa**);

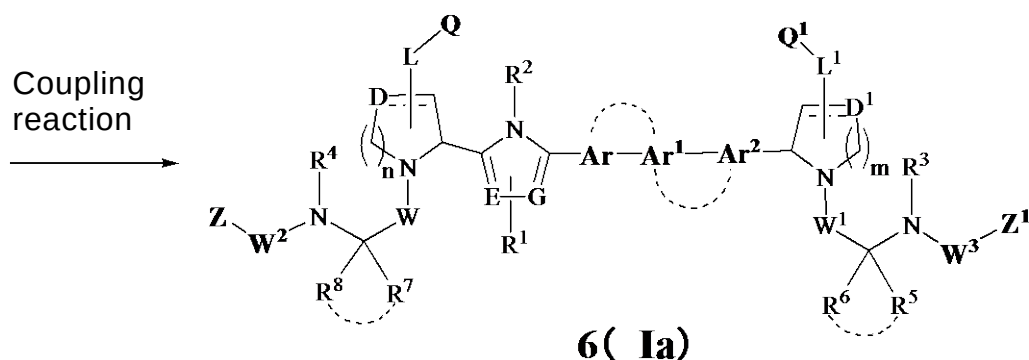


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Method 2: Compound SM3 and compound SM4 were carried out by a catalytic coupling reaction to get compound **6 (Ia)**;



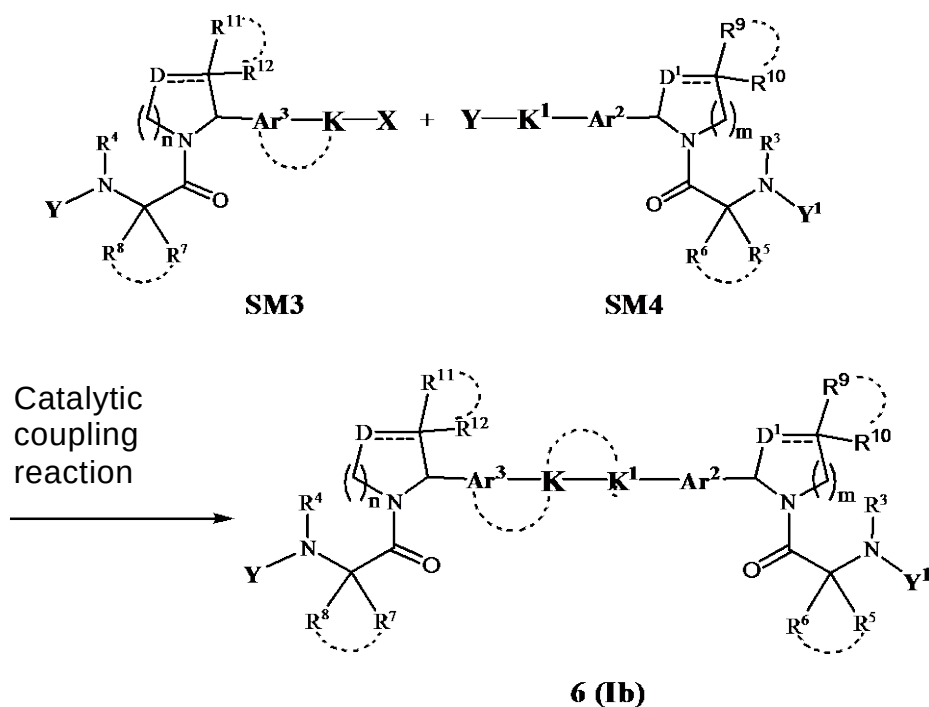
10



In the following examples, heterocyclic functional group containing compounds **SM3** (**SM-3a to SM-3cw**) of structural formula series 1 and heterocyclic functional group containing compounds **SM4** (**SM-4a to SM-4bw**) of structural formula series 2 were carried out by a catalytic coupling reaction (see reaction scheme 3) by a composition of chemical preparation techniques to synthesize a series of novel compounds **6** of formula **Ia** and **Ib** (**6a-6ep** and **6fa-6gq**, refer to structural formula series 3 as shown below for more details).

Method 3:

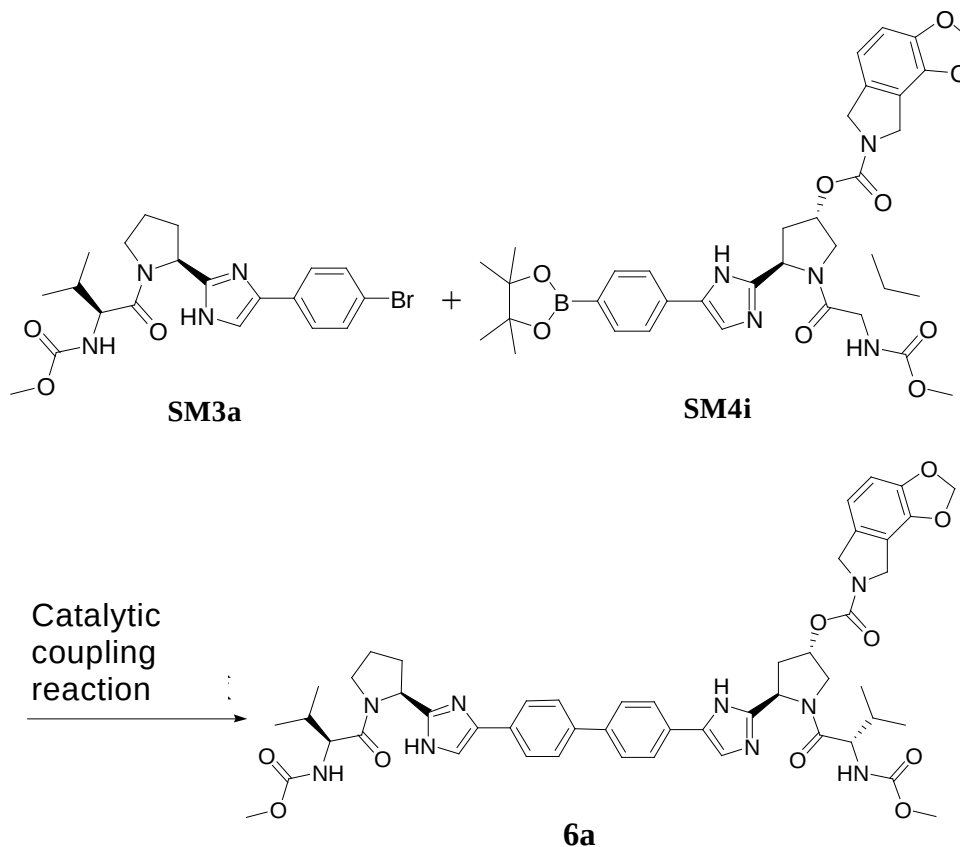
Compounds **6fa-6gq** (**Ib**) are synthesized by the catalytic coupling reaction of compounds **SM3** and compounds **SM4**:



In the following examples, heterocyclic functional group containing compounds **SM3** (**SM-3a to SM-3cw**) of structural formula series 1 and heterocyclic functional group

containing compounds **SM4** (**SM-4a to SM-4bw**) of structural formula series **2** were carried out by a catalytic coupling reaction (see reaction scheme 3) to synthesize a series of novel compounds **6a-6gq** of formulae **Ia-Ib** (see structural formula series3).

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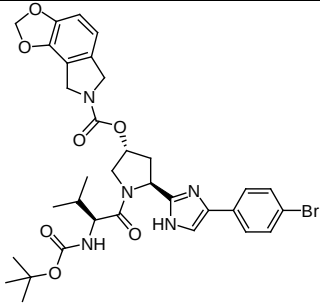
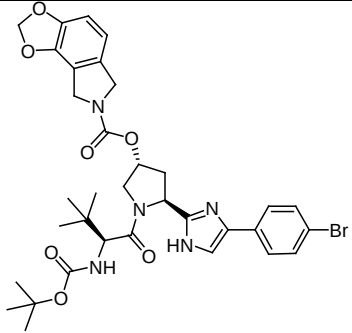
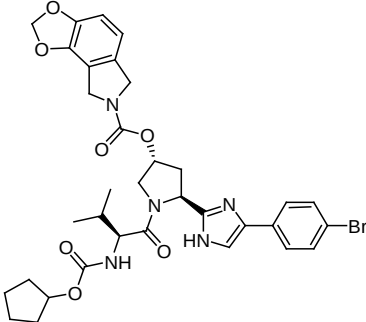
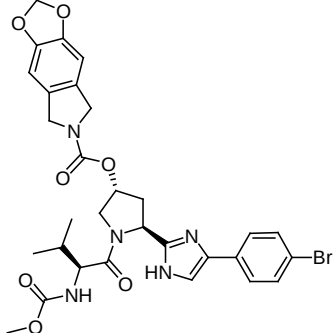
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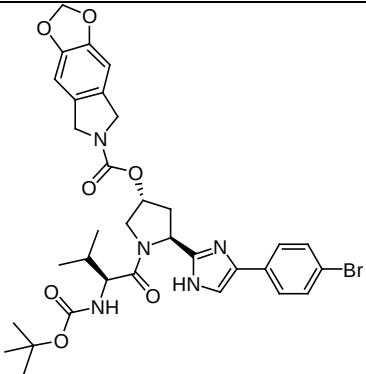
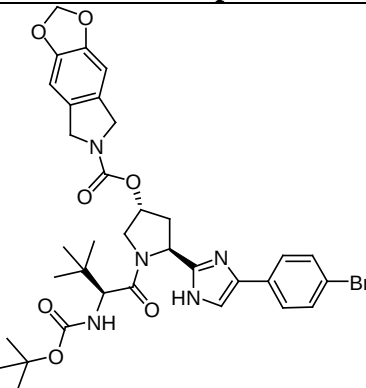
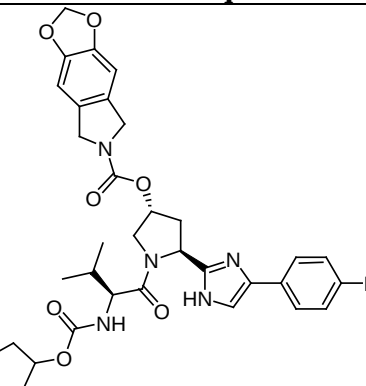
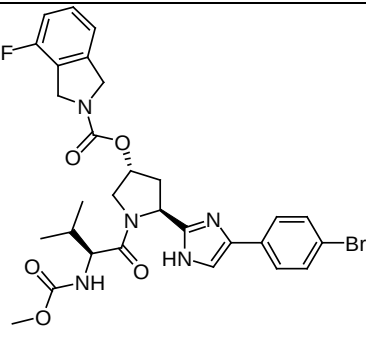
Structural formula series **1** and **2** correspond to the material compounds **SM3** and **SM4**, respectively. Both are required for the synthesis of target compound **Ia** of this invention, and their structural formulae are as follows:

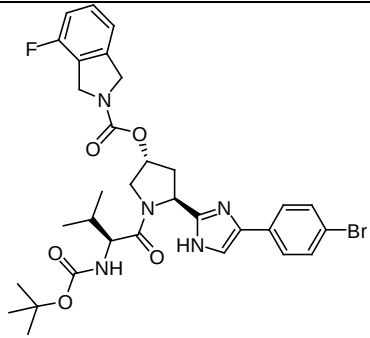
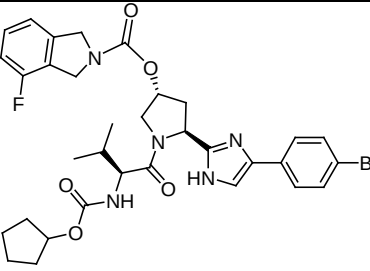
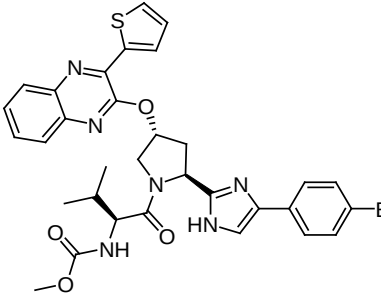
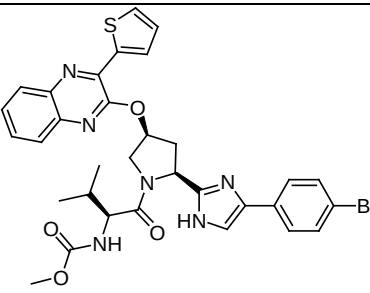
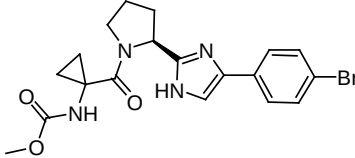
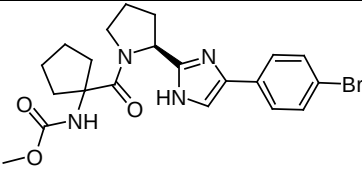
Material compounds **SM3** (**SM-3a to SM-3cw**) of structural formula series **1**:

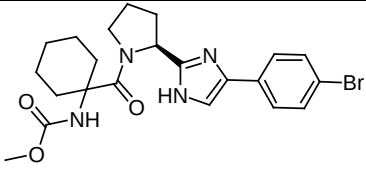
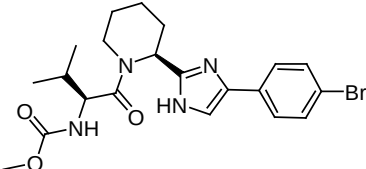
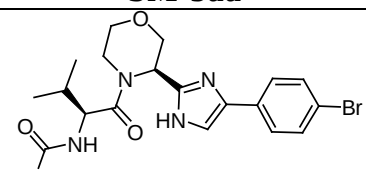
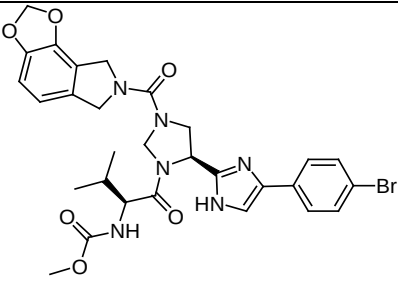
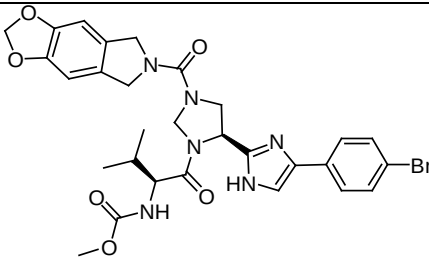
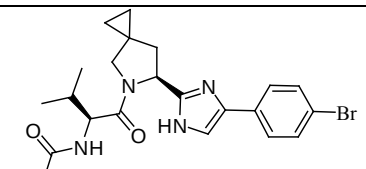
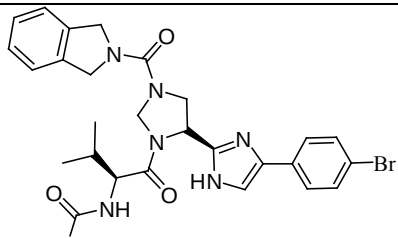
No.	Structural formula of material compounds SM3
1	SM-3a
2	

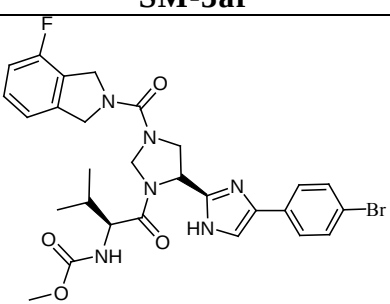
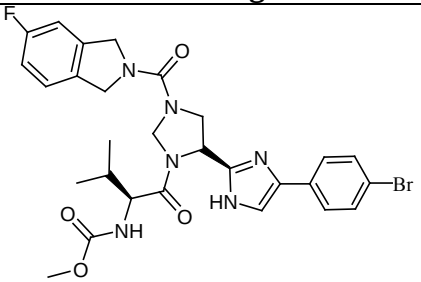
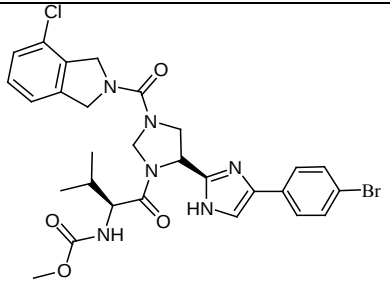
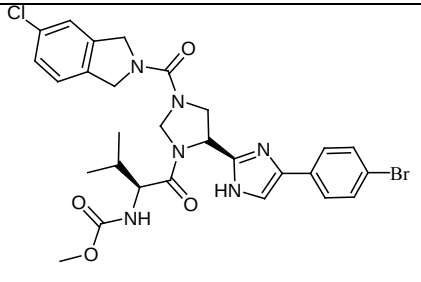
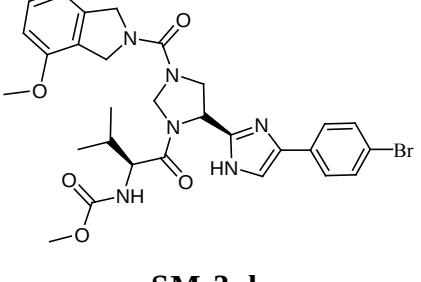
	SM-3b
3	
4	SM-3c
5	SM-3d
6	SM-3e
7	SM-3f
8	SM-3g
9	SM-3h
	SM-3i

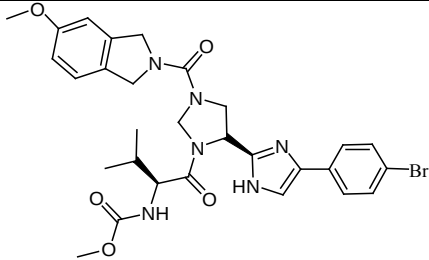
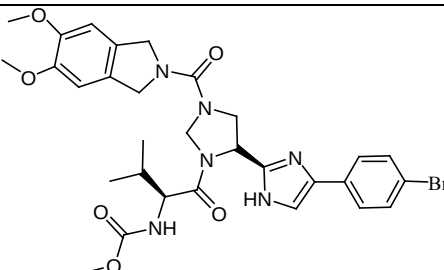
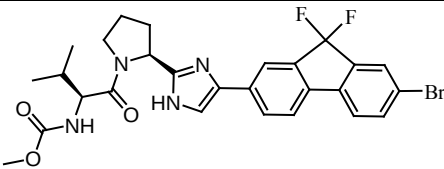
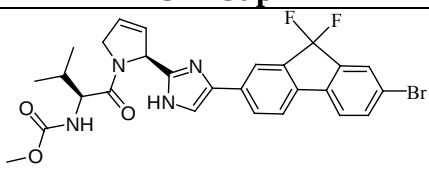
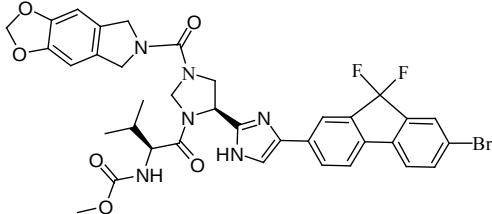
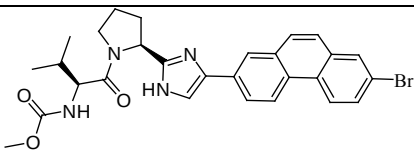
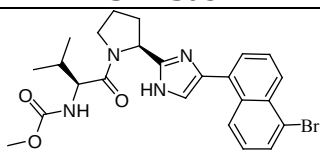
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11	 SM-3k
12	 SM-3m
13	 SM-3n

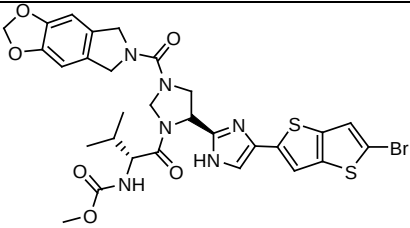
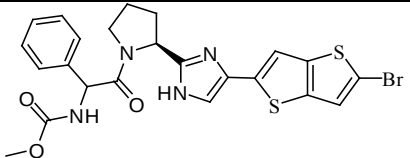
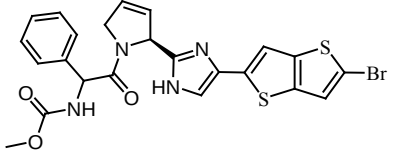
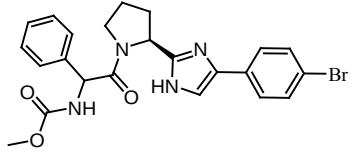
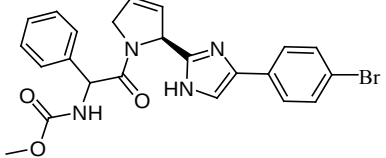
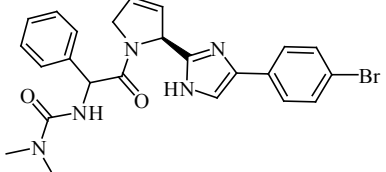
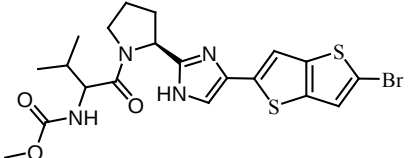
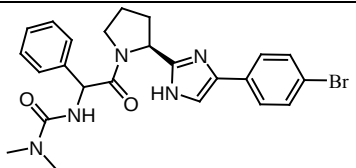
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15	 SM-3q
16	 SM-3r
17	 SM-3s

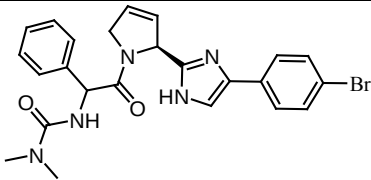
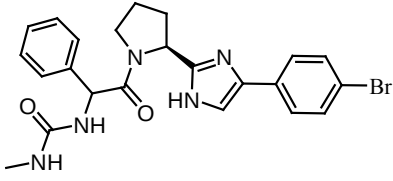
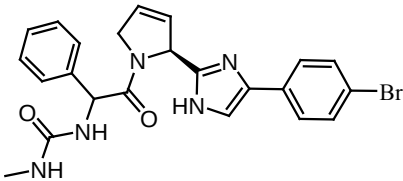
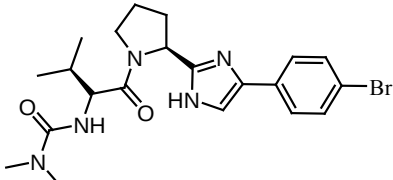
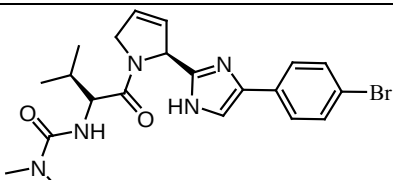
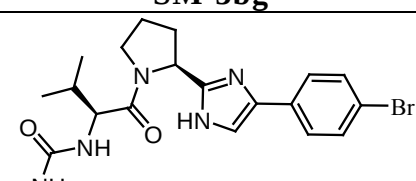
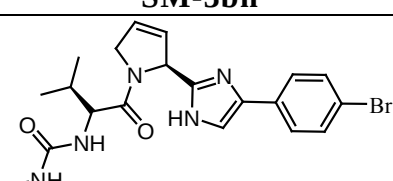
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20	 SM-3v
21	 SM-3w
22	 SM-3x
23	 SM-3y

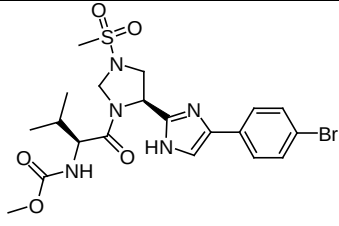
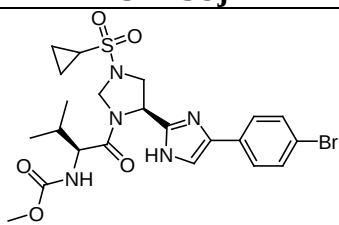
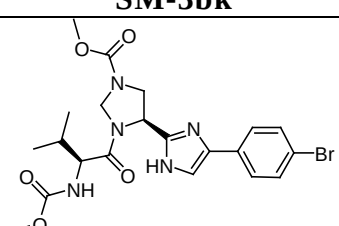
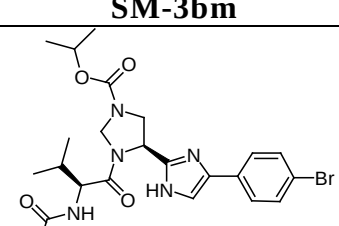
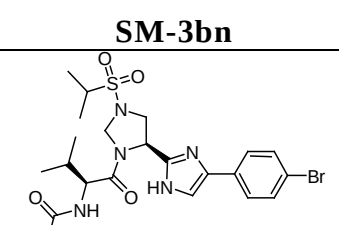
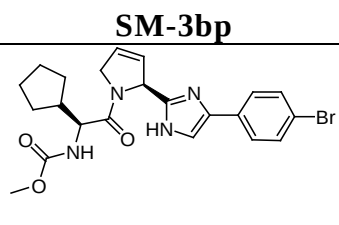
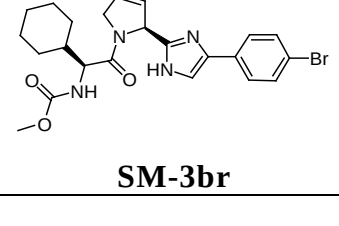
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26	 SM-3ab
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29	 SM-3ae
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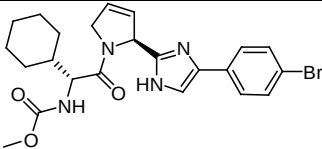
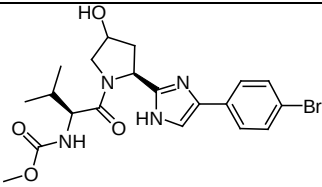
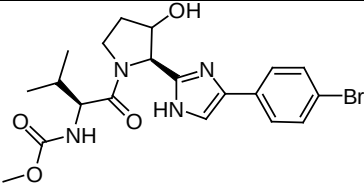
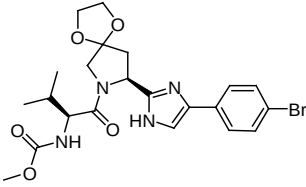
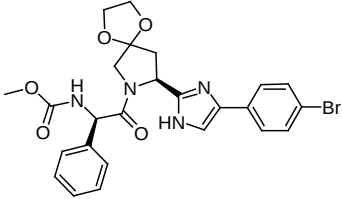
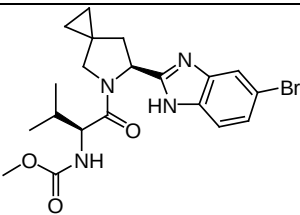
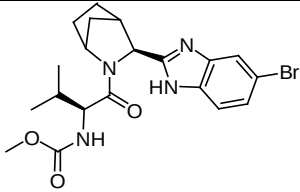
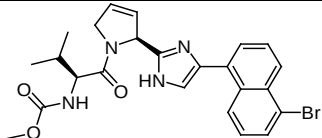
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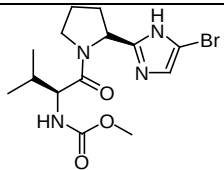
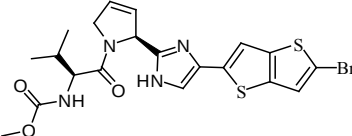
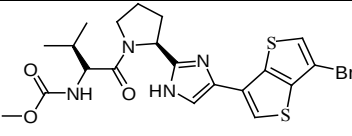
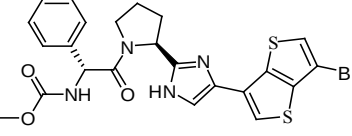
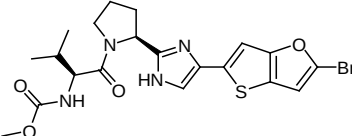
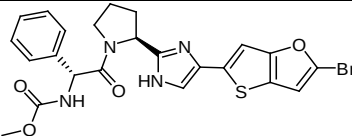
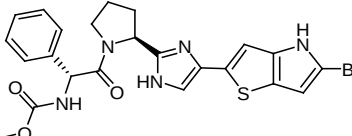
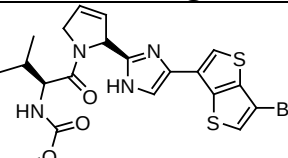
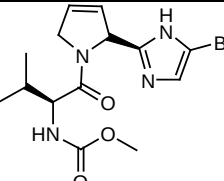
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37	 SM-3an
38	 SM-3ap
39	 SM-3aq
40	 SM-3ar
41	 SM-3as
42	 SM-3at

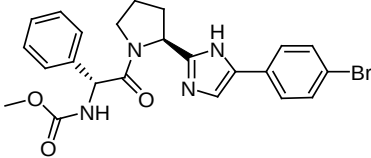
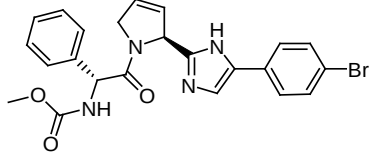
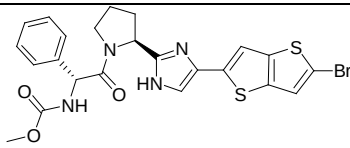
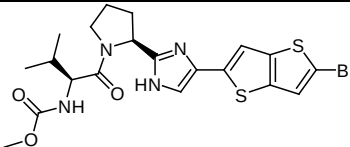
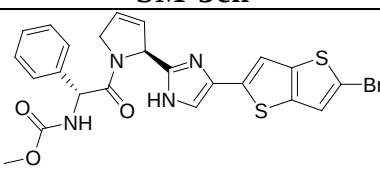
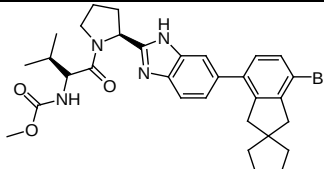
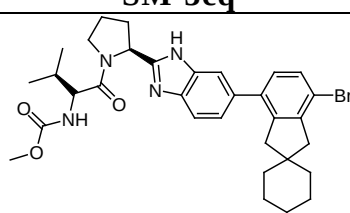
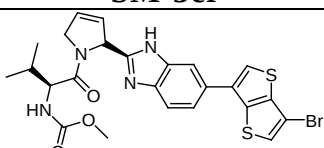
43	 SM-3au
44	 SM-3av
45	 SM-3aw
46	 SM-3ax
47	 SM-3ay
48	 SM-3az
49	 SM-3ba
50	 SM-3bb

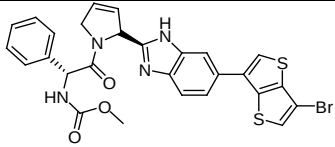
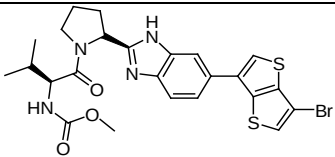
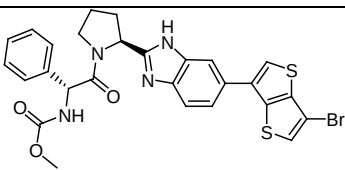
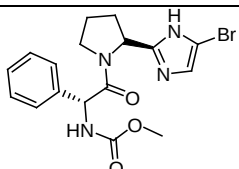
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52	 SM-3bd
53	 SM-3be
54	 SM-3bf
55	 SM-3bg
56	 SM-3bh
57	 SM-3bi

58	 SM-3bj
59	 SM-3bk
60	 SM-3bm
61	 SM-3bn
62	 SM-3bp
63	 SM-3bq
64	 SM-3br

65	 SM-3bs
66	 SM-3bt
67	 SM-3bu
68	 SM-3bv
69	 SM-3bw
70	 SM-3bx
71	 SM-3by
72	

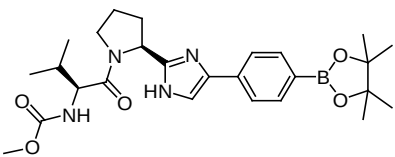
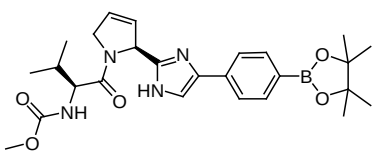
	SM-3bz
73	
	SM-3ca
74	
	SM-3cb
75	
	SM-3cc
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78	
	SM-3cf
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	SM-3cg
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	SM-3ch
81	

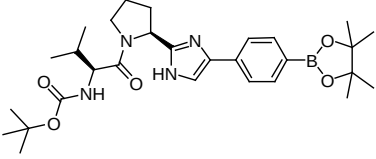
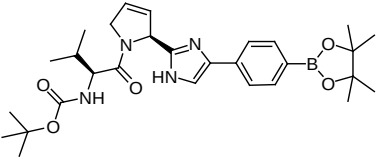
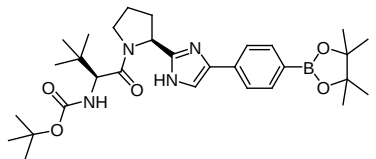
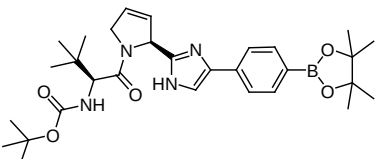
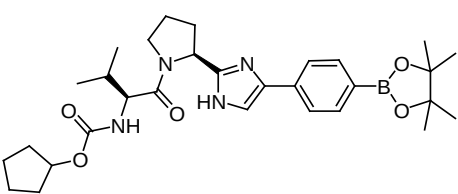
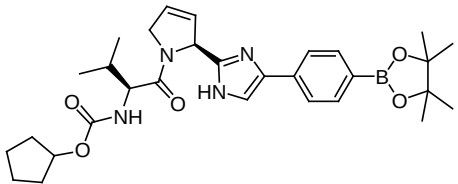
	SM-3ci
82	
83	SM-3cj
	
84	SM-3ck
	
85	SM-3cm
	
86	SM-3cn
	
87	SM-3cp
	
88	SM-3cq
	
89	SM-3cr
	
	SM-3cs

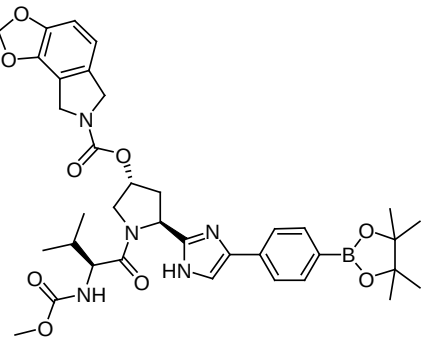
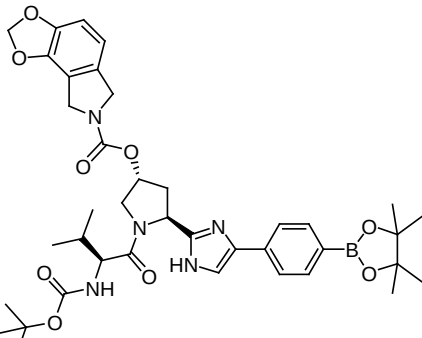
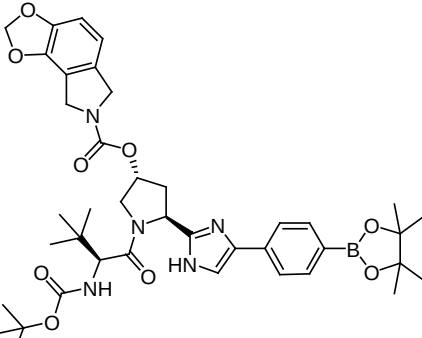
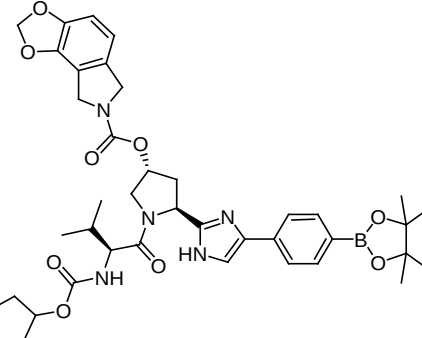
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91	 SM-3cu
92	 SM-3cv
93	 SM-3cw

