HCV PROTEASE INHIBITORS

BACKGROUND

Hepatitis C virus (HCV), a (+)-sense single-stranded RNA virus, is the major causative agent for most cases of non-A, non-B hepatitis. Infection by HCV is a compelling human health problem. See, e.g., WO 05/007681; WO 89/04669; EP 381216; Alberti et al., *J. Hepatology*, 31 (Suppl. 1), 17-24 (1999); Alter, *J. Hepatology*, 31 (Suppl. 1), 88-91 (1999); and Lavanchy, *J. Viral Hepatitis*, 6, 35-47 (1999).

Hepatitis caused by HCV infection is difficult to treat since the virus can quickly mutate and escape the natural immune response. The only anti-HCV therapies currently available are interferon-α, interferon-α/ribavirin combination, and pegylated interferon-α. However, sustained response rates for interferon-α or interferon-α/ribavirin combination were found to be <50% and patients suffer greatly from side effects of these therapeutic agents. See, e.g., Walker, *DDT*, 4, 518-529 (1999); Weiland, *FEMS Microbial. Rev.*, 14, 279-288 (1994); and WO 02/18369. Thus, there remains a need for developing more effective and better-tolerated therapeutic drugs.

An HCV protease necessary for viral replication contains about 3000 amino acids. It includes a nucleocapsid protein (C), envelope proteins (E1 and E2), and several non-structural proteins (NS2, NS3, NS4a, NS5a, and NS5b).

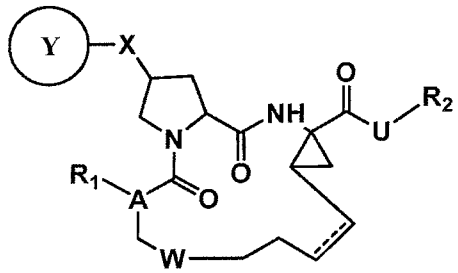
NS3 protein possesses serine protease activity and is considered essential for viral replication and infectivity. The essentiality of the NS3 protease was inferred from the fact that mutations in the yellow fever virus NS3 protease decreased viral infectivity. See, e.g., Chamber et al., *Proc. Natl. Acad. Sci.* USA 87, 8898-8902 (1990). It was also demonstrated that mutations at the active site of the HCV NS3 protease completely inhibited the HCV infection in chimpanzee model. See, e.g., Rice et al., *J. Virol.* 74 (4) 2046-51 (2000). Further, the HCV NS3 protease was found to facilitate proteolysis at the NS3/NS4a, NS4a/NS4b, NS4b/NS5a, NS5a/NS5b junctions and was thus responsible for generating four viral proteins during viral replication. See, e.g., US 2003/0207861. Consequently, the HCV NS3 protease enzyme is an attractive target in treating HCV infection. Potential NS3 HCV protease inhibitors can be found in WO 02/18369, WO 00/09558, WO 00/09543, WO 99/64442, WO 99/07733, WO 99/07734, WO 99/50230,

WO 98/46630, WO 98/17679, WO 97/43310, US 5,990,276, Dunsdon et al., *Biorg. Med. Chem. Lett.* 10, 1571-1579 (2000); Llinas-Brunet et al., *Biorg. Med. Chem. Lett.* 10, 2267-2270 (2000); and S. LaPlante et al., Biorg. Med. Chem. Lett. 10, 2271-2274 (2000).

SUMMARY

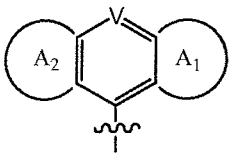
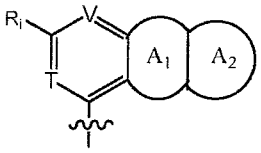
This invention is based on unexpected discoveries that certain macrocyclic compounds block activity of NS3-4A proteases, decrease HCV RNA levels, inhibit HCV protease mutants resistant to other inhibitors, and show a prolonged half-life in the blood system.

In one aspect, this invention relates to compounds of formula (I):

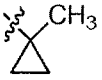


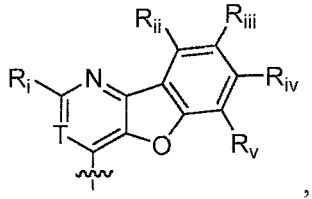
Formula (I)

wherein R_1 is -H, -OH, C_{1-6} alkyl, C_{1-6} alkoxyl, C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, heteroaryl, -Z-R, or –NH-Z-R; in which R is H, or is a moiety selected from C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, and heteroaryl, each of which is optionally mono-, di- or tri-substituted with halo, nitro, cyano, amino, C_{1-6} alkyl, C_{1-6} alkoxyl, C_{2-6} alkenyl, C_{2-6} alkynyl, aryl, or heteroaryl; and Z is -C(O)-, -C(O)O-, -C(O)C(O)O-, -C(O)C(O)NH-, -C(O)NR'-, -OC(S)-, - C(S)NR'-, or -C(NH)O-, R' being H, C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, or heteroaryl; R_2 is H, or is a moiety selected from C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, and heteroaryl, each of which is optionally mono-, di-, or tri-substituted with halo, nitro, cyano, amino, C_{1-6} alkyl, C_{1-6} alkoxyl, C_{2-6} alkenyl, C_{2-6} alkynyl, aryl, or heteroaryl; A is N or CH; U is -O-, -NH-, -NH(CO)-, -NHS(O)-, or -$NHSO_2$-; W is -$(CH_2)_m$-, -$NH(CH_2)_n$-, -$(CH_2)_nNH$-, -$O(CH_2)_n$-, -$(CH_2)_nO$-, -$S(CH_2)_n$-, -$(CH_2)_nS$-, -S(O)-, -$SO(CH_2)_n$-, -$(CH_2)_nS(O)$-, -$SO_2(CH_2)_n$-, or -$(CH_2)_nSO_2$-, m being 1, 2, or 3 and n being

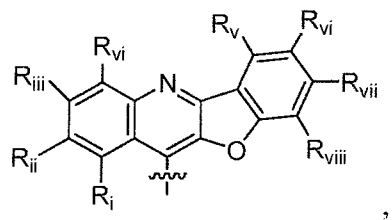
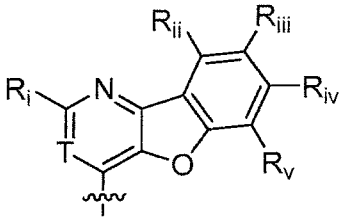
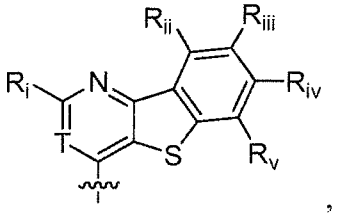
0, 1, or 2; X is -O-, -S-, -NH-, or -OCH_2-; Y is  or , in which each of V and T, independently, is -CH- or -N-; each of A_1 and A_2, independently, is a moiety selected from C_{4-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, and heteroaryl, each of which is optionally mono-, di-, or tri-substituted with halo, nitro, cyano, amino, C_{1-6} alkyl, C_{1-6} alkoxyl, C_{2-6} alkenyl, C_{2-6} alkynyl, aryl, or heteroaryl, or optionally fused with C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, or heteroaryl; and R_i is H, halo, nitro, cyano, or amino, or is a moiety selected from C_{1-6} alkyl, C_{1-6} alkoxyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, and heteroaryl, each of C_{1-6} alkyl, C_{1-6} alkoxyl, C_{2-6} alkenyl, and C_{2-6} alkynyl being optionally mono-, di- or tri-substituted with halo, nitro, cyano, amino, C_{1-6} alkyl, C_{1-6} alkoxyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, or heteroaryl, and each of C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, and heteroaryl being optionally mono-, di- or tri-substituted with halo, nitro, cyano, amino, C_{1-6} alkyl, C_{1-6} alkoxyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, or heteroaryl, or optionally fused with C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, or heteroaryl; and ≡ is a single bond or a double bond.

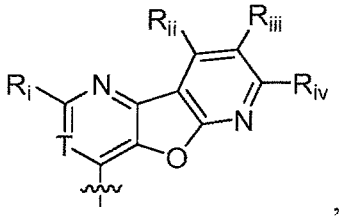
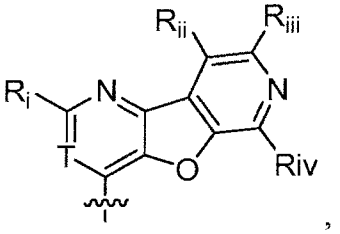
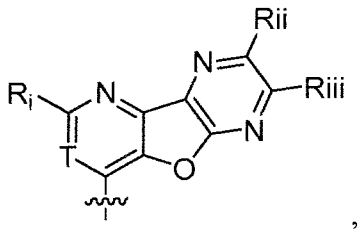
The groups assigned to variables U, W, X, and Z are bi-valent. Each of the groups is presented above in the same orientation as that in which the variable is presented in the formula. Take for example the group -NHSO- assigned to the variable U, which, as shown in the formula, is interposed between C=O and R_2. The N atom in this –NHS(O)- group is bonded to C=O and the S atom bonded to R_2. As another example, the group –C(O)O- assigned to the variable Z is interposed between NH and R (i.e., -NH-Z-R). The C atom in –C(O)O- is bonded to NH and the O atom bonded to R.

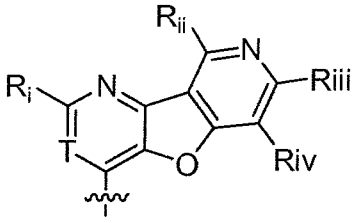
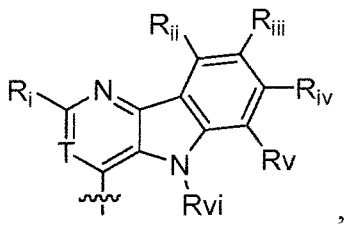
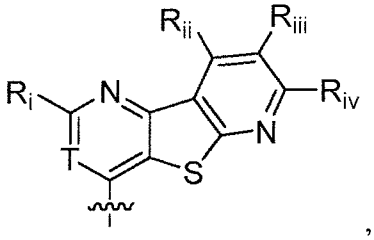
Referring to Formula (I), a subset of the compounds feature that R_1 is –NH-Z-R, in which Z is -C(O)-, -C(O)O-, -C(O)C(O)O-, or -C(O)C(O)NH-; R_2 is  or ;

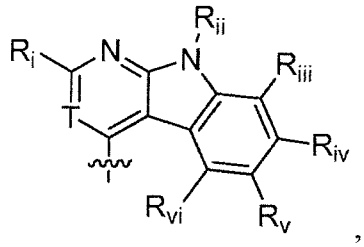
X is O; A is CH; W is $-CH_2CH_2-$, $-OCH_2-$, $-SCH_2-$, or $-SOCH_2-$; U is $-NHSO_2-$; ⎓ is a double bond; or Yis  , in which T is CH or N; R_i is phenyl or thioazolyl optionally substituted with halo, amino, C_{1-6} alkyl, or C_{1-6} alkoxyl; and each of R_{ii}, R_{iii}, R_{iv}, and R_v, independently, is H, halo, nitro, cyano, amino, C_{1-6} alkyl, C_{1-6} alkoxyl, C_{2-6} alkenyl, or C_{2-6} alkynyl, or is a moiety selected from C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, and heteroaryl, each of which is optionally mono-, di-, or tri-substituted with halo, nitro, cyano, amino, C_{1-6} alkyl, C_{1-6} alkoxyl, C_{2-6} alkenyl, C_{2-6} alkynyl, aryl, or heteroaryl, or optionally fused with C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, or heteroaryl. Examples of R_1 are –NH-C(O)O-t-Bu, –NH-C(O)O-cyclopentyl, and–NH-C(O)-furyl.

Another subset of the compounds feature that Y is

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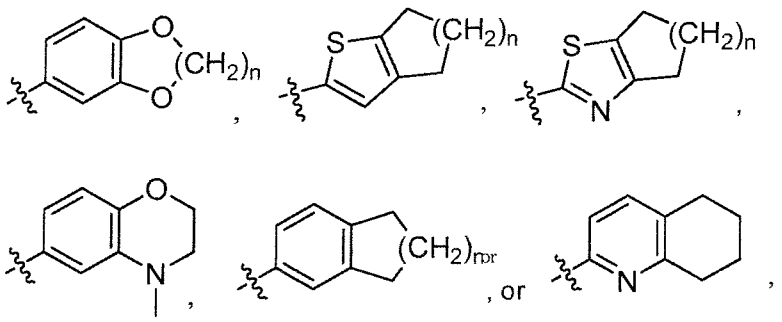
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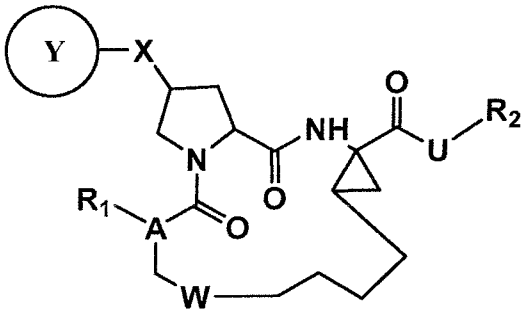
wherein each of R_i, R_{ii}, R_{iii}, R_{iv}, R_v, and R_{vi}, independently, is H, halo, nitro, cyano, amino, C_{1-6} alkyl, C_{1-6} alkoxyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, or heteroaryl, each of cycloalkyl, heterocycloalkyl, aryl, and heteroaryl being optionally mono-, di- or tri-substituted with halo, nitro, cyano, amino, C_{1-6} alkyl, C_{1-6} alkoxyl, C_{2-6} alkenyl, C_{2-6} alkynyl, aryl, or heteroaryl; and optionally fused with C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, or heteroaryl.

In the above compounds, R_i can be, e.g.,



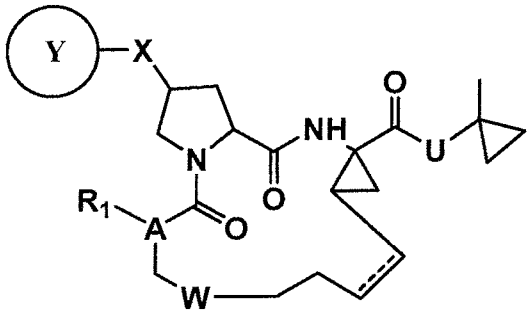
in which the n is 1 or 2.

In one embodiment, the compounds of this invention have the following formula:



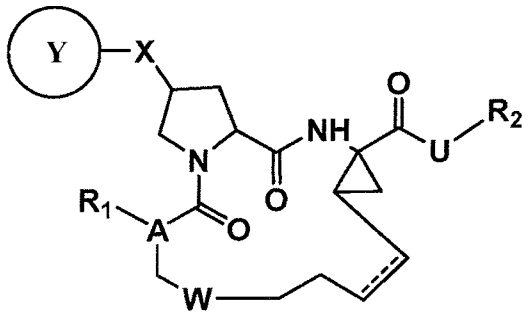
wherein R_1, R_2, A, U, W, X, and Y are as defined above.

In another embodiment, the compounds of this invention have the following formula:



wherein R_1, A, U, W, X, and Y are as defined above.

In yet another embodiment, the compounds of this invention have the following formula:



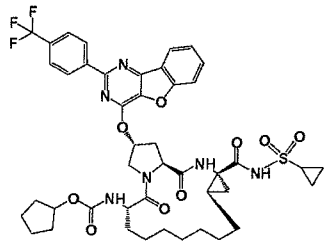
wherein R_1 is -H, -OH, C_{1-6} alkyl, C_{1-6} alkoxyl, C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, heteroaryl, or -Z-R; in which R is H, or is a moiety selected from C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, and heteroaryl, each of which is optionally mono-, di-, or tri-substituted with halo, nitro, cyano, amino, C_{1-6} alkyl, C_{1-6} alkoxyl, C_{2-6} alkenyl, C_{2-6} alkynyl, aryl, or heteroaryl; and Z is -C(O)-, -C(O)O-, -C(O)C(O)O-, -C(O)C(O)NH-, -C(O)NR'-, -OC(S)-, - C(S)NR'-, or -C(NH)O-, R' being H, C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, or heteroaryl; and R_2, A, U, W, X, and Y are as defined above.

The term "alkyl" refers to a saturated, linear or branched hydrocarbon moiety, such as $-CH_3$ or $-CH(CH_3)_2$. The term "alkoxy" refers to an -O-(C_{1-6} alkyl) radical. The term "alkenyl" refers to a linear or branched hydrocarbon moiety that contains at least one double bond, such as $-CH=CH-CH_3$. The term "alkynyl" refers to a linear or

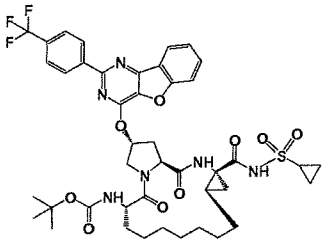
branched hydrocarbon moiety that contains at least one triple bond, such as -C≡C-CH_3. The term "cycloalkyl" refers to a saturated, cyclic hydrocarbon moiety, such as cyclohexyl. The term "cycloalkenyl" refers to a non-aromatic, cyclic hydrocarbon moiety that contains at least one double bond, such as cyclohexenyl. The term "heterocycloalkyl" refers to a saturated, cyclic moiety having at least one ring heteroatom (e.g., N, O, or S), such as 4-tetrahydropyranyl. The term "heterocycloalkenyl" refers to a non-aromatic, cyclic moiety having at least one ring heteroatom (e.g., N, O, or S) and at least one ring double bond, such as pyranyl. The term "aryl" refers to a hydrocarbon moiety having one or more aromatic rings. Examples of aryl moieties include phenyl (Ph), phenylene, naphthyl, naphthylene, pyrenyl, anthryl, and phenanthryl. The term "heteroaryl" refers to a moiety having one or more aromatic rings that contain at least one heteroatom (e.g., N, O, or S). Examples of heteroaryl moieties include furyl, furylene, fluorenyl, pyrrolyl, thienyl, oxazolyl, imidazolyl, thiazolyl, pyridyl, pyrimidinyl, quinazolinyl, quinolyl, isoquinolyl and indolyl. The term "amino" refers to a radical of $-NH_2$, -NH-(C_{1-6} alkyl), or -N(C_{1-6} alkyl)$_2$.

Alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, and heteroaryl mentioned herein include both substituted and unsubstituted moieties, unless specified otherwise. Possible substituents on cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, and heteroaryl include, but are not limited to, C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_2-C_{10} alkynyl, C_3-C_{20} cycloalkyl, C_3-C_{20} cycloalkenyl, C_1-C_{20} heterocycloalkyl, C_1-C_{20} heterocycloalkenyl, C_1-C_{10} alkoxy, aryl, aryloxy, heteroaryl, heteroaryloxy, amino, C_1-C_{10} alkylamino, C_1-C_{20} dialkylamino, arylamino, diarylamino, C_1-C_{10} alkylsulfonamino, arylsulfonamino, C_1-C_{10} alkylimino, arylimino, C_1-C_{10} alkylsulfonimino, arylsulfonimino, hydroxyl, halo, thio, C_1-C_{10} alkylthio, arylthio, C_1-C_{10} alkylsulfonyl, arylsulfonyl, acylamino, aminoacyl, aminothioacyl, amidino, guanidine, ureido, cyano, nitro, nitroso, azido, acyl, thioacyl, acyloxy, carboxyl, and carboxylic ester. On the other hand, possible substituents on alkyl, alkenyl, or alkynyl include all of the above-recited substituents except C_1-C_{10} alkyl. Cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, and heteroaryl can also be fused with each other.

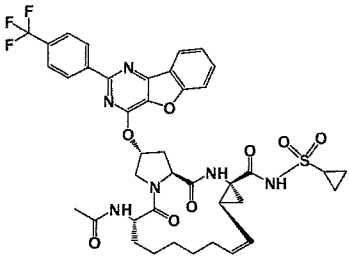
Shown below are 281 exemplary compounds of this invention.