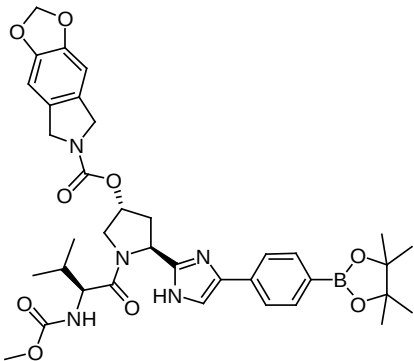
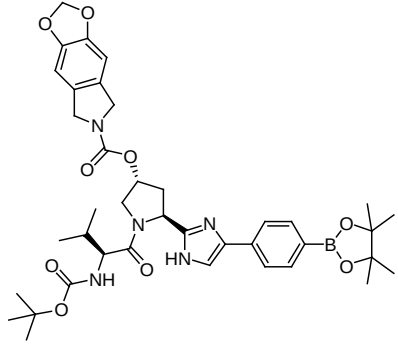
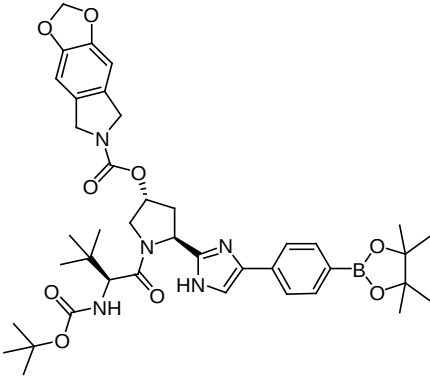
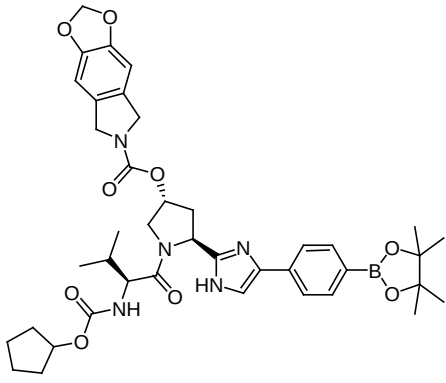
The following structural formula series 2 is a concrete example of the materials **SM4** (**SM-4a to SM-4bw**) for synthesis of key structure of compounds of this invention, their structure formula is as shown below:

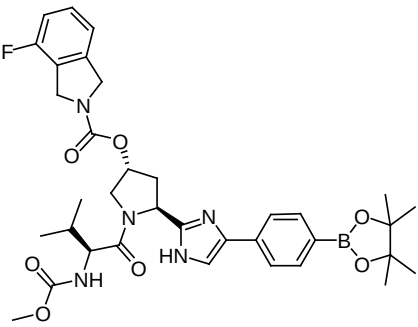
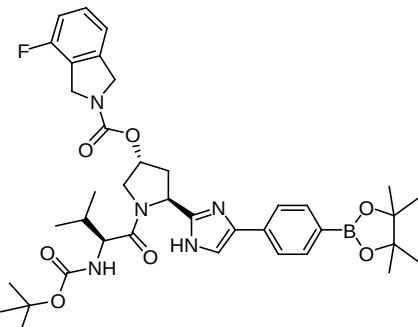
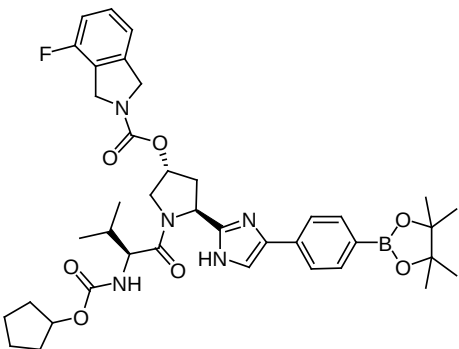
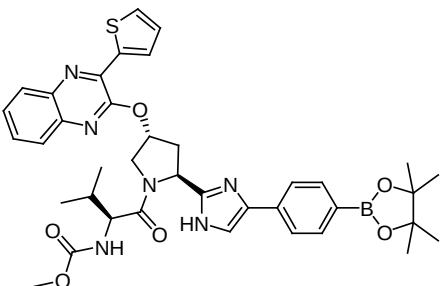
5 Material compounds **SM4** (**SM-4a to SM-4bw**) of structural formula series 2:

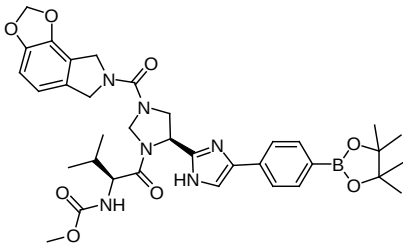
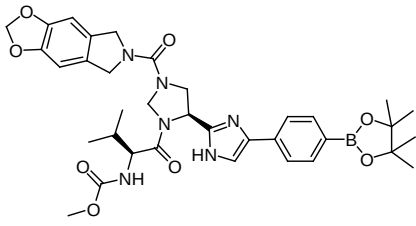
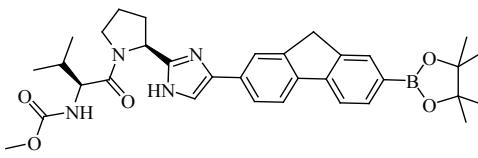
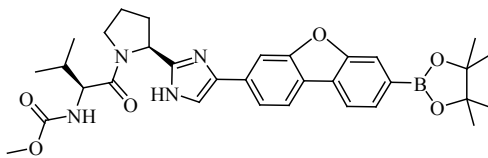
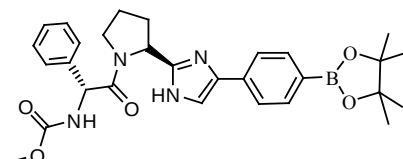
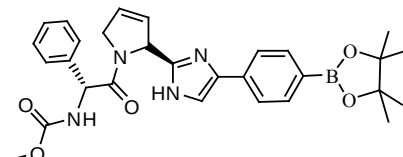
NO.	Structural formula of material compounds SM4
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2	 SM-4b

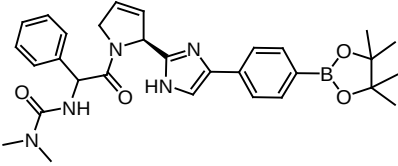
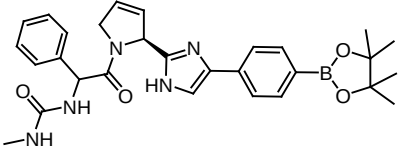
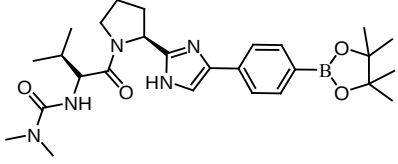
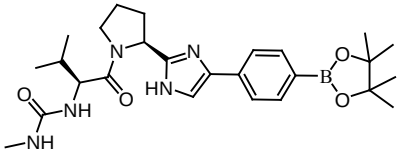
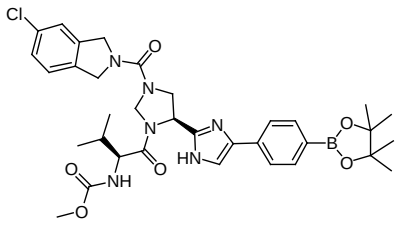
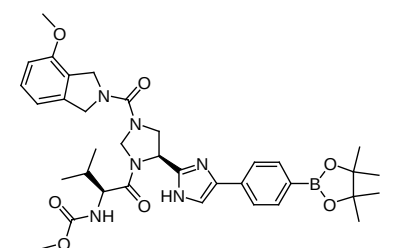
3	 SM-4c
4	 SM-4d
5	 SM-4e
6	 SM-4f
7	 SM-4g
8	 SM-4h

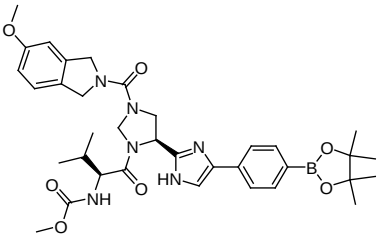
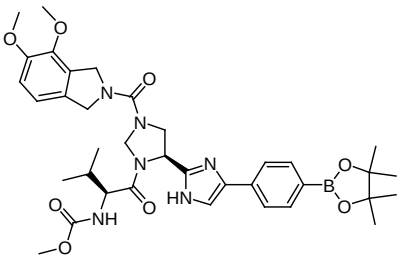
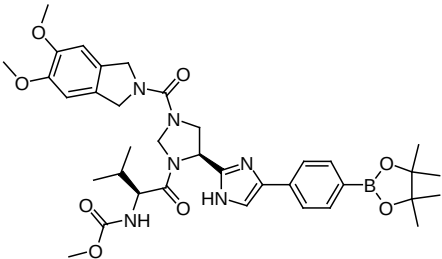
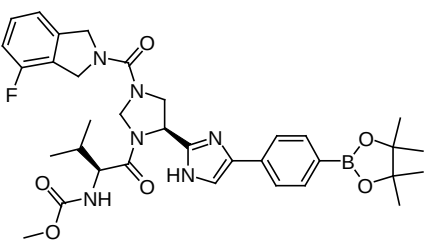
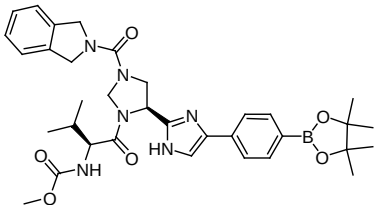
9	 SM-4i
10	 SM-4j
11	 SM-4k
12	 SM-4m

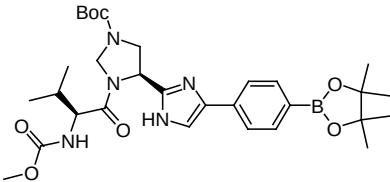
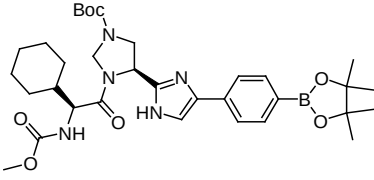
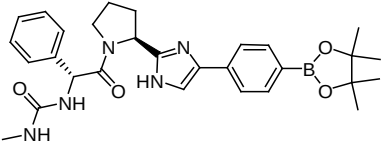
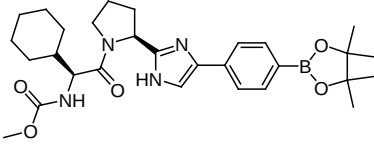
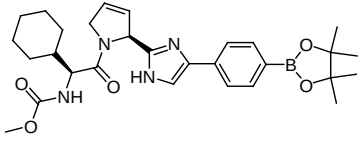
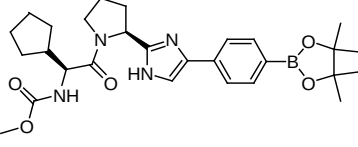
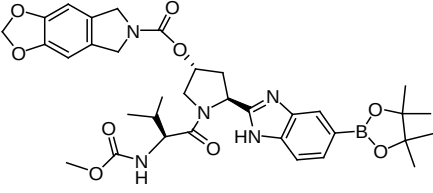
13	 SM-4n
14	 SM-4p
15	 SM-4q
16	 SM-4r

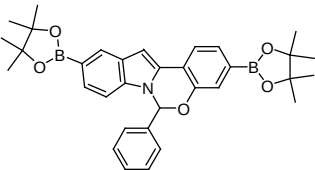
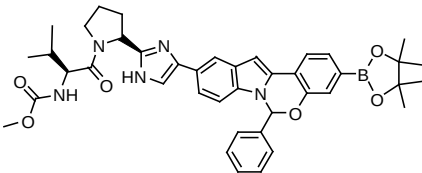
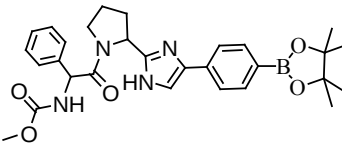
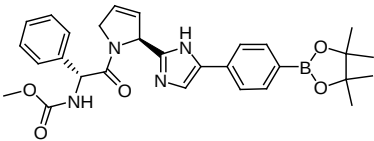
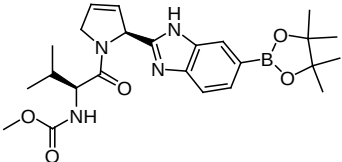
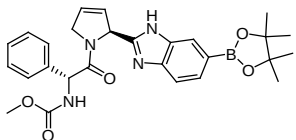
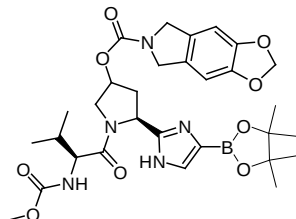
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18	 SM-4t
19	 SM-4u
20	 SM-4v

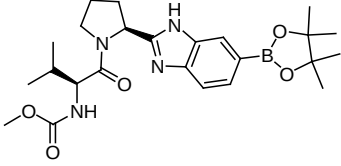
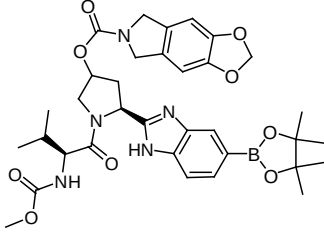
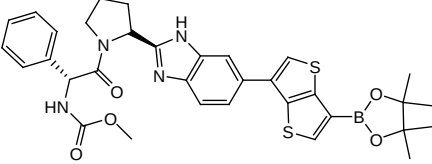
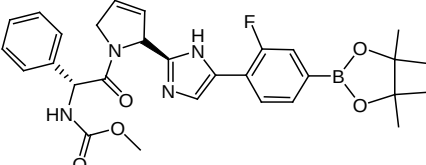
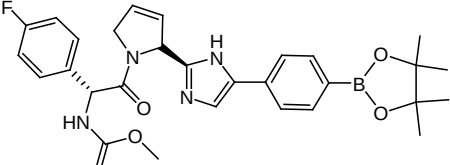
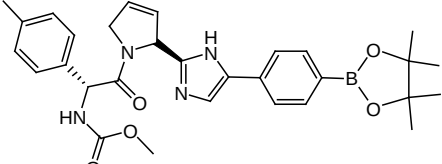
27	 SM-4ac
28	 SM-4ad
29	 SM-4ae
30	 SM-4af
31	 SM-4ag
32	 SM-4ah

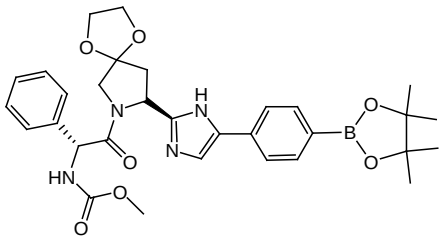
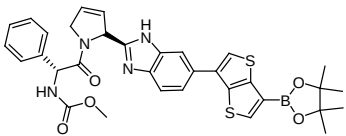
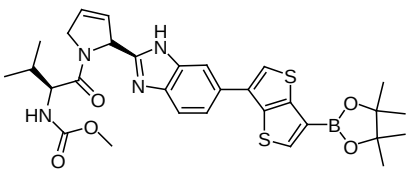
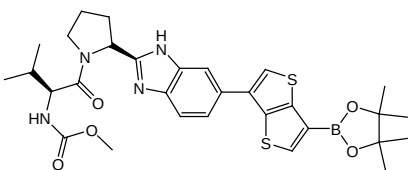
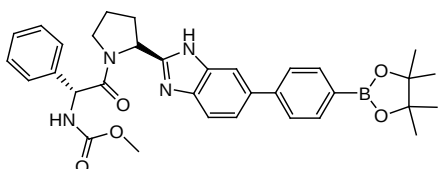
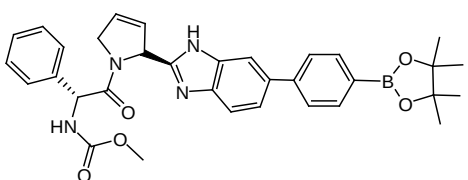
33	 SM-4ai
34	 SM-4aj
35	 SM-4ak
36	 SM-4am
37	 SM-4an
38	 SM-4ap

39	 SM-4aq
40	 SM-4ar
41	 SM-4as
42	 SM-4at
43	 SM-4au

44	 SM-4av
45	 SM-4aw
46	 SM-4ax
47	 SM-4ay
48	 SM-4az
49	 SM-4ba
50	 SM-4bb

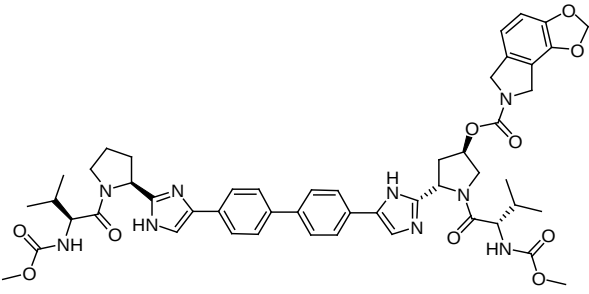
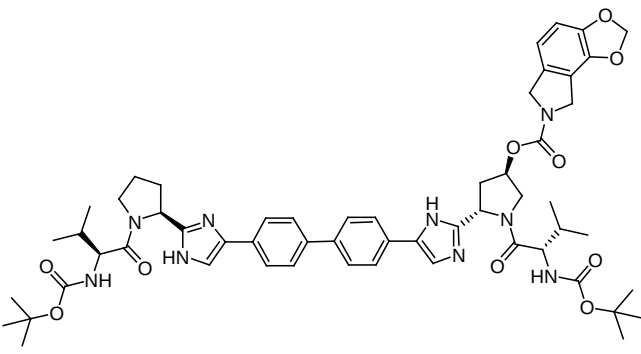
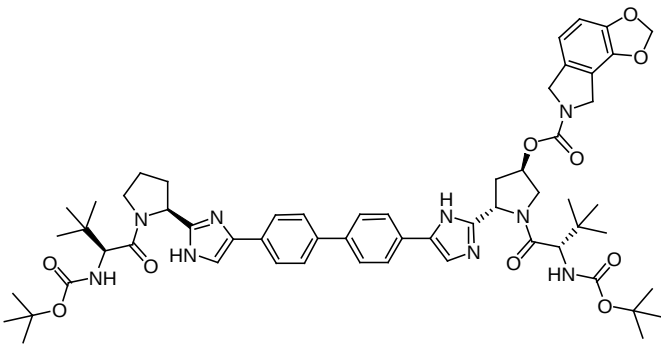
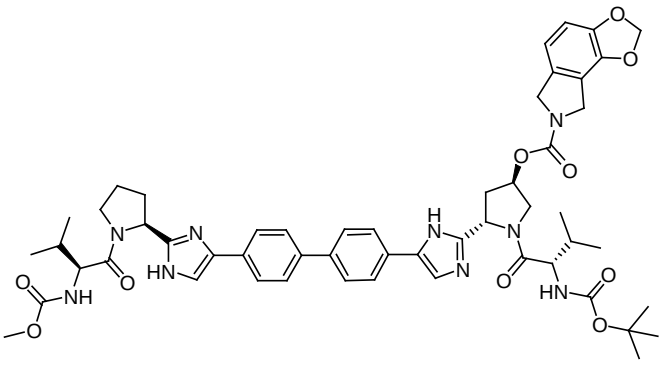
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52	 SM-4bd
53	 SM-4be
54	 SM-4bf
55	 SM-4bg
56	 SM-4bh
57	 SM-4bi

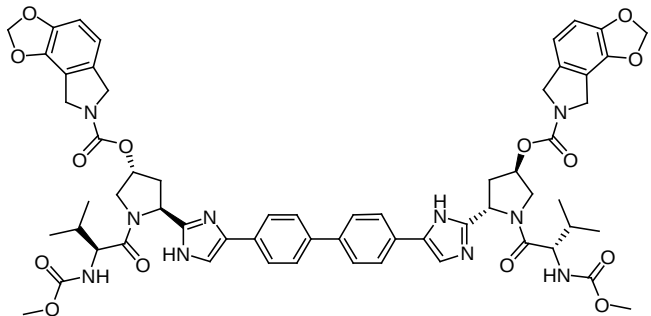
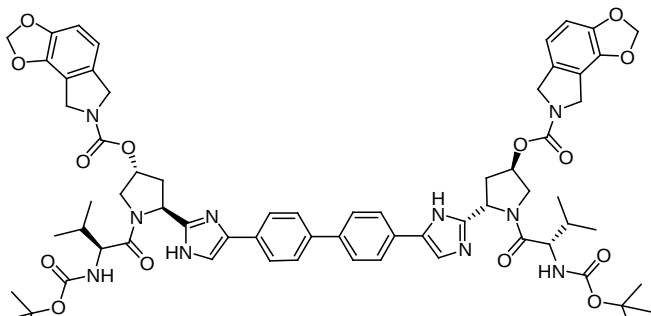
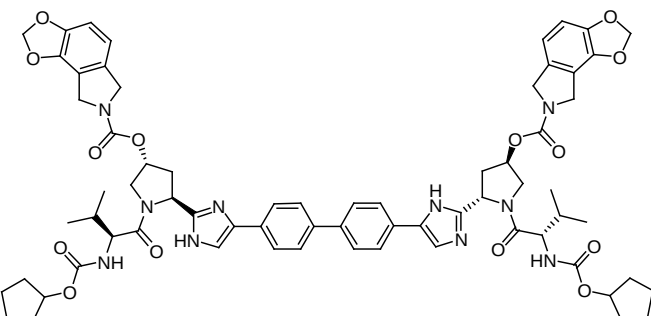
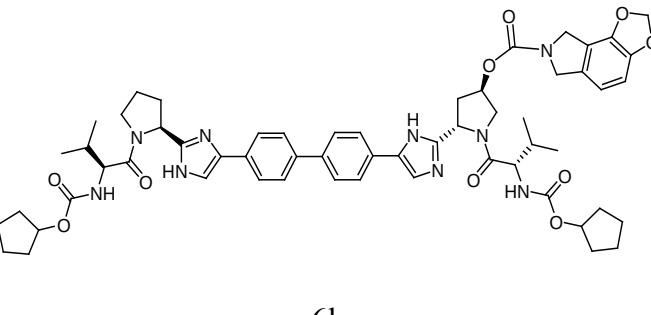
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59	 SM-4bk
60	 SM-4bm
61	 SM-4bn
62	 SM-4bp
63	 SM-4bq

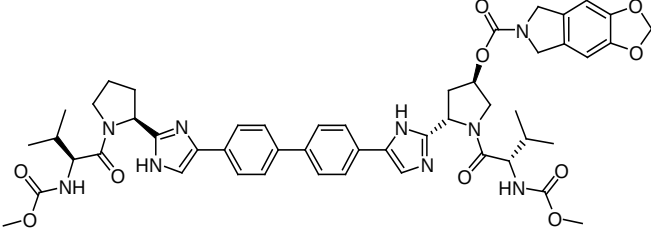
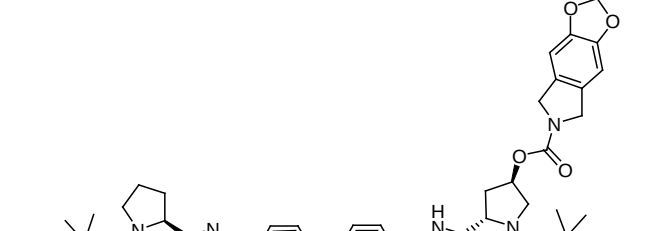
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66	 SM-4bt
67	 SM-4bu
68	 SM-4bv
69	 SM-4bw

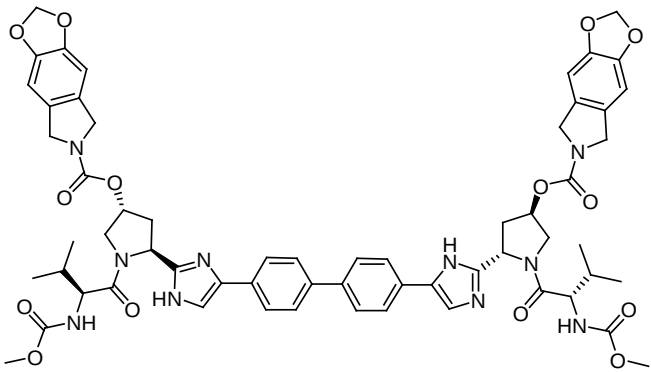
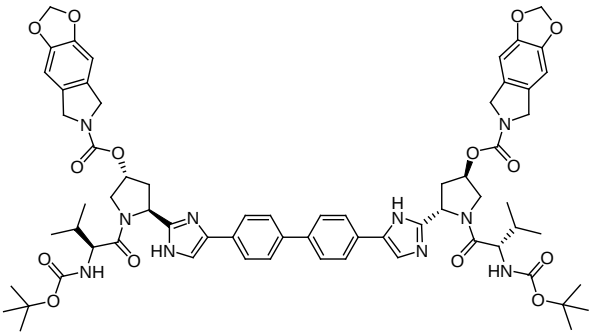
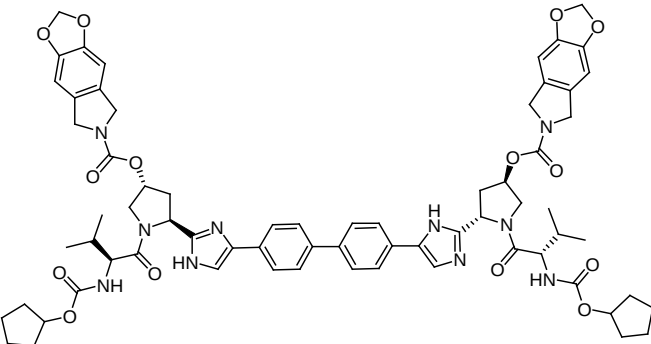
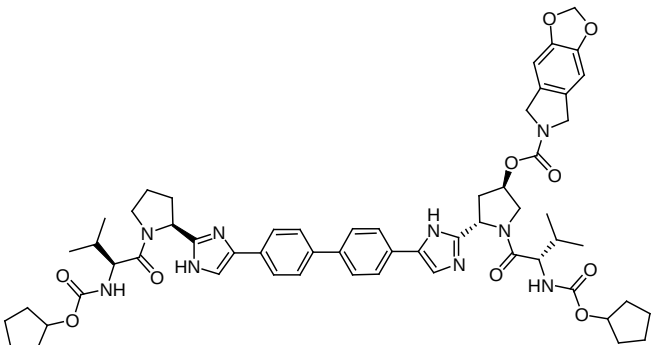
The following are concrete examples of target compounds **6a-6ep (Ia)** and target compounds **6fa-6gq (Ib)** of structural formula series 3 synthesized in accordance with the above-mentioned reaction scheme 3.

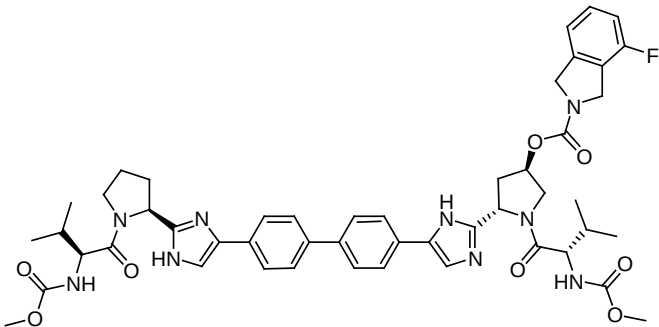
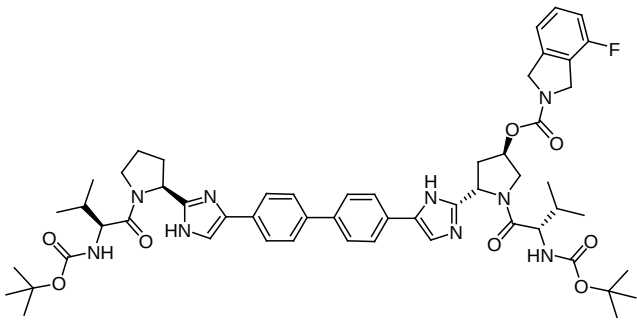
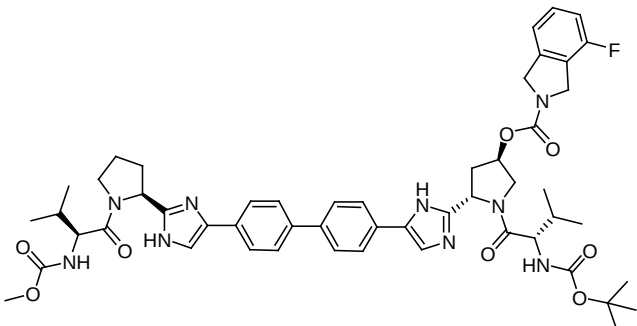
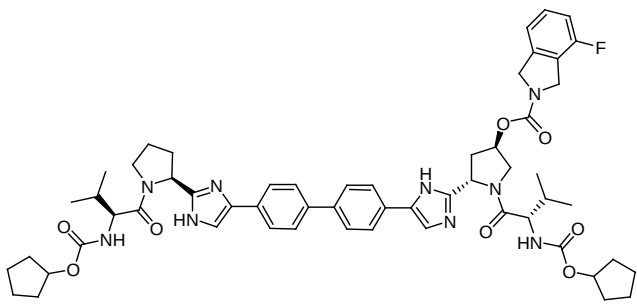
Below are compounds **6a-6ep** as represented by Formula **Ia**:

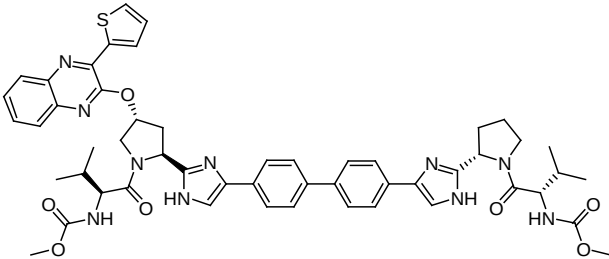
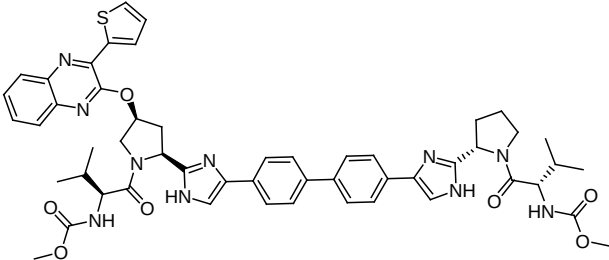
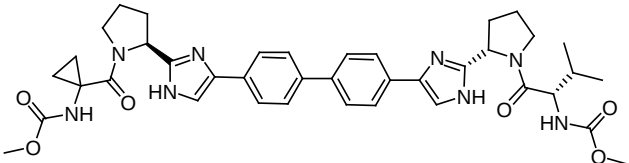
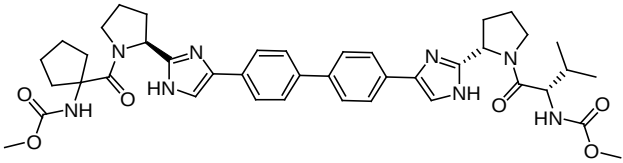
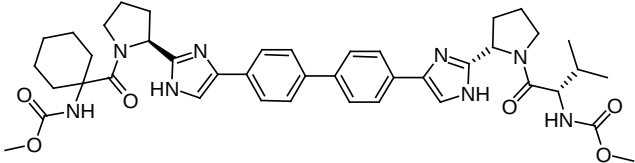
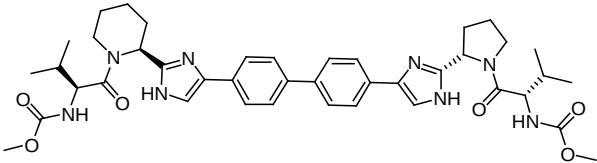
NO.	Compounds as represented by Formula Ia
Ia-1	 6a
Ia-2	 6b
Ia-3	 6c
Ia-4	 6d

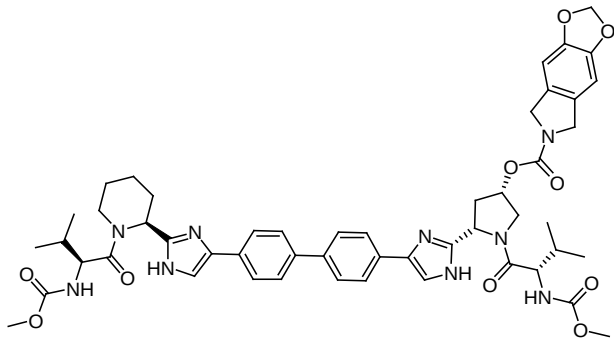
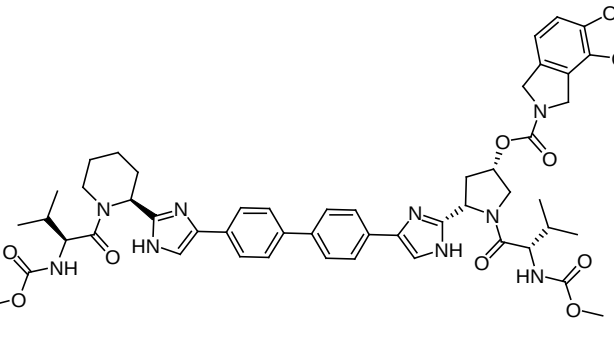
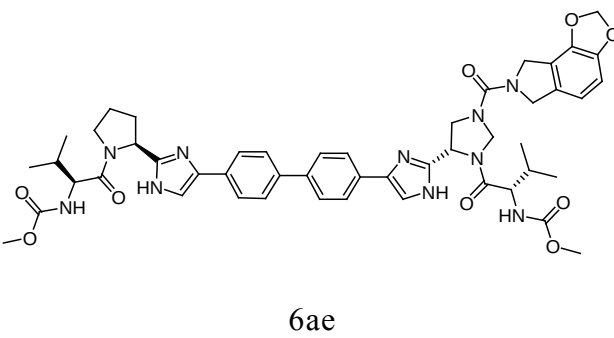
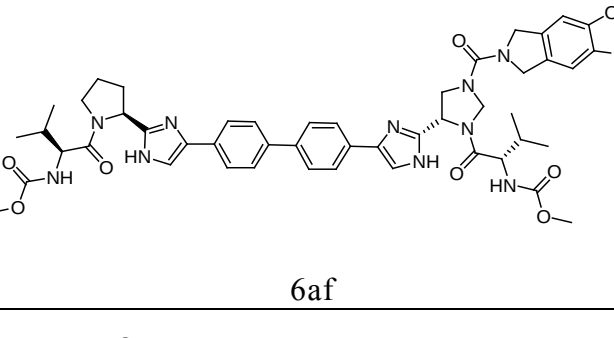
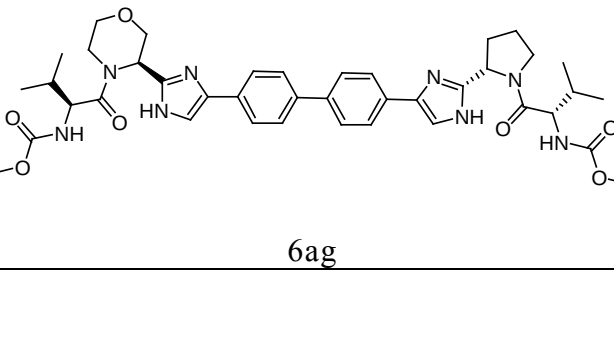
Ia-5	 6e
Ia-6	 6f
Ia-7	 6g
Ia-8	 6h