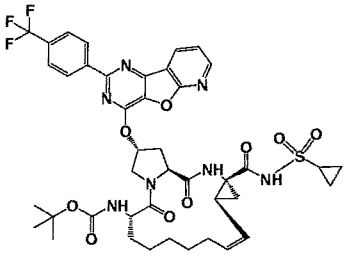
Compound 1



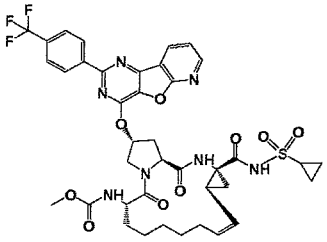
Compound 2



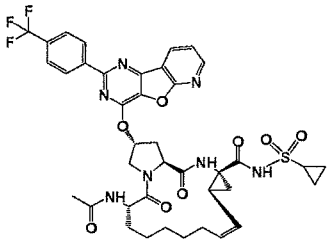
Compound 3



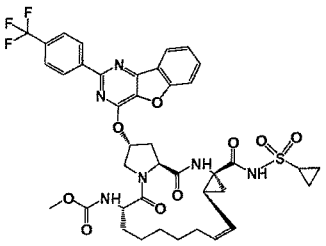
Compound 4



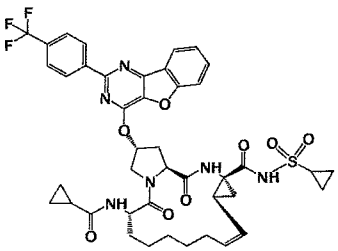
Compound 5



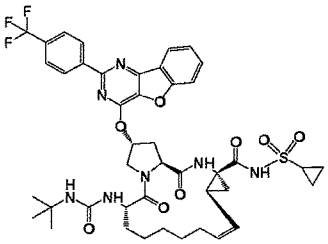
Compound 6



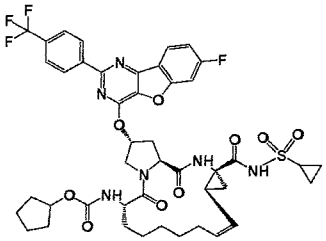
Compound 7



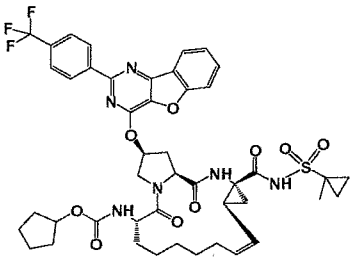
Compound 8



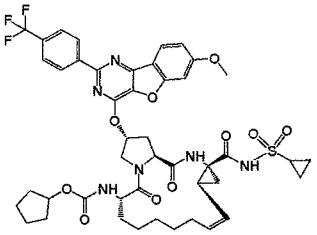
Compound 9



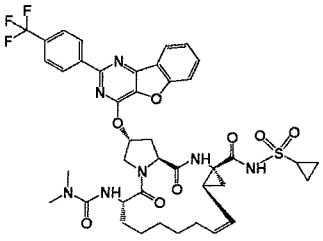
Compound 10



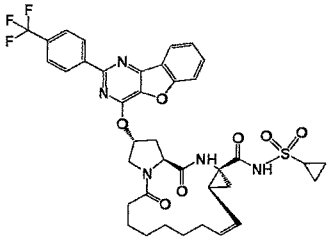
Compound 11



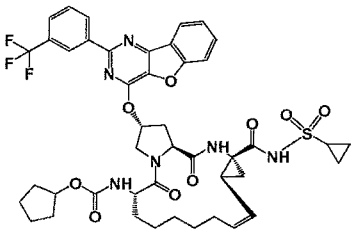
Compound 12



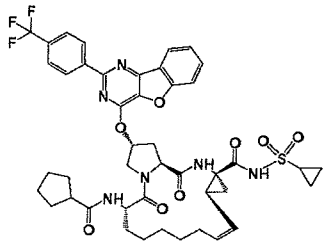
Compound 13



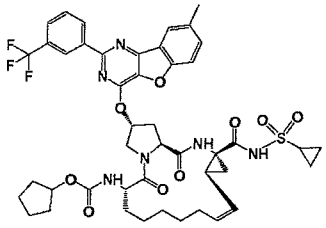
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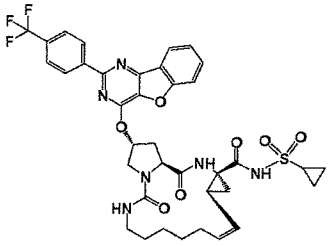
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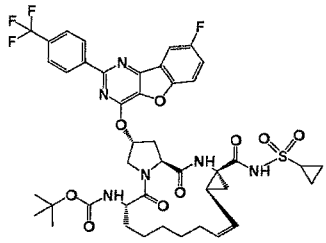
Compound 16



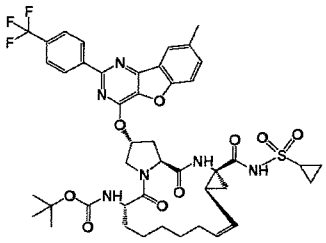
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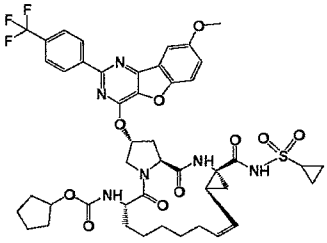
Compound 18



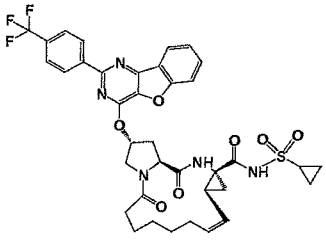
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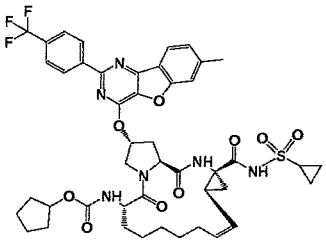
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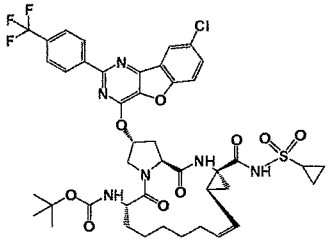
Compound 21



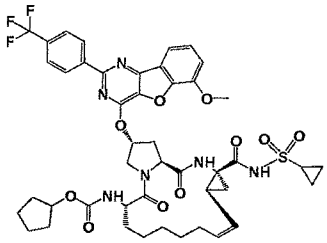
Compound 22



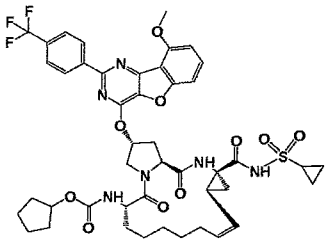
Compound 23



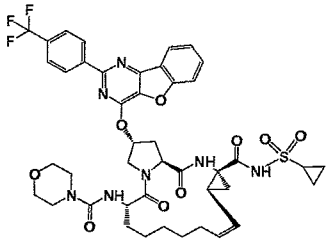
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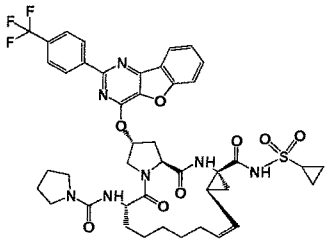
Compound 25



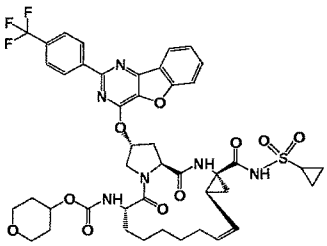
Compound 26



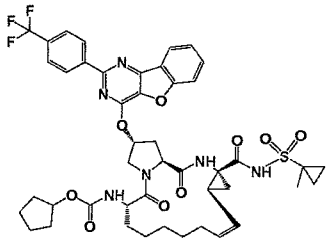
Compound 27



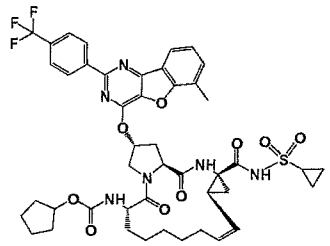
Compound 28



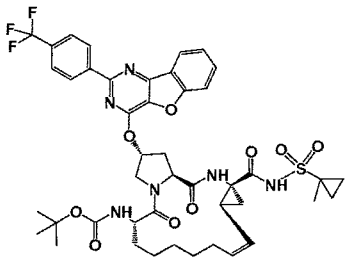
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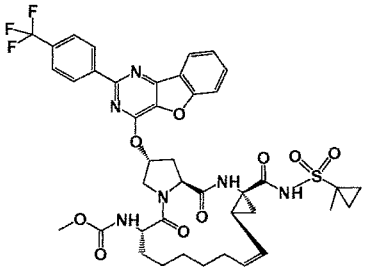
Compound 30



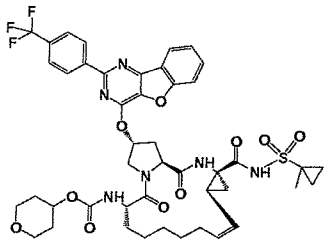
Compound 31



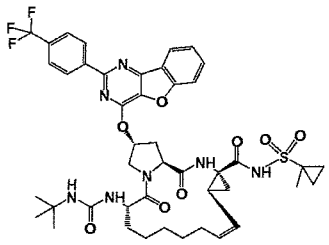
Compound 32



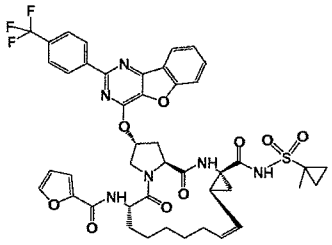
Compound 33



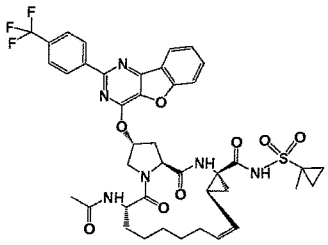
Compound 34



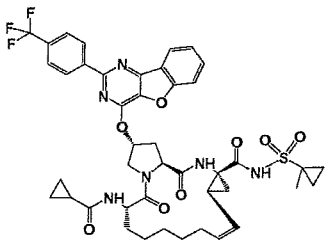
Compound 35



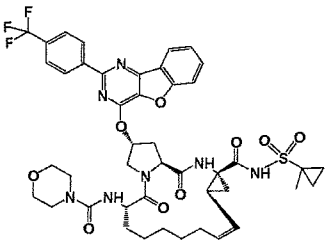
Compound 36



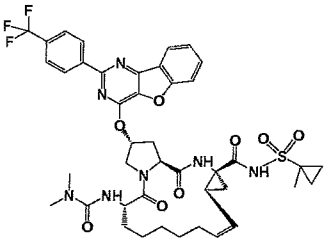
Compound 37



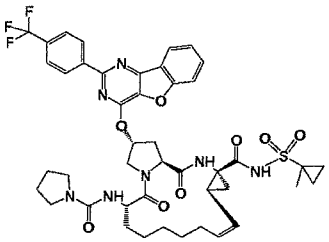
Compound 38



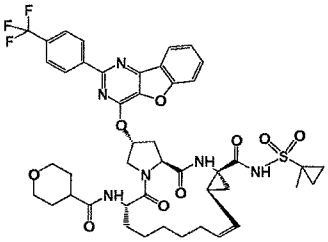
Compound 39



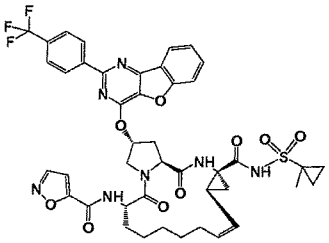
Compound 40



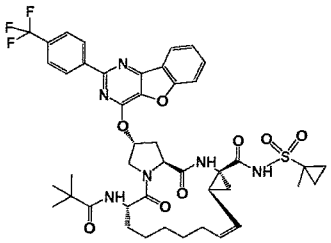
Compound 41



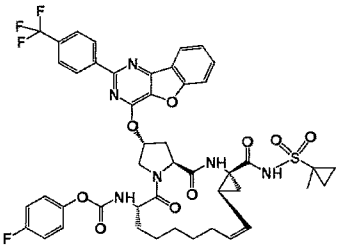
Compound 42



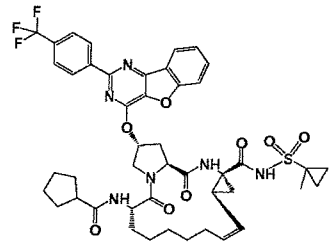
Compound 43



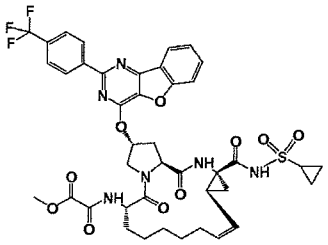
Compound 44



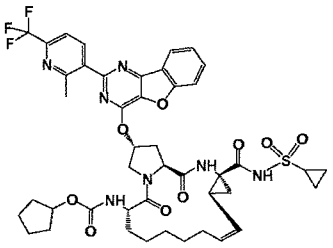
Compound 45



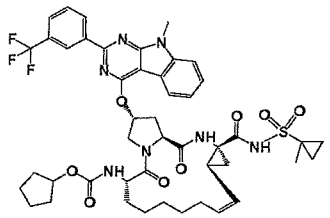
Compound 46



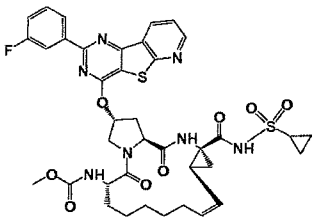
Compound 47



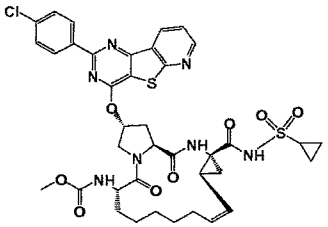
Compound 48



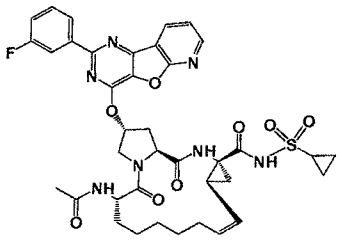
Compound 49



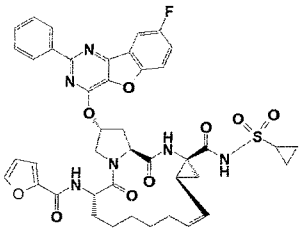
Compound 50



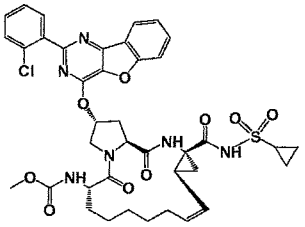
Compound 51



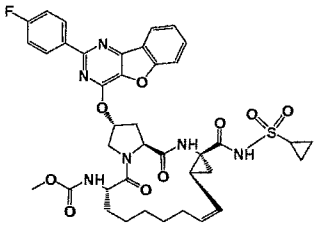
Compound 52



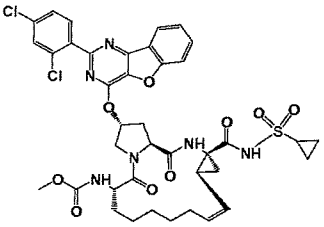
Compound 53



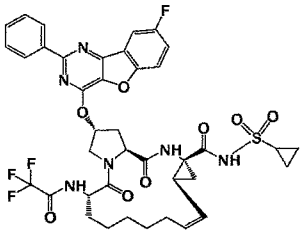
Compound 54



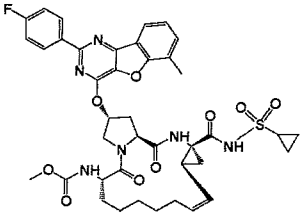
Compound 55



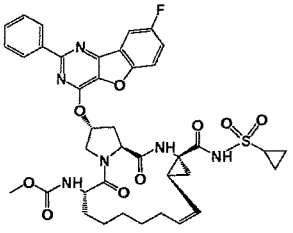
Compound 56



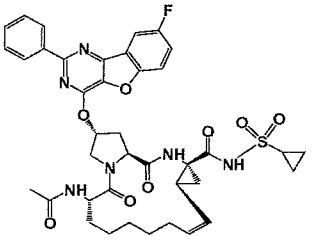
Compound 57



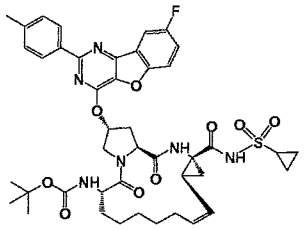
Compound 58



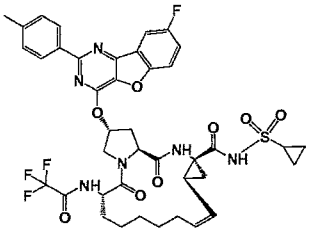
Compound 59



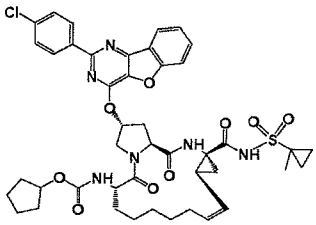
Compound 60



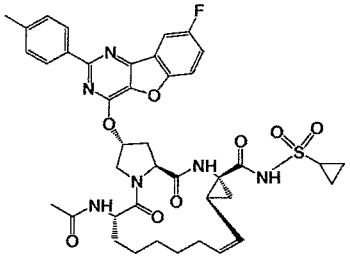
Compound 61



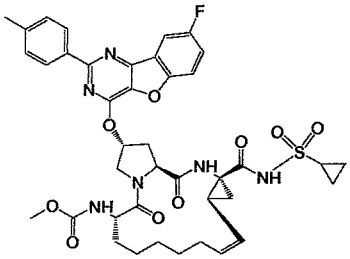
Compound 62



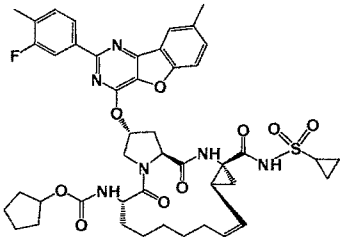
Compound 63



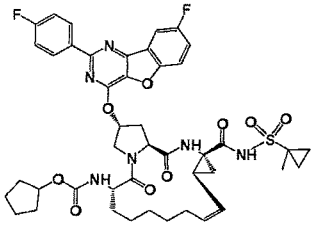
Compound 64



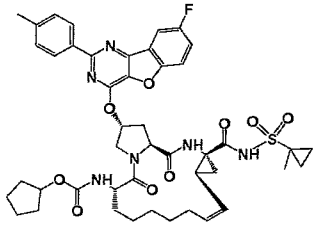
Compound 65



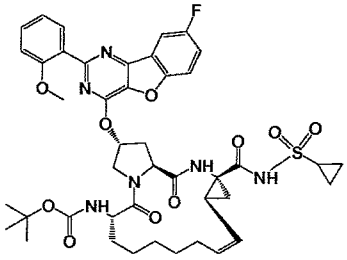
Compound 66



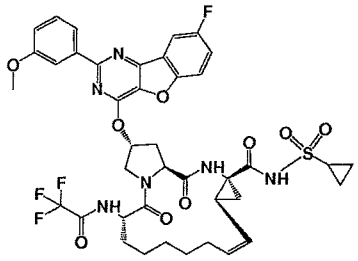
Compound 67



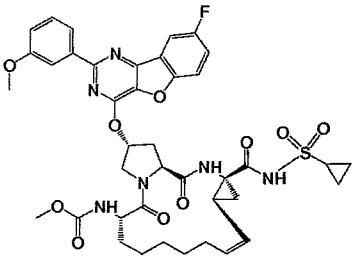
Compound 68



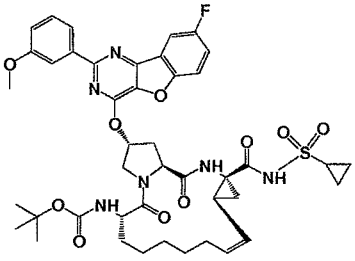
Compound 69



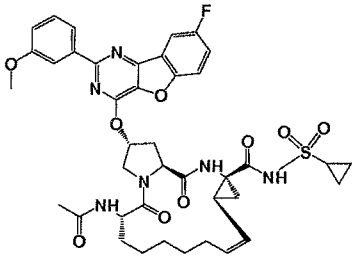
Compound 70



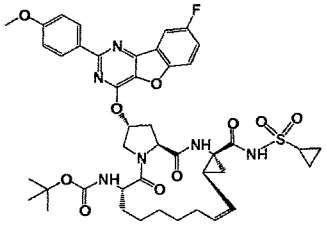
Compound 71



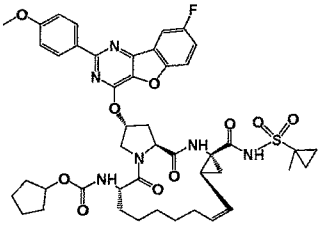
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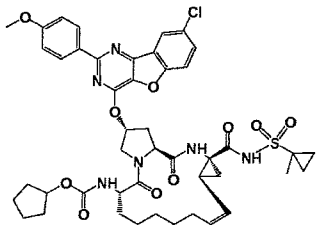
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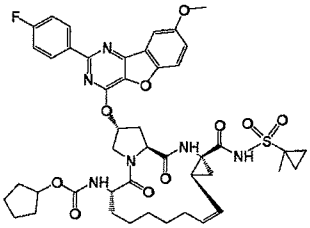
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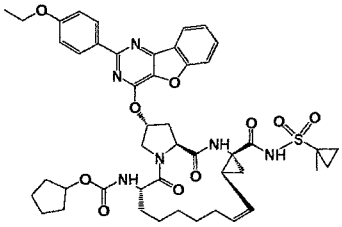
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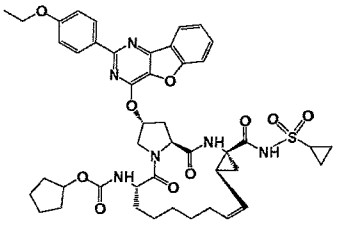
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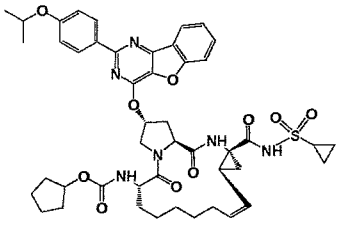
Compound 77