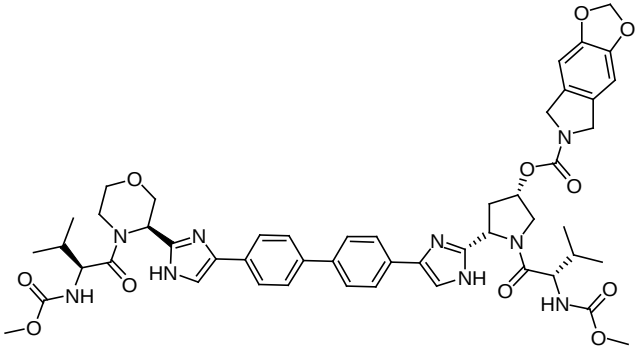
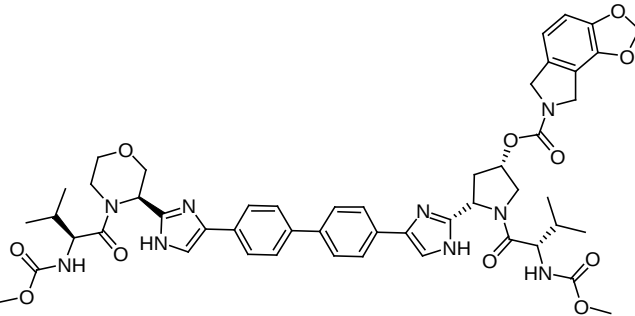
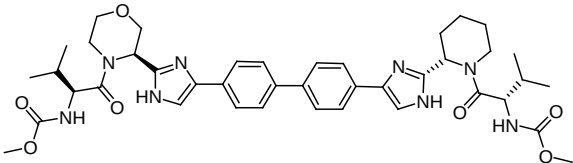
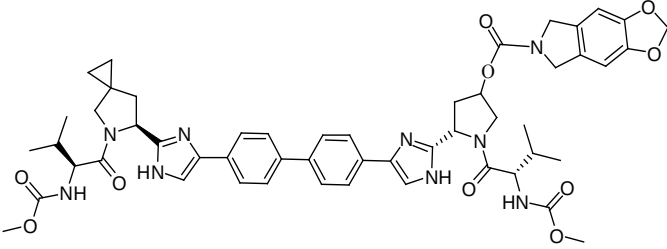
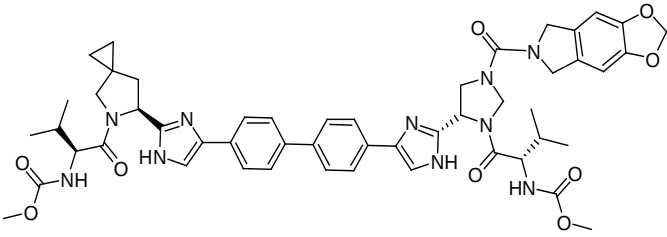
Ia-9	 6i
Ia-10	 6j
Ia-11	 6k
Ia-12	 6m

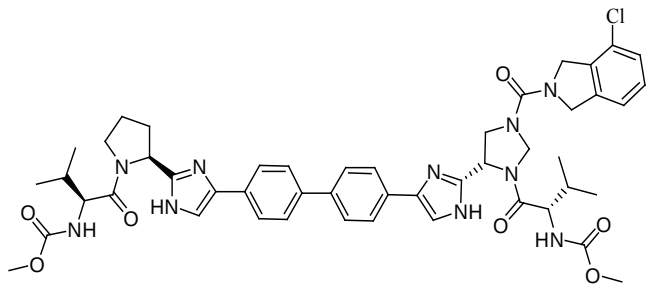
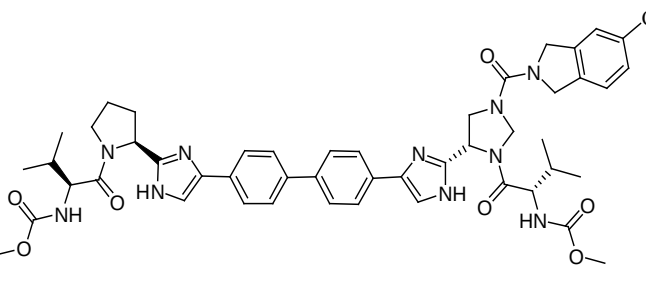
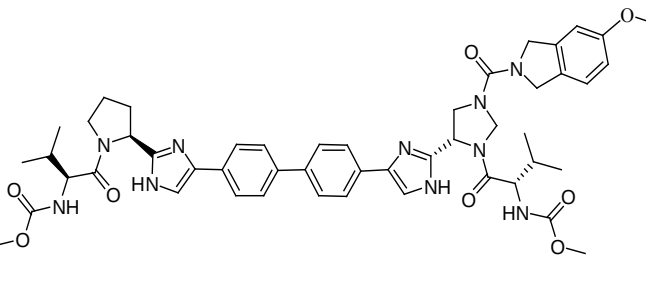
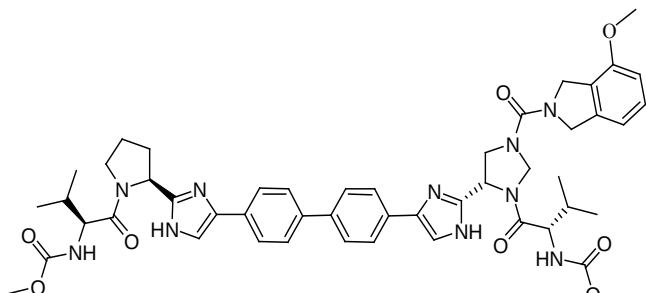
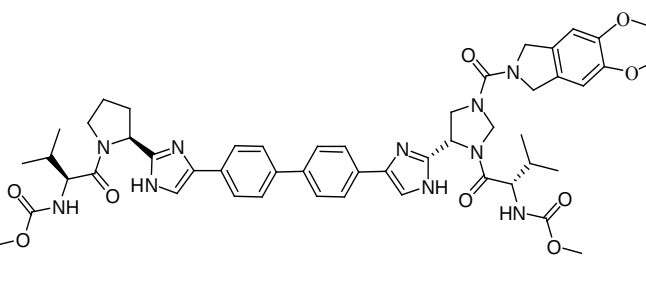
Ia-13	 6n
Ia-14	 6p
Ia-15	 6q
Ia-16	 6r

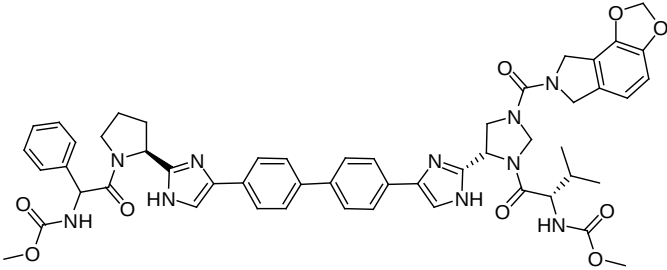
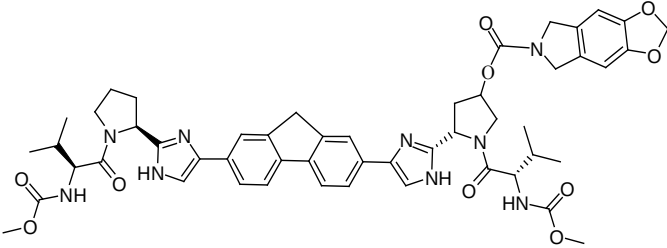
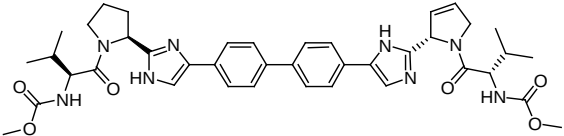
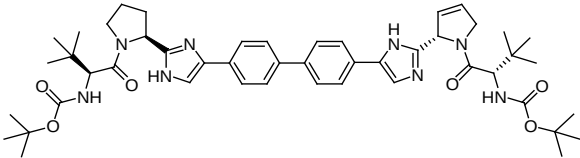
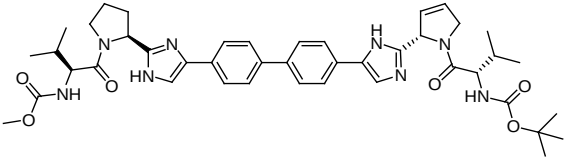
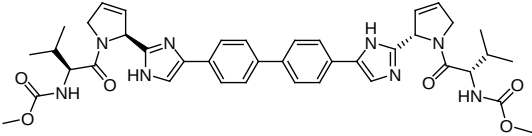
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Ia-18	 6t
Ia-19	 6u
Ia-20	 6v

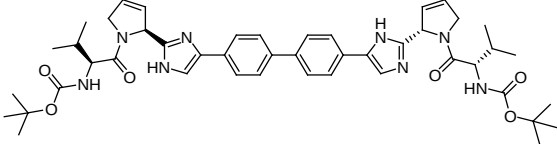
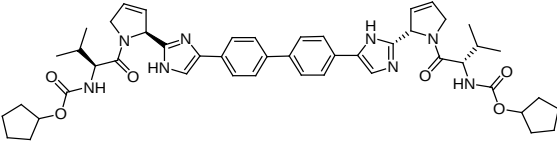
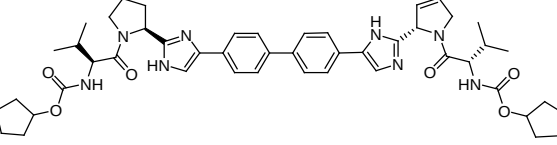
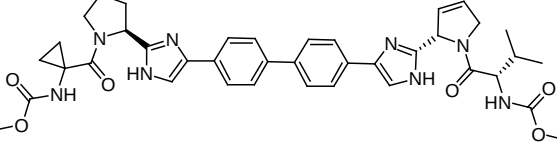
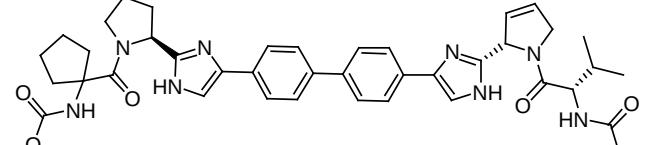
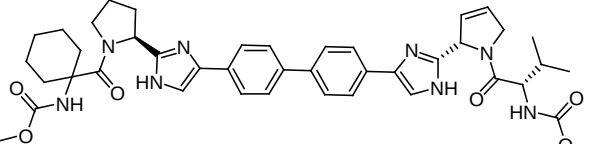
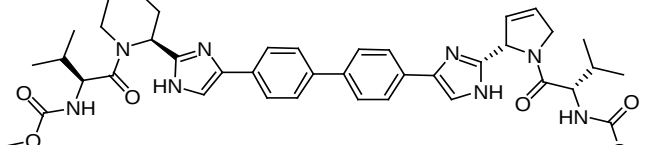
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Ia-22	 6x
Ia-23	 6y
Ia-24	 6z
Ia-25	 6aa
Ia-26	 6ab

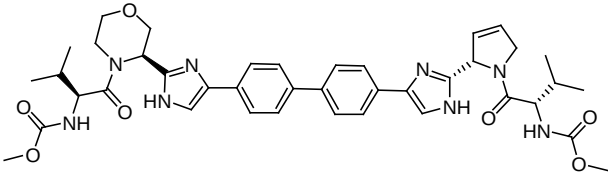
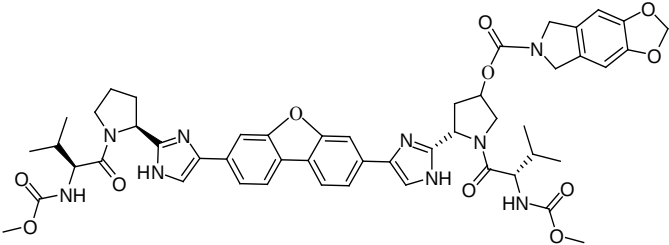
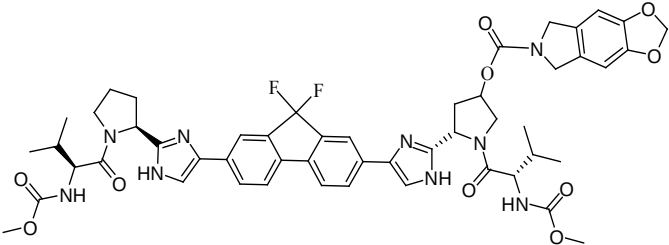
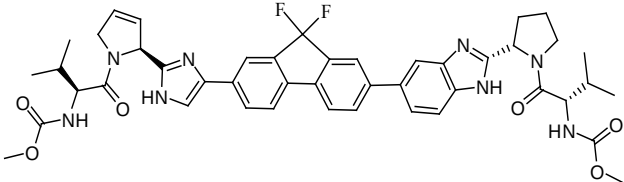
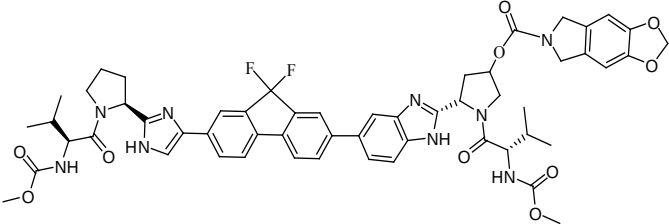
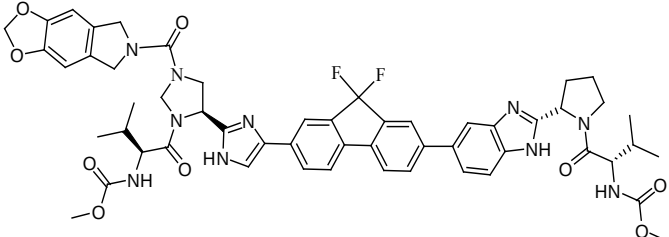
Ia-27	 6ac
Ia-28	 6ad
Ia-29	 6ae
Ia-30	 6af
Ia-31	 6ag

Ia-32	 6ah
Ia-33	 6ai
Ia-34	 6aj
Ia-35	 6ak
Ia-36	 6am

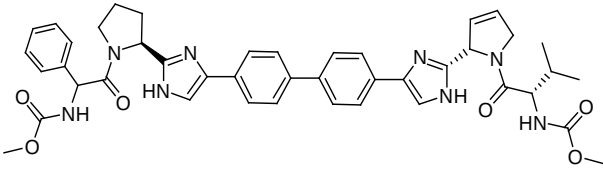
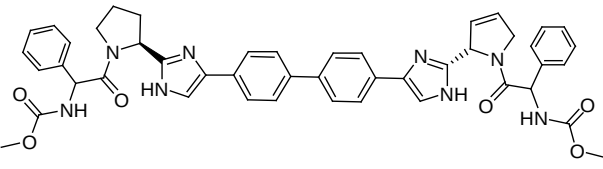
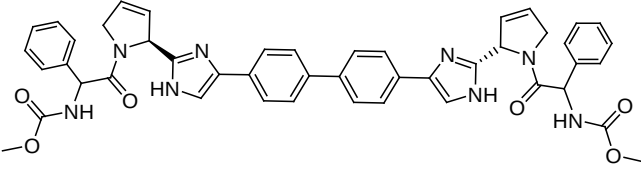
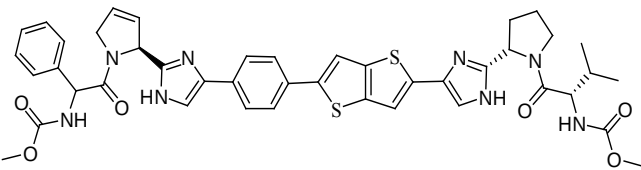
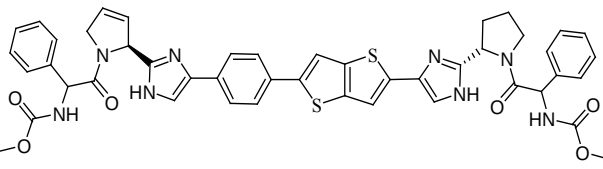
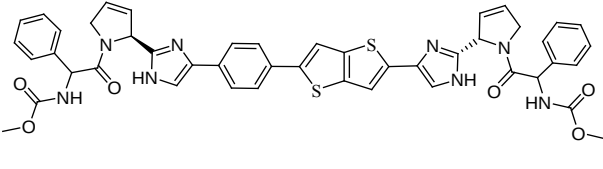
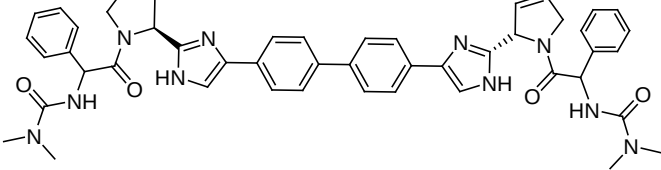
Ia-42	 6at
Ia-43	 6au
Ia-44	 6av
Ia-45	 6aw
Ia-46	 6ax

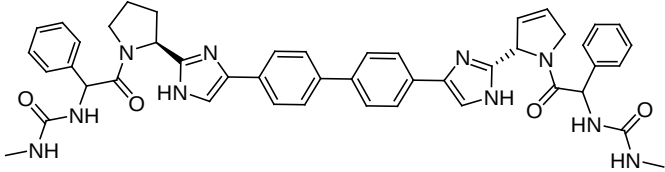
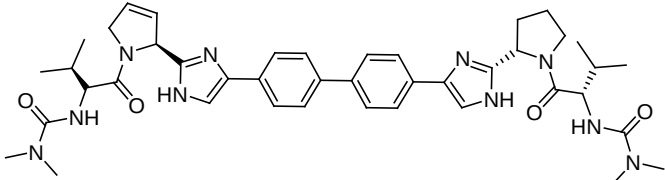
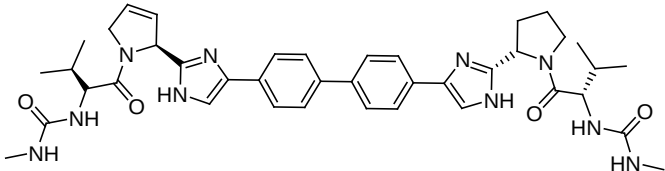
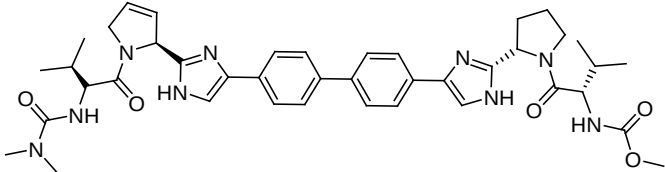
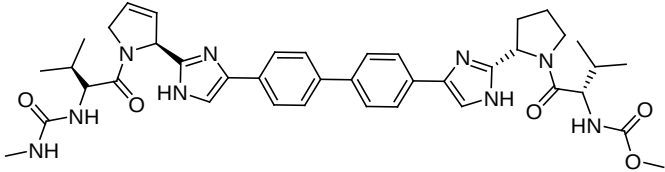
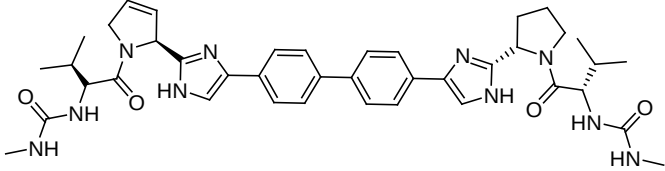
Ia-47	 6ay
Ia-48	 6az
Ia-49	 6ba
Ia-50	 6bb
Ia-51	 6bc
Ia-52	 6bd

Ia-53	 6be
Ia-54	 6bf
Ia-55	 6bg
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Ia-58	 6bj
Ia-59	 6bk

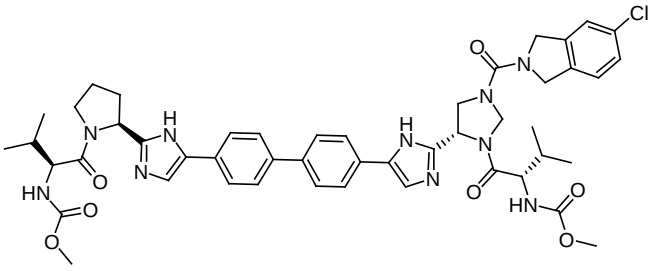
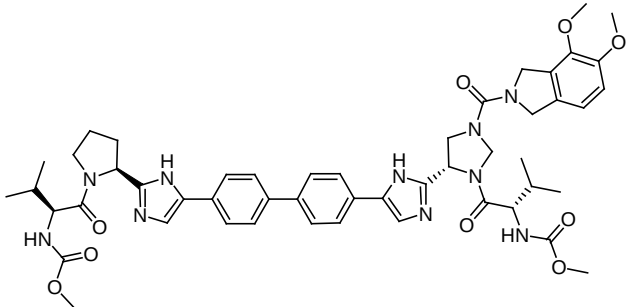
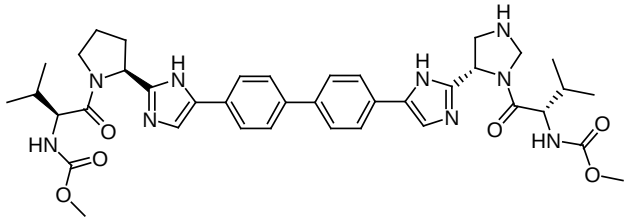
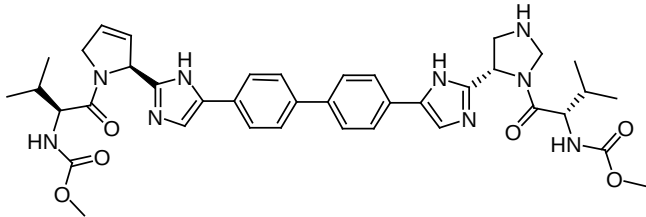
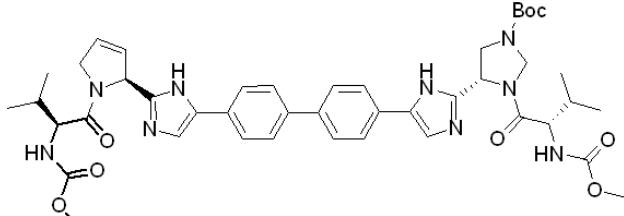
Ia-60	 6bm
Ia-61	 6bn
Ia-62	 6bp
Ia-63	 6bq
Ia-64	 6br
Ia-65	

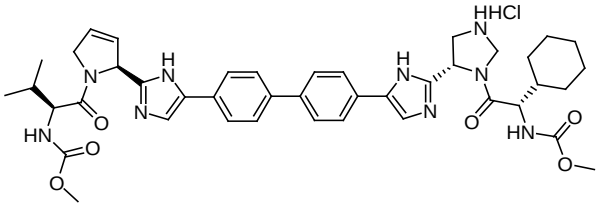
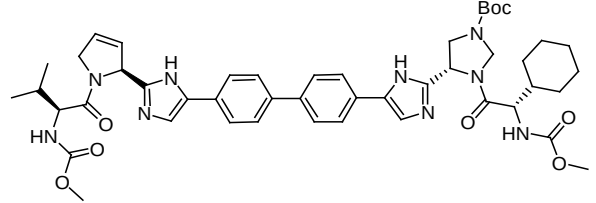
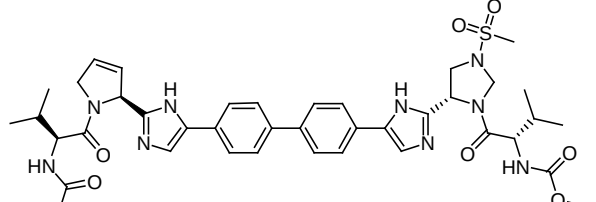
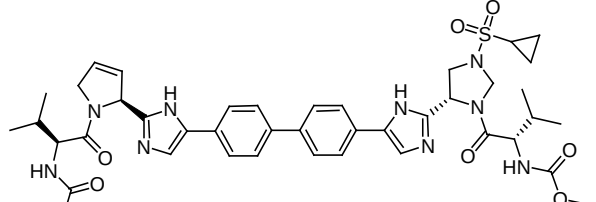
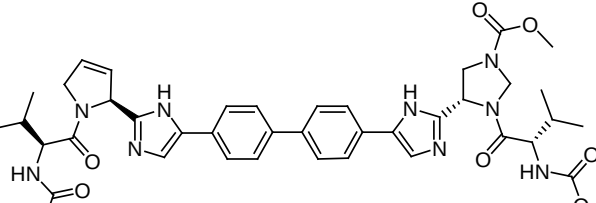
	6bs
Ia-66	
	6bt
Ia-67	
	6bu
Ia-68	
	6bv
Ia-69	
	6bw
Ia-70	
	6bx

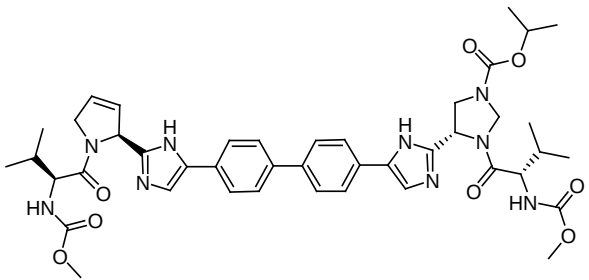
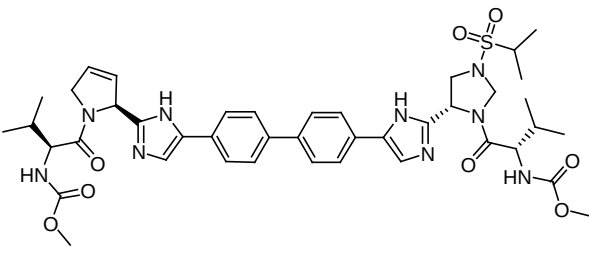
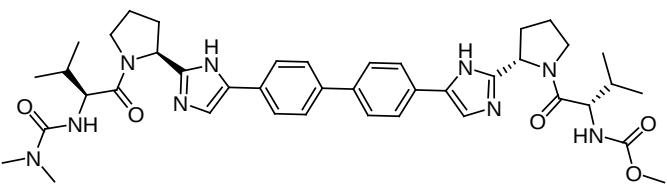
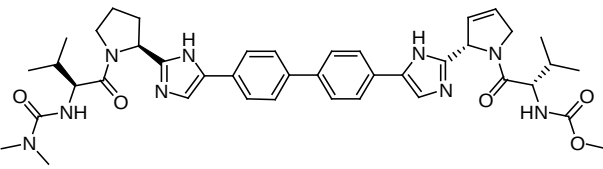
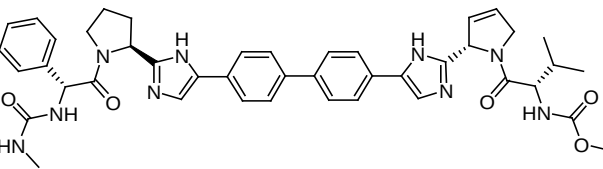
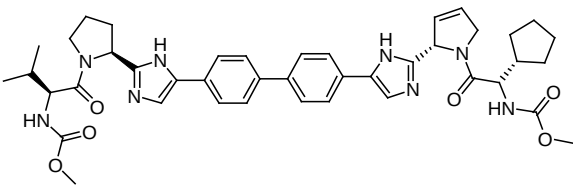
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Ia-73	 6ca
Ia-74	 6cb
Ia-75	 6cc
Ia-76	 6cd
Ia-77	 6ce

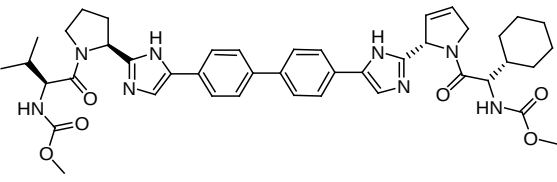
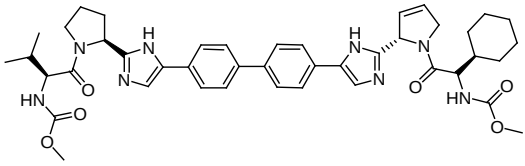
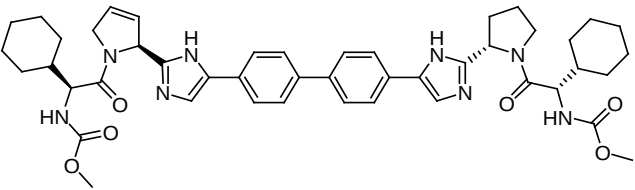
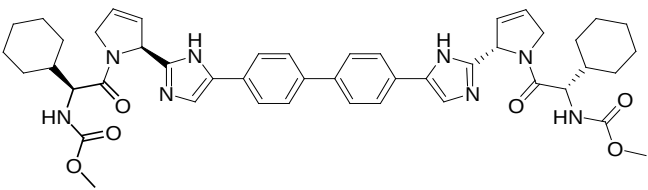
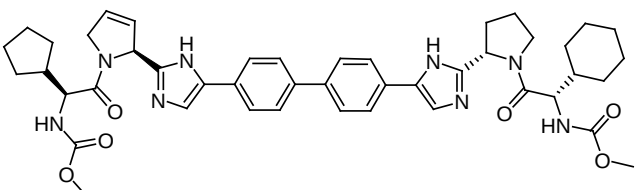
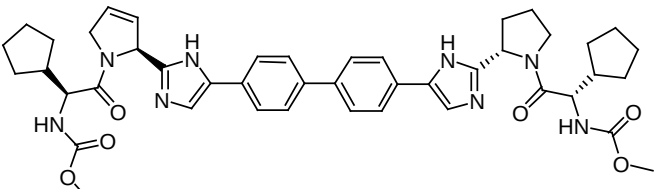
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Ia-80	 6ch
Ia-81	 6ci
Ia-82	 6cj
Ia-83	 6ck

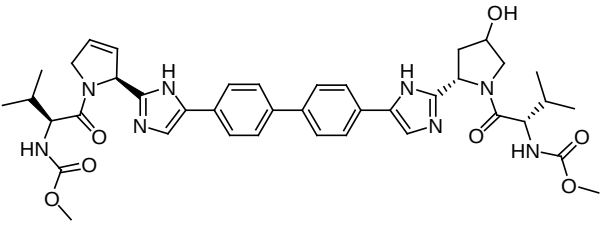
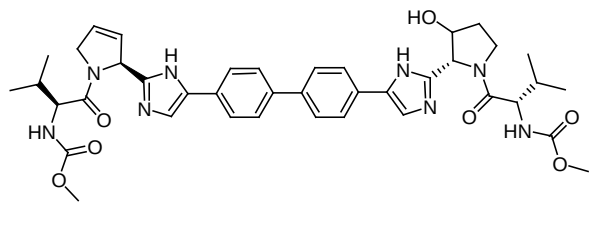
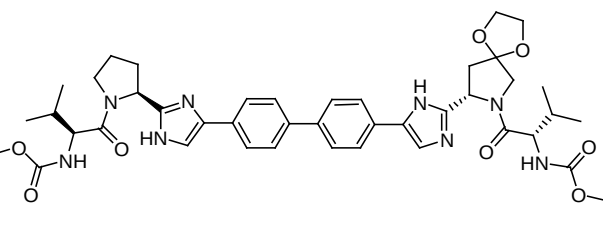
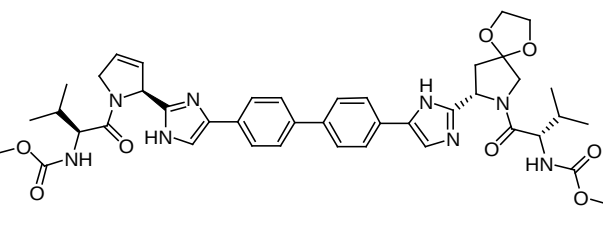
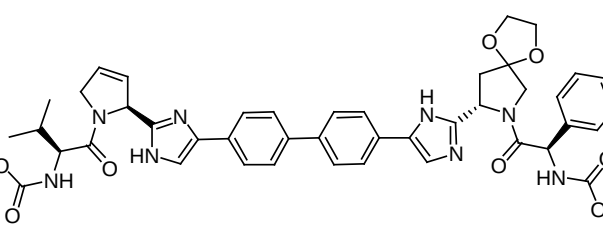
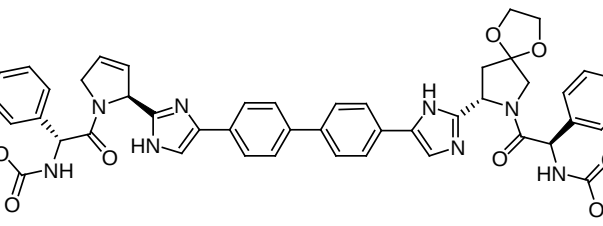
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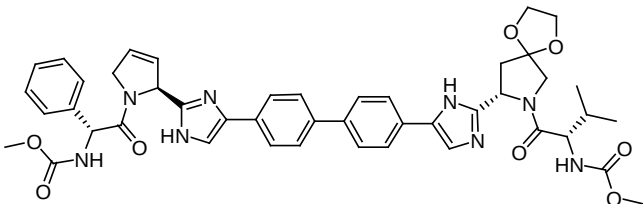
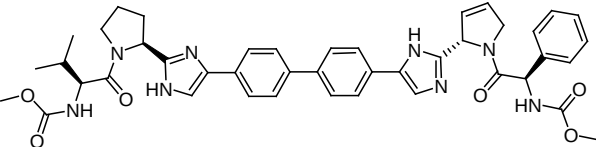
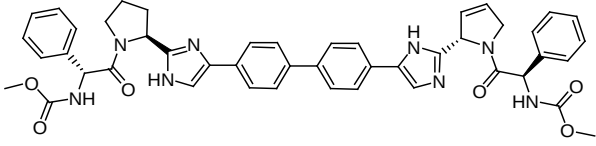
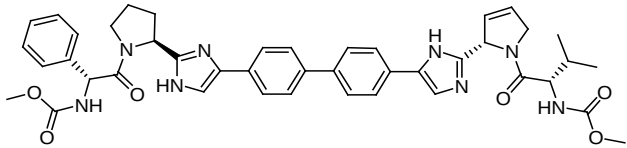
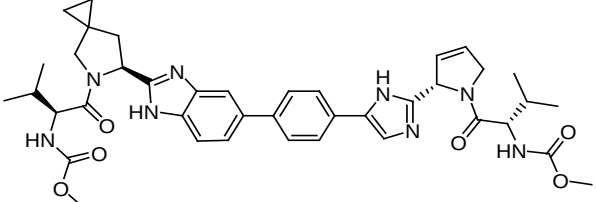
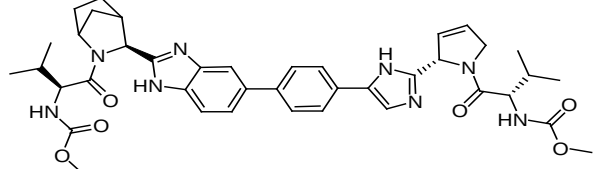
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Ia-85	 6cq
Ia-86	 6cu
Ia-87	 6cv
Ia-88	 6cw

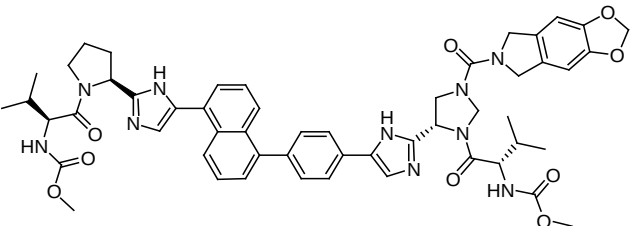
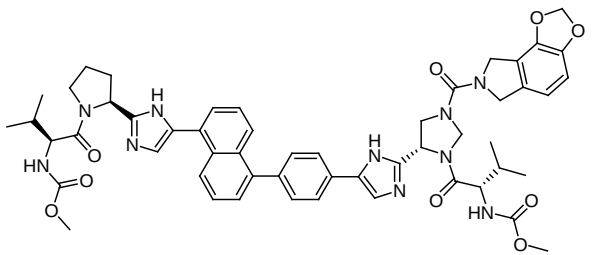
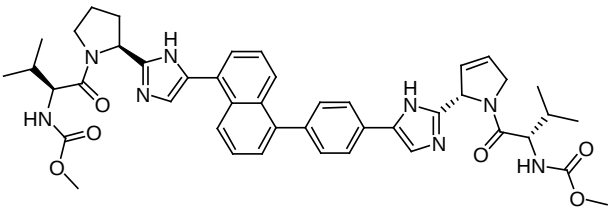
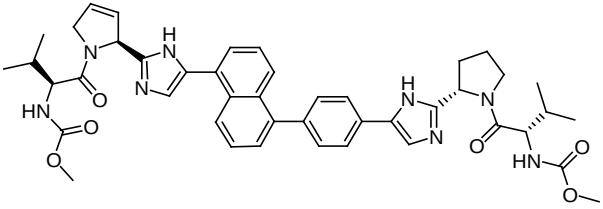
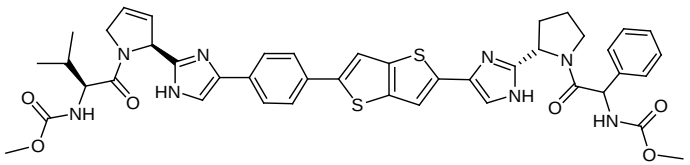
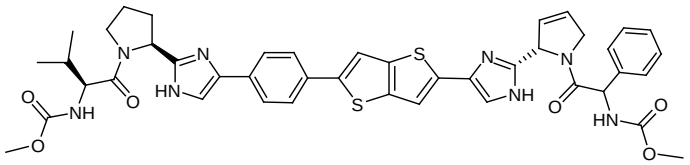
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Ia-90	 6cy
Ia-91	 6cz
Ia-92	 6da
Ia-93	 6db

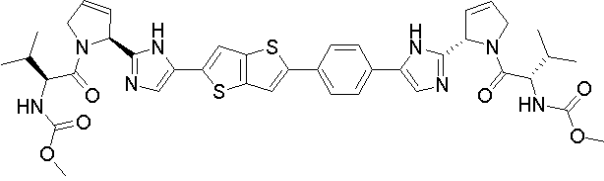
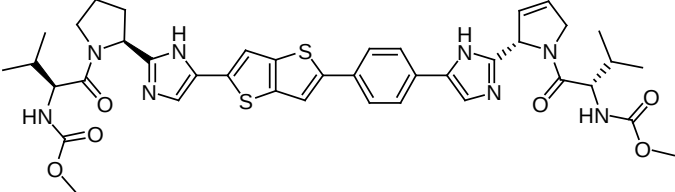
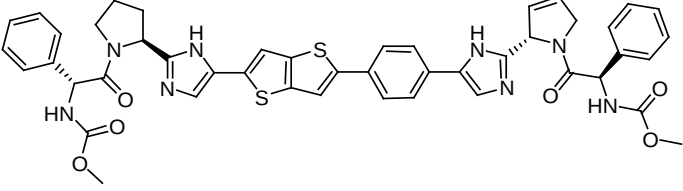
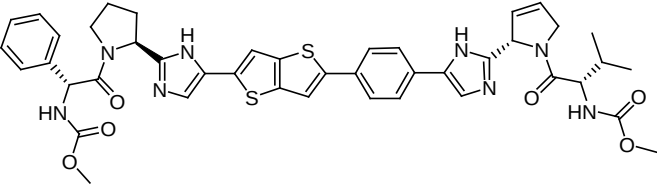
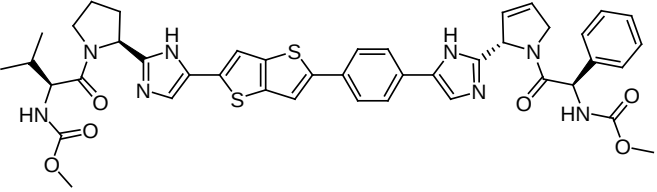
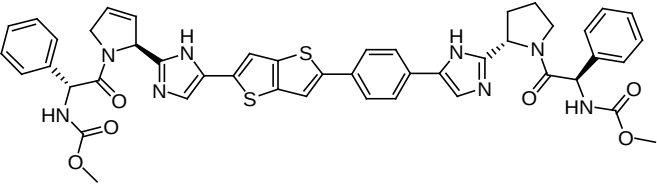
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Ia-95	 6dd
Ia-96	 6de
Ia-97	 6df
Ia-98	 6dg
Ia-99	 6dh

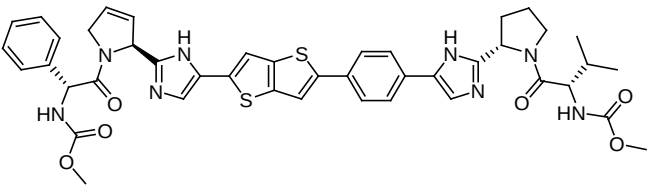
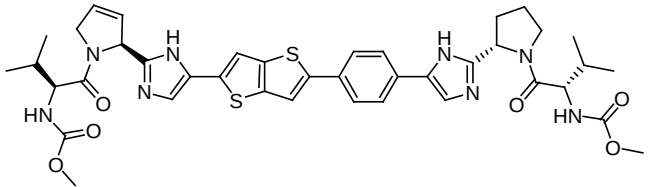
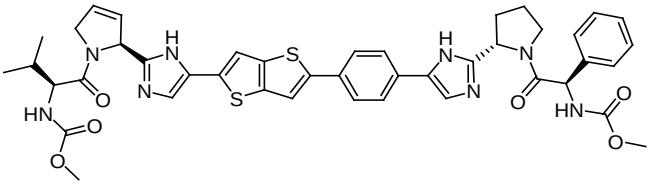
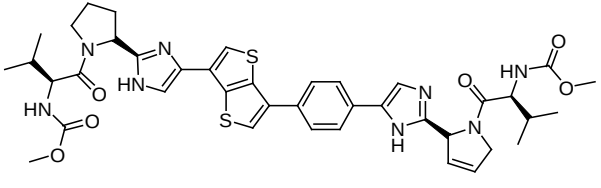
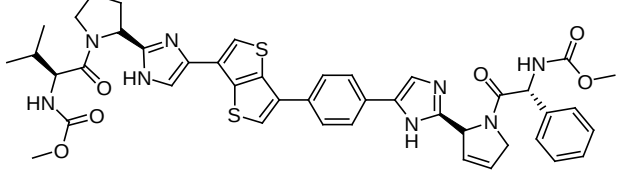
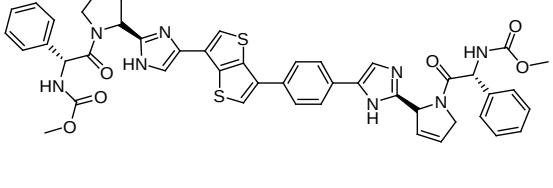
Ia-100	 Chemical structure of Ia-100: A symmetrical molecule featuring a central biphenyl core. Each phenyl ring is substituted with a 1H-imidazole ring. The imidazole rings are further substituted with a 2-methoxy-1-methylpyrrolidine-3-carboxamide group. The stereochemistry at the chiral centers is (1S,2S) for the left side and (1R,2R) for the right side. 6di
Ia-101	 Chemical structure of Ia-101: A symmetrical molecule featuring a central biphenyl core. Each phenyl ring is substituted with a 1H-imidazole ring. The imidazole rings are further substituted with a 2-methoxy-1-methylpyrrolidine-3-carboxamide group. The stereochemistry at the chiral centers is (1S,2S) for the left side and (1R,2R) for the right side. 6dj
Ia-102	 Chemical structure of Ia-102: A symmetrical molecule featuring a central biphenyl core. Each phenyl ring is substituted with a 1H-imidazole ring. The imidazole rings are further substituted with a 2-methoxy-1-methylpyrrolidine-3-carboxamide group. The stereochemistry at the chiral centers is (1S,2S) for the left side and (1R,2R) for the right side. 6dk
Ia-103	 Chemical structure of Ia-103: A symmetrical molecule featuring a central biphenyl core. Each phenyl ring is substituted with a 1H-imidazole ring. The imidazole rings are further substituted with a 2-methoxy-1-methylpyrrolidine-3-carboxamide group. The stereochemistry at the chiral centers is (1S,2S) for the left side and (1R,2R) for the right side. 6dm
Ia-104	 Chemical structure of Ia-104: A symmetrical molecule featuring a central biphenyl core. Each phenyl ring is substituted with a 1H-imidazole ring. The imidazole rings are further substituted with a 2-methoxy-1-methylpyrrolidine-3-carboxamide group. The stereochemistry at the chiral centers is (1S,2S) for the left side and (1R,2R) for the right side. 6dn
Ia-105	 Chemical structure of Ia-105: A symmetrical molecule featuring a central biphenyl core. Each phenyl ring is substituted with a 1H-imidazole ring. The imidazole rings are further substituted with a 2-methoxy-1-methylpyrrolidine-3-carboxamide group. The stereochemistry at the chiral centers is (1S,2S) for the left side and (1R,2R) for the right side. 6dp

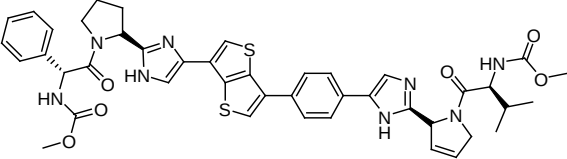
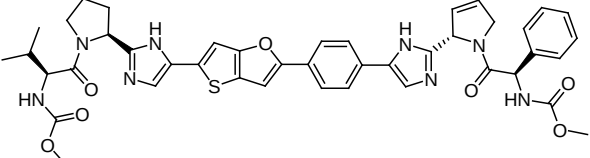
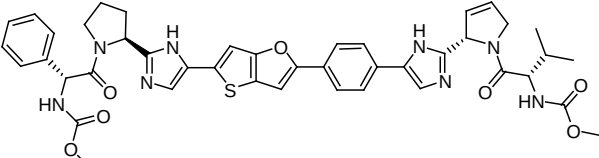
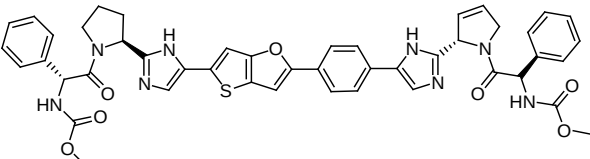
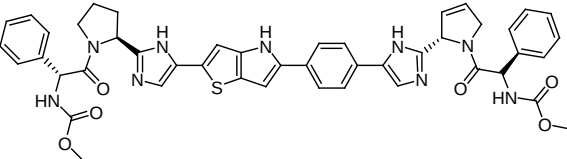
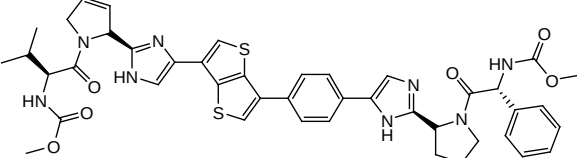
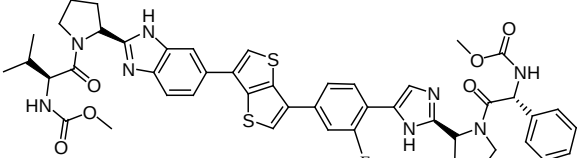
Ia-106	 6dq
Ia-107	 6dr
Ia-108	 6ds
Ia-109	 6dt
Ia-110	 6du
Ia-111	 6dv

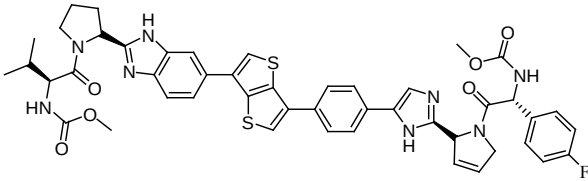
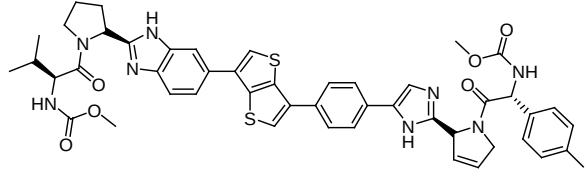
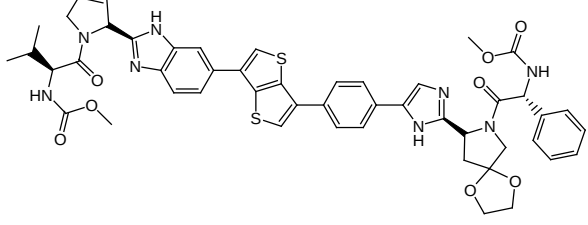
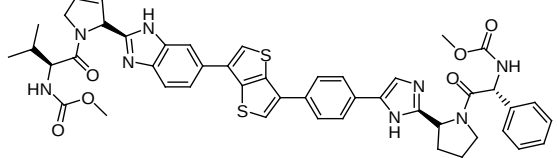
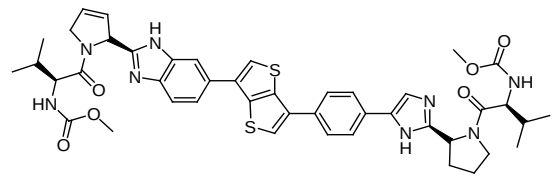
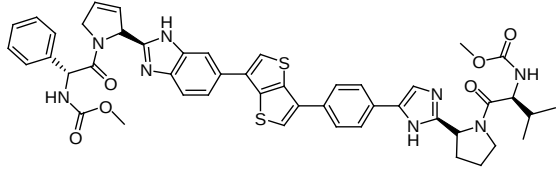
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Ia-113	 6dy
Ia-114	 6dz
Ia-115	 6ea
Ia-116	 6eb
Ia-117	 6ec

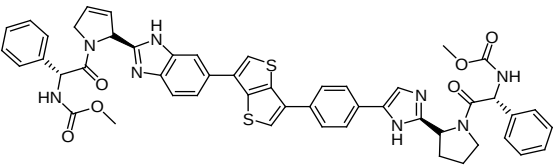
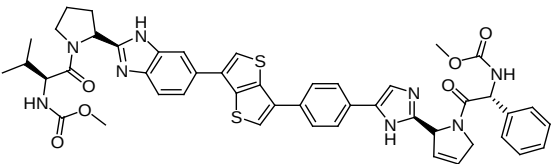
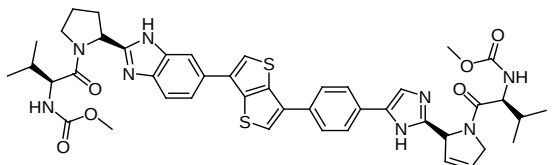
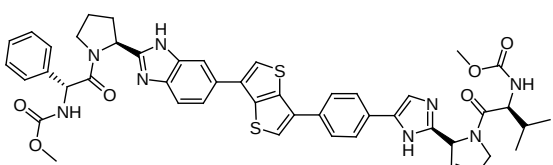
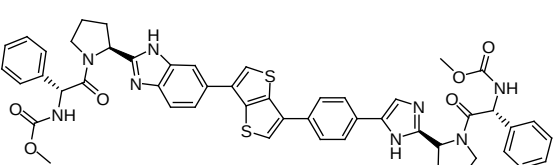
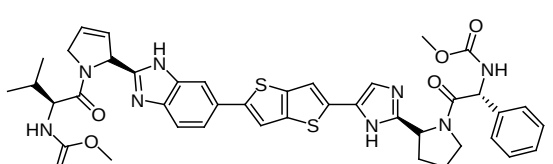
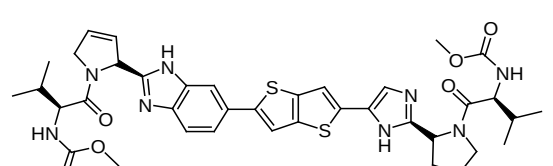
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Ia-119	 6ee
Ia-120	 6ef
Ia-121	 6eg
Ia-122	 6eh
Ia-123	 6ei

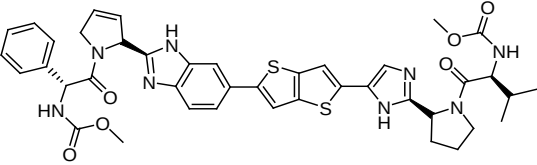
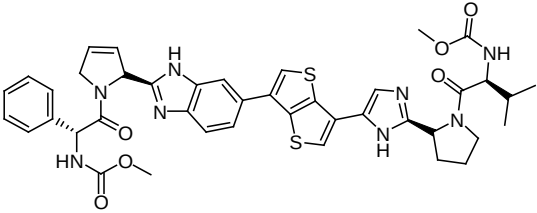
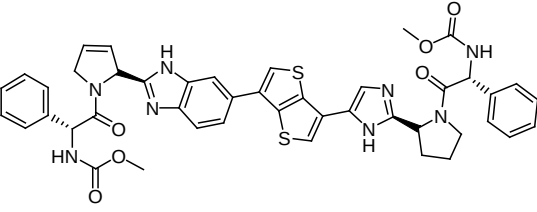
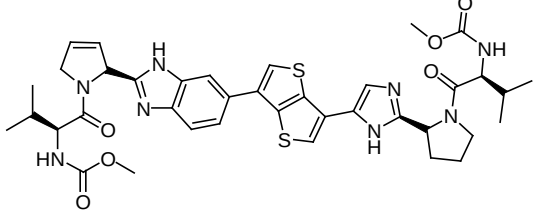
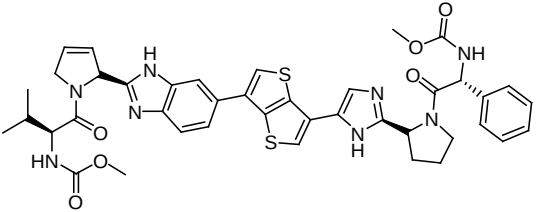
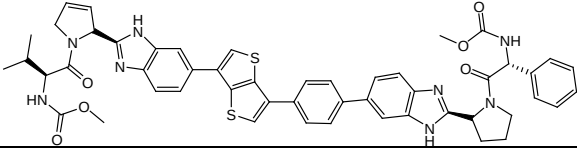
Ib-1	 6fa
Ib-2	 6fb
Ib-3	 6fc
Ib-4	 6fd
Ib-5	 6fe
Ib-6	 6ff

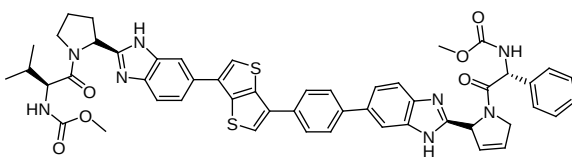
Ib-7	 6fg
Ib-8	 6fh
Ib-9	 6fi
Ib-10	 6fj
Ib-11	 6fk
Ib-12	 6fm

Ib-13	 6fn
Ib-14	 6fp
Ib-15	 6fq
Ib-16	 6fr
Ib-17	 6fs
Ib-18	 6ft
Ib-19	

	6fu
Ib-20	 Chemical structure of Ib-20: A complex molecule featuring a central benzothiazole core. The left side is substituted with a 1-methoxy-2-methyl-3-((1-methyl-2-oxo-2-(propan-2-ylideneamino)ethyl)amino)propan-1-yl group. The right side is substituted with a 1-methoxy-2-((1-methyl-2-oxo-2-(propan-2-ylideneamino)ethyl)amino)propan-1-yl group. The central benzothiazole is linked to a 4-((1-methyl-2-oxo-2-(propan-2-ylideneamino)ethyl)amino)phenyl group.
Ib-21	 Chemical structure of Ib-21: Similar to Ib-20, but the right side is substituted with a 1-methoxy-2-((1-methyl-2-oxo-2-(propan-2-ylideneamino)ethyl)amino)propan-1-yl group.
Ib-22	 Chemical structure of Ib-22: Similar to Ib-20, but the right side is substituted with a 1-methoxy-2-((1-methyl-2-oxo-2-(propan-2-ylideneamino)ethyl)amino)propan-1-yl group.
Ib-23	 Chemical structure of Ib-23: Similar to Ib-20, but the right side is substituted with a 1-methoxy-2-((1-methyl-2-oxo-2-(propan-2-ylideneamino)ethyl)amino)propan-1-yl group.
Ib-24	 Chemical structure of Ib-24: Similar to Ib-20, but the right side is substituted with a 1-methoxy-2-((1-methyl-2-oxo-2-(propan-2-ylideneamino)ethyl)amino)propan-1-yl group.
Ib-25	 Chemical structure of Ib-25: Similar to Ib-20, but the right side is substituted with a 1-methoxy-2-((1-methyl-2-oxo-2-(propan-2-ylideneamino)ethyl)amino)propan-1-yl group.

Ib-26	 6gb
Ib-27	 6gc
Ib-28	 6gd
Ib-29	 6ge
Ib-30	 6gf
Ib-31	 6gg
Ib-32	

	6gh
Ib-33	
	6gi
Ib-34	
	6gj
Ib-35	
	6gk
Ib-36	
	6gm
Ib-37	
	6gn
Ib-38	

	6gp
Ib-39	
	6gq

This invention also discloses the application of the described compounds as represented by Formula Ia or Ib, their stereoisomers, tautomers, isotope isomers, esterified or amidated prodrugs, pharmaceutically acceptable salts in the preparation of HCV
5 inhibiting drugs.

This invention also discloses the application of the mixture of one or more compositions selected from the described compounds as represented by Formula Ia or Ib, their stereoisomers, tautomers, isotope isomers, esterified or amidated prodrugs and pharmaceutically acceptable salts in the preparation of HCV inhibiting drugs.

10 This invention also discloses a pharmaceutical composition comprising the described compounds as represented by Formula Ia or Ib, their stereoisomers, tautomers, isotope isomers, esterified or amidated prodrugs, or pharmaceutically acceptable salts, and pharmaceutically acceptable excipient(s).

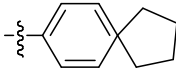
The described pharmaceutical composition in this invention may also contain one or
15 more ingredients selected from immunoregulants, HCV-NS3/4A inhibitors, HCV-NS5B inhibitors, HCV inhibitors in the categories of nucleosides, nucleoside derivatives and non-nucleosides, HBV inhibitors, HIV inhibitors, anti-cancer drugs and anti-inflammatory drugs. Wherein, the described immunoregulants are preferably interferon or interferon derivatives; wherein the described interferon is preferably pegylated interferon; the
20 described HIV inhibitors include ritonavir and/or ribavirin; the described HBV inhibitors include lamivudine, telbivudine, adefovir, emtricitabine, entecavir, tenofovir and clevudine; the described HIV inhibitors include ritonavir and/or ribavirin; the described HCV protease inhibitor is preferably VX-950, ZN2007, ABT-450, RG-7227, TMC-435, MK-5172, MK-7009, ACH-1625, GS-9256, TG2349, BMS-650032, IDX320, yimidasvir
25 phosphate, or seraprevir potassium; the described HCV polymerase inhibitor is preferably GS-5885, TMC647055, ABT-267, BMS-791325, PPI-383, or ALS-002158.

In the described pharmaceutical composition of this invention, the content of the described compounds as represented by Formula Ia or Ib, their stereoisomers, tautomers, isotope isomers, esterified or amidated prodrugs and pharmaceutically acceptable salts is preferably 0.01%-99.9% (mass percent); the described mass percent means the percentage of the mass of compounds as represented by Formula **Ia**, compounds as represented by Formula **Ib**, their stereoisomers, tautomers, esterified or amidated prodrugs and pharmaceutically acceptable salts in total mass of the pharmaceutical composition. This invention also discloses the application of the described pharmaceutical compositions in the preparation of HCV-inhibiting medicine.

Unless otherwise specifically provided herein, the described alkyl group refers to branched chain and linear chain saturated fatty hydrocarbonyl containing 1~20 carbon atoms, preferably 1~10 carbon atoms, and more preferably 1~8 carbon atoms, e.g. methyl, ethyl, n-propyl, isopropyl, n-butyl, tert-butyl, isobutyl, pentyl, hexyl, heptyl, octyl, nonyl, decyl, 4,4-dimethyl pentyl, 2,2,4-trimethyl pentyl, hendecyl, lauryl, and their isomers; and any of the above-mentioned alkyls that has 1~4 substituents selected from aryl, heterocyclic aryl, cycloalkyl, cycloalkenyl, epoxyl, heterocyclic radical, alkoxyl carbonyl, aryloxycarbonyl, heterocyclic oxyl, alkyl amino, alkylaminocarbonyl, arylamino, heterocyclic amino, aryl sulfonyl, alkylaminosulfonyl, heterocyclic aminosulfonyl, alkylsulfonamino, heterocyclic sulfonamino, arylsulfonamino, alkyl aminosulfonamino, alkylcarbonylamino, fused aryl, fused alkylaryl, fused alkyl, fused epoxyl, alkylureido, alkyl group, alkyl sulphide, alkylthioureido, ureido or thioureido.

Unless otherwise specifically provided herein, the described alkoxyl refers to a radical formed by the connection of alkyl and oxygen atom, i.e., " $R-O\dot{}$ ", R represents alkyl radical.

Unless otherwise specifically provided herein, the described aryl refers to any stable monocyclic or bicyclic radical, with each nucleus consisting of up to 7 atoms, wherein at least one ring is aromatic; in the case of bicyclic nucleus, fused nucleus is excluded but

spiro nucleus is included. For example, phenyl or  and any of the aryl radicals having one or more of the following radicals as substituents: aryl, heterocyclic aryl, cycloalkyl, cycloalkenyl, epoxyl, heterocyclic radical, alkoxyl carbonyl,

aryloxycarbonyl, heterocyclic oxyl, alkyl amino, alkylaminocarbonyl, arylamino, heterocyclic amino, aryl sulfonyl, alkylaminosulfonyl, heterocyclic aminosulfonyl, alkylsulfonamino, heterocyclic sulfonamino, arylsulfonamino, alkyl aminosulfonamino, alkylcarbonylamino, fused aryl, fused cyclic alkylaryl, fused cyclic alkyl, fused epoxyl, alkylureido, alkyl, alkyl sulphide, alkylthioureido, ureido or thioureido, for example, biphenyl.

Unless otherwise specifically provided herein, the described heterocyclic aryl refers to a stable monocyclic or bicyclic ring whose nucleus consists of up to 7 atoms, wherein at least one ring is an aromatic one containing 1-4 hetero-atoms selected from O, N, and S; and the above-mentioned heterocyclic aryl containing one or more substituents selected from the undermentioned radicals defined in this invention: aryl, heterocyclic aryl, cycloalkyl, cycloalkenyl, epoxyl, heterocyclic radical, alkoxyl carbonyl, aryloxycarbonyl, heterocyclic oxyl, alkyl amino, alkylaminocarbonyl, arylamino, heterocyclic amino, aryl sulfonyl, alkylaminosulfonyl, heterocyclic aminosulfonyl, alkylsulfonamino, heterocyclic sulfonamino, arylsulfonamino, alkyl aminosulfonamino, alkylcarbonylamino, fused aryl, fused alkylaryl, fused alkyl, fused epoxyl, alkylureido, alkyl, alkyl sulphide, alkylthioureido, ureido or thioureido. Heterocyclic aryl radicals that fall into the scope of this definition include but are not limited to acridinyl, carbazolyl, cinnolinyl, quinoxalyl, pyrazolyl, indyl, benzotriazolyl, furyl, thiophene thiofuryl, benzothiazolyl, benzothiophenyl, benzofuranyl, quinolinyl, isoquinolyl, oxazolyl, isoxazolyl, indyl, pyrazinyl, pyridazinyl, pyridyl, pyrimidinyl, pyrrolyl, tetrahydroquinolinyl. According to the following definition of heterocyclic nucleus, heterocyclic aryls are deemed to include the N-oxide derivatives of any nitrogen-containing heterocyclic aryls. When a heterocyclic aryl substituent is a bicyclic substituent and one of the nucleus is a non-aromatic one or hetero-atom free, it is understandable that the two nucleus are connected via the aromatic ring or the heteroatom-containing ring.

Unless otherwise specifically provided herein, the described alkyl sulphide refers to a radical formed by connecting the alkyl radical to sulfur atom, i.e., " $R-S^{\frac{\cdot}{2}}$ ", wherein R represents an alkyl radical.

Unless otherwise specifically provided herein, the described aryloxy refers to a radical formed by connecting the aryl group to an oxygen atom, i.e., " $R-O^{\frac{\cdot}{2}}$ ", wherein R

represents an aryl radical.

Unless otherwise specifically provided herein, the described arylamino radical refers to a radical formed by substituting a hydrogen in "NH₃" with an aryl radical.

Unless otherwise specifically provided herein, the described cycloalkyl radical refers
5 to a total-carbon monocyclic or polycyclic radical that is free of any double bond on its nucleus. It is preferably a cycloalkyl radical consisting of 1~3 rings of 3~20 carbons, more preferably, 3~10 carbons, for example: cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, cyclodecanyl and cyclolauryl; the cycloalkyl radical can be substituted by 1~4 substituents as defined herein, i.e. deuterium, halogen, alkyl, alkoxy,
10 hydroxyl, aryl, aryloxy, arylalkyl, cycloalkyl, alkylamino, amido, oxygen, acyl, arylcarbonylamino, amino, nitrile, mercapto, alkyl sulphide and alkyl.

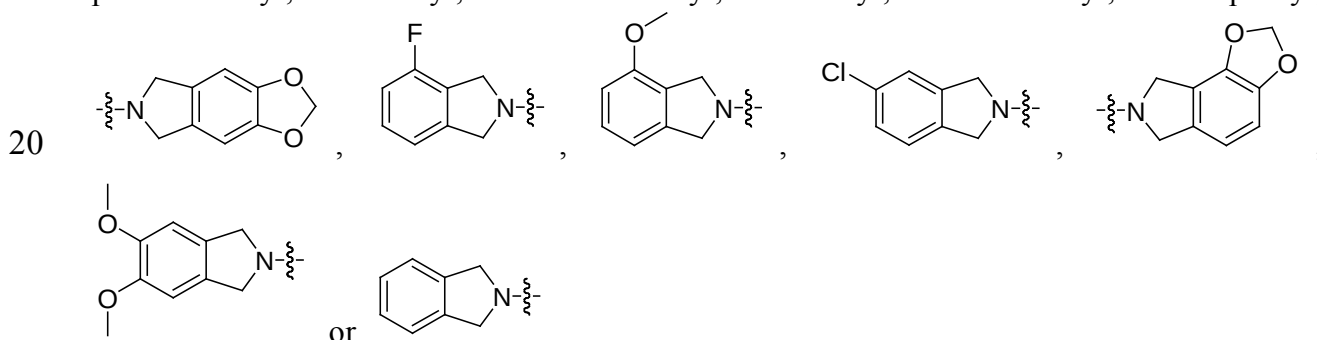
Unless otherwise specifically provided herein, the described cycloalkenyl refers to a total-carbon monocyclic or polycyclic radical, wherein every nucleus can contain one or more double bonds but none of such nucleus should be with a conjugated π electric system.
15 It is preferably a cycloalkenyl whose nucleus is consisted of 3~20 carbons, more preferably of 3~10 carbons, e.g., cyclopropenyl, cyclobutenyl, cyclopentenyl, cyclohexenyl, cycloheptenyl, cyclooctenyl, cyclodecenyl and cyclododecenyl; the cycloalkenyl can be substituted by one or more substituent defined in this invention, including deuterium, halogen, alkyl, alkoxy, hydroxyl, aryl, aryloxy, arylalkyl,
20 cycloalkyl, alkylamino, amido, oxygen, carbonyl, arylcarbonylamino, amino, nitrile, mercapto, alkyl sulphide and alkyl. When substitution of cycloalkenyl take place on a carbon-carbon double bond and the double bond is saturated, cycloalkyl will form.

Unless otherwise specifically provided herein, the described epoxy refers to a cycloalkyl connected to an etheryl-containing radical.

25 Unless otherwise specifically provided herein, the described heterocyclic radical refers to an aromatic or non-aromatic heterocyclic ring that contain one or more hetero-atoms selected from O, N and S, and may include bicyclic radicals. Therefore, heterocyclic radicals include the above-mentioned heterocyclic aryls and their dihydro or tetrahydro analogs. Other examples of heterocyclic radicals include but are not limited to
30 the following: benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl, benzothiazolyl, benzothiophenyl, benzoxazolyl, carbolinyl, furyl, imidazolyl, dihydroindyl, indyl, indazolyl, isobenzofuranyl, isoazaindenyl, isoquinolyl, isothiazolyl, isoxazolyl,

oxazolyl, oxazoliny, isooxazoliny, oxy-cyclobutyl, pyranyl, pyraziny, pyrazolyl, pyridaziny, pyridinopyridyl, pyridaziny, pyridyl, pyrimidiny, pyrrolyl, quinazoliny, quinoliny, quinoxalyl, tetrahydropyranyl, thiadiazolyl, thiazolyl, thiophene thiofuryl, triazolyl, azetidiny, 1,4-dioxanyl, hexahydroazepiny, piperaziny, piperidyl, pyrrolealkyl
 5 group, morpholiny, thio-morpholiny, dihydrobenzimidazolyl, dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuryl, dihydroimidazolyl, dihydroindyl, dihydroisoxazolyl, dihydroisothiazolyl, dihydrooxdiazolyl, dihydrooxazolyl, dihydropyraziny, dihydropyrazolyl, dihydropyridyl, dihydropyrimidiny, dihydropyrrolyl, dihydroquinoliny, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl,
 10 dihydrothiophene thiofuryl, dihydrotriazolyl, dihydroazetidiny, methylenedioxybenzoyl, tetrahydrofuryl and tetrahydrothiophene thiofuryl and their N-oxides. Heterocyclic radicals can be connected via carbon atom or hetero-atom to nucleus molecule.

Unless otherwise specifically provided herein, the described fused aryl refers to a polycyclic organic compound formed by the fused connection of two or more aryl radicals
 15 and/or heterocyclic aryl radicals, the described fused aryl radical may have substituents defined in this invention such as alkyl, alkoxy, alkyl sulphide, aryloxy, arylamino, heterocyclic radical, cycloalkyl, cycloalkenyl, epoxy, aryl, halogen, carbonyl, hydroxyl, heterocyclic aryl in a reasonable way. For example, naphthalenyl, anthracenyl, quinonyl, phenanthrenyl, fluorenyl, Benzimidazolyl, furofuryl, thienothienyl, acenaphthyl,



Unless otherwise specifically provided herein, the described fused ring alkylaryl radical refers to an aryl radical whose aromatic nucleus has hydrogen(s) substituted by fused ring alkyl radicals.

25 Unless otherwise specifically provided herein, the described fused ring alkyl radical refers to a non-aromatic polycyclic system formed by the reduction of one or more double bonds on the fused aryl nucleus.

Unless otherwise specifically provided herein, the described fused ring ether radical

refers to a radical formed by connecting an oxygen to a fused aryl or fused alkyl radical, i.e., “ $\text{R}-\text{O}-\dot{\text{X}}$ ”, wherein R represents a fused aryl or a fused alkyl radical.

Unless otherwise specifically provided herein, the described alkoxy carbonyl refers to a radical formed by connecting an alkoxy radical to a carbonyl radical, i.e., “ $\text{R}-\text{O}-\text{C}(=\text{O})-\dot{\text{X}}$ ”,
5 wherein R represents an alkyl radical.

Unless otherwise specifically provided herein, the described aryloxy carbonyl radical refers to a radical formed by connecting an aryloxy radical to a carbonyl radical, i.e., “ $\text{R}-\text{O}-\text{C}(=\text{O})-\dot{\text{X}}$ ”, wherein R represents an aryl radical.