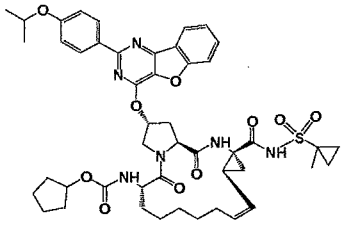
Compound 78



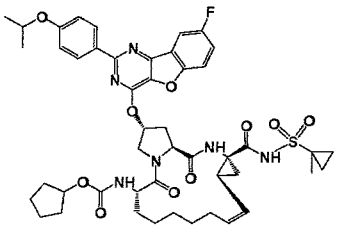
Compound 79



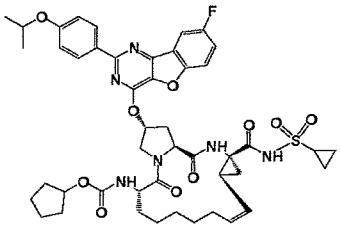
Compound 80



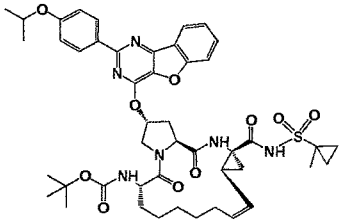
Compound 81



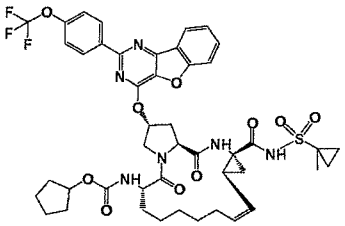
Compound 82



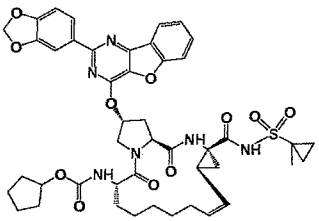
Compound 83



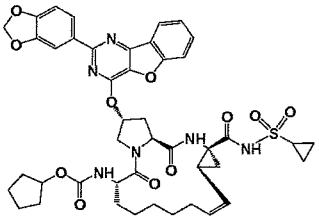
Compound 84



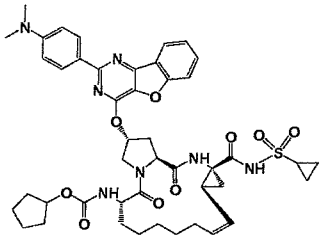
Compound 85



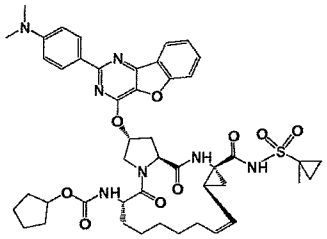
Compound 86



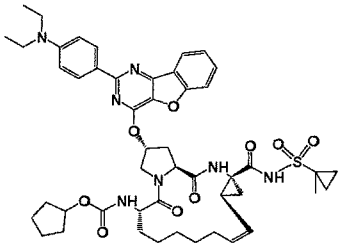
Compound 87



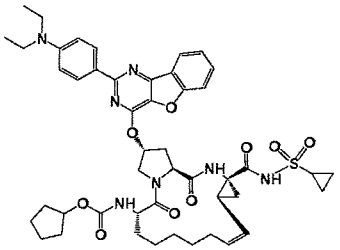
Compound 88



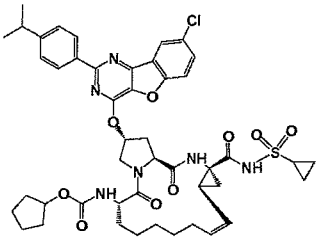
Compound 89



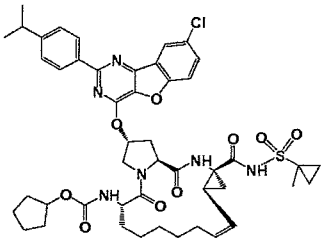
Compound 90



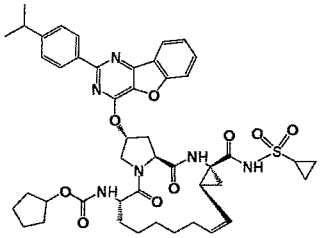
Compound 91



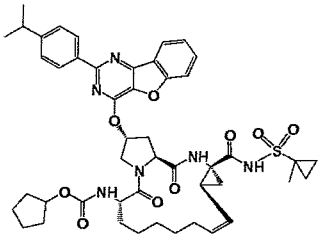
Compound 92



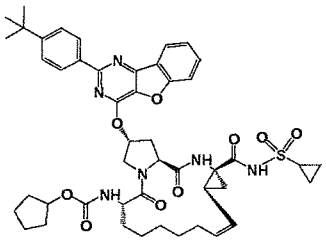
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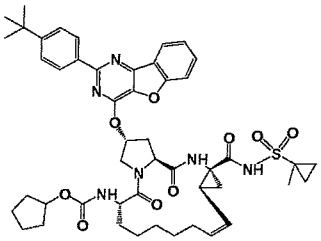
Compound 94



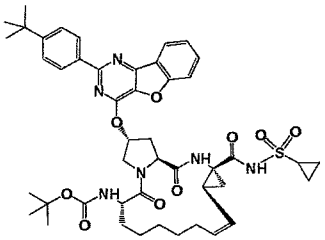
Compound 95



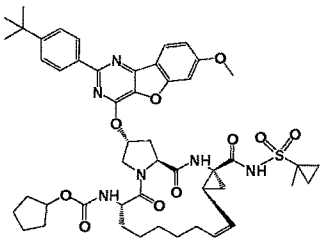
Compound 96



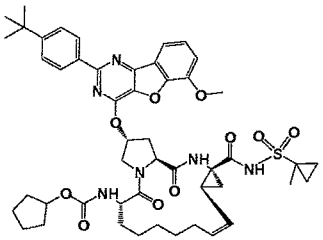
Compound 97



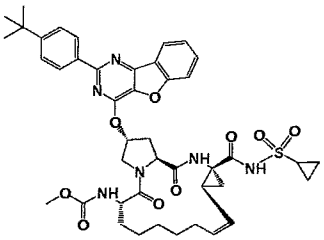
Compound 98



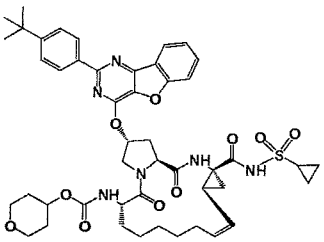
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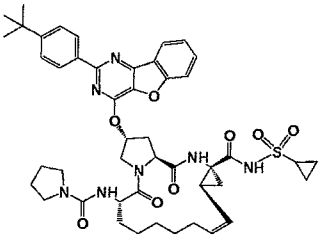
Compound 100



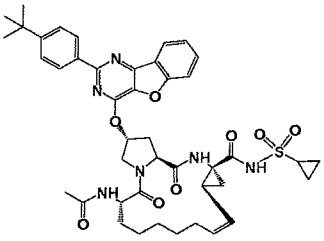
Compound 101



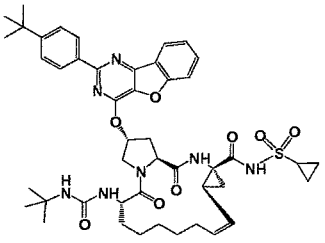
Compound 102



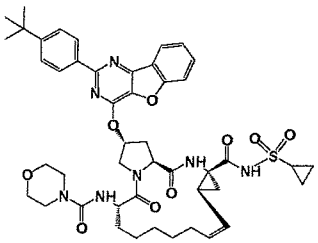
Compound 103



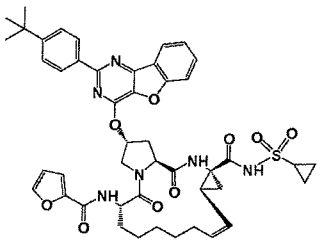
Compound 104



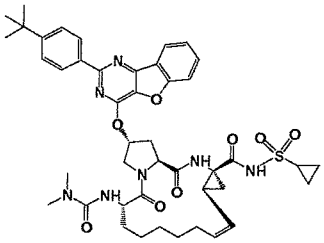
Compound 105



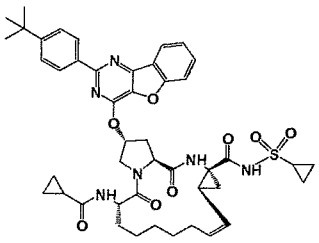
Compound 106



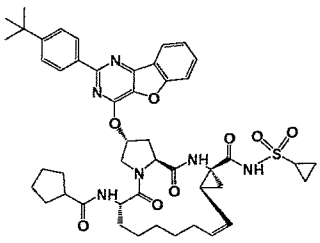
Compound 107



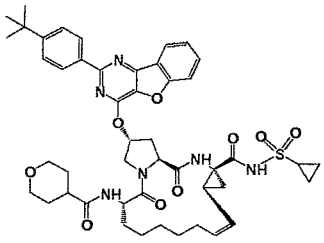
Compound 108



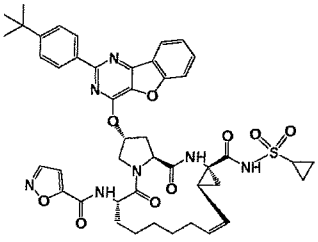
Compound 109



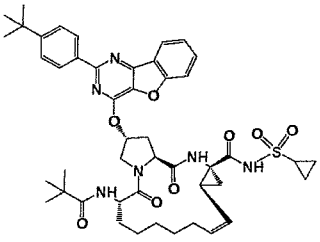
Compound 110



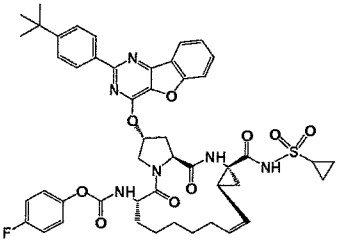
Compound 111



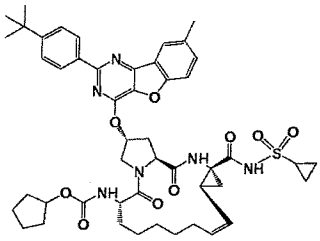
Compound 112



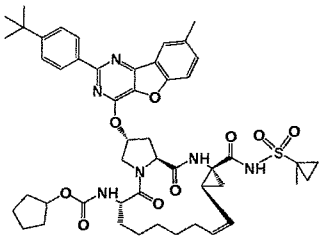
Compound 113



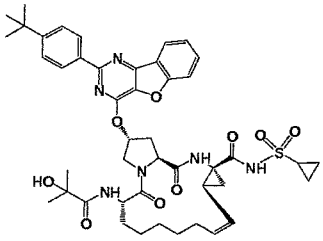
Compound 114



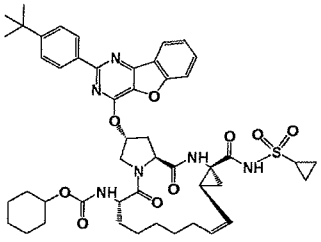
Compound 115



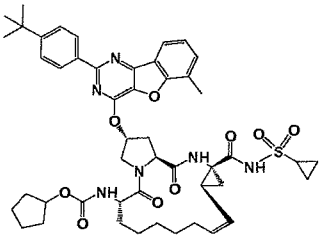
Compound 116



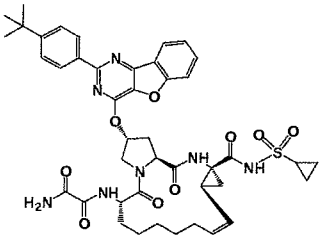
Compound 117



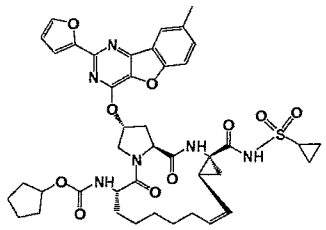
Compound 118



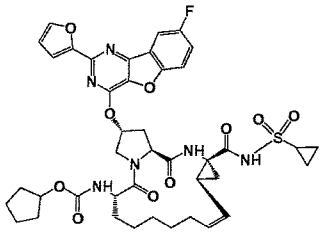
Compound 119



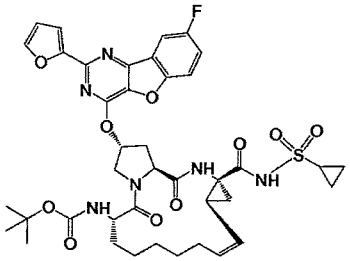
Compound 120



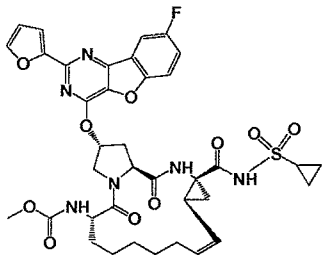
Compound 121



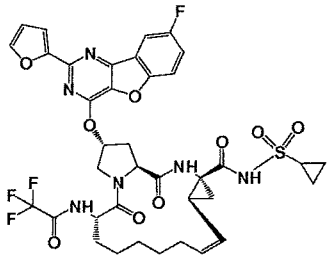
Compound 122



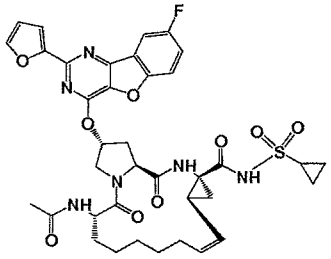
Compound 123



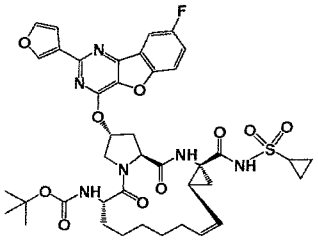
Compound 124



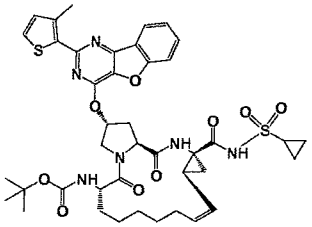
Compound 125



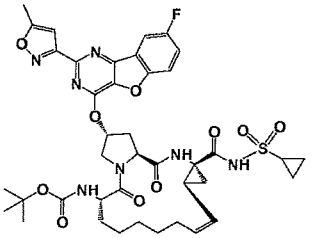
Compound 126



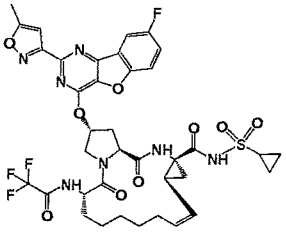
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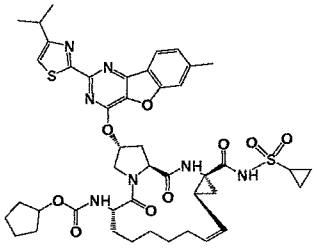
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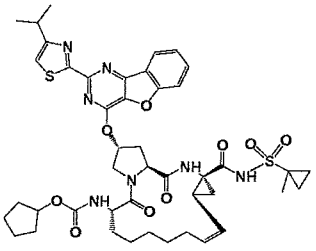
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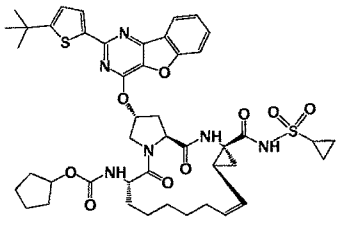
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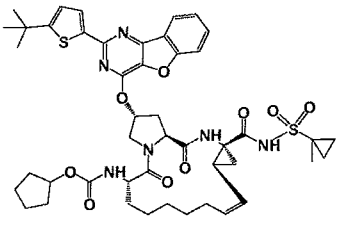
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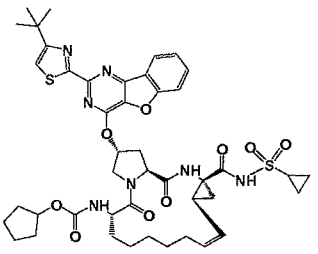
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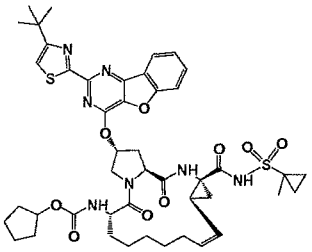
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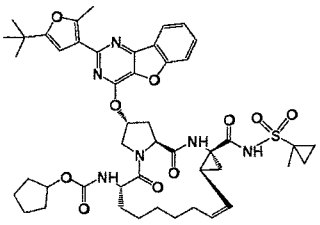
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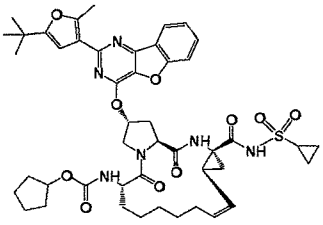
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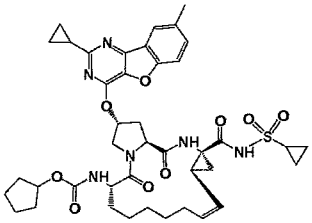
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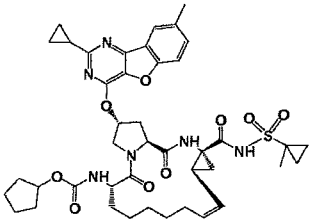
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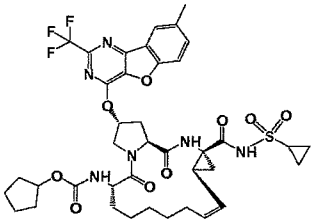
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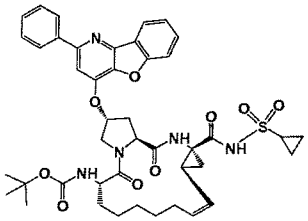
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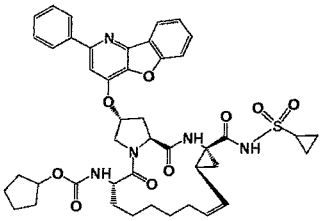
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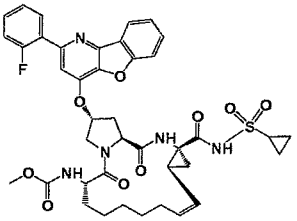
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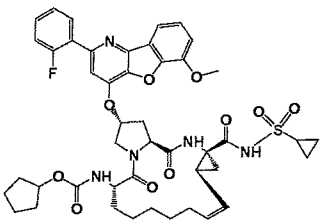
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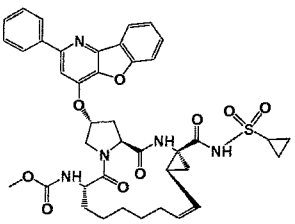
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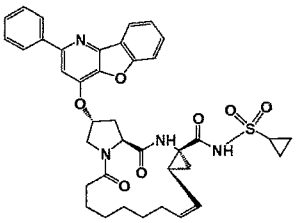
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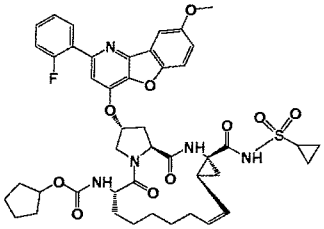
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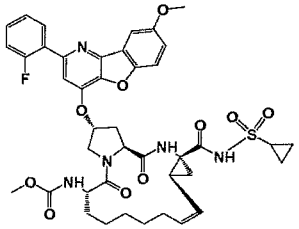
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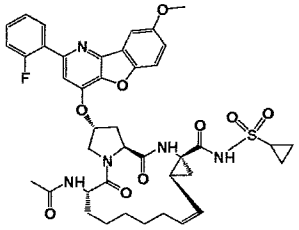
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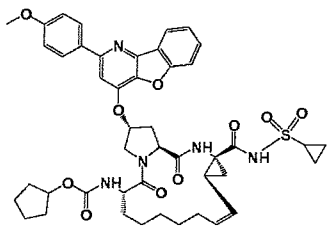
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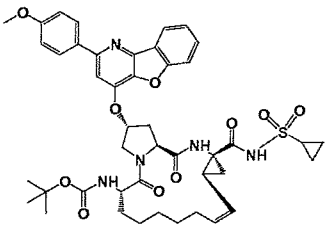
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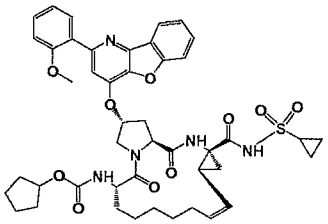
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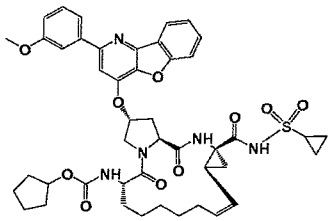
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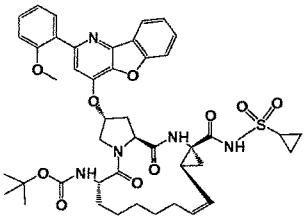
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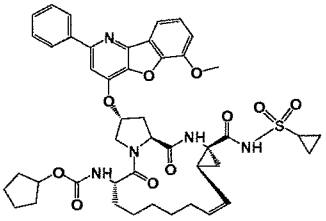
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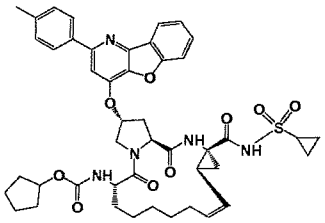
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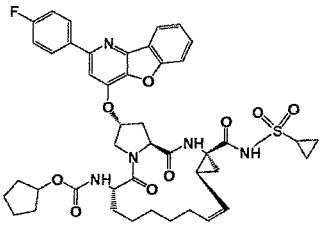
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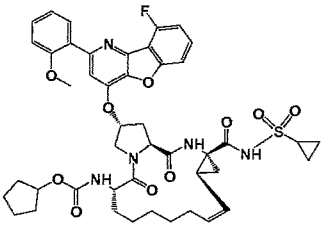
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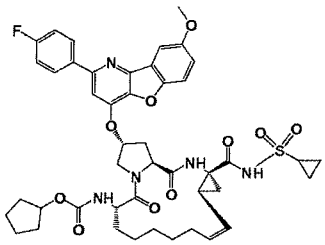
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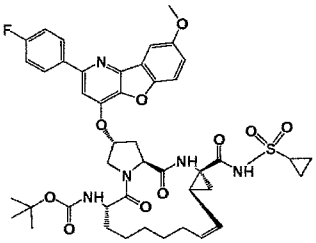
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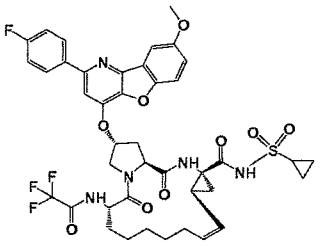
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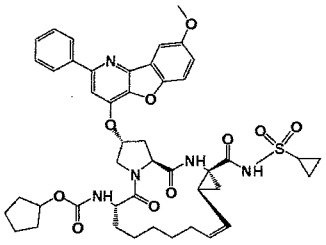
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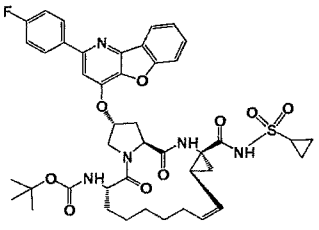
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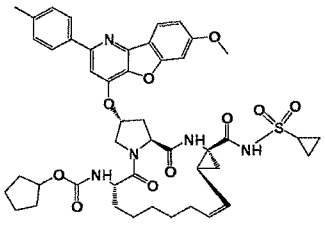
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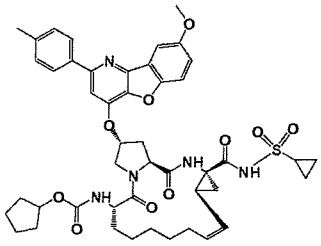
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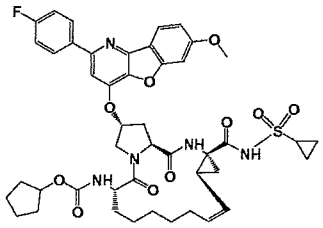
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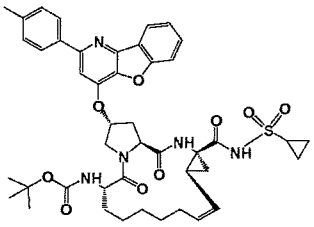
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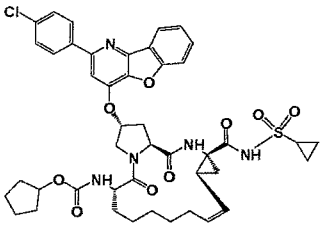
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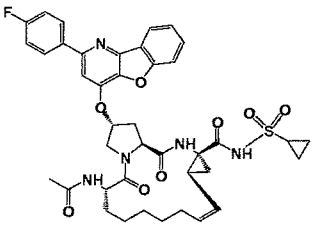
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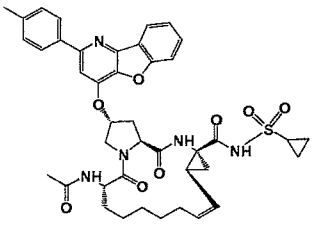
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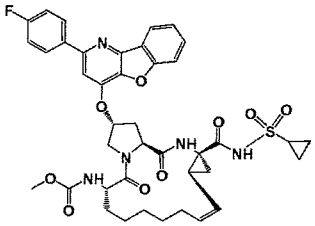
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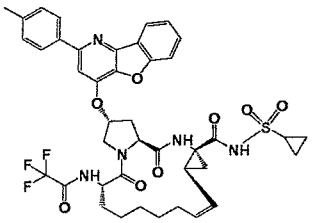
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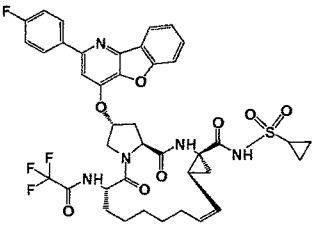
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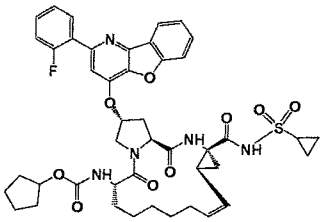
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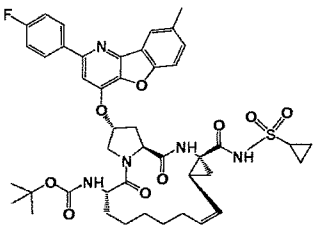
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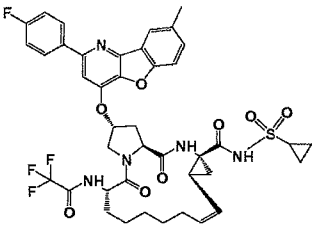
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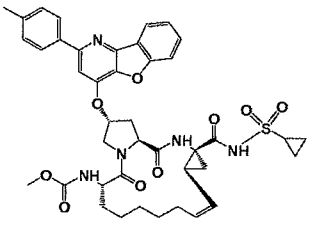
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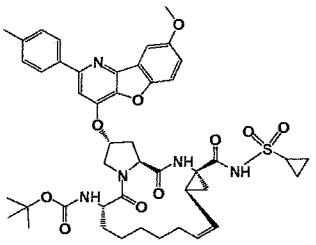
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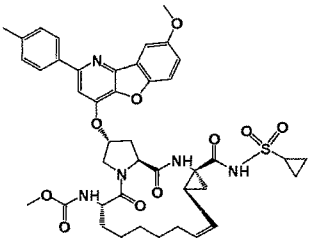
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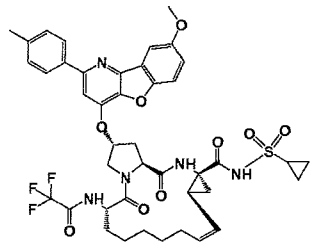
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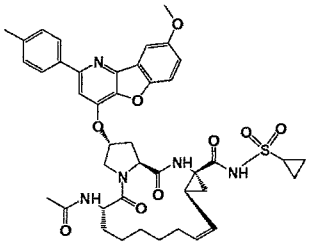
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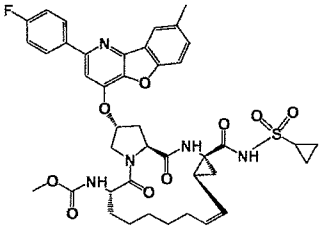
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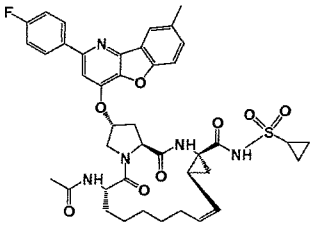
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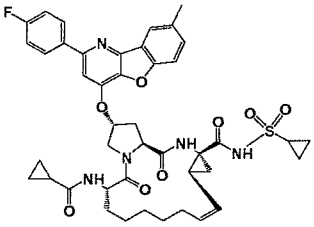
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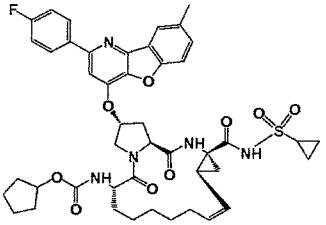
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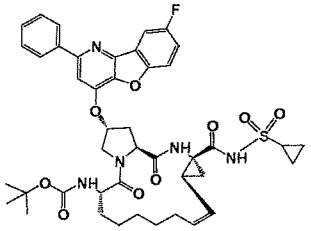
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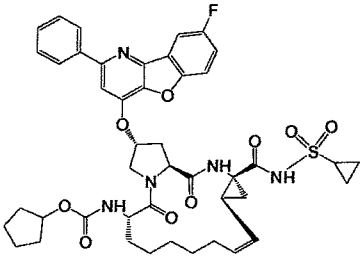
Compound 185