Unless otherwise specifically provided herein, the described heterocyclic oxy radical
10 refers to a radical formed by connecting a heterocyclic radical to an oxygen atom, i.e., “ $\text{R}-\text{O}-\dot{\text{X}}$ ”, wherein R represents a heterocyclic radical.

Unless otherwise specifically provided herein, the described alkyl amino radical refers to a radical formed by connecting an alkyl radical to an amino radical, i.e., “ $\text{R}-\text{N}(\text{H})-\dot{\text{X}}$ ”,
wherein R represents an alkyl radical.

Unless otherwise specifically provided herein, the described alkylaminocarbonyl
15 radical refers to a radical formed by connecting an alkyl amino radical to a carbonyl radical, i.e., “ $\text{R}-\text{N}(\text{H})-\text{C}(=\text{O})-\dot{\text{X}}$ ”, wherein R represents an alkyl radical.

Unless otherwise specifically provided herein, the described arylamino radical refers to a radical formed by connecting an aryl radical to an amino radical, i.e., “ $\text{R}-\text{N}(\text{H})-\dot{\text{X}}$ ”,
20 wherein R represents an aryl group.

Unless otherwise specifically provided herein, the described heterocyclic amino radical refers to a radical formed by connecting a heterocyclic radical to an amino radical, i.e., “ $\text{R}-\text{N}(\text{H})-\dot{\text{X}}$ ”, wherein R represents a heterocyclic radical.

Unless otherwise specifically provided herein, the described arylaminosulfonyl radical
25 refers to a radical formed by connecting an arylamino radical to a sulfonyl radical, i.e.,

“ $\begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{N}-\text{S} \\ | \quad || \\ \text{H} \quad \text{O} \end{array}$ ”, wherein R represents an aryl group.

Unless otherwise specifically provided herein, the described alkylaminosulfonyl radical refers to a radical formed by connecting an alkyl amino radical to a sulfonyl radical,

i.e., “ $\begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{N}-\text{S} \\ | \quad || \\ \text{H} \quad \text{O} \end{array}$ ”, wherein R represents an alkyl group.

5 Unless otherwise specifically provided herein, the described heterocyclic aminosulfonyl radical refers to a radical formed by connecting a heterocyclic amino

radical to a sulfonyl group, i.e., “ $\begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{N}-\text{S} \\ | \quad || \\ \text{H} \quad \text{O} \end{array}$ ”, wherein R represents a heterocyclic radical.

Unless otherwise specifically provided herein, the described alkylsulfonamino refers to a radical formed by connecting an alkyl radical to Sulfonamino group formed by

10 connecting, i.e., “ $\text{R}-\overset{\text{O}_2}{\text{S}}-\overset{\text{H}}{\underset{\cdot}{\text{N}}}$ ”, wherein R represents an alkyl radical.

Unless otherwise specifically provided herein, the described Heterocyclic ringSulfonamino refers to a radical formed by connecting a heterocyclic radical to a sulfonamino radical, i.e., “ $\text{R}-\overset{\text{O}_2}{\text{S}}-\overset{\text{H}}{\underset{\cdot}{\text{N}}}$ ”, wherein R represents a heterocyclic radical.

15 Unless otherwise specifically provided herein, the described arylsulfonamino radical refers to a radical formed by connecting an aryl radical to a sulfonamino radical, i.e., “ $\text{R}-\overset{\text{O}_2}{\text{S}}-\overset{\text{H}}{\underset{\cdot}{\text{N}}}$ ”, wherein R represents an aryl group.

Unless otherwise specifically provided herein, the described alkyl aminosulfonamino radical refers to a radical formed by connecting an alkyl amino radical to a sulfonamino radical, i.e., “ $\text{R}-\overset{\text{H}}{\text{N}}-\overset{\text{O}_2}{\text{S}}-\overset{\text{H}}{\underset{\cdot}{\text{N}}}$ ”, wherein R represents an alkyl group.

20 Unless otherwise specifically provided herein, the described alkylcarbonylamino radical refers to a radical formed by connecting an alkyl radical to a carbonyl radical and an amino radical in succession, i.e., “ $\text{R}-\overset{\text{H}}{\text{N}}-\overset{\text{O}_2}{\text{S}}-\overset{\text{H}}{\underset{\cdot}{\text{N}}}$ ”, wherein R represents an alkyl group.

Unless otherwise specifically provided herein, the described alkylureido radical refers to a radical formed by connecting an alkyl radical to a ureido radical and an amino radical

in succession, i.e., “ $\text{R}-\text{NH}-\text{C}(=\text{O})-\text{NH}-\text{}$ ”, wherein R represents an alkyl group.

Unless otherwise specifically provided herein, the described alkylthioureido radical
5 refers to a radical formed by connecting an alkyl radical to a thioureido radical in

succession, i.e., “ $\text{R}-\text{NH}-\text{C}(=\text{S})-\text{NH}-\text{}$ ”, wherein R represents an alkyl group.

In this invention, the term halogen refers to fluorine, chlorine, bromine, iodine or astatine.

In this invention, the term hydroxyl radical refers to $-\text{OH}$.

In this invention, the term amino radical refers to $-\text{NH}_2$.

10 In this invention, the term nitrile radical refers to $-\text{CN}$.

In this invention, the term carboxyl refers to $-\text{COOH}$.

In this invention, the term sulfonyl refers to $-\text{S}(=\text{O})_2-$.

In this invention, the term sulfonamino radical refers to $-\text{SO}_2\text{NH}-$.

In this invention, the term carbonyl refers to $-\text{C}(=\text{O})-$.

15 In this invention, the term ureido radical refers to $-\text{NH}-\text{C}(=\text{O})-\text{NH}-$.

In this invention, the term thioureido radical refers to $-\text{NH}-\text{C}(=\text{S})-\text{NH}-$.

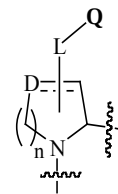
In this invention, the substituent radicals may be preceded by a C_{x1-y1} ($x1$ and $y1$ are integers), e.g. “ C_{x1-y1} ” alkyl, “ C_{x1-y1} ” alkoxy, “ C_{x1-y1} ” alkyl sulphide, “ C_{x1-y1} ” aryl, “ C_{x1-y1} ” heterocyclic aryl, “ C_{x1-y1} ” cycloalkyl, “ C_{x1-y1} ” cycloalkenyl, “ C_{x1-y1} ” epoxy,

“C_{x1-y1}” heterocyclic radical, “C_{x1-y1}” alkoxy carbonyl, “C_{x1-y1}” aryloxy carbonyl, “C_{x1-y1}” heterocyclic oxyl, “C_{x1-y1}” alkyl amino, “C_{x1-y1}” alkylaminocarbonyl, “C_{x1-y1}” arylamino, “C_{x1-y1}” heterocyclic amino, “C_{x1-y1}” aryl sulfonyl, “C_{x1-y1}” alkylaminosulfonyl, “C_{x1-y1}” heterocyclic aminosulfonyl, “C_{x1-y1}” alkylsulfonamino, “C_{x1-y1}” heterocyclic sulfonamino, “C_{x1-y1}” arylsulfonamino, “C_{x1-y1}” alkyl aminosulfonamino, “C_{x1-y1}” alkylcarbonylamino, “C_{x1-y1}” fused aryl, “C_{x1-y1}” fused alkylaryl, “C_{x1-y1}” fused alkyl, “C_{x1-y1}” fused epoxyl, “C_{x1-y1}” alkylureido or “C_{x1-y1}” alkylthioureido. This C_{x1-y1} denotes the number of the number of skeleton carbon atoms (carbon atoms in substituent groups are excluded). For example, C₁~C₂₀ alkyl denotes a C₁~C₂₀ alkyl radical that has 1~20 carbon atoms in its skeleton structure (not substituted).

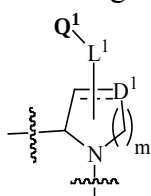
In the art without departing from common sense, the above-mentioned preferred conditions can be combined at discretion to yield preferred embodiments of the invention. The reagents and raw materials used in the invention are all commercially available.

The advantages of this invention are as follows:

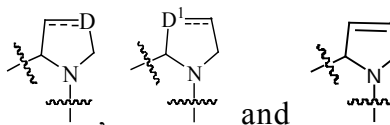
1) the design and introduction of novel heterocyclic functional groups that contain



the following two substituent groups “L, Q and/or L¹, Q¹” or double bond(s):



and ; and heterocyclic functional groups of Formula **Ib** that contain no



substituent groups “L, Q and L¹, Q¹” : (D = CH), and the

synthesis of a group of novel heterocyclic functional group containing linear polypeptide compounds capable of effectively inhibiting HCV, especially novel heterocyclic functional group containing compounds with high selectivity in inhibiting HCV NS5A.

2) The compounds of this invention are advantageous for its obvious HCV NS5A inhibitory activity, this invention also further develops and optimizes the structure of multiple novel heterocyclic rings containing linear compounds that effectively inhibit

HCV infection.

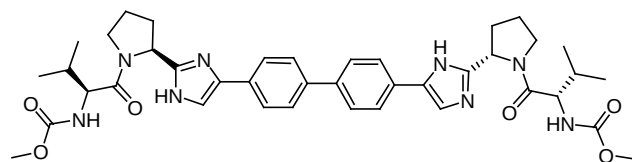
3) This invention discloses several compound (**6dy** and **6fm**) which, identified in the study of the correlation between HCV NS5A inhibitors' structure and their activities, demonstrate high HCV NS5A inhibitory activity superior to that of known
5 NCEs in clinical trial (e.g.: BMS790052) and low toxicity at high dosage and no observable side effects, thus laying down a solid foundation for the development of a highly effective anti-HCV new drug.

4) The compounds of this invention are mainly for inhibiting HCV NS5A and can be used in composition with one or more drugs to inhibit HCV and other viruses. They
10 are promising in the development of more and better new drugs for the society.

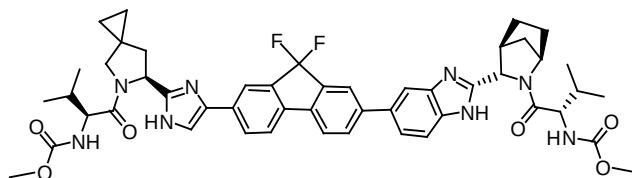
Detailed Description of the Preferred Embodiments

It should be understood that these embodiments are merely illustrative of the present invention and are not intended that the invention should be limited thereto. Any
15 of the following embodiments that is not provided with specific experiment method and conditions was carried out by Zannan SciTech or other CROs with routine method under conventional conditions or with a method selected in accordance with instructions book of materials or with methods specified in WO2008/021927 A2, WO2010/132601 A1, WO2011/075615 A1 and other references to get key
20 intermediates SM1, SM2, SM3, and SM4 of this invention.

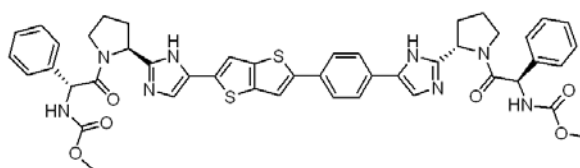
Compounds of this invention may containing tricyclic functional group(s) and one or more heterocyclic rings with an asymmetric center. Therefore, such compounds may be in the form of a mixture of mesomer and racemate, single antimer, and/or tautomer. Compounds 6a-6ax(**Ia**) prepared in the invention are chiral heterocyclic compounds;
25 the optical purity of natural amino acids and non-natural amino acids in products is determined by polarimeter and/or chromatographic column. The structural characterization of every final products(including compounds **6a-6gq** and the following reference compounds: **Ref-1**(BMS790052), **Ref-2**(GS5885), **Ref-3**, **Ref-4(DIX-719)**) is done by LC-MS and ¹H-NMR analysis.



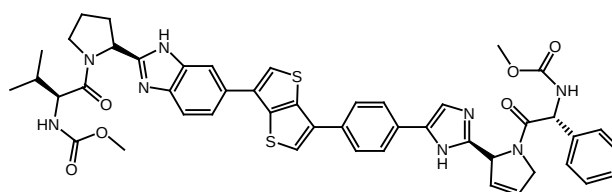
Ref-1 (BMS790052)



Ref-2 (GS-5885)



Ref-3



Ref-4 (DIX-719)

5 The synthesis and effects of the compounds and intermediates of this invention are illustrated with the following embodiments.

Apparatuses and raw materials used in the embodiments are as follows:

IR spectra data are obtained with Fourier Transform AVATAR™ 360 E.S.P™ IR spectrometer (Thermo Nicolet) and represented in cm^{-1} .

10 ¹HNMR spectra are obtain with Varian Mercury Plus NMR analyzer at 400 or 500 MHz. Chemical shift is recorded in ppm with tetramethylsilane(TMS) as internal standard(CHCl_3 : $\delta = 7.26$ ppm). The recorded data include the following: chemical shift and its splitting constants and coupling constants(s: singlet; d : doublet; t: triplet; q: quartet; br: broad peak; m: multiplet).

15 Unless otherwise specified, MS data are analyzed with LS-MS (Finnigan LCQ Advantage); all reactions are carried out in argon atmosphere under anhydrous and anaerobic conditions. Solid metal organic compounds are stored in drier under argon atmosphere.

Tetrahydrofuran and ether are added natrium and benzophenone and then distilled.

Dichlormethane(DCM), pentane and hexane are subjected to calcium hydride. The special raw materials and intermediates used in the invention are ordered from and provided by Zannan SciTech, all other chemical reagents are purchased from Shanghai Reagent Company, Aldrich, Acros, and/or other reagent suppliers. Where the amount of any intermediate or product is insufficient for the next step experiment during the synthesis process, such intermediate or product will be synthesized repetitively until sufficient amount is obtained. EC₅₀t tests and MTD tests are carried out by WuXi AppTec and or other CROs for the compounds prepared in the invention.

Key to Abbreviations of chemical materials, reagents and solvents used in the invention and its embodiments:

AIBN: Azobisisobutyronitrile

Boc: Butoxycarbonyl

(Boc)₂O: Di-tert-butyl pyrocarbonate

CDI: N,N'-carbonyldiimidazole

DBU: 1,8-Diazabicyclo[5.4.0]undec-7-ene

EDCI: N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride

HATU: 2-(7-Aza-1H-benzotriazole-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate

NBS: N-bromo-succinimide

DMAP: 4-Dimethylaminopyridine

DIEA: N,N-Diisopropylethylamine

SOCl₂: Thionyl chloride

Pd/C: Palladium carbon

HMTA: Hexamethylenetetramine

HOAc: Glacial acetic acid

HBr: Hydrobromic acid

HCl: Hydrochloric acid

TFA: Trifluoroacetic acid

TsOH: para-Toluenesulfonic acid

K₂CO₃: Potassium carbonate

ACN: Acetonitrile

DCM: Dichlormethane

DMF: N,N-dimethylformamide

DMSO: Dimethyl sulfoxide

Et₂O: Diethyl ether

EA: Acetoacetate

5 PE: Petroleum ether

THF: Tetrahydrofuran

TBME: tert-Butyl Methyl Ether

Embodiment 1

10 Synthesis of compound **6a**

SM-3a (0.11g, 0.24mmol) and **SM-4i** (0.168g, 0.24mmol, 1.0eq.) were dissolved in 5mL of DMF, added potassium carbonate (0.1g, 0.72mmol, 3.0eq.) and water (3mL) under stirring and nitrogen gas, heated to 100°C, then added tetrakis(triphenylphosphine)palladium (0.01g) in one go, allowed to react thoroughly at
15 100°C under stirring. When HPLC analysis showed that the reactants had reacted completely, the reaction liquid was filtered, added water and acetoacetate for extraction; the organic phase was combined, rinsed with salt solution, dried with dessicant, and finally separated and purified by column chromatography to get a yellow solid product **6a** (68mg), yield: 30%.

20 Product **6a**'s ¹HNMR (300MHz, CDCl₃) spectrum: δ 7.49-7.84 (m, 8H), 7.22-7.24 (m, 2H), 6.65-6.78 (m, 2H), 5.98-5.99 (m, 2H), 5.51-5.55 (m, 2H), 5.43-5.51 (m, 2H), 5.27-5.31 (m, 1H), 4.60-4.72 (m, 4H), 4.12-4.38 (m, 3H), 3.85-3.91 (m, 1H), 3.64-3.74 (m, 4H), 3.49 (s, 3H), 2.54-2.61 (m, 1H), 2.36-2.42 (m, 1H), 1.91-2.28 (m, 5H), 0.85-0.91 (m, 12H). MS analysis confirms that **6a**'s ESI-MS [(M+H)⁺]: theoretical m/z:
25 944.4; measured value: 944.5.

Embodiment 2

Synthesis of compound **6b**

The synthesis method of compound **6b** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6b**,
30 wherein compounds **SM-3c** (0.24mmol) and **SM-4j** (0.24mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6b** (0.062g) was obtained, yield: 25%.

¹H NMR (500 MHz, CDCl₃) of product **6b**: δ 7.48-7.84 (m, 8H), 6.66-6.77 (m, 2H), 5.98 (m, 2H), 5.14-5.57 (m, 5H), 4.60-4.72 (m, 4H), 4.13-4.32 (m, 3H), 3.84 (m, 2H), 3.71 (m, 1H), 3.37 (m, 1H), 2.58 (m, 1H), 1.93-2.36 (m, 8H), 1.25-1.45 (m, 20H), 0.87-1.13 (m, 12H). MS analysis confirms that **6b**'s ESI-MS [(M+H)⁺]: theoretical m/z: 1028.5; measured value: 1028.6.

Embodiment 3

Synthesis of compound **6c**

The synthesis method of compound **6c** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6c**, wherein compounds **SM-3e** (0.24mmol) and **SM-4k** (0.24mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6c** (0.078g) was obtained, yield: 31%.

MS analysis confirms that **6c**'s ESI-MS [(M+H)⁺]: theoretical m/z: 1056.6; measured value: 1056.7.

Embodiment 4

Synthesis of compound **6d**

The synthesis method of compound **6d** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6d**, wherein compounds **SM-3a** (0.29mmol) and **SM-4j** (0.29mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6d** (0.16g) was obtained, yield: 57%.

¹H NMR (300 MHz, CDCl₃) of product **6d**: δ 7.31-7.79 (m, 8H), 7.22-7.27 (m, 2H), 6.66-6.78 (m, 2H), 5.98-5.99 (m, 2H), 5.28-5.56 (m, 4H), 4.62-4.69 (m, 4H), 4.20-4.59 (m, 3H), 3.88-3.97 (m, 1H), 3.62-3.75 (m, 4H), 1.78-2.01 (m, 8H), 1.36-1.46 (m, 9H), 0.89-0.94 (m, 12H). MS analysis confirms that **6d**'s ESI-MS [(M+H)⁺]: theoretical m/z: 986.5; measured value: 986.6.

Embodiment 5

Synthesis of compound **6e**

The synthesis method of compound **6e** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6e**, wherein compounds **SM-3i** (0.14mmol) and **SM-4j** (0.14mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6e** (0.048g) was obtained, yield:

30%.

¹H NMR (500 MHz, CDCl₃) of product **6e**: δ 7.82 (brs, 2H), 7.50-7.61 (m, 6H), 6.66-6.78 (m, 4H), 5.98 (s, 2H), 5.97 (s, 2H), 5.55 (brs, 2H), 5.39-5.46 (m, 4H), 4.60-4.74 (m, 8H), 4.21-4.25 (m, 4H), 3.84-3.85 (m, 2H), 3.49 (s, 6H), 2.57 (m, 2H), 1.93-1.94 (m, 2H), 1.73 (m, 4H), 1.32 (m, 1H), 1.12 (m, 1H), 0.82-0.88 (m, 12H). MS analysis confirms that **6e**'s ESI-MS [(M+H)⁺]: theoretical m/z: 1149.5; measured value: 1149.6.

Embodiment 6

Synthesis of compound **6f**

The synthesis method of compound **6f** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6f**, wherein compounds **SM-3j** (0.23mmol) and **SM-4j** (0.23mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6f** (0.12g) was obtained, yield: 42.3%.

¹H NMR (500 MHz, CDCl₃) of product **6f**: δ 7.62-7.83 (m, 8H), 6.68-6.78 (m, 4H), 5.96-5.98 (m, 4H), 5.55 (s, 2H), 5.47 (s, 2H), 5.15 (m, 2H), 4.61-4.72 (m, 8H), 4.12-4.22 (m, 4H), 3.85 (m, 2H), 3.49 (s, 6H), 2.58 (m, 2H), 1.74-1.92 (m, 4H), 1.25-1.35 (m, 20H), 1.12 (m, 2H), 0.84 (s, 12H). MS analysis confirms that **6f**'s ESI-MS [(M+H)⁺]: theoretical m/z: 1233.6; measured value: 1233.6.

Embodiment 7

Synthesis of compound **6g**

The synthesis method of compound **6g** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6g**, wherein compounds **SM-3m** (0.08mmol) and **SM-4m** (0.08mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6g** (0.013g) was obtained, yield: 14%.

¹H NMR (CD₃OD, 400 MHz) of product **6g**: δ 7.38-7.34 (m, 1H), 7.00-6.96 (m, 2H), 6.11-6.03 (m, 1H), 5.43-5.39 (m, 1H), 5.29-5.27 (m, 1H), 4.65-4.64 (m, 2H), 4.62 (s, 2H), 4.57 (s, 2H). MS analysis confirms that **6g**'s ESI-MS [(M+H)⁺]: theoretical m/z: 1257.6; measured value: 1257.6.

Embodiment 8

Synthesis of compound **6h**

The synthesis method of compound **6h** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6h**, wherein compounds **SM-3g** (0.05mmol) and **SM-4m** (0.05mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6h** (0.01g) was obtained, yield: 20%.

¹H NMR (CD₃OD, 400 MHz) of product **6h**: δ 7.38-7.34 (m, 1H), 7.00-6.96 (m, 2H), 6.11-6.03 (m, 1H), 5.43-5.39 (m, 1H), 5.29-5.27 (m, 1H), 4.65-4.64 (m, 2H), 4.62 (s, 2H), 4.57 (s, 2H). MS analysis confirms that **6h**'s ESI-MS [(M+H)⁺]: theoretical m/z: 1052.5; measured value: 1052.6.

Embodiment 9

Synthesis of compound **6i**

The synthesis method of compound **6i** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6i**, wherein compounds **SM-3a** (0.19mmol) and **SM-4n** (0.19mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6i** (0.10g) was obtained, yield: 55%.

¹H NMR (500 MHz, CDCl₃) of product **6i**: δ 7.62-7.83 (m, 8H), 6.72 (s, 1H), 6.66 (s, 1H), 5.97 (s, 2H), 5.44-5.54 (m, 4H), 5.28 (m, 1H), 4.57-4.69 (m, 4H), 4.34 (m, 1H), 4.25 (m, 1H), 4.17 (m, 1H), 3.83-3.86 (m, 2H), 3.74-3.76 (m, 1H), 3.70 (s, 3H), 3.65 (m, 1H), 3.50 (s, 3H), 2.57 (m, 1H), 2.36 (m, 1H), 2.20 (m, 1H), 2.09-2.10 (m, 1H), 1.79-1.98 (m, 5H), 1.04-1.16 (m, 2H), 0.84-0.89 (m, 12H). MS analysis confirms that **6i**'s ESI-MS [(M+H)⁺]: theoretical m/z: 944.4; measured value: 944.5.

Embodiment 10

Synthesis of compound **6j**

The synthesis method of compound **6j** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6j**, wherein compounds **SM-3c** (0.19mmol) and **SM-4p** (0.19mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6j** (0.04g) was obtained, yield: 20%.

¹H NMR (500 MHz, CDCl₃) of product **6j**: δ 7.83 (m, 2H), 7.51-7.64 (m, 6H), 6.72 (s, 1H), 6.64 (s, 1H), 5.97 (m, 2H), 5.14-5.56 (m, 5H), 4.55-4.67 (m, 4H), 4.13-4.31 (m, 3H), 3.82 (m, 2H), 3.48-3.60 (m, 2H), 2.57 (m, 1H), 2.32 (m, 1H), 1.72-2.07 (m, 7H),

1.08-1.32 (m, 20H), 0.84-0.90 (m, 12H). MS analysis confirms that **6j**'s ESI-MS [(M+H)⁺]: theoretical m/z: 1028.5; measured value: 1028.6.

Embodiment 11

5 Synthesis of compound **6k**

The synthesis method of compound **6k** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6k**, wherein compounds **SM-3e** (0.21mmol) and **SM-4q** (0.21mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6k** (0.045g) was obtained, yield:

10 20%.

¹H NMR (500 MHz, CDCl₃) of product **6k**: δ 7.62-7.81 (m, 8H), 6.71 (s, 1H), 6.62 (s, 1H), 5.97 (s, 2H), 5.16-5.50 (m, 5H), 4.58-4.66 (m, 4H), 4.28-4.35 (m, 2H), 4.21-4.23 (d, J = 9.5 Hz, 1H), 3.90 (m, 1H), 3.78 (m, 1H), 3.66 (m, 1H), 3.42 (m, 1H), 2.58 (m, 1H), 2.34 (m, 1H), 2.01-2.09 (m, 2H), 1.49-1.64 (m, 5H), 1.32 (s, 9H), 1.26 (s, 9H),
15 0.82-0.93 (m, 18H). MS analysis confirms that **6k**'s ESI-MS [(M+H)⁺]: theoretical m/z: 1056.6; measured value: 1056.7.

Embodiment 12

Synthesis of compound **6m**

20 The synthesis method of compound **6m** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6m**, wherein compounds **SM-3a** (0.38mmol) and **SM-4p** (0.38mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6m** (0.3g) was obtained, yield: 79%.

25 ¹H NMR (500 MHz, CDCl₃) of product **6m**: δ 7.58-7.82 (m, 8H), 6.71 (s, 1H), 6.64 (s, 1H), 5.97 (s, 2H), 5.46-5.55 (m, 3H), 5.18-5.28 (m, 2H), 4.56-4.66 (m, 4H), 4.35 (m, 1H), 4.15-4.24 (m, 2H), 3.84-3.89 (m, 2H), 3.67-3.75 (m, 5H), 2.58 (m, 1H), 2.37 (m, 1H), 2.22 (m, 1H), 2.10 (m, 1H), 1.91-2.05 (m, 3H), 1.36 (s, 9H), 1.07-1.13 (m, 4H),
0.84-0.90 (m, 12H)). MS analysis confirms that **6m**'s ESI-MS [(M+H)⁺]: theoretical
30 m/z: 986.5; measured value: 986.6.

Embodiment 13

Synthesis of compound **6n**

The synthesis method of compound **6n** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6n** wherein compounds **SM-3n** (0.24mmol) and **SM-4n** (0.24mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6n** (0.054g) obtained, yield: 19.3

¹H NMR (500 MHz, CDCl₃) of product **6n**: δ 7.83 (brs, 2H), 7.50-7.63 (m, 6H), 6.72 (s, 2H), 6.66 (s, 2H), 5.97 (s, 4H), 5.36-5.54 (m, 6H), 4.57-4.68 (m, 8H), 4.24-4.27 (m, 2H), 4.16-4.19 (m, 2H), 3.84-3.85 (m, 2H), 3.51 (s, 6H), 2.55-2.59 (m, 2H), 1.92-1.94 (m, 2H), 1.66-1.68 (m, 4H), 1.32 (m, 1H), 1.12 (m, 1H), 0.84-0.88 (m, 12H). MS analysis confirms that **6n**'s ESI-MS [(M+H)⁺]: theoretical m/z: 1149.5; measured value:

1149.6

Embodiment 14

Synthesis of compound **6p**

The synthesis method of compound **6p** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6p** wherein compounds **SM-3p** (0.32mmol) and **SM-4p** (0.32mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6p** (0.20g) obtained, yield: 50%

¹H NMR (500 MHz, CDCl₃) of product **6p**: δ 7.83 (brs, 2H), 7.51-7.63 (m, 6H), 6.71 (s, 2H), 6.64 (s, 2H), 5.97 (s, 4H), 5.48-5.54 (m, 4H), 5.17 (m, 2H), 4.55-4.66 (m, 8H), 4.14-4.22 (m, 4H), 3.59-3.84 (m, 2H), 2.58 (m, 2H), 1.69-2.05 (m, 6H), 1.26-1.36 (m, 20H), 0.84-0.90 (m, 12H). MS analysis confirms that **6p**'s ESI-MS [(M+H)⁺]: theoretical m/z: 1233.6; measured value: 1233.6

Embodiment 15

Synthesis of compound **6q**

The synthesis method of compound **6q** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6q** wherein compounds **SM-3r** (0.16mmol) and **SM-4r** (0.16mmol) were used in place of

compounds **SM-3a** and **SM-4i**, a yellow solid product **6q** (0.02g) obtained, yield: 10%
¹H NMR (500 MHz, CDCl₃) of product **6q**: δ 7.83-7.84 (m, 2H), 7.52-7.63 (m, 6H), 6.72 (s, 2H), 6.65 (s, 2H), 5.97 (s, 4H), 5.43-5.53 (m, 4H), 5.21 (m, 2H), 4.57-4.77 (m,

8H), 4.29 (m, 4H), 3.80-3.82 (m, 2H), 3.49 (m, 2H), 2.57 (m, 2H), 1.88-1.91 (m, 2H), 1.59-1.70 (m, 16H), 1.12-1.33 (m, 6H), 0.81-0.85 (m, 12H) MS analysis confirms that **6q**'s ESI-MS [(M+H)⁺]: theoretical m/z: 1257.6; measured value: 1257.7

5

Embodiment 16

Synthesis of compound **6r**

The synthesis method of compound **6r** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6r** wherein compounds **SM-3g** (0.09mmol) and **SM-4r** (0.09mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6r** (0.044g) obtained, yield: 47.8%

¹H NMR (500 MHz, CDCl₃) of product **6r**: δ 7.85-7.84 (m, 2H), 7.60 (m, 6H), 6.72 (s, 1H), 6.66 (s, 1H), 5.97 (s, 2H), 5.54 (m, 2H), 5.10-5.31 (m, 5H), 4.57-4.78 (m, 4H), 4.22-4.34 (m, 3H), 3.86 (m, 2H), 3.68 (m, 1H), 3.15-3.46 (m, 1H), 2.58 (m, 1H), 2.36 (m, 1H), 2.22-2.24 (m, 2H), 1.99-2.11 (m, 5H), 1.15-1.50 (m, 18H), 0.74-0.90 (m, 12H) MS analysis confirms that **6r**'s ESI-MS [(M+H)⁺]: theoretical m/z: 1052.5; measured value: 1052.6

Embodiment 17

Synthesis of compound **6s**

The synthesis method of compound **6s** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6s** wherein compounds **SM-3a** (0.17mmol) and **SM-4s** (0.17mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6s** (0.05g) obtained, yield: 31%

¹H NMR (500 MHz, CDCl₃) of product **6s**: δ 7.85-7.84 (m, 2H), 7.60 (m, 6H), 6.72 (s, 1H), 6.66 (s, 1H), 5.97 (s, 2H), 5.54 (m, 2H), 5.10-5.31 (m, 5H), 4.57-4.78 (m, 4H), 4.22-4.34 (m, 3H), 3.86 (m, 2H), 3.68 (m, 1H), 3.15-3.46 (m, 1H), 2.58 (m, 1H), 2.36 (m, 1H), 2.22-2.24 (m, 2H), 1.99-2.11 (m, 5H), 1.15-1.50 (m, 18H), 0.74-0.90 (m, 12H) MS analysis confirms that **6s**'s ESI-MS [(M+H)⁺]: theoretical m/z: 918.4; measured value: 918.5

30

Embodiment 18

Synthesis of compound **6t**

The synthesis method of compound **6t** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6t** wherein compounds **SM-3c** (0.38mmol) and **SM-4t** (0.38mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6t** (0.25g) obtained, yield: 65%

¹H NMR (500 MHz, CDCl₃) of product **6t**: δ 7.72-7.82 (m, 2H), 7.59 (s, 4H), 6.95-7.07 (m, 3H), 5.48-5.55 (m, 3H), 5.13-5.30 (m, 4H), 4.71-4.81 (m, 4H), 4.20-4.32 (m, 4H), 3.84-3.47 (m, 5H), 2.59-2.59 (m, 1H), 1.89-2.34 (m, 5H), 1.26 (s, 18H), 0.85-0.88 (m, 12H). MS analysis confirms that **6t**'s ESI-MS [(M+H)⁺]: theoretical m/z: 1002.5; measured value: 1002.6

10

Embodiment 19

Synthesis of compound **6u**

The synthesis method of compound **6u** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6u**

wherein compounds **SM-3a** (0.15mmol) and **SM-4t** (0.15mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6u** (0.051g) obtained, yield: 35%

¹H NMR (500 MHz, CDCl₃) of product **6u**: δ 7.58 (s, 4H), 7.21-7.23 (m, 1H), 6.95-7.06 (m, 3H), 6.80-6.82 (m, 1H), 5.46-5.53 (m, 3H), 5.23-5.30 (m, 3H), 4.71-4.80 (m, 3H), 4.32-4.33 (m, 1H), 4.19-4.20 (m, 1H), 3.82-3.85 (m, 1H), 3.65-3.74 (m, 4H), 2.94-2.96 (m, 1H), 2.88-2.89 (m, 1H), 2.62 (s, 4H), 2.33-2.34 (m, 1H), 2.18-2.22 (m, 2H), 1.89-2.10 (m, 4H), 1.25-1.31 (m, 9H), 0.83-0.8 (m, 12H). MS analysis confirms that **6u**'s ESI-MS [(M+H)⁺]: theoretical m/z: 960.5; measured value: 960.6

20

Embodiment 20

Synthesis of compound **6v**

The synthesis method of compound **6v** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6v**

wherein compounds **SM-3g** (0.09mmol) and **SM-4u** (0.09mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6v** (0.034g) obtained, yield: 37%

¹H NMR (500 MHz, CDCl₃) of product **6v**: δ 7.77-7.82 (m, 3H), 7.54-7.62 (m, 5H), 6.95-7.08 (m, 3H), 6.02-6.05 (m, 1H), 5.83-5.85 (m, 1H), 5.52 (s, 1H), 5.39-5.44 (m, 2H), 5.30-5.32 (m, 1H), 5.22-5.24 (m, 1H), 5.06-5.08 (m, 1H), 4.68-4.86 (m, 5H),

30

4.42-4.44 (m, 1H), 4.32-4.36 (m, 1H), 4.24-4.25 (m, 2H), 3.97-4.00 (m, 1H), 3.88-3.91 (m, 1H), 2.66-2.68 (m, 1H), 2.42-2.45 (m, 1H), 2.31-2.34 (m, 1H), 2.19-2.30 (m, 2H), 2.12-2.18 (m, 1H), 1.63-1.84 (m, 16H), 1.24-1.26 (m, 2H), 1.09-1.16 (m, 4H), 0.86-0.96 (m, 6H). MS analysis confirms that **6v**'s ESI-MS [(M+H)⁺]: theoretical m/z:

5 1026.5; measured value: 1026.6

Embodiment 21

10 Synthesis of compound **6w**

The synthesis method of compound **6w** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6w** wherein compounds **SM-3v** (0.19mmol) and **SM-4a** (0.19mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6w** (0.07g) obtained, yield: 38%