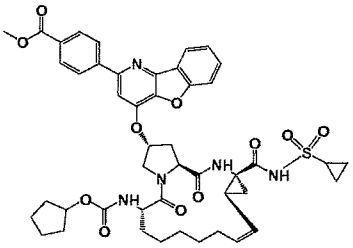
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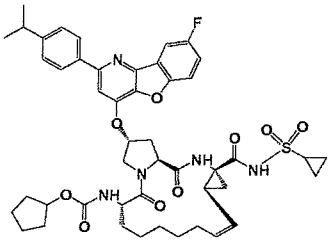
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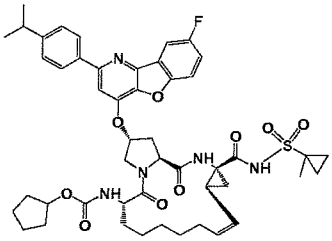
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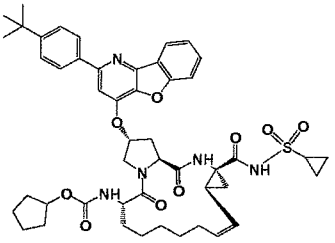
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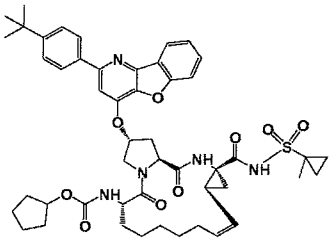
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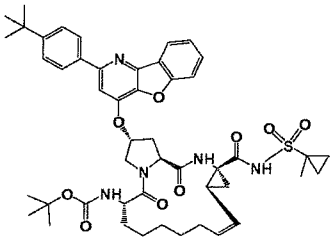
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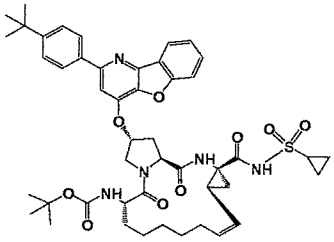
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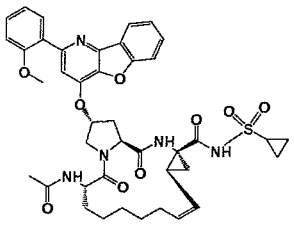
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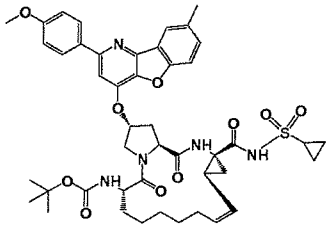
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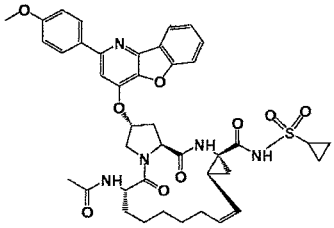
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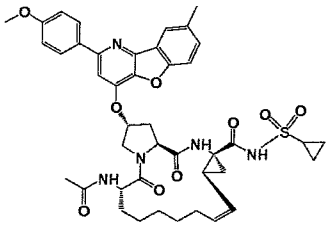
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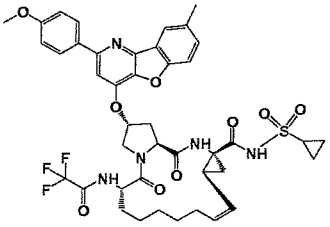
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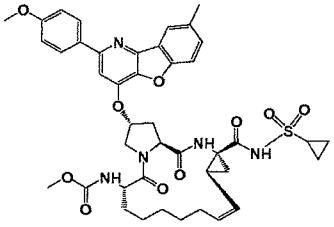
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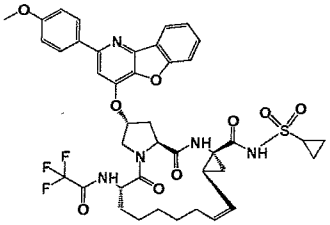
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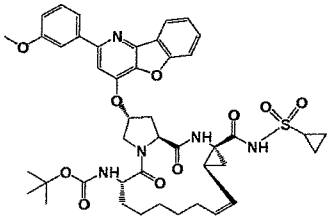
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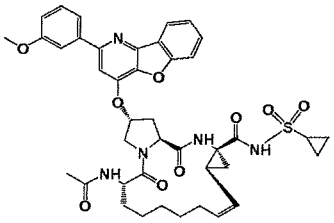
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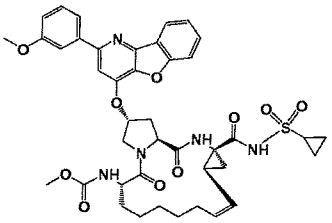
Compound 202