15 ¹H NMR (500 MHz, CDCl₃) of product **6w**: δ 8.11 (m, 1H), 8.01-8.00 (m, 1H), δ 7.84-7.79 (m, 2H), 7.64-7.45 (m, 10H), 7.21-7.13 (m, 3H), 5.61-5.58 (m, 1H), 5.53-5.51 (m, 1H), 5.45-5.43 (m, 1H), 5.27-5.25 (m, 1H), 4.51-4.48 (m, 1H), 4.35-4.27 (m, 2H), 4.13-4.09 (m, 1H), 3.85-3.84 (m, 1H), 3.67 (s, 3H), 3.40 (s, 3H), 2.20-2.96 (m, 8H), 0.89-0.83 (m, 12H). MS analysis confirms that **6w**'s ESI-MS [(M+H)⁺]:

20 theoretical m/z: 965.4; measured value: 965.5

Embodiment 22

Synthesis of compound **6x**

The synthesis method of compound **6x** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6x** wherein compounds **SM-3w** (0.47mmol) and **SM-4a** (0.47mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6x** (0.16g) obtained, yield: 35%

25 ¹H NMR (500 MHz, CDCl₃) of product **6x**: δ 8.04-8.02 (m, 1H), δ 7.90-7.88 (m, 1H), 7.68-7.52 (m, 11H), 7.36-7.32 (m, 2H), 7.22-7.24 (m, 2H), 5.55-5.48 (m, 3H), 5.28 (m, 2H), 4.42-4.34 (m, 2H), 3.88-3.86 (m, 2H), 3.71 (s, 6H), 2.40-2.01 (m, 8H), 0.92-0.89 (m, 12H) MS analysis confirms that **6x**'s ESI-MS [(M+H)⁺]: theoretical m/z: 965.4; measured value: 965.5

Embodiment 23

Synthesis of compound **6y**

5 The synthesis method of compound **6y** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6y** wherein compounds **SM-3x** (0.51mmol) and **SM-4a** (0.51mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6y** (0.07g) obtained, yield: 19%
10 ¹H NMR (500 MHz, CDCl₃) of product **6y**: δ 7.68-7.47 (m, 7H), 7.33-7.18 (m, 3H), 5.54-5.53 (m, 1H), 5.35-5.25 (m, 2H), 4.35-4.30 (m, 1H), 3.87-3.85 (m, 1H), 3.76-3.69 (m, 6H), 3.30(m, 1H), 2.91 (m, 1H), 2.38-2.35 (m, 2H), 2.34-1.92 (m, 7H), 1.38-1.20 (m, 12H), 0.95-0.85 (m, 6H). MS analysis confirms that **6y**'s ESI-MS [(M+H)⁺]: theoretical m/z: 723.4; measured value: 723.5

Embodiment 24

Synthesis of compound **6z**

The synthesis method of compound **6z** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6z** wherein compounds **SM-3y** (0.54mmol) and **SM-4a** (0.54mmol) were used in place of
20 compounds **SM-3a** and **SM-4i**, a yellow solid product **6z** (0.204g) obtained, yield: 50%
¹H NMR (500 MHz, CDCl₃) of product **6z**: δ 7.76-7.56 (m, 7H), 7.34-7.21 (m, 3H), 5.51-5.26 (m, 3H), 4.34-4.33 (m, 1H), 3.84-3.60 (m, 7H), 3.51 (m, 1H), 2.76-2.74 (m, 1H), 2.40-2.33 (m, 2H), 2.38-1.95 (m, 13H), 1.26-1.23 (m, 4H), 0.93-0.86 (m, 6H). MS analysis confirms that **6z**'s ESI-MS [(M+H)⁺]: theoretical m/z: 751.4; measured value:
25 751.5

Embodiment 25

Synthesis of compound **6aa**

The synthesis method of compound **6aa** was the same with that in Embodiment 1; the
30 product was carried out by one-step catalytic coupling reaction to get product **6aa** wherein compounds **SM-3z** (0.54mmol) and **SM-4a** (0.54mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6aa** (0.142g) obtained, yield:

34%

¹H NMR (500 MHz, CDCl₃) of product **6aa**: δ 7.82-7.49 (m, 6H), 7.34-7.19 (m, 4H), 5.54-5.49 (m, 1H), 5.36-5.27 (m, 1H), 4.37-4.28 (m, 1H), 3.57-3.55 (m, 6H), 2.98 (m, 1H), 2.34-2.33 (m, 2H), 2.27-1.57 (m, 12H), 1.44-1.21 (m, 8H), 0.94-0.87 (m, 6H). MS analysis confirms that **6aa**'s ESI-MS [(M+H)⁺]: theoretical m/z: 765.4; measured value: 765.5

Embodiment 26

Synthesis of compound **6ab**

10 The synthesis method of compound **6ab** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ab** wherein compounds **SM-3aa** (7.36mmol) and **SM-4a** (7.36mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6ab** (3.6g) obtained, yield: 65%
¹H NMR (500 MHz, CDCl₃) of product **6ab**: δ 7.85-7.76 (m, 2H), 7.67-7.56 (m, 5H),
15 7.40-7.37 (m, 2H), 7.22-7.16 (m, 1H), 5.51-5.45 (m, 2H), 5.40-5.30 (m, 2H), 4.45-4.36 (m, 2H), 3.88-3.86(m, 2H), 3.71 (s, 6H), 2.87-2.85 (m, 1H), 2.51-1.74 (m, 11H) , 1.10-0.80 (m, 12H). MS analysis confirms that **6ab**'s ESI-MS [(M+H)⁺]: theoretical m/z: 753.4; measured value: 753.5

Embodiment 27

Synthesis of compound **6ac**

20 The synthesis method of compound **6ac** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ac** wherein compounds **SM-3aa** (0.19mmol) and **SM-4n** (0.19mmol) were used in place of
25 compounds **SM-3a** and **SM-4i**, a yellow solid product **6ac** (0.08g) obtained, yield: 42%
¹H NMR (500 MHz, CDCl₃) of product **6ac**: δ 7.81-7.45 (m, 8H), 7.37-7.22 (m, 4H), 6.72-6.62 (m, 2H), 5.97-5.93 (m, 2H), 5.55-5.35 (m, 3H), 4.71-4.57 (m, 4H), 4.26-4.12 (m, 2H), 3.77-3.70 (m, 3H), 3.51-3.43 (m, 3H), 2.83 (m, 1H), 2.57-2.47 (m, 2H), 2.07-1.77 (m, 9H), 1.12-1.11 (m, 6H), 0.84-0.82 (m, 6H). MS analysis confirms that
30 **6ac**'s ESI-MS [(M+H)⁺]: theoretical m/z: 958.4; measured value: 958.5

Embodiment 28

Synthesis of compound **6ad**

The synthesis method of compound **6ad** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ad** wherein compounds **SM-3aa** (0.20mmol) and **SM-4i** (0.20mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6ad** (0.064g) obtained, yield: 33%

¹H NMR (500 MHz, CDCl₃) of product **6ad**: δ 7.80-7.46 (m, 8H), 7.37-7.22 (m, 4H), 6.78-6.66 (m, 2H), 5.98-5.97 (m, 2H), 5.56-5.34 (m, 3H), 4.75-4.59 (m, 4H), 4.25-4.17 (m, 2H), 3.86-3.64 (m, 3H), 3.49-3.46 (m, 3H), 2.82 (m, 1H), 2.58-2.47 (m, 2H), 2.08-1.76 (m, 9H), 1.12-1.11 (m, 6H), 0.86-0.84 (m, 6H). MS analysis confirms that **6ad**'s ESI-MS [(M+H)⁺]: theoretical m/z: 958.4; measured value: 958.5

Embodiment 29

Synthesis of compound **6ae**

The synthesis method of compound **6ae** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ae** wherein compounds **SM-3a** (0.13mmol) and **SM-4ac** (0.13mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6ae** (0.021g) obtained, yield: 17%

¹H NMR (500 MHz, CDCl₃) of product **6ae**: δ 7.81-7.55 (m, 8H), 7.34-7.22 (m, 4H), 6.80-6.69 (m, 2H), 5.99-5.97 (m, 1H), 5.57-5.56 (m, 1H), 5.32-5.17 (m, 2H), 4.93-4.72 (m, 4H), 4.35-4.25 (m, 2H), 3.74-3.69 (m, 6H), 2.96 (m, 1H), 2.37-2.36 (m, 1H), 2.24-1.76 (m, 8H), 1.16-0.79 (m, 12H). MS analysis confirms that **6ae**'s ESI-MS [(M+H)⁺]: theoretical m/z: 929.4; measured value: 929.5

Embodiment 30

Synthesis of compound **6af**

The synthesis method of compound **6af** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6af** wherein compounds **SM-3a** (0.16mmol) and **SM-4ad** (0.16mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6af** (0.015g) obtained, yield: 10%

¹H NMR (500 MHz, CDCl₃) of product **6af**: δ 7.77-7.54 (m, 8H), 7.28-7.22 (m, 2H),

6.73-6.68 (m, 2H), 6.00-5.98 (m, 2H), 5.61-5.46 (m, 2H), 5.35-5.22 (m, 2H), 4.85-4.75 (m, 4H), 4.365-4.10 (m, 2H), 3.72-3.70 (m, 6H), 2.95 (m, 1H), 2.39 (m, 1H), 2.03-1.81 (m, 8H), 1.10-0.90 (m, 12H). MS analysis confirms that **6af**'s ESI-MS [(M+H)⁺]: theoretical m/z: 929.4; measured value: 929.5

5

Embodiment 31

Synthesis of compound **6ag**

The synthesis method of compound **6ag** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ag** wherein compounds **SM-3ab** (0.24mmol) and **SM-4a** (0.24mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6ag** (0.15g) obtained, yield: 65%
¹H NMR (500 MHz, CDCl₃) of product **6ag**: δ 7.83-7.53 (m, 7H), 7.47-7.19 (m, 3H), 5.50-5.48 (m, 1H), 5.27-5.26 (m, 1H), 5.08-5.03 (m, 1H), 4.54-4.48 (m, 1H), 4.40-4.33 (m, 1H), 4.01-3.82 (m, 3H), 3.70 (m, 6H), 2.95-2.90 (m, 1H), 2.38-2.37 (m, 1H),
15 2.23-1.83 (m, 8H), 1.27-1.11 (m, 6H), 0.97-0.86 (m, 6H). MS analysis confirms that **6ag**'s ESI-MS [(M+H)⁺]: theoretical m/z: 755.4; measured value: 755.5

Embodiment 32

Synthesis of compound **6ah**

The synthesis method of compound **6ah** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ah** wherein compounds **SM-3ab** (0.24mmol) and **SM-4n** (0.24mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6ah** (0.033g) obtained, yield: 14.2%
¹H NMR (500 MHz, CDCl₃) of product **6ah**: δ 7.80-7.59 (m, 8H), 7.27 (m, 2H), 6.71-6.65 (m, 2H), 5.96 (s, 2H), 5.46-5.38 (m, 3H), 5.08-5.03 (m, 1H), 4.68-4.53 (m, 5H), 3.79-3.70 (m, 3H), 3.57-3.50 (m, 3H), 2.91-2.84 (m, 2H), 2.15-1.88 (m, 10H), 1.26-1.11 (m, 6H), 0.93-0.86 (m, 6H). MS analysis confirms that **6ah**'s ESI-MS [(M+H)⁺]: theoretical m/z: 960.4; measured value: 960.5

30

Embodiment 33

Synthesis of compound **6ai**

The synthesis method of compound **6ai** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ai** wherein compounds **SM-3ab** (0.03mmol) and **SM-4i** (0.03mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6ai** (0.075g) obtained, yield:

25%

¹H NMR (500 MHz, CDCl₃) of product **6ai**: δ 7.80-7.58 (m, 8H), 7.28-7.23 (m, 2H), 6.78-6.66 (m, 2H), 5.98-5.97 (m, 2H), 5.47-5.37 (m, 3H), 5.08-5.04 (m, 1H), 4.75-4.53 (m, 5H), 4.24-4.21 (m, 2H), 3.79-3.65 (m, 3H), 3.57-3.49 (m, 3H), 2.92 (m, 1H), 2.57 (m, 1H), 2.15-1.73 (m, 8H), 1.28-1.11 (m, 6H), 0.83-0.75 (m, 6H). MS analysis confirms that **6ai**'s ESI-MS [(M+H)⁺]: theoretical m/z: 960.4; measured value: 960.5

Embodiment 34

Synthesis of compound **6aj**

The synthesis method of compound **6aj** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6aj** wherein compounds **SM-3ab** (0.36mmol) and **SM-4aa** (0.36mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6aj** (0.15g) obtained, yield: 43%

¹H NMR (500 MHz, CDCl₃) of product **6aj**: δ 7.85-7.39 (m, 8H), 5.58-5.54 (m, 1H), 5.41-5.35 (m, 1H), 5.09-5.05 (m, 1H), 4.60 (m, 1H), 4.54-4.40 (m, 2H), 4.31-4.30 (m, 1H), 4.20-4.18 (m, 1H), 4.02 (m, 1H), 3.80 (m, 3H), 3.72-3.43 (m, 3H), 3.04-3.03 (m, 2H), 2.98-2.84 (m, 2H), 2.45 (m, 1H), 2.30 (m, 1H), 1.76-1.62 (m, 2H), 1.49-1.33 (m, 2H), 1.15-1.12 (m, 6H), 0.95-0.87 (m, 6H). MS analysis confirms that **6aj**'s ESI-MS [(M+H)⁺]: theoretical m/z: 769.4; measured value: 769.5

Embodiment 35

Synthesis of compound **6ak**

The synthesis method of compound **6ak** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ak**, wherein compounds **SM-3ae** (0.2mmol) and **SM-4n** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6ak** was obtained (yield: 51%). MS analysis confirms that **6ak**'s ESI-MS [(M+H)⁺]: theoretical m/z: 970.4; measured value: 970.6.

Embodiment 36

Synthesis of compound **6am**

The synthesis method of compound **6am** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6am**, wherein compounds **SM-3ae** (0.2mmol) and **SM-4ad** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6am** was obtained (yield: 53%). MS analysis confirms that **6am**'s ESI-MS [(M+H)⁺]: theoretical m/z: 955.4; measured value: 955.6.

Embodiment 37

Synthesis of compound **6an**

The synthesis method of compound **6an** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6an**, wherein compounds **SM-3ae** (0.2mmol) and **SM-4i** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6an** was obtained (yield: 52%). MS analysis confirms that **6an**'s ESI-MS [(M+H)⁺]: theoretical m/z: 970.4; measured value: 970.6.

Embodiment 38

Synthesis of compound **6ap**

The synthesis method of compound **6ap** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ap**, wherein compounds **SM-3ae** (0.2mmol) and **SM-4ac** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6ap** was obtained (yield: 53%). MS analysis confirms that **6ap**'s ESI-MS [(M+H)⁺]: theoretical m/z: 955.4; measured value: 955.6.

Embodiment 39

Synthesis of compound **6aq**

The synthesis method of compound **6aq** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6aq**, wherein compounds **SM-3af** (0.2mmol) and **SM-4a** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6aq** was obtained (yield: 53%). MS analysis confirms that **6aq**'s ESI-MS [(M+H)⁺]: theoretical m/z: 885.4; measured

value: 885.5.

Embodiment 40

Synthesis of compound **6ar**

- 5 The synthesis method of compound **6ar** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ar**, wherein compounds **SM-3ag** (0.2mmol) and **SM-4a** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6ar** was obtained (yield: 55%). MS analysis confirms that **6ar**'s ESI-MS [(M+H)⁺]: theoretical m/z: 903.4; measured
10 value: 903.5.

Embodiment 41

Synthesis of compound **6as**

- The synthesis method of compound **6as** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6as**,
15 wherein compounds **SM-3ah** (0.2mmol) and **SM-4a** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6as** was obtained (yield: 54%). MS analysis confirms that **6as**'s ESI-MS [(M+H)⁺]: theoretical m/z: 903.4; measured
value: 903.5.

20 Embodiment 42

Synthesis of compound **6at**

- The synthesis method of compound **6at** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6at**, wherein compounds **SM-3ai** (0.2mmol) and **SM-4a** (0.2mmol) were used in place of
25 compounds **SM-3a** and **SM-4i**, a yellow solid product **6at** was obtained (yield: 51%). MS analysis confirms that **6at**'s ESI-MS [(M+H)⁺]: theoretical m/z: 919.4; measured
value: 919.5.

Embodiment 43

Synthesis of compound **6au**

- 30 The synthesis method of compound **6au** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6au**, wherein compounds **SM-3aj** (0.2mmol) and **SM-4a** (0.2mmol) were used in place of

compounds **SM-3a** and **SM-4i**, a yellow solid product **6au** was obtained (yield: 52%). MS analysis confirms that **6au**'s ESI-MS [(M+H)⁺]: theoretical m/z: 919.4; measured value: 919.5.

5 Embodiment 44

Synthesis of compound **6av**

The synthesis method of compound **6av** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6av**, wherein compounds **SM-3am** (0.2mmol) and **SM-4a** (0.2mmol) were used in place of
10 compounds **SM-3a** and **SM-4i**, a yellow solid product **6av** was obtained (yield: 63%).
¹H NMR (500 MHz, CDCl₃) of product **6av**: δ 7.54-7.80 (m, 9H), 7.17-7.22 (m, 3H), 6.76-6.85 (m, 3H), 5.60-5.72 (m, 2H), 5.19-5.44 (m, 4H), 4.82-4.92 (m, 5H), 3.97-4.34 (m, 4H), 3.79-3.82 (m, 3H), 3.68-3.73 (m, 6H), 2.95 (m, 1H), 2.37 (m, 1H), 2.20-2.21 (m, 1H), 1.98-2.11 (m, 4H), 0.88-0.95 (m, 12H). MS analysis confirms that **6av**'s
15 ESI-MS [(M+H)⁺]: theoretical m/z: 915.4; measured value: 915.5

Embodiment 45

Synthesis of compound **6aw**

The synthesis method of compound **6aw** was the same with that in Embodiment 1; the
20 product was carried out by one-step catalytic coupling reaction to get product **6aw**, wherein compounds **SM-3ak** (0.2mmol) and **SM-4a** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6aw** was obtained (yield: 61%).
¹H NMR (500 MHz, CDCl₃) of product **6aw**: δ 7.48-7.80 (m, 9H), 7.16-7.25 (m, 4H), 6.83-6.84 (m, 1H), 6.72-6.73 (m, 1H), 5.70-5.78 (m, 2H), 5.22-5.41 (m, 4H), 4.74-4.98
25 (m, 5H), 4.28-4.30 (m, 2H), 4.01-4.13 (m, 2H), 3.81 (s, 3H), 3.64-3.66 (m, 6H), 2.92 (m, 1H), 2.38 (m, 1H), 2.17-2.18 (m, 1H), 1.94-2.07 (m, 4H), 0.85-0.91 (m, 12H). MS analysis confirms that **6aw**'s ESI-MS [(M+H)⁺]: theoretical m/z: 915.4; measured value: 915.5

Embodiment 46

30 Synthesis of compound **6ax**

The synthesis method of compound **6ax** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ax**,

wherein compounds **SM-3an** (0.2mmol) and **SM-4a** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6ax** was obtained (yield: 54%).

¹H NMR (500 MHz, CDCl₃) of product **6ax**: δ 7.54-7.84 (m, 9H), 7.23 (s, 1H), 7.20 (s, 1H), 6.79 (s, 2H), 6.74 (s, 1H), 6.81-6.87 (m, 2H), 5.58-5.70 (m, 2H), 5.46 (m, 1H), 5.19-5.34 (m, 3H), 4.72-4.92 (m, 5H), 3.97-4.35 (m, 4H), 3.86-3.89 (m, 6H), 3.69-3.74 (m, 6H), 2.96 (m, 1H), 2.38 (m, 1H), 2.22 (m, 1H), 1.99-2.12 (m, 4H), 0.89-0.96 (m, 12H). MS analysis confirms that **6ax**'s ESI-MS [(M+H)⁺]: theoretical m/z: 945.4; measured value: 945.6

10

Embodiment 47

Synthesis of compound **6ay**

The synthesis method of compound **6ay** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ay** wherein compounds **SM-3ac** (0.2mmol) and **SM-4ag** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6ay** was obtained (yield: 53%).

15

MS analysis confirms that **6ay**'s ESI-MS [(M+H)⁺]: theoretical m/z: 963.4; measured value: 963.5.

Embodiment 48

20 Synthesis of compound **6az**

The synthesis method of compound **6az** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6az** wherein compounds **SM-3n** (0.2mmol) and **SM-4ae** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6az** was obtained (yield: 56%).

25

MS analysis confirms that **6az**'s ESI-MS [(M+H)⁺]: theoretical m/z: 956.4; measured value: 956.5.

Embodiment 49

Synthesis of compound **6ba**

30

The synthesis method of compound **6ba** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ba** wherein compounds **SM-3a** (0.55mmol) and **SM-4b** (0.55mmol) were used in place of

compounds **SM-3a** and **SM-4i**, a yellow solid product **6ba** (0.13g) obtained, yield: 32%
¹H NMR (500 MHz, CDCl₃) of product **6ba**: δ 7.50-7.63 (m, 6H), 7.16-7.23 (m, 2H),
6.26 (s, 1H), 6.06-6.08 (m, 1H), 5.98 (s, 1H), 5.58-5.59 (m, 2H), 5.24-5.30 (m, 1H),
4.72-4.75 (m, 1H), 4.47-4.49 (m, 1H), 4.28-4.36 (m, 2H), 3.83-3.88 (m, 1H), 3.70 (s,
5 6H), 2.93-2.94 (m, 1H), 2.34-2.38 (m, 1H), 2.16-2.24 (m, 1H), 1.98-2.11 (m, 4H),
0.83-0.91 (m, 12H). MS analysis confirms that **6ba**'s ESI-MS [(M+H)⁺]: theoretical
m/z: 737.4; measured value: 737.5

Embodiment 50

10 Synthesis of compound **6bb**

The synthesis method of compound **6bb** was the same with that in Embodiment 1; the
product was carried out by one-step catalytic coupling reaction to get product **6bb**
wherein compounds **SM-3e** (0.057mmol) and **SM-4f** (0.057mmol) were used in place
of compounds **SM-3a** and **SM-4i**, a yellow solid product **6bb** (0.013g) obtained, yield:

15 27.5%

¹H NMR (500 MHz, CDCl₃) of product **6bb**: δ 7.57-7.72 (m, 4H), 7.16-7.23 (m, 2H),
6.29 (s, 1H), 6.00-6.07 (m, 2H), 5.24-5.36 (m, 3H), 4.75, 4.76 (d, 1H), 4.45-4.57 (m,
2H), 4.27-4.36 (m, 2H), 3.88 (s, 1H), 3.67-3.68 (m, 1H), 2.20-2.34 (m, 2H), 1.99-2.09
(m, 2H), 1.46 (s, 18H), 0.93 (m, 18H). MS analysis confirms that **6bb**'s ESI-MS
20 [(M+H)⁺]: theoretical m/z: 849.5; measured value: 849.6

Embodiment 51

Synthesis of compound **6bc**

The synthesis method of compound **6bc** was the same with that in Embodiment 1; the
25 product was carried out by one-step catalytic coupling reaction to get product **6bc**
wherein compounds **SM-3a** (0.31mmol) and **SM-4d** (0.31mmol) were used in place of
compounds **SM-3a** and **SM-4i**, a yellow solid product **6bc** (0.048g) obtained, yield:
20%

¹H NMR (500 MHz, CDCl₃) of product **6bc**: δ 7.46-7.54 (m, 4H), 7.15-7.24 (m, 2H),
30 6.29 (s, 1H), 6.07-6.08 (m, 1H), 6.00 (s, 1H), 5.50-5.52 (m, 1H), 5.23-5.27 (m, 2H),
4.69-4.72 (m, 1H), 4.25-4.47 (m, 3H), 3.83-3.86 (m, 1H), 3.70 (s, 3H), 2.34-2.38 (m,
1H), 1.95-2.23 (m, 5H), 1.46 (s, 6H), 0.88-0.93 (m, 12H). MS analysis confirms that

6bc's ESI-MS [(M+H)⁺]: theoretical m/z: 779.4; measured value: 779.5

Embodiment 52

Synthesis of compound **6bd**

- 5 The synthesis method of compound **6bd** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6bd** wherein compounds **SM-3b** (0.32mmol) and **SM-4b** (0.32mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6bd** (0.08g) obtained, yield: 33.7%
- 10 ¹H NMR (500 MHz, CDCl₃) of product **6bd**: δ 7.77-7.80 (m, 2H), 7.56-7.60 (m, 4H), 7.20-7.23 (m, 2H), 6.30-6.33 (m, 2H), 6.08-6.09 (m, 2H), 5.99 (s, 2H), 5.34-5.39 (m, 2H), 4.72-4.74 (m, 2H), 4.42-4.45 (m, 2H), 4.27-4.30 (m, 2H), 3.71 (s, 6H), 1.96-2.01 (m, 2H), 1.25-1.34 (m, 6H), 0.87-0.90 (m, 6H). MS analysis confirms that **6bd**'s ESI-MS [(M+H)⁺]: theoretical m/z: 735.4; measured value: 735.4

15

Embodiment 53

Synthesis of compound **6be**

- The synthesis method of compound **6be** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6be**
- 20 wherein compounds **SM-3d** (0.29mmol) and **SM-4d** (0.29mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6be** (0.10g) obtained, yield: 42%
- ¹H NMR (500 MHz, CDCl₃) of product **6be**: δ 7.70-7.76 (m, 2H), 7.47-7.60 (m, 4H), 7.21-7.25 (m, 2H), 6.28-6.32 (m, 2H), 6.07-6.08 (m, 2H), 6.01 (s, 2H), 5.21-5.23 (m, 2H), 4.69-4.72 (m, 2H), 4.44-4.47 (m, 2H), 4.25-4.29 (m, 2H), 1.94-1.99 (m, 2H), 1.46
- 25 (s, 18H), 0.82-0.89 (m, 12H). MS analysis confirms that **6be**'s ESI-MS [(M+H)⁺]: theoretical m/z: 819.5; measured value: 819.5

Embodiment 54

Synthesis of compound **6bf**

- 30 The synthesis method of compound **6bf** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6bf** wherein compounds **SM-3h** (0.11mmol) and **SM-4h** (0.11mmol) were used in place of

compounds **SM-3a** and **SM-4i**, a yellow solid product **6bf** (0.031g) obtained, yield: 33.6%

¹H NMR (500 MHz, CDCl₃) of product **6bf**: δ 7.47-7.63 (m, 6H), 7.15-7.23 (m, 2H), 7.21-7.24 (m, 2H), 6.07-6.08 (m, 2H), 6.00 (s, 2H), 5.30-5.32 (m, 2H), 5.08-5.09 (m, 2H), 4.73-4.76 (m, 2H), 4.48-4.51 (m, 2H), 4.27-4.30 (m, 2H), 1.94-2.00 (m, 2H), 1.83-1.86 (m, 4H), 1.71 (s, 8H), 1.58 (s, 4H), 0.90-0.91 (m, 12H). MS analysis confirms that **6bf**'s ESI-MS [(M+H)⁺]: theoretical m/z: 843.5; measured value: 843.6

Embodiment 55

10 Synthesis of compound **6bg**

The synthesis method of compound **6bg** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6bg** wherein compounds **SM-3g** (0.11mmol) and **SM-4h** (0.11mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6bg** (0.014g) obtained, yield:

15 15%

¹H NMR (CD₃OD, 400 MHz) of product **6bg**: δ 7.38-7.34 (m, 1H), 7.00-6.96 (m, 2H), 6.11-6.03 (m, 1H), 5.43-5.39 (m, 1H), 5.29-5.27 (m, 1H), 4.65-4.64 (m, 2H), 4.62 (s, 2H), 4.57 (s, 2H). MS analysis confirms that **6bg**'s ESI-MS [(M+H)⁺]: theoretical m/z: 845.5; measured value: 843.6

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Embodiment 56

Synthesis of compound **6bh**

The synthesis method of compound **6bh** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6bh** wherein compounds **SM-3x** (0.4mmol) and **SM-4b** (0.4mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6bh** (0.165g) obtained, yield: 57.5%

¹H NMR (500 MHz, CDCl₃) of product **6bh**: δ 7.66-7.52 (m, 8H), 7.20 (m, 2H), 6.23 (m, 1H), 6.23 (m, 1H), 6.06-6.05 (m, 1H), 5.98 (m, 1H), 5.73 (m, 1H), 5.53-5.52 (m, 1H), 5.35 (m, 1H), 4.74-4.71 (m, 1H), 4.49-4.47 (m, 1H), 4.29-4.26 (m, 1H), 3.77-3.69 (m, 6H), 2.33-2.32 (m, 1H), 2.09-1.95 (m, 4H), 1.32-1.24 (m, 4H), 0.91-0.80 (m, 6H). MS analysis confirms that **6bh**'s ESI-MS [(M+H)⁺]: theoretical m/z: 721.3; measured

30

value: 721.5

Embodiment 57

Synthesis of compound **6bi**

- 5 The synthesis method of compound **6bi** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6bi** wherein compounds **SM-3y** (0.41mmol) and **SM-4b** (0.41mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6bi** (0.13g) obtained, yield: 42.5%
- 10 ¹H NMR (500 MHz, CDCl₃) of product **6bi**: δ 7.76-7.55 (m, 8H), 7.26-7.23 (m, 2H), 6.29-6.28 (m, 1H), 6.08-6.07 (m, 1H), 5.99 (m, 1H), 5.51-5.49 (m, 1H), 5.37 (m, 1H), 4.75-4.72 (m, 1H), 4.47-4.44 (m, 1H), 4.30-4.27 (m, 1H), 3.72-3.70 (m, 6H), 2.77-2.74 (m, 1H), 2.39-2.34 (m, 1H), 2.15-1.73 (m, 10H), 1.26 (m, 1H), 0.90-0.85 (m, 6H). MS analysis confirms that **6bi**'s ESI-MS [(M+H)⁺]: theoretical m/z: 749.4; measured value:
- 15 749.5

Embodiment 58

Synthesis of compound **6bj**

- 20 The synthesis method of compound **6bj** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6bj** wherein compounds **SM-3z** (0.39mmol) and **SM-4b** (0.39mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6bj** (0.10g) obtained, yield: 33.5%
- 25 ¹H NMR (500 MHz, CDCl₃) of product **6bj**: δ 7.75-7.46 (m, 6H), 7.35-7.24 (m, 4H), 6.08-5.99 (m, 1H), 5.52-5.48 (m, 1H), 4.75-4.72 (m, 1H), 4.47-4.44 (m, 1H), 4.30-4.28 (m, 1H), 3.76-3.58 (m, 6H), 2.39 (m, 2H), 2.14-1.55 (m, 11H), 1.26 (m, 6H), 0.94-0.88 (m, 6H)。质谱分析确证, **6bj**的ESI-MS [(M+H)⁺]: m/z 理论值 763.4, 实测值 763.5. MS analysis confirms that **6bj**'s ESI-MS [(M+H)⁺]: theoretical m/z: 763.4; measured value: 763.5

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Embodiment 59

Synthesis of compound **6bk**

The synthesis method of compound **6bk** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6bk** wherein compounds **SM-3aa** (0.22mmol) and **SM-4b** (0.22mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6bk** (0.10g) obtained, yield: 61%
5 ¹H NMR (500 MHz, CDCl₃) of product **6bk**: δ 7.81-7.52 (m, 6H), 7.38-7.20 (m, 4H), 6.09 (m, 1H), 6.0 (m, 1H), 5.43 (m, 1H), 4.73-4.70 (m, 1H), 4.48-4.43 (m, 1H), 4.32-4.29 (m, 1H), 3.70-3.63 (m, 6H), 2.85-2.83 (m, 1H), 2.09-1.48 (m, 11H), 1.11 (m, 6H), 0.92-0.85 (m, 6H). MS analysis confirms that **6bk**'s ESI-MS [(M+H)⁺]: theoretical m/z: 751.4; measured value: 751.5

10

Embodiment 60

Synthesis of compound **6bm**

The synthesis method of compound **6bm** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6bm**
15 wherein compounds **SM-3ab** (5.83mmol) and **SM-4b** (5.83mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6bm** (3.0g) obtained, yield: 54%
¹H NMR (500 MHz, CDCl₃) of product **6bm**: δ 7.76-7.42 (m, 9H), 7.28-7.21 (m, 1H), 6.24 (m, 1H), 6.10-6.09 (m, 1H), 5.99 (m, 1H), 5.45-5.46 (m, 1H), 5.13-5.04 (m, 1H), 4.74-4.71 (m, 1H), 4.53-4.52 (m, 2H), 4.41-4.28 (m, 2H), 4.14-4.00 (m, 2H), 3.70 (m,
20 6H), 2.94 (m, 1H), 2.11-1.99 (m, 3H), 1.27-1.12 (m, 6H), 0.95-0.87 (m, 6H). MS analysis confirms that **6bm**'s ESI-MS [(M+H)⁺]: theoretical m/z: 753.4; measured value: 753.5

Embodiment 61

Synthesis of compound **6bn**

The synthesis method of compound **6bn** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6bn** wherein compounds **SM-3n** (0.2mmol) and **SM-4af** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6bn** was obtained (yield: 61%).
MS analysis confirms that **6bn**'s ESI-MS [(M+H)⁺]: theoretical m/z: 958.4; measured
30 value: 958.5.

Embodiment 62

Synthesis of compound **6bp**

The synthesis method of compound **6bp** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6bp** wherein compounds **SM-3ap** (0.2mmol) and **SM-4n** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6bp** was obtained (yield: 56%). MS analysis confirms that **6bp**'s ESI-MS [(M+H)⁺]: theoretical m/z: 992.4; measured value: 992.5.

Embodiment 63

Synthesis of compound **6bq**

The synthesis method of compound **6bq** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6bq** wherein compounds **SM-3aq** (0.2mmol) and **SM-4bj** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6bq** was obtained (yield: 53%). MS analysis confirms that **6bq**'s ESI-MS [(M+H)⁺]: theoretical m/z: 835.4; measured value: 835.5.

Embodiment 64

Synthesis of compound **6br**

The synthesis method of compound **6br** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6br** wherein compounds **SM-3ap** (0.2mmol) and **SM-4n** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6br** was obtained (yield: 52%). MS analysis confirms that **6br**'s ESI-MS [(M+H)⁺]: theoretical m/z: 1042.4; measured value: 1042.5.

Embodiment 65

Synthesis of compound **6bs**

The synthesis method of compound **6bs** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6bs** wherein compounds **SM-3ar** (0.2mmol) and **SM-4bj** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6bs** was obtained (yield: 54%).

MS analysis confirms that **6bs**'s ESI-MS [(M+H)⁺]: theoretical m/z: 1027.4; measured value: 1027.5.

Embodiment 66

5 Synthesis of compound **6bt**

The synthesis method of compound **6bt** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6bt** wherein compounds **SM-3as** (0.2mmol) and **SM-4bi** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6bt** was obtained (yield: 52%).

10 MS analysis confirms that **6bt**'s ESI-MS [(M+H)⁺]: theoretical m/z: 968.4; measured value: 968.5.

Embodiment 67

Synthesis of compound **6bu**

15 The synthesis method of compound **6bu** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6bu** wherein compounds **SM-3at** (0.2mmol) and **SM-4ad** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6bu** was obtained (yield: 56%).

MS analysis confirms that **6bu**'s ESI-MS [(M+H)⁺]: theoretical m/z: 979.4; measured
20 value: 979.5.

Embodiment 68

Synthesis of compound **6bv**

25 The synthesis method of compound **6bv** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6bv** wherein compounds **SM-3au** (0.2mmol) and **SM-4a** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6bv** was obtained (yield: 53%).

MS analysis confirms that **6bv**'s ESI-MS [(M+H)⁺]: theoretical m/z: 991.3; measured
30 value: 991.4.

Embodiment 69

Synthesis of compound **6bw**

The synthesis method of compound **6bw** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6bw** wherein compounds **SM-3av** (0.2mmol) and **SM-4ad** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6bw** was obtained (yield: 52%).

5 MS analysis confirms that **6bw**'s ESI-MS [(M+H)⁺]: theoretical m/z: 1025.3; measured value: 1025.4.

Embodiment 70

Synthesis of compound **6bx**

10 The synthesis method of compound **6bx** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6bx** wherein compounds **SM-3ay** (0.2mmol) and **SM-4a** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6bx** was obtained (yield: 54%). MS analysis confirms that **6bx**'s ESI-MS [(M+H)⁺]: theoretical m/z: 771.4; measured
15 value: 771.4.

Embodiment 71

Synthesis of compound **6by**

The synthesis method of compound **6by** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6by**
20 wherein compounds **SM-3b** (0.2mmol) and **SM-4ag** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6by** was obtained (yield: 56%). MS analysis confirms that **6by**'s ESI-MS [(M+H)⁺]: theoretical m/z: 771.4; measured
value: 771.4.

25 Embodiment 72

Synthesis of compound **6bz**

The synthesis method of compound **6bz** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6bz** wherein compounds **SM-3ax** (0.2mmol) and **SM-4ah** (0.2mmol) were used in place of
30 compounds **SM-3a** and **SM-4i**, a yellow solid product **6bz** was obtained (yield: 61%). MS analysis confirms that **6bz**'s ESI-MS [(M+H)⁺]: theoretical m/z: 805.3; measured
value: 805.4.

Embodiment 73

Synthesis of compound **6ca**

The synthesis method of compound **6ca** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ca** wherein compounds **SM-3ay** (0.2mmol) and **SM-4ah** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6ca** was obtained (yield: 53%). MS analysis confirms that **6ca**'s ESI-MS [(M+H)⁺]: theoretical m/z: 803.3; measured value: 803.4.

Embodiment 74

Synthesis of compound **6cb**

The synthesis method of compound **6cb** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6cb** wherein compounds **SM-3ba** (0.2mmol) and **SM-4ah** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6cb** was obtained (yield: 53%). MS analysis confirms that **6cb**'s ESI-MS [(M+H)⁺]: theoretical m/z: 833.3; measured value: 833.4.

Embodiment 75

Synthesis of compound **6cc**

The synthesis method of compound **6cc** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6cc** wherein compounds **SM-3av** (0.2mmol) and **SM-4ah** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6cc** was obtained (yield: 58%). MS analysis confirms that **6cc**'s ESI-MS [(M+H)⁺]: theoretical m/z: 867.3; measured value: 867.3.

Embodiment 76

Synthesis of compound **6cd**

The synthesis method of compound **6cd** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6cd**

wherein compounds **SM-3aw** (0.2mmol) and **SM-4ah** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6cd** was obtained (yield: 54%). MS analysis confirms that **6cd**'s ESI-MS [(M+H)⁺]: theoretical m/z: 865.2; measured value: 865.3.

5

Embodiment 77

Synthesis of compound **6ce**

The synthesis method of compound **6ce** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ce** wherein compounds **SM-3bb** (0.2mmol) and **SM-4ai** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6ce** was obtained (yield: 57%). MS analysis confirms that **6ce**'s ESI-MS [(M+H)⁺]: theoretical m/z: 831.4; measured value: 831.5.

15

Embodiment 78

Synthesis of compound **6cf**

The synthesis method of compound **6cf** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6cf** wherein compounds **SM-3bd** (0.2mmol) and **SM-4aj** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6cf** was obtained (yield: 56%). MS analysis confirms that **6cf**'s ESI-MS [(M+H)⁺]: theoretical m/z: 803.3; measured value: 803.4.

20

Embodiment 79

Synthesis of compound **6cg**

The synthesis method of compound **6cg** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6cg** wherein compounds **SM-3bg** (0.2mmol) and **SM-4ak** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6cg** was obtained (yield: 52%). MS analysis confirms that **6cg**'s ESI-MS [(M+H)⁺]: theoretical m/z: 763.4; measured value: 763.5

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Embodiment 80

Synthesis of compound **6ch**

The synthesis method of compound **6ch** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ch** wherein compounds **SM-3bi** (0.2mmol) and **SM-4am** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6ch** was obtained (yield: 53%). MS analysis confirms that **6ch**'s ESI-MS [(M+H)⁺]: theoretical m/z: 735.4; measured value: 735.5

Embodiment 81

Synthesis of compound **6ci**

The synthesis method of compound **6ci** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ci** wherein compounds **SM-3bg** (0.2mmol) and **SM-4a** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6ci** was obtained (yield: 53%). MS analysis confirms that **6ci**'s ESI-MS [(M+H)⁺]: theoretical m/z: 750.4; measured value: 750.5

Embodiment 82

Synthesis of compound **6cj**

The synthesis method of compound **6cj** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6cj** wherein compounds **SM-3bi** (0.2mmol) and **SM-4a** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6cj** was obtained (yield: 59%). MS analysis confirms that **6cj**'s ESI-MS [(M+H)⁺]: theoretical m/z: 736.4; measured value: 736.5

Embodiment 83

Synthesis of compound **6ck**

The synthesis method of compound **6ck** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ck** wherein compounds **SM-3bi** (0.2mmol) and **SM-4am** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6ck** was obtained (yield: 53%).

MS analysis confirms that **6ck's** ESI-MS [(M+H)⁺]: theoretical m/z: 735.4; measured value: 735.5

Embodiment 84

5 Synthesis of compound **6cm**

The synthesis method of compound **6cm** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6cm** wherein compounds **SM-3a** (0.2mmol) and **SM-4an** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6cm** (110mg) obtained, yield:

10 54%

¹H NMR (500 MHz, CDCl₃) of product **6cm**: δ 7.74-7.80 (m, 1H), 7.53-7.62 (m, 8H), 7.26-7.28 (m, 3H), 7.18-7.22 (m, 3H), 5.56-5.67 (m, 2H), 5.44 (m, 1H), 4.74-4.94 (m, 5H), 4.34 (m, 1H), 4.23 (m, 1H), 4.08 (m, 1H), 3.85 (m, 1H), 3.67-3.73 (m, 6H), 2.92 (m, 1H), 2.37 (m, 1H), 2.22 (m, 1H), 2.00-2.11 (m, 4H), 0.90-0.91 (m, 12H). MS

15 analysis confirms that **6cm's** ESI-MS [(M+H)⁺]: theoretical m/z: 919.4; measured value: 919.5

Embodiment 85

Synthesis of compound **6cq**

20 The synthesis method of compound **6cq** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6cq** wherein compounds **SM-3a** (0.2mmol) and **SM-4ar** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6cq** (83mg) obtained, yield: 43%.

25 ¹H NMR (500 MHz, CDCl₃) of product **6cq**: δ 7.46-7.75 (m, 9H), 7.12-7.30 (m, 3H), 6.81-6.87 (m, 2H), 5.64-5.74 (m, 2H), 5.17-5.41 (m, 4H), 4.56-4.93 (m, 5H), 3.94-4.30 (m, 4H), 3.81-3.85 (m, 6H), 3.63-3.65 (m, 6H), 2.83 (m, 1H), 2.33 (m, 1H), 2.17 (m, 1H), 1.96-2.07 (m, 4H), 0.86-0.89 (m, 12H). MS analysis confirms that **6cq's** ESI-MS [(M+H)⁺]: theoretical m/z: 945.5; measured value: 945.7

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Embodiment 86

Synthesis of compound **6cu**

The synthesis method of compound **6cu** was the same with that in Embodiment 1; the

system was carried out by one-step catalytic coupling reaction to get a product, which was then removed Boc, neutralized and purified to get compound **6cu**, wherein compounds **SM-3a** (0.2mmol) and **SM-4av** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i** to get a yellow solid Boc protected product(310mg),
5 yield: 25%. 10mL of 3N HCl/Et₂O was added, the system was allowed to react at room temperature until the reactants have reacted completely, adjusted pH to alkaline, subjected to purification with preparation TLC to get a yellow solid **6cu** (55mg), yield of the above-mentioned 2-step reaction: 37%.

H NMR (500 MHz, CDCl₃) of product **6cu**: δ 7.50-7.78 (m, 9H), 7.02-7.35 (m, 3H),
10 5.67 (m, 2H), 5.13-5.26 (m, 2H), 4.69-4.75 (m, 2H), 4.35-4.41 (m, 2H), 4.13-4.14 (m, 1H), 3.88 (m, 1H), 3.71 (s, 6H), 3.35 (m, 1H), 2.18-2.39 (m, 2H), 2.00-2.11 (m, 4H), 0.91 (s, 12H). MS analysis confirms **6cu**'s ESI-MS [(M+H)⁺]: theoretical m/z: 740.4; measured value: 740.5.

Embodiment 87

15 Synthesis of compound **6cv**

The synthesis method of compound **6cv** was the same with that in Embodiment 1, the system was then carried out by one-step catalytic coupling reaction to get a product, which was removed Boc, neutralized, purified to get **6cv**, wherein compounds **SM-3b** (0.2mmol) and **SM-4av** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**
20 to get a yellow solid Boc protected product(110mg), which was added 10mL of 3N HCl/Et₂O, allowed to react at room temperature until reactants have gone, adjusted pH to alkaline, subjected to purification with preparation TLC to get a yellow solid **6cv** (47mg); yield of the above-mentioned 2-step reaction: 32%.

MS analysis confirms **6cv**'s ESI-MS [(M+H)⁺]: theoretical m/z: 738.4; measured value:
25 738.5.

Embodiment 88

Synthesis of compound **6cw**

The synthesis method of compound **6cw** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6cw** wherein compounds **SM-3b** (0.2mmol) and **SM-4av** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6cw** was obtained (yield: 35%).
30

MS analysis confirms that **6cw**'s ESI-MS [(M+H)⁺]: theoretical m/z: 838.4; measured

value: 838.6

Embodiment 89

Synthesis of compound **6cx**

- 5 The synthesis method of compound **6cx** was the same with that in Embodiment 1, the system was then carried out by one-step catalytic coupling reaction to get a Boc protected product, then the Boc was removed to get **6cx**, wherein compounds **SM-3b** (0.2mmol) and **SM-4aw** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i** to get 13mg of a yellow solid product, yield: 10%. 10mg of the product was taken,
10 added 10mL of 3N HCl/ether, allowed to react thoroughly at room temperature under stirring. The reaction liquid was concentrated to get a yellow solid **6cx**, yield: 32%. MS analysis confirms **6cx**'s ESI-MS $[(M+H)^+]$: theoretical m/z: 778.5; measured value: 778.6.

Embodiment 90

15 Synthesis of compound **6cy**

- The synthesis method of compound **6cy** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6cy**, wherein compounds **SM-3b** (0.2mmol) and **SM-4aw** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6cy** (33mg) was obtained, yield:
20 23%. MS analysis confirms that **6cy**'s ESI-MS $[(M+H)^+]$: theoretical m/z: 878.5; measured value: 878.6.

Embodiment 91

Synthesis of compound **6cz**

- 25 The synthesis method of compound **6cz** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6cz**, wherein compounds **SM-3bj** (0.2mmol) and **SM-4b** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6cz** was obtained, yield: 29%.
¹H NMR (500 MHz, CDCl₃) of product **6cz**: δ 7.62-7.78 (m, 10H), 5.98-6.09 (m, 2H),
30 5.43-5.59 (m, 2H), 4.49-4.60 (m, 4H), 3.70-3.75 (m, 8H), 3.01 (s, 3H), 2.78 (m, 1H), 0.89-0.91 (m, 12H). MS analysis confirms that **6cz**'s ESI-MS $[(M+H)^+]$: theoretical m/z: 816.3; measured value: 816.5.

Embodiment 92

Synthesis of compound **6da**

The synthesis method of compound **6da** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6da**, wherein compounds **SM-3bk** (0.2mmol) and **SM-4b** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6da** was obtained, yield: 32%. MS analysis confirms that **6da**'s ESI-MS $[(M+H)^+]$: theoretical m/z: 842.4; measured value: 842.5.

Embodiment 93

Synthesis of compound **6db**

The synthesis method of compound **6db** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6db**, wherein compounds **SM-3bm** (0.2mmol) and **SM-4b** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6db** was obtained, yield: 22%. MS analysis confirms that **6db**'s ESI-MS $[(M+H)^+]$: theoretical m/z: 796.4; measured value: 796.6.

Embodiment 94

Synthesis of compound **6dc**

The synthesis method of compound **6dc** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6dc**, wherein compounds **SM-3bn** (0.2mmol) and **SM-4b** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6dc** was obtained, yield: 33%. MS analysis confirms that **6dc**'s ESI-MS $[(M+H)^+]$: theoretical m/z: 824.4; measured value: 824.5.

Embodiment 95

Synthesis of compound **6dd**

The synthesis method of compound **6dd** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6dd**, wherein compounds **SM-3bp** (0.2mmol) and **SM-4b** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6dd** (20mg) was obtained, yield: 28%.

MS analysis confirms that **6dd**'s ESI-MS $[(M+H)^+]$: theoretical m/z: 844.4; measured

value: 844.5.

Embodiment 96

Synthesis of compound **6de**

The synthesis method of compound **6de** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6de**, wherein compounds **SM-3bf** (0.2mmol) and **SM-4a** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6de** was obtained, yield: 35%.

¹H NMR (500 MHz, CDCl₃) of product **6de**: δ 7.81 (m, 1H), 7.53-7.59 (m, 8H), 7.34 (s, 1H), 7.24 (s, 1H), 7.19 (s, 1H), 5.55-5.56 (d, *J* = 8.5 Hz, 1H), 5.10-5.12 (d, *J* = 8.5 Hz, 1H), 4.48-4.51 (t, *J* = 7.5 Hz, 1H), 4.33-4.36 (m, 1H), 3.97 (m, 1H), 3.85 (m, 1H), 3.70 (s, 3H), 3.45 (m, 1H), 3.14 (m, 1H), 2.95 (s, 6H), 2.34-2.39 (m, 2H), 2.19-2.24 (m, 2H), 1.97-2.10 (m, 6H), 0.86-0.91 (m, 12H). MS analysis confirms that **6de**'s ESI-MS [(M+H)⁺]: theoretical m/z: 752.4; measured value: 752.5.

Embodiment 97

Synthesis of compound **6df**

The synthesis method of compound **6df** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6df**, wherein compounds **SM-3bf** (0.2mmol) and **SM-4b** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6df** was obtained, yield: 35%.

¹H NMR (500 MHz, CDCl₃) of product **6df**: δ 7.82-7.86 (m, 1H), 7.54-7.68 (m, 8H), 7.34 (s, 1H), 7.19-7.23 (m, 2H), 6.24-6.28 (m, 1H), 5.98-6.08 (m, 2H), 5.44-5.53 (m, 1H), 5.26 (m, 1H), 5.08-5.09 (m, 1H), 4.71 (m, 1H), 4.49-4.51 (m, 1H), 4.28-4.34 (m, 1H), 3.94-3.95 (m, 1H), 3.70 (s, 3H), 3.43 (m, 1H), 3.15 (m, 1H), 2.92 (s, 6H), 1.97-2.20 (m, 6H), 1.05-1.10 (m, 6H), 0.88 (s, 6H). MS analysis confirms that **6df**'s ESI-MS [(M+H)⁺]: theoretical m/z: 750.4; measured value: 750.5.

Embodiment 98

Synthesis of compound **6dg**

The synthesis method of compound **6dg** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6dg**, wherein compounds **SM-3b** (0.2mmol) and **SM-4ax** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6dg** was obtained, yield: 36%.

¹H NMR (500 MHz, CDCl₃) of product **6dg**: δ 7.10-7.71 (m, 17H), 5.97-6.15 (m, 3H),

5.41-5.55 (m, 3H), 4.73 (m, 1H), 4.48-4.55 (m, 1H), 4.26 (m, 1H), 4.03 (m, 1H), 3.69 (s, 3H), 3.30 (m, 1H), 2.72 (m, 1H), 2.44 (s, 3H), 1.97-2.27 (m, 6H), 0.88-0.99 (m, 6H). MS analysis confirms that **6dg**'s ESI-MS [(M+H)⁺]: theoretical m/z: 770.4; measured value: 770.5.

5 Embodiment 99

Synthesis of compound **6dh**

The synthesis method of compound **6dh** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6dh**, wherein compounds **SM-3bq** (0.2mmol) and **SM-4a** (0.2mmol) were used in place of
10 compounds **SM-3a** and **SM-4i**, a yellow solid product **6dh** was obtained, yield: 22%. MS analysis confirms that **6dh**'s ESI-MS [(M+H)⁺]: theoretical m/z: 763.4; measured value: 763.5.

Embodiment 100

Synthesis of compound **6di**

15 The synthesis method of compound **6di** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6di**, wherein compounds **SM-3br** (0.2mmol) and **SM-4a** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6di** was obtained, yield: 38%. MS analysis confirms that **6di**'s ESI-MS [(M+H)⁺]: theoretical m/z: 777.4; measured
20 value: 777.4.

Embodiment 101

Synthesis of compound **6dj**

The synthesis method of compound **6dj** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6dj**,
25 wherein compounds **SM-3bs** (0.2mmol) and **SM-4a** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6dj** was obtained, yield: 46%. ¹H NMR (500 MHz, CDCl₃) of product **6dj**: δ 7.59-7.47 (m, 10H), 6.26 (m, 1H), 6.08 (m, 1H), 5.99 (m, 1H), 5.26 (s, 1H), 4.77 (m, 1H), 4.54 (m, 1H), 4.35 (m, 1H), 4.28 (m, 1H), 3.87 (m, 1H), 3.73 (s, 6H), 2.39 (m, 2H), 2.21-1.69 (m, 14H), 1.26 (d, 6H). MS
30 analysis confirms that **6dj**'s ESI-MS [(M+H)⁺]: theoretical m/z: 777.4; measured value: 777.5.

Embodiment 102

Synthesis of compound **6dk**

The synthesis method of compound **6dk** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6dk**, wherein compounds **SM-3br** (0.2mmol) and **SM-4ay** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6dk** was obtained, yield: 36%. MS analysis confirms that **6dk**'s ESI-MS [(M+H)⁺]: theoretical m/z: 817.4; measured value: 817.6.

Embodiment 103

Synthesis of compound **6dm**

The synthesis method of compound **6dm** is the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6dm**, wherein compounds **SM-3br** (0.2mmol) and **SM-4az** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6dm** was obtained, yield: 38%. MS analysis confirms that **6dm**'s ESI-MS [(M+H)⁺]: theoretical m/z: 815.4; measured value: 815.5.

Embodiment 104

Synthesis of compound **6dn**

The synthesis method of compound **6dn** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6dn**, wherein compounds **SM-3bq** (0.2mmol) and **SM-4ay** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6dn** was obtained, yield: 30%. MS analysis confirms that **6dn**'s ESI-MS [(M+H)⁺]: theoretical m/z: 803.4; measured value: 803.5.

Embodiment 105

Synthesis of compound **6dp**

The synthesis method of compound **6dp** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6dp**, wherein compounds **SM-3bq** (0.2mmol) and **SM-4ba** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6dp** was obtained, yield: 28%. ¹H NMR (500 MHz, CDCl₃) of product **6dp**: δ 8.02 (s, 1H), 7.85-7.55 (m, 9H), 6.34 (m, 1H), 6.09 (m, 1H), 5.99 (m, 1H), 5.42 (m, 1H), 5.36 (m, 1H), 4.81 (m, 1H), 4.44 (m, 1H), 4.38 (m, 1H), 3.90 (m, 1H), 3.71 (s, 6H), 3.50 (m, 1H), 2.34-2.01 (m, 16H). MS

analysis confirms that **6dp**'s ESI-MS [(M+H)⁺]: theoretical m/z: 789.4; measured value: 789.5.

Embodiment 106

Synthesis of compound **6dq**

- 5 The synthesis method of compound **6dq** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6dq**, wherein compounds **SM-3bt** (0.2mmol) and **SM-4b** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6dq** was obtained, yield: 36%. ¹H NMR (500 MHz, CDCl₃) of product **6dq**: δ 7.53-7.22 (m, 8H), 6.21 (m, 1H), 6.10 (m, 1H), 6.03 (m, 1H), 5.46 (m, 1H), 5.39 (m, 1H), 4.74 (m, 1H), 4.60 (m, 1H), 4.32 (m, 1H), 4.21 (m, 1H), 3.99 (m, 1H), 3.86 (m, 1H), 3.72 (s, 3H), 3.69 (s, 3H), 2.62 (m, 1H), 2.44 (m, 1H), 2.06-1.72 (m, 6H), 1.26 (d, 12H). MS analysis confirms that **6dq**'s ESI-MS [(M+H)⁺]: theoretical m/z: 753.4; measured value: 753.5.

Embodiment 107

15 Synthesis of compound **6dr**

- The synthesis method of compound **6dr** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6dr**, wherein compounds **SM-3bu** (0.2mmol) and **SM-4b** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6dr** was obtained, yield: 33%.
20 MS analysis confirms that **6dr**'s ESI-MS [(M+H)⁺]: theoretical m/z: 753.4; measured value: 753.5.

Embodiment 108

Synthesis of compound **6ds**

- The synthesis method of compound **6ds** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ds**, wherein compounds **SM-3bv** (0.2mmol) and **SM-4a** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6ds** was obtained, yield: 38%.
25 MS analysis confirms that **6ds**'s ESI-MS [(M+H)⁺]: theoretical m/z: 797.4; measured value: 797.5.

30 Embodiment 109

Synthesis of compound **6dt**

The synthesis method of compound **6dt** was the same with that in Embodiment 1; the

product was carried out by one-step catalytic coupling reaction to get product **6dt**, wherein compounds **SM-3bv** (0.2mmol) and **SM-4b** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6dt** was obtained, yield: 41%. MS analysis confirms that **6dt**'s ESI-MS [(M+H)⁺]: theoretical m/z: 795.4; measured value: 795.5.

Embodiment 110

Synthesis of compound **6du**

The synthesis method of compound **6du** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6du**, wherein compounds **SM-3bw** (0.2mmol) and **SM-4b** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6du** was obtained, yield: 39%. ¹H NMR (500 MHz, CDCl₃) of product **6du**: δ 7.16-7.82 (m, 15H), 5.98-6.26 (m, 3H), 5.35-5.53 (m, 1H), 4.71-4.74 (m, 1H), 4.48-4.51 (m, 1H), 3.91-4.04 (m, 6H), 3.62-3.69 (m, 8H), 2.47-2.38 (m, 1H), 2.04-2.08 (m, 1H), 1.69-2.00 (m, 1H), 1.05-0.87 (m, 6H). MS analysis confirms that **6du**'s ESI-MS [(M+H)⁺]: theoretical m/z: 829.4; measured value: 829.5.

Embodiment 111

Synthesis of compound **6dv**

The synthesis method of compound **6dv** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6dv**, wherein compounds **SM-3bw** (0.2mmol) and **SM-4ah** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6dv** was obtained, yield: 34%. MS analysis confirms that **6dv**'s ESI-MS [(M+H)⁺]: theoretical m/z: 863.3; measured value: 863.5.

Embodiment 112

Synthesis of compound **6dw**

The synthesis method of compound **6dw** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6dw**, wherein compounds **SM-3bv** (0.2mmol) and **SM-4ah** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6dw** was obtained, yield: 37%. MS analysis confirms that **6dw**'s ESI-MS [(M+H)⁺]: theoretical m/z: 829.4; measured value: 829.4.

Embodiment 113

Synthesis of compound **6dy**

The synthesis method of compound **6dy** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6dy**, wherein compounds **SM-3ay** (0.2mmol) and **SM-4a** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6dy** was obtained, yield: 42%.
¹H NMR (500 MHz, CDCl₃) of product **6dy**: δ 7.65-7.18 (m, 15H), 6.23 (m, 1H), 6.01 (m, 1H), 5.89 (m, 1H), 5.50 (m, 1H), 5.39 (m, 1H), 5.25 (m, 1H), 4.52 (m, 1H), 4.34 (m, 1H), 4.12 (m, 1H), 3.84 (m, 1H), 3.67 (s, 3H), 3.61 (s, 3H), 2.34-1.83 (m, 6H), 1.23 (d, 6H). MS analysis confirms that **6dy**'s ESI-MS [(M+H)⁺]: theoretical m/z: 771.4; measured value: 771.4.

Embodiment 114

Synthesis of compound **6dz**

The synthesis method of compound **6dz** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6dz**, wherein compounds **SM-3ck** (0.2mmol) and **SM-4bf** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6dz** was obtained, yield: 38%.
¹H NMR (500 MHz, CDCl₃) of product **6dz**: δ 7.71-7.40 (m, 20H), 6.28 (m, 1H), 6.04 (m, 1H), 5.99 (m, 1H), 5.50 (m, 1H), 5.39 (m, 1H), 4.54 (m, 1H), 4.12 (m, 1H), 3.98 (m, 1H), 3.68 (s, 3H), 3.65 (s, 3H), 2.23-1.82 (m, 6H). MS analysis confirms that **6dz**'s ESI-MS [(M+H)⁺]: theoretical m/z: 805.3; measured value: 805.5.

Embodiment 115

Synthesis of compound **6ea**

The synthesis method of compound **6ea** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ea**, wherein compounds **SM-3ay** (0.2mmol) and **SM-4b** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6ea** was obtained, yield: 33%.
¹H NMR (500 MHz, CDCl₃) of product **6ea**: δ 7.67-7.20 (m, 13H), 6.26 (s, 1H), 6.15 (s, 1H), 6.08 (m, 1H), 5.99 (m, 1H), 5.59 (m, 1H), 5.46 (m, 1H), 5.31 (m, 1H), 4.76 (m, 1H), 4.48 (m, 1H), 4.30 (m, 1H), 3.70 (s, 3H), 3.65 (s, 3H), 3.22 (m, 1H), 2.24-1.92 (m, 6H), 1.26 (d, 6H). MS analysis confirms that **6ea**'s ESI-MS [(M+H)⁺]: theoretical m/z: 771.4; measured value: 771.5.

Embodiment 116

Synthesis of compound **6eb**

The synthesis method of compound **6eb** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6eb**, wherein compounds **SM-3bx** (0.2mmol) and **SM-4b** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6eb** was obtained, yield: 37%. MS analysis confirms that **6eb**'s ESI-MS [(M+H)⁺]: theoretical m/z: 737.4; measured value: 737.4.

Embodiment 117

Synthesis of compound **6ec**

The synthesis method of compound **6ec** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ec**, wherein compounds **SM-3by** (0.2mmol) and **SM-4b** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6ec** was obtained, yield: 43%. MS analysis confirms that **6ec**'s ESI-MS [(M+H)⁺]: theoretical m/z: 737.4; measured value: 737.5.

Embodiment 118

Synthesis of compound **6ee**

The synthesis method of compound **6ee** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ee**, wherein compounds **SM-3at** (0.2mmol) and **SM-4ad** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6ee** was obtained, yield: 52%. MS analysis confirms that **6ee**'s ESI-MS [(M+H)⁺]: theoretical m/z: 979.4; measured value: 979.5.

Embodiment 119

Synthesis of compound **6ef**

The synthesis method of compound **6ef** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ef**, wherein compounds **SM-3at** (0.2mmol) and **SM-4b** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6ef** was obtained, yield: 51%. MS analysis confirms that **6ef**'s ESI-MS [(M+H)⁺]: theoretical m/z: 787.4; measured value: 787.5.

Embodiment 120

Synthesis of compound **6eg**

The synthesis method of compound **6eg** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6eg**, wherein compounds **SM-3bz** (0.2mmol) and **SM-4a** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6eg** was obtained, yield: 58%. MS analysis confirms that **6eg**'s ESI-MS [(M+H)⁺]: theoretical m/z: 787.4; measured value: 787.5.

Embodiment 121

Synthesis of compound **6eh**

The synthesis method of compound **6eh** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6eh**, wherein compounds **SM-3cm** (0.2mmol) and **SM-4b** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6eh** was obtained, yield: 53%. MS analysis confirms that **6eh**'s ESI-MS [(M+H)⁺]: theoretical m/z: 833.3; measured value: 833.4.

Embodiment 122

Synthesis of compound **6ei**

The synthesis method of compound **6ei** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ei**, wherein compounds **SM-3cp** (0.2mmol) and **SM-4a** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6ei** was obtained, yield: 47%. MS analysis confirms that **6ei**'s ESI-MS [(M+H)⁺]: theoretical m/z: 833.3; measured value: 833.4.

Embodiment 123

Synthesis of compound **6ej**

The synthesis method of compound **6ej** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ej**, wherein compounds **SM-3ci** (0.2mmol) and **SM-4bd** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6ej** was obtained, yield: 43%. MS analysis confirms that **6ej**'s ESI-MS [(M+H)⁺]: theoretical m/z: 880.4; measured value: 880.5.

Embodiment 124

Synthesis of compound **6ek**

The synthesis method of compound **6ek** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ek**, wherein compounds **SM-3cq** (0.2mmol) and **SM-4b** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6ek** (81mg) was obtained, yield: 46%.

MS analysis confirms that **6ek**'s ESI-MS [(M+H)⁺]: theoretical m/z: 881.5; measured value: 881.5.

Embodiment 125

Synthesis of compound **6em**

The synthesis method of compound **6em** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6em**, wherein compounds **SM-3cq** (0.2mmol) and **SM-4bf** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6em** (75mg) was obtained, yield: 41%.

MS analysis confirms that **6em**'s ESI-MS [(M+H)⁺]: theoretical m/z: 915.5; measured value: 915.6.

Embodiment 126

Synthesis of compound **6en**

The synthesis method of compound **6en** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6en**, wherein compounds **SM-3cr** (0.2mmol) and **SM-4bg** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6en** (94mg) was obtained, yield: 54%.

MS analysis confirms that **6en**'s ESI-MS [(M+H)⁺]: theoretical m/z: 869.5; measured value: 869.5.

Embodiment 127

Synthesis of compound **6ep**

The synthesis method of compound **6ep** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ep**, wherein compounds **SM-3cr** (0.2mmol) and **SM-4bh** (0.2mmol) were used in place of

compounds **SM-3a** and **SM-4i**, a yellow solid product **6ep** (71mg) was obtained, yield: 39%.

MS analysis confirms that **6ep**'s ESI-MS [(M+H)⁺]: theoretical m/z: 903.5; measured value: 903.5.

5 Embodiment 128

Synthesis of compound **6fa**

The synthesis method of compound **6fa** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6fa**, wherein compounds **SM-3cb** (0.2mmol) and **SM-4b** (0.2mmol) were used in place of
10 compounds **SM-3a** and **SM-4i**, a yellow solid product **6fa** (69mg) was obtained, yield: 43%.

MS analysis confirms that **6fa**'s ESI-MS [(M+H)⁺]: theoretical m/z: 865.3; measured value: 865.3.

Embodiment 129

15 Synthesis of compound **6fb**

The synthesis method of compound **6fb** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6fb**, wherein compounds **SM-3cn** (0.2mmol) and **SM-4b** (0.2mmol) were used in place of
20 compounds **SM-3a** and **SM-4i**, a yellow solid product **6fb** (32mg) was obtained, yield: 20%.

¹H NMR (500 MHz, CDCl₃) of product **6fb**: δ 7.39-7.10 (m, 8H), 6.09 (s, 1H), 5.99 (s, 1H), 5.49 (s, 1H), 5.25 (s, 1H), 4.74 (m, 1H), 4.38 (m, 1H), 4.32 (m, 1H), 3.91 (s, 1H), 3.71 (s, 6H), 2.38 (m, 2H), 2.19 (m, 2H), 2.09-2.07 (m, 4H), 1.28 (s, 6H), 1.27 (s, 6H).

MS analysis confirms that **6fb**'s ESI-MS [(M+H)⁺]: theoretical m/z: 799.3; measured
25 value: 799.3.

Embodiment 130

Synthesis of compound **6fc**

The synthesis method of compound **6fc** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6fc**,
30 wherein compounds **SM-3cm** (0.2mmol) and **SM-4bf** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6fc** (46mg) was obtained, yield: 26%.

¹H NMR (500 MHz, CDCl₃) of product **6fc**: δ 7.92-7.27 (m, 18H), 6.24 (s, 1H), 6.19 (s, 1H), 5.97 (s, 1H), 5.89 (s, 1H), 5.48 (m, 1H), 5.28 (s, 1H), 4.55 (m, 1H), 4.10 (s, 1H), 3.76 (s, 6H), 2.32-2.03 (m, 6H). MS analysis confirms that **6fc**'s ESI-MS [(M+H)⁺]: theoretical m/z: 867.3; measured value: 867.3.

5 Embodiment 131

Synthesis of compound **6fd**

The synthesis method of compound **6fd** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6fd**, wherein compounds **SM-3cm** (0.2mmol) and **SM-4b** (0.2mmol) were used in place of
10 compounds **SM-3a** and **SM-4i**, a yellow solid product **6fd** (59mg) was obtained, yield: 25%.

¹H NMR (500 MHz, CDCl₃) of product **6fd**: δ 7.46-7.41 (m, 13H), 6.20 (s, 1H), 6.09 (s, 1H), 5.99 (s, 1H), 5.51 (m, 1H), 5.31 (m, 1H), 4.78 (m, 1H), 4.57 (m, 1H), 4.31 (m, 1H), 3.70 (s, 6H), 3.24 (m, 1H), 2.24-1.92 (m, 6H), 1.28 (s, 6H). MS analysis confirms that
15 **6fd**'s ESI-MS [(M+H)⁺]: theoretical m/z: 833.3; measured value: 833.3.

Embodiment 132

Synthesis of compound **6fe**

The synthesis method of compound **6fe** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6fe**,
20 wherein compounds **SM-3cn** (0.2mmol) and **SM-4bf** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6fd** (53mg) was obtained, yield: 35%.

¹H NMR (500 MHz, CDCl₃) of product **6fe**: δ 7.47-7.32 (m, 13H), 6.16 (s, 1H), 5.98 (s, 1H), 5.92 (s, 1H), 5.53 (m, 1H), 5.47 (m, 1H), 5.23 (m, 1H), 4.61 (m, 1H), 4.37 (m, 1H),
25 3.88 (m, 1H), 3.74 (s, 6H), 2.34-2.03 (m, 6H), 1.27 (s, 6H). MS analysis confirms that **6fe**'s ESI-MS [(M+H)⁺]: theoretical m/z: 833.3; measured value: 833.3.

Embodiment 133

Synthesis of compound **6ff**

The synthesis method of compound **6ff** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ff**,
30 wherein compounds **SM-3cp** (0.2mmol) and **SM-4ag** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6ff** (40mg) was obtained, yield:

26%.

¹H NMR (500 MHz, CDCl₃) of product **6ff**: δ 7.46-7.31 (m, 18H), 6.27 (s, 1H), 6.12 (s, 1H), 5.99 (s, 1H), 5.90 (s, 1H), 5.52 (m, 1H), 5.33 (s, 1H), 4.53 (m, 1H), 4.11 (s, 1H), 3.69 (s, 6H), 2.34-1.99 (m, 6H). MS analysis confirms that **6ff**'s ESI-MS [(M+H)⁺]:
5 theoretical m/z: 867.3; measured value: 867.3.

Embodiment 134

Synthesis of compound **6fg**

The synthesis method of compound **6fg** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6fg**,
10 wherein compounds **SM-3cp** (0.2mmol) and **SM-4a** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6fg** (81mg) was obtained, yield: 48%.

¹H NMR (500 MHz, CDCl₃) of product **6fg**: δ 7.47-7.40 (m, 13H), 6.24 (s, 1H), 5.97 (s, 1H), 5.90 (s, 1H), 5.58 (m, 1H), 5.27 (s, 1H), 4.62 (m, 1H), 4.36 (m, 1H), 4.12 (m, 1H),
15 3.88 (m, 1H), 3.73 (s, 6H), 2.18-2.02 (m, 6H), 1.26 (s, 6H). MS analysis confirms that **6fg**'s ESI-MS [(M+H)⁺]: theoretical m/z: 833.3; measured value: 833.3.

Embodiment 135

Synthesis of compound **6fh**

The synthesis method of compound **6fh** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6fh**,
20 wherein compounds **SM-3cb** (0.2mmol) and **SM-4a** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6fh** (63mg) was obtained, yield: 38%.

¹H NMR (500 MHz, CDCl₃) of product **6fh**: δ 7.55-7.13 (m, 8H), 6.07 (s, 1H), 5.98 (s, 1H), 5.57 (s, 1H), 5.28 (s, 1H), 4.79 (m, 1H), 4.60 (m, 1H), 4.39 (m, 1H), 4.33 (s, 1H),
25 3.73 (s, 6H), 2.39 (m, 1H), 2.25 (m, 1H), 2.11-2.07 (m, 6H), 1.07 (s, 6H), 0.94 (s, 6H). MS analysis confirms that **6fh**'s ESI-MS [(M+H)⁺]: theoretical m/z: 799.3; measured value: 799.3.

Embodiment 136

Synthesis of compound **6fi**

The synthesis method of compound **6fi** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6fi**,

wherein compounds **SM-3cb** (0.2mmol) and **SM-4ag** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6fi** (59mg) was obtained, yield: 35%.

¹H NMR (500 MHz, CDCl₃) of product **6fi**: δ 7.45-7.39 (m, 13H), 6.18 (s, 1H), 6.06 (s, 1H), 5.95 (s, 1H), 5.61 (m, 1H), 5.30 (m, 1H), 4.77 (m, 1H), 4.56 (m, 1H), 4.30 (m, 1H), 3.70 (s, 3H), 3.63 (s, 3H), 3.22 (s, 1H), 2.25-1.91 (m, 6H), 1.26 (s, 6H). MS analysis confirms that **6fi**'s ESI-MS [(M+H)⁺]: theoretical m/z: 833.3; measured value: 833.3.

Embodiment 137

Synthesis of compound **6fj**

The synthesis method of compound **6fj** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6fj**, wherein compounds **SM-3cc** (0.2mmol) and **SM-4b** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6fj** (61mg) was obtained, yield: 37%.

MS analysis confirms that **6fj**'s ESI-MS [(M+H)⁺]: theoretical m/z: 799.3; measured value: 799.4.

Embodiment 138

Synthesis of compound **6fk**

The synthesis method of compound **6fk** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6fk**, wherein compounds **SM-3cc** (0.2mmol) and **SM-4bf** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6fk** (59mg) was obtained, yield: 35%.

MS analysis confirms that **6fk**'s ESI-MS [(M+H)⁺]: theoretical m/z: 833.3; measured value: 833.4.

Embodiment 139

Synthesis of compound **6fm**

The synthesis method of compound **6fm** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6fm**, wherein compounds **SM-3cd** (0.2mmol) and **SM-4bf** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6fm** (57mg) was obtained, yield: 32%.

MS analysis confirms that **6fm**'s ESI-MS [(M+H)⁺]: theoretical m/z: 867.3; measured value: 867.5.

Embodiment 140

Synthesis of compound **6fn**

- 5 The synthesis method of compound **6fn** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6fn**, wherein compounds **SM-3cd** (0.2mmol) and **SM-4b** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6fn** (59mg) was obtained, yield: 35%.
- 10 ¹H NMR (500 MHz, CDCl₃) of product **6fn**: δ 7.20-7.66 (m, 13H), 5.99-6.26 (m, 3H), 5.56-5.58 (m, 1H), 5.31-5.32 (m, 1H), 4.73-4.76 (m, 2H), 4.49-4.51 (m, 1H), 3.79-3.82 (m, 2H), 3.68-3.71 (m, 5H), 3.54 (s, 3H), 1.93-2.04 (m, 5H), 0.90-0.91 (m, 6H). MS analysis confirms that **6fn**'s ESI-MS [(M+H)⁺]: theoretical m/z: 833.3; measured value: 833.5.

15 Embodiment 141

Synthesis of compound **6fp**

- The synthesis method of compound **6fp** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6fp**, wherein compounds **SM-3ce** (0.2mmol) and **SM-4bf** (0.2mmol) were used in place of
- 20 compounds **SM-3a** and **SM-4i**, a yellow solid product **6fp** (60mg) was obtained, yield: 37%.
- MS analysis confirms that **6fp**'s ESI-MS [(M+H)⁺]: theoretical m/z: 817.3; measured value: 817.3.

Embodiment 142

25 Synthesis of compound **6fq**

- The synthesis method of compound **6fq** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6fq**, wherein compounds **SM-3cf** (0.2mmol) and **SM-4b** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6fq** (52mg) was obtained, yield:
- 30 32%.
- MS analysis confirms that **6fq**'s ESI-MS [(M+H)⁺]: theoretical m/z: 817.3; measured value: 817.3.

Embodiment 143

Synthesis of compound **6fr**

The synthesis method of compound **6fr** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6fr**, wherein compounds **SM-3cf** (0.2mmol) and **SM-4bf** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6fr** (55mg) was obtained, yield: 32%.

MS analysis confirms that **6fr**'s ESI-MS [(M+H)⁺]: theoretical m/z: 851.3; measured value: 851.3.

Embodiment 144

Synthesis of compound **6fs**

The synthesis method of compound **6fs** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6fs**, wherein compounds **SM-3cg** (0.2mmol) and **SM-4bf** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6fs** (67mg) was obtained, yield: 39%.

MS analysis confirms that **6fs**'s ESI-MS [(M+H)⁺]: theoretical m/z: 850.3; measured value: 850.5.

Embodiment 145

Synthesis of compound **6ft**

The synthesis method of compound **6ft** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ft**, wherein compounds **SM-3ch** (0.2mmol) and **SM-4ag** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6ft** (82mg) was obtained, yield: 48%.

MS analysis confirms that **6ft**'s ESI-MS [(M+H)⁺]: theoretical m/z: 833.3; measured value: 833.5.

Embodiment 146

Synthesis of compound **6fu**

The synthesis method of compound **6fu** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6fu**, wherein compounds **SM-3cs** (0.25mmol) and **SM-4bn** (0.25mmol) were used in place

of compounds **SM-3a** and **SM-4i**, a yellow solid product **6fu** (57mg) was obtained, yield: 25%.

MS analysis confirms that **6fu**'s ESI-MS [(M+H)⁺]: theoretical m/z: 901.3; measured value: 901.4.

5 Embodiment 147

Synthesis of compound **6fv**

The synthesis method of compound **6fv** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6fv**, wherein compounds **SM-3cu** (0.25mmol) and **SM-4bp** (0.25mmol) were used in place
10 of compounds **SM-3a** and **SM-4i**, a yellow solid product **6fv** (48mg) was obtained, yield: 21%.

MS analysis confirms that **6fv**'s ESI-MS [(M+H)⁺]: theoretical m/z: 901.3; measured value: 901.4.

Embodiment 148

15 Synthesis of compound **6fw**

The synthesis method of compound **6fw** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6fw**, wherein compounds **SM-3cu** (0.25mmol) and **SM-4bq** (0.25mmol) were used in place
20 of compounds **SM-3a** and **SM-4i**, a yellow solid product **6fw** (72mg) was obtained, yield: 32%.

MS analysis confirms that **6fw**'s ESI-MS [(M+H)⁺]: theoretical m/z: 897.3; measured value: 897.4.

Embodiment 149

Synthesis of compound **6fx**

25 The synthesis method of compound **6fx** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6fx**, wherein compounds **SM-3cs** (0.25mmol) and **SM-4br** (0.25mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6fx** (81mg) was obtained, yield: 36%.

30 MS analysis confirms that **6fx**'s ESI-MS [(M+H)⁺]: theoretical m/z: 941.3; measured value: 941.4.

Embodiment 150

Synthesis of compound **6fy**

The synthesis method of compound **6fy** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6fy**, wherein compounds **SM-3cs** (1.0mmol) and **SM-4ag** (1.0mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6fy** (374mg) was obtained, yield: 43%.

¹H NMR (500 MHz, CDCl₃) of product **6fy**: δ 7.19-7.84 (m, 15H), 5.92-6.17 (m, 3H), 5.55-5.68 (m, 2H), 4.54-4.68 (m, 1H), 4.39-4.41 (m, 1H), 4.12-4.15 (m, 1H), 3.95-3.98 (m, 1H), 3.63-3.71 (m, 7H), 2.81 (m, 1H), 2.42-2.43 (m, 1H), 2.28-2.31 (m, 1H), 2.10-2.16 (m, 2H), 0.93-0.97 (m, 6H). MS analysis confirms that **6fy**'s ESI-MS [(M+H)⁺]: theoretical m/z: 883.3; measured value: 883.4.

Embodiment 151

Synthesis of compound **6fz**

The synthesis method of compound **6fz** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6fz**, wherein compounds **SM-3cs** (0.35mmol) and **SM-4a** (0.35mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6fz** (200mg) was obtained.

¹H NMR (500 MHz, CDCl₃) of product **6fz**: δ 7.33-7.86 (m, 10H), 6.08-6.27 (m, 3H), 5.57-5.61 (m, 1H), 5.27 (m, 1H), 4.81-4.83 (m, 1H), 4.56-4.59 (m, 1H), 4.20-4.38 (m, 2H), 3.66-3.89 (m, 7H), 2.39 (m, 1H), 2.26 (m, 1H), 2.02-2.06 (m, 4H), 1.05-1.10 (m, 3H), 0.84-0.96 (m, 9H). MS analysis confirms that **6fz**'s ESI-MS [(M+H)⁺]: theoretical m/z: 849.3; measured value: 849.4.

Embodiment 152

Synthesis of compound **6ga**

The synthesis method of compound **6ga** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ga**, wherein compounds **SM-3ct** (0.35mmol) and **SM-4a** (0.35mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6ga** (190mg) was obtained.

¹H NMR (500 MHz, CDCl₃) of product **6ga**: δ 7.16-7.86 (m, 15H), 5.97-6.26 (m, 3H), 5.47-5.62 (m, 2H), 5.26-5.29 (m, 1H), 4.58-4.62 (m, 1H), 4.36 (m, 1H), 4.03-4.22 (m, 1H), 3.64-3.89 (m, 7H), 2.36-2.40 (m, 1H), 2.21-2.24 (m, 1H), 2.02-2.11 (m, 3H), 0.83-0.91 (m, 6H). MS analysis confirms that **6ga**'s ESI-MS [(M+H)⁺]: theoretical m/z:

883.3; measured value: 883.4.

Embodiment 153

Synthesis of compound **6gb**

The synthesis method of compound **6gb** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6gb**, wherein compounds **SM-3ct** (0.44mmol) and **SM-4ag** (0.44mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6gb** (180mg) was obtained.

¹H NMR (500 MHz, CDCl₃) of product **6gb**: δ 7.13-7.97 (m, 20H), 5.95-6.26 (m, 4H), 5.33-5.53 (m, 3H), 4.55-4.63 (m, 1H), 4.01-4.21 (m, 1H), 3.64-3.79 (m, 7H), 2.21-2.26 (m, 1H), 1.90-2.04 (m, 3H). MS analysis confirms that **6gb**'s ESI-MS [(M+H)⁺]: theoretical m/z: 917.3; measured value: 917.4.

Embodiment 154

Synthesis of compound **6gc**

The synthesis method of compound **6gc** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6gc**, wherein compounds **SM-3cu** (12.5mmol) and **SM-4bf** (12.5mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6gc** (4.3g) was obtained, yield: 39%.

¹H NMR (500 MHz, CDCl₃) of product **6gc**: δ 7.61-7.26 (m, 10H), 6.09 (m, 1H), 6.01 (m, 1H), 5.54 (m, 1H), 5.46 (m, 1H), 4.77 (m, 1H), 4.56 (m, 1H), 4.39 (m, 1H), 4.33 (m, 1H), 3.93 (m, 1H), 3.71 (d, 6H), 2.92 (m, 1H), 2.42-2.04 (m, 7H), 1.26 (d, 12H). MS analysis confirms that **6gc**'s ESI-MS [(M+H)⁺]: theoretical m/z: 883.3; measured value: 883.4.

Embodiment 155

Synthesis of compound **6gd**

The synthesis method of compound **6gd** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6gd**, wherein compounds **SM-3cu** (0.44mmol) and **SM-4b** (0.44mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6gd** (100mg) was obtained, yield: 26%.

¹H NMR (500 MHz, CDCl₃) of product **6gd**: δ 7.61-7.26 (m, 10H), 6.09 (m, 1H), 6.01 (m, 1H), 5.54 (m, 1H), 5.46 (m, 1H), 4.77 (m, 1H), 4.56 (m, 1H), 4.39 (m, 1H), 4.33 (m,

1H), 3.93 (m, 1H), 3.71 (d, 6H), 2.92 (m, 1H), 2.42-2.04 (m, 7H), 1.26 (d, 12H). MS analysis confirms that **6gd**'s ESI-MS [(M+H)⁺]: theoretical m/z: 849.3; measured value: 849.4.

Embodiment 156

5 Synthesis of compound **6ge**

The synthesis method of compound **6ge** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6ge**, wherein compounds **SM-3cv** (0.37mmol) and **SM-4b** (0.37mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6ge** (40mg) was obtained, yield: 12%.

¹H NMR (500 MHz, CDCl₃) of product **6ge**: δ 7.71-7.24 (m, 15H), 6.09 (m, 2H), 5.53 (m, 2H), 4.76 (d, 1H), 4.53 (s, 1H), 4.31 (m, 1H), 4.13 (m, 1H), 3.74 (d, 6H), 3.32 (m, 1H), 2.89 (m, 1H), 2.31-1.99 (m, 6H), 1.28 (d, 6H). MS analysis confirms that **6ge**'s ESI-MS [(M+H)⁺]: theoretical m/z: 883.3; measured value: 883.4.

Embodiment 157

15 Synthesis of compound **6gf**

The synthesis method of compound **6gf** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6gf**, wherein compounds **SM-3cv** (0.39mmol) and **SM-4bf** (0.39mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6gf** (50mg) was obtained, yield: 14%.

MS analysis confirms that **6gf**'s ESI-MS [(M+H)⁺]: theoretical m/z: 917.3; measured value: 917.4.

Embodiment 158

25 Synthesis of compound **6gg**

The synthesis method of compound **6gg** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6gg**, wherein compounds **SM-3cm** (0.39mmol) and **SM-4bg** (0.39mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6gg** (31mg) was obtained, yield: 16%.

¹H NMR (500 MHz, CDCl₃) of product **6gg**: δ 7.26-7.47 (m, 11H), 6.10-6.33 (m, 3H), 5.27-5.44 (m, 2H), 4.78-4.81 (m, 1H), 4.46-4.58 (m, 1H), 4.19-4.31 (m, 1H), 3.66-3.77

(m, 7H), 3.21-3.23 (m, 1H), 2.81-2.94 (m, 1H), 2.20-2.23 (m, 1H), 2.07 (m, 1H), 1.88-1.91 (m, 2H), 0.84-0.89 (m, 6H). MS analysis confirms that **6gg**'s ESI-MS [(M+H)⁺]: theoretical m/z: 807.3; measured value: 807.4.

Embodiment 159

5 Synthesis of compound **6gh**

The synthesis method of compound **6gh** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6gg**, wherein compounds **SM-3cn** (0.86mmol) and **SM-4bg** (0.86mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6gh** (190mg) was obtained, yield: 29%.

¹H NMR (500 MHz, CDCl₃) of product **6gh**: δ 7.14-7.70 (m, 6H), 6.06-6.23 (m, 3H), 5.56-5.58 (m, 1H), 5.23 (m, 1H), 4.80 (m, 1H), 4.55-4.61 (m, 1H), 4.18-4.38 (m, 2H), 3.60-3.87 (m, 7H), 2.34-2.37 (m, 1H), 2.18-2.21 (m, 1H), 2.00-2.10 (m, 4H), 0.88-0.92 (m, 12H). MS analysis confirms that **6gh**'s ESI-MS [(M+H)⁺]: theoretical m/z: 773.3; measured value: 773.4.

Embodiment 160

Synthesis of compound **6gi**

The synthesis method of compound **6gi** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6gi**, wherein compounds **SM-3cn** (0.80mmol) and **SM-4bh** (0.80mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6gi** (260mg) was obtained, yield: 42%.

¹H NMR (500 MHz, CDCl₃) of product **6gi**: δ 7.00-7.54 (m, 11H), 5.97-6.28 (m, 3H), 5.45-5.55 (m, 2H), 5.24 (m, 1H), 4.57-4.60 (m, 1H), 4.35 (m, 1H), 3.64-3.88 (m, 7H), 3.53-3.55 (m, 1H), 2.88-2.92 (m, 1H), 2.34-2.35 (m, 1H), 2.19-2.22 (m, 1H), 2.04-2.09 (m, 2H), 0.88-0.96 (m, 6H). MS analysis confirms that **6gi**'s ESI-MS [(M+H)⁺]: theoretical m/z: 807.3; measured value: 807.3.

Embodiment 161

Synthesis of compound **6gj**

The synthesis method of compound **6gj** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6gj**, wherein compounds **SM-3ca** (0.31mmol) and **SM-4bs** (0.31mmol) were used in place

of compounds **SM-3a** and **SM-4i**, a yellow solid product **6gj** (35mg) was obtained, yield: 14%.

MS analysis confirms that **6gj**'s ESI-MS [(M+H)⁺]: theoretical m/z: 807.3; measured value: 807.4.

5

Embodiment 162

Synthesis of compound **6gk**

The synthesis method of compound **6gk** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6gk**, wherein compounds **SM-3cw** (0.31mmol) and **SM-4bs** (0.31mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6gk** (30mg) was obtained, yield: 11%.

10

MS analysis confirms that **6gk**'s ESI-MS [(M+H)⁺]: theoretical m/z: 841.3; measured value: 841.4.

15

Embodiment 163

Synthesis of compound **6gm**

The synthesis method of compound **6gm** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6gm**, wherein compounds **SM-3ca** (0.33mmol) and **SM-4bt** (0.33mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6gm** (50mg) was obtained, yield: 20%.

20

MS analysis confirms that **6gm**'s ESI-MS [(M+H)⁺]: theoretical m/z: 773.3; measured value: 773.4.

Embodiment 164

Synthesis of compound **6gn**

The synthesis method of compound **6gn** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6gn**, wherein compounds **SM-3cw** (0.25mmol) and **SM-4bt** (0.25mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6gn** (29mg) was obtained, yield: 14%.

30

MS analysis confirms that **6gn**'s ESI-MS [(M+H)⁺]: theoretical m/z: 807.3; measured value: 807.4.

Embodiment 165

Synthesis of compound **6gp**

The synthesis method of compound **6gp** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6gp**, wherein compounds **SM-3cw** (0.25mmol) and **SM-4bt** (0.25mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6gp** (32mg) was obtained, yield: 13%.

MS analysis confirms that **6gp**'s ESI-MS [(M+H)⁺]: theoretical m/z: 933.3; measured value: 933.4.

Embodiment 166

Synthesis of compound **6gq**

The synthesis method of compound **6gq** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **6gq**, wherein compounds **SM-3cu** (0.25mmol) and **SM-4bw** (0.25mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **6gq** (37mg) was obtained, yield: 15%.

MS analysis confirms that **6gq**'s ESI-MS [(M+H)⁺]: theoretical m/z: 933.3; measured value: 933.4.

Embodiment 167

Synthesis of compound **Ref-3**

The synthesis method of compound **Ref-3** was the same with that in Embodiment 1; the product was carried out by one-step catalytic coupling reaction to get product **Ref-3**, wherein compounds **SM-3cm** (0.2mmol) and **SM-4ag** (0.2mmol) were used in place of compounds **SM-3a** and **SM-4i**, a yellow solid product **Ref-3** (69mg) was obtained, yield: 40%.

¹H NMR (500 MHz, CDCl₃) of product **Ref-3**: δ 10.53 (s, 1H), 7.75-7.14 (m, 17H), 6.13 (m, 2H), 5.46 (m, 2H), 5.31 (m, 2H), 3.80 (m, 6H), 3.23 (m, 2H), 2.91 (m, 2H), 2.23-1.67 (m, 12H). MS analysis confirms that **Ref-3**'s ESI-MS [(M+H)⁺]: theoretical m/z: 869.3; measured value: 869.3.

Embodiment of treatment effect

The autonomous replication level of HCV in liver cells in vitro is very low, and the only animal that can be infected by HCV is chimpanzee, therefore there is no appropriate animal model currently available for preclinical pharmacodynamic study. Some researchers have transplanted human liver tissue infected with HCV in vitro into immune deficient mice to establish an in vivo mice model, but these mice are hard to raise and the model is unstable and short of normal immunologic reaction. Moreover, the model has significant difference with the pathogenic process of hepatitis C, therefore, it has not been used for animal model to assess the action of anti-HCV medicine yet. The progress of the development of anti-viral drugs for the treatment of HCV infection had been very slow because the pathogenic mechanism and life cycle of HCV were unclear before 1999 due to the lack of cell culture system for effective multiplication of HCV. But researchers managed to achieve a breakthrough in 1999 after numerous attempts. An effective cell culture model-replicon system in which HCV is capable of autonomous replication in transfected human hepatic carcinoma cell line Huh-7 had been established in that year on the basis of subgenomic HCV RNA built with genetic engineering.

The above-mentioned cell culture model-replicon system which has been widely accepted in the industry is used in this invention for ex vivo experiments and subsequent assessment of drugs based on the experiment results. The resulted ex vivo experiment results for HCV NS5, a target site of action of anti-HCV drugs include:

- 1) inhibitory action(IC_{50}) of the compounds on the activity of HCV NS5 replicase;
- 2) inhibitory action(EC_{50}) of the compounds on HCV NS5 replicon;

Currently available foreign preclinical and clinical studies suggest the ex vivo experiment results are consistent with relevant in vivo activity tests.

The therapeutic effect of the compounds of this invention on HCV infection can be preliminarily assessed through the following preclinical in vitro inhibitory action test and can be further confirmed in clinical trials. Other methods used in the invention are also quite familiar to professionals in this field with ordinary technical knowledge.

Method for testing the anti-viral activity(EC_{50}) in HCV NS5A replicon system:

The viral replication level in infected cells was determined by testing Renilla luciferase with the newly established dual-reporter gene replicon system. There was a good linear relation between the expression level of the reporter gene and the HCV RNA

replication level and viral protein expression level. The anti-viral activity was determined for 3 replicates in 3 replicate cells at five(5) 1:2 diluted concentration gradients, with 1 to 2 positive controls. The EC₅₀ of the compounds was calculated in the end.

- 5 The compounds of the invention, or their stereoisomers, tautomers, esterified or amidated prodrugs, or pharmaceutically acceptable salts and mixtures have been subjected to test to determined their therapeutic effects in the treatment of HCV infection. The results show they have significant HCV NS5 inhibitory effect. Moreover, the results of **6a-6ep(Ia)**, **6fa-6gq(Ib)** and reference compounds **Ref-1(BMS-790052)**, **Ref-2(GS5885)**, **Ref-3** in HCV-NS5 inhibition test reveal that the cyclopentanyl/hexamethyleneamino radical containing linear polypeptide compounds **6a-6ep**, **6fa-6gq** and reference compounds **Ref-1**, **Ref-2**, **Ref-3** have good HCV inhibitory results. The detailed testing results of the HCV-NS5A inhibitory activity of compounds **6a-6ep** and reference compounds **Ref-1**, **Ref-2**, **Ref-3** are listed in Table 1 as shown below; in the Table, the results are marked with an “A” when the inhibitory activity(EC₅₀) is ≥ 50 nM, or with a “B” when the inhibitory activity(EC₅₀) is in the range of 1.0-49.9nM, or with a “C” when the inhibitory activity(EC₅₀) is in the range of 0.001-0.999nM. The replicons GT-1a, GT-1b, GT-2a, GT-3a, GT-4a, GT-5a and GT-6a used for the test are routine replicons commercially available in this field. The detailed testing data of HCV NS5A replicon inhibition test are as shown in Table 1 and Table 2.

Table 1: HCV NS5A replicon inhibitory activity test results of compounds (**6a-6gq**) of the invention

No.	Compound NO.	NS5A Inhibitory Activity (EC ₅₀ of GT-1a subtype inhibition)	No.	Compound NO.	NS5A Inhibitory Activity (EC ₅₀ of GT-1a subtype inhibition)
1	6a	C	86	6cu	C
2	6b	A	87	6cv	C
3	6c	A	88	6cw	C
4	6d	B	89	6cx	C

5	6e	A	90	6cy	C
6	6f	A	91	6cz	C
7	6g	A	92	6da	C
8	6h	A	93	6db	C
9	6i	C	94	6dc	C
10	6j	A	95	6dd	C
11	6k	A	96	6de	C
12	6m	B	97	6df	C
13	6n	A	98	6dg	C
14	6p	A	99	6dh	C
15	6q	A	100	6di	C
16	6r	A	101	6dj	B
17	6s	C	102	6dk	C
18	6t	A	103	6dm	C
19	6u	B	104	6dn	C
20	6v	A	105	6dp	C
21	6w	A	106	6dq	C
22	6x	C	107	6dr	C
23	6y	C	108	6ds	C
24	6z	C	109	6dt	C
25	6aa	C	110	6du	C
26	6ab	C	111	6dv	C
27	6ac	C	112	6dw	C
28	6ad	C	113	6dy	C
29	6ae	C	114	6dz	C
30	6af	C	115	6ea	C
31	6ag	C	116	6eb	C
32	6ah	C	117	6ec	C
33	6ai	C	118	6ed	C
34	6aj	C	119	6ee	C
35	6ak	C	120	6ef	C

36	6am	C	121	6eg	C
37	6an	C	122	6eh	C
38	6ap	C	123	6ei	C
39	6aq	C	124	6ej	C
40	6ar	C	125	6ek	B
41	6as	C	126	6em	B
42	6at	C	127	6en	B
43	6au	C	128	6ep	B
44	6av	C	129	6fa	C
45	6aw	C	130	6fb	C
46	6ax	C	131	6fc	C
47	6ay	C	132	6fd	C
48	6az	C	133	6fe	C
49	6ba	C	134	6ff	C
50	6bb	A	135	6fg	C
51	6bc	B	136	6fh	C
52	6bd	C	137	6fi	C
53	6be	C	138	6fj	C
54	6bf	A	139	6fk	C
55	6bg	A	140	6fm	C
56	6bh	C	141	6fn	C
57	6bi	C	142	6fp	C
58	6bj	C	143	6fq	C
59	6bk	C	144	6fr	C
60	6bm	C	145	6fs	C
61	6bn	C	146	6ft	C
62	6bp	C	147	6fu	C
63	6bq	C	148	6fv	C
64	6br	C	149	6fw	C
65	6bs	A	150	6fx	C
66	6bt	C	151	6fy	C

67	6bu	C	152	6fz	C
68	6bv	C	153	6ga	C
69	6bw	C	154	6gb	C
70	6bx	C	155	6gc	C
71	6by	C	156	6ge	C
72	6bz	C	157	6gf	C
73	6ca	C	158	6gg	C
74	6cb	A	159	6gh	C
75	6cc	A	160	6gi	C
76	6cd	A	161	6gj	C
77	6ce	C	162	6gk	C
78	6cf	C	163	6gm	C
79	6cg	C	164	6gn	C
80	6ch	C	165	6gp	C
81	6ci	C	166	6gq	C
82	6cj	C	167	Ref-1	C
83	6ck	C	168	Ref-2	C
84	6cm	C	169	Ref-3	C
85	6cq	B	170	Ref-4	C

Table 2: The highly-effective HCV NS5A replicon inhibiting compounds of this invention and their activity test results

No.	Compound NO.	Inhibitory activity against various HCV-NS5A subtypes(EC ₅₀ , GT-1a to GT-6a)						
		GT-1a	GT-1b	GT-2a	GT-3a	GT-4a	GT-5a	GT-6a
1	6ba	39	12	16	173	10	23	221
2	6dy	11	14	6	15	8	23	24
3	6fc	21	11	5	15	8	23	111
4	6fd	20	5	7	26	5	13	55
5	6fg	9	13	8	24	12	29	23
6	6fz	7	N/A	N/A	N/A	N/A	N/A	N/A

7	6gc	11	N/A	N/A	N/A	N/A	N/A	N/A
8	6gd	4	N/A	N/A	N/A	N/A	N/A	N/A
9	Ref-1	52	21	29	218	11	36	118
10	Ref-2	88	N/A	N/A	N/A	N/A	N/A	N/A
11	Ref-3	51	N/A	N/A	N/A	N/A	N/A	N/A
12	Ref-4	22	N/A	N/A	N/A	N/A	N/A	N/A

N/A: Not Available.

The results in Table 2 suggest that compounds **6a-6ep(Ia)** and **6fa-6gq(Ib)** of this invention have excellent HCV NS5A inhibitory activity and are among the novel HCV NS5A inhibitors that have good activity; some compounds (e.g. compounds **6dy**, **6fg**, **6fz**, **6gc** and **6gd** in Table 2), in particular, have inhibitory activity significantly superior to that of **Ref-1**(BMS-790052), **Ref-2**(GS5885), **Ref-3** and **Ref-4** (Idenix compound IDX-719), therefore some novel compounds (e.g. **6dy**, **6fg**, **6fz**, **6gc** and **6gd**) designed and prepared in this invention are of value that deserves further test and promotion.

10 MTD screening test

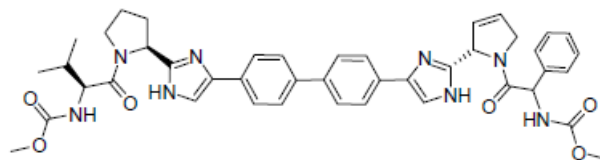
Method: ICR mice, 10 mice/group, 5 males and 5 females. A treatment group and a control group are set up for every drugs, respectively, mice in control group were administered 0.5%CMC-Na solution, i.e. the solvent of the drugs. The mice were fasted overnight but granted free access to water before the administration. Their body weight before the administration of drugs is in the range of 18.8~24.1 g. The mice were administered the drugs by peroral lavage at the dosage of 40 mL/kg. The mice were closely observed 3 hours after the administration and twice a day afterwards for 7 days, one in the morning and one in the afternoon. At the end of the observation period, 2 mice (1 male and 1 female) were randomly selected from each treatment group and subjected to histopathological examination of part of their tissues and organs.

In order to test the toxicity of some of the novel heterocyclic compounds **6a-6ep(Ia)**, **6fa-6gq(Ib)** of this invention and some highly active compounds in reference compounds Ref-1, Ref-2, Ref-3 (e.g.: **6ba**, **6bx**, **6by**, **6bz**, **6dy**, **6fb**, **6fc**, **6fd**, **6fg**, **6ft**), healthy mice of body weight 18-22g were subjected to administration of the drugs by lavage at daily single dosage of 2000mg/kg for 5 consecutive days and close observations for 7 consecutive days for assessment of the acute toxicity of the trial

drugs on body based on the mice's toxic reaction (Acute Toxicity Study, MTD). The results show the overall toxicity of the compound group of the invention is very low ($LD_{50} > 10000$), most mice (80%-100%) survive the administration. Two third of the novel heterocyclic compounds that have good HCV inhibiting activity ($EC_{50}: < 0.05nM$) after administration of the drugs by lavage at the dosage of 2000mg/kg yield a survival rate of 100%. The experiment results show the compounds of the invention have good therapeutic effect in the treatment of HCV infection and demonstrate significant inhibitory effect against HCV NS5A. Two third of the novel compounds that show high HCV inhibiting activity have very low overall toxicity (survive rate of mice after administration: 100%). It is believed that these compounds are generally nontoxic.

CLAIMS

1. A chemical compound as represented by Formula Ia-70, its stereoisomers, tautomers, pharmaceutically acceptable salts, or their isotopic substitutions in which the hydrogen, oxygen, or nitrogen is replaced by its corresponding isotope,

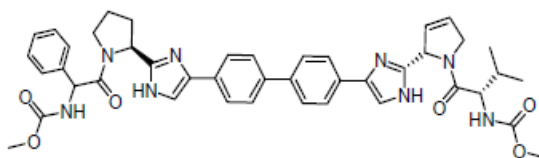


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Ia-70.

2. A chemical compound as represented by Formula Ia-71, its stereoisomers, tautomers, pharmaceutically acceptable salts, or their isotopic substitutions in which the hydrogen, oxygen, or nitrogen is replaced by its corresponding isotope,

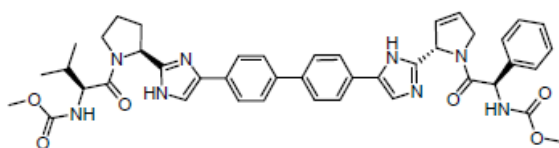
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Ia-71.

3. A chemical compound as represented by Formula Ia-113, its stereoisomers, tautomers, pharmaceutically acceptable salts, or their isotopic substitutions in which the hydrogen, oxygen, or nitrogen is replaced by its corresponding isotope,

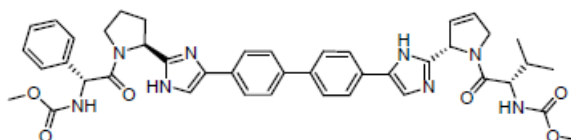
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Ia-113.

4. A chemical compound as represented by Formula Ia-115, its stereoisomers, tautomers, pharmaceutically acceptable salts, or their isotopic substitutions in which the hydrogen, oxygen, or nitrogen is replaced by its corresponding isotope,

20



Ia-115.

5 5. A chemical compound as represented by Formula Ia-70, Ia-71, Ia-113 or Ia-115 in any one of claims 1-4, their stereoisomers, tautomers, pharmaceutically acceptable salts are used in preparation of HCV inhibitor drugs.

10 6. A kind of pharmaceutical composition, comprising a chemical compound as represented by Formula Ia-70, Ia-71, Ia-113 or Ia-115 in any one of claims 1-4, their stereoisomers, tautomers, pharmaceutically acceptable salts, and pharmaceutical acceptable excipient.

15 7. A kind of pharmaceutical composition according to claim 6, which includes: Immunomodulators, hepatitis C virus (HCV) NS3/4A inhibitors, HCV-NS5B inhibitors, HCV inhibitors of the nucleoside and non-nucleoside and nucleoside derivatives, hepatitis B viral (HBV) inhibitors, antiviral human immunodeficiency virus (HIV) inhibitors, anti-cancer drugs and anti-inflammatory drugs.

20 8. A kind of pharmaceutical composition according to claim 7, wherein: the described immunomodulators are interferon or interferon derivatives;

The described HBV inhibitors include Lamivudine, Telbivudine, Adefovir Dipivoxil, Emtricitabine, Entecavir, Tenofovir and Telbivudine;

The described anti-HIV inhibitors include ritonavir and/or ribavirin,

25 The described HCV protease inhibitors include VX-950, ZN2007, ABT-450, RG-7227, TMC-435, MK-5172, MK-7009, ACH-1625, GS-9256, TG2349, BMS-650032, IDX320, Yimitasvir phosphate capsule or Seraprevir potassium;

The described hepatitis C virus polymerase inhibitor comprises GS-5885, TMC647055, ABT-267, BMS-791325, PPI-383 or ALS-002158.

30 9. A kind of pharmaceutical composition according to claim 8, wherein the described interferon is pegylated interferon.