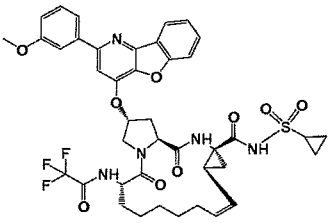
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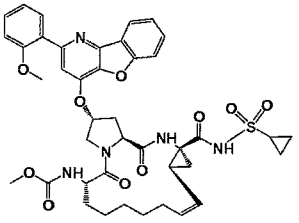
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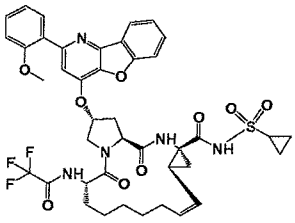
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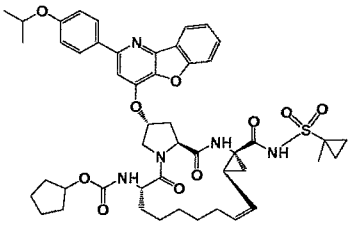
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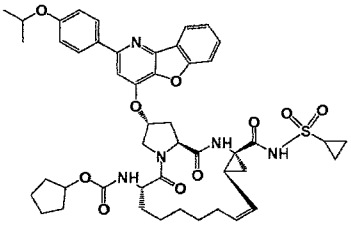
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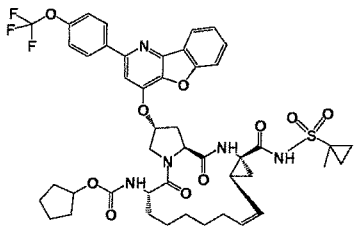
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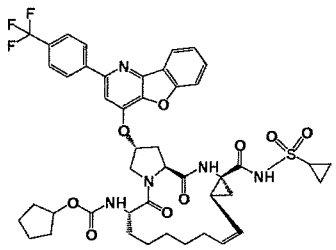
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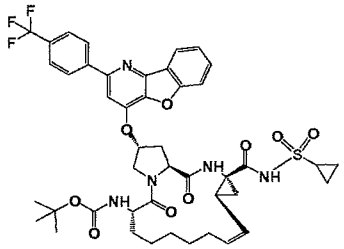
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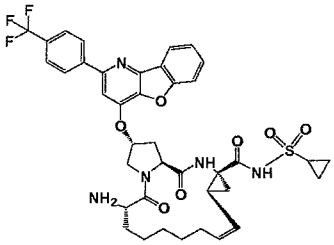
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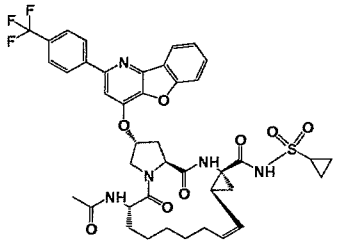
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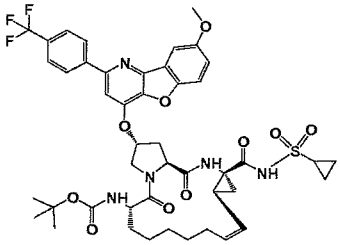
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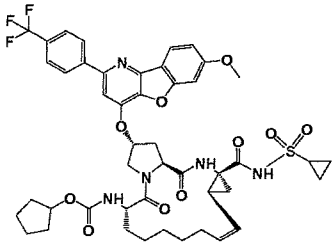
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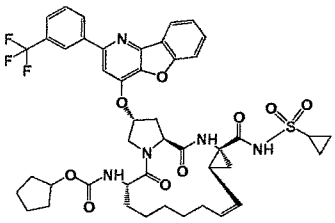
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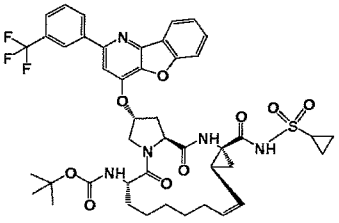
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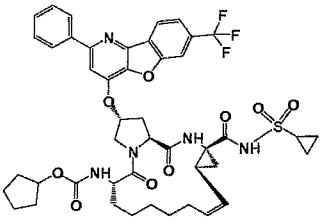
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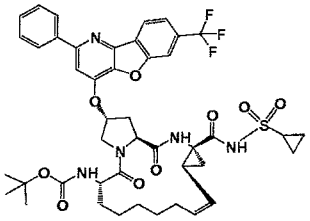
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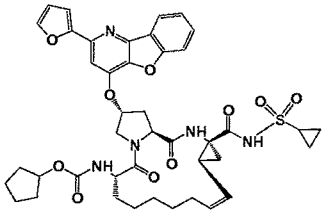
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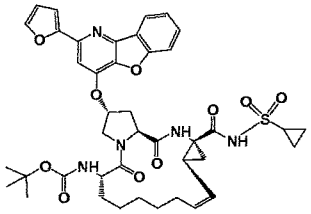
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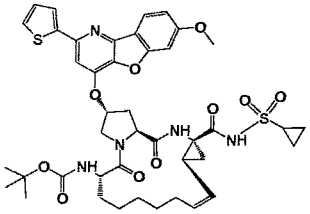
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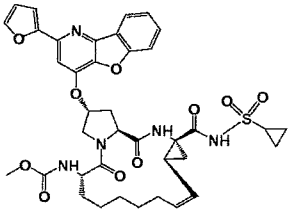
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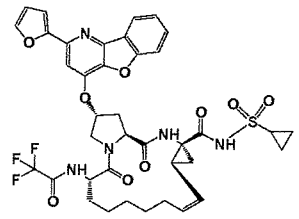
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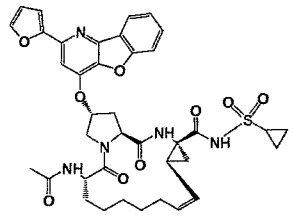
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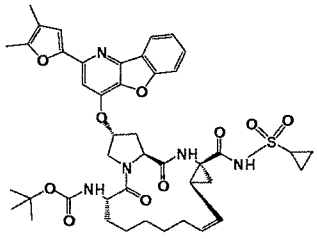
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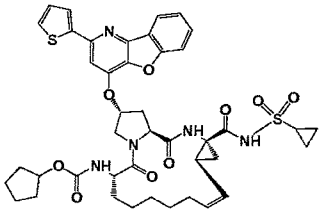
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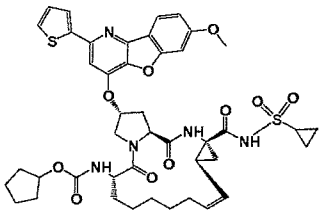
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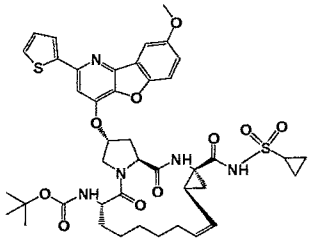
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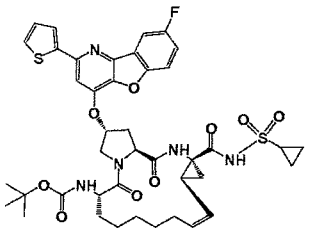
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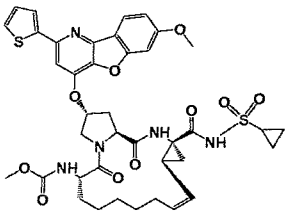
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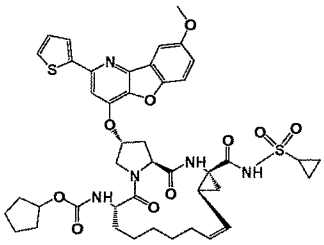
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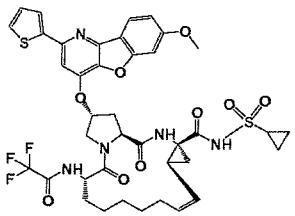
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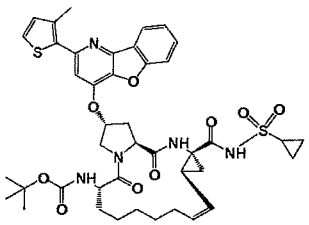
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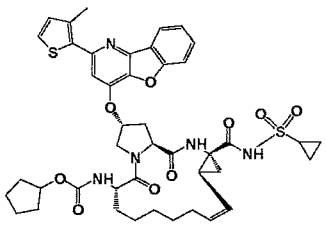
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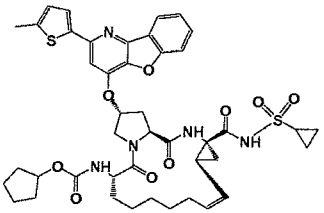
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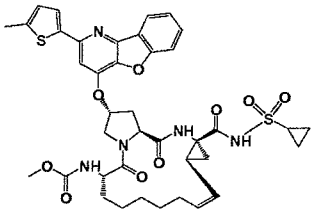
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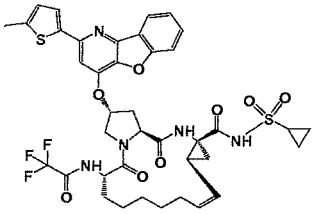
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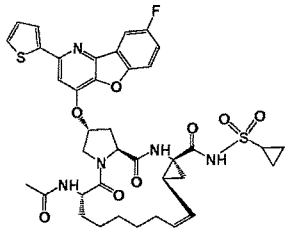
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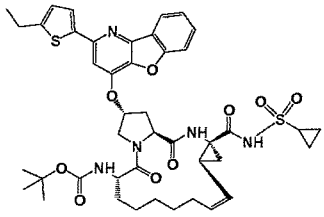
Compound 239



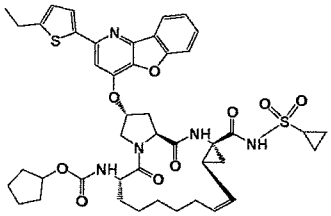
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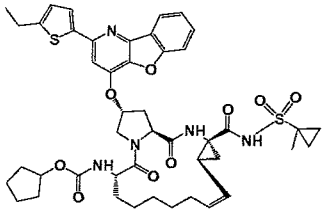
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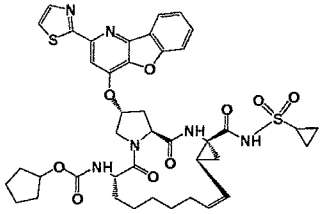
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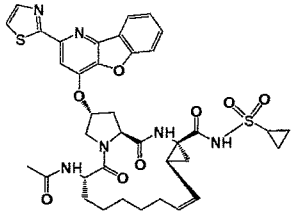
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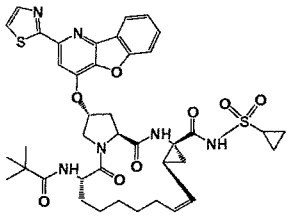
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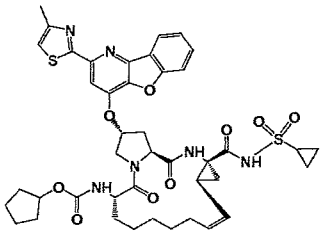
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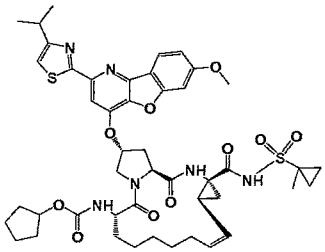
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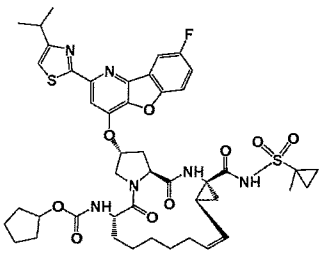
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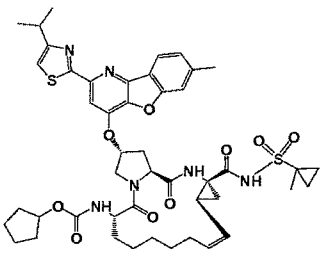
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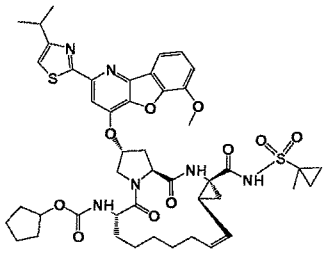
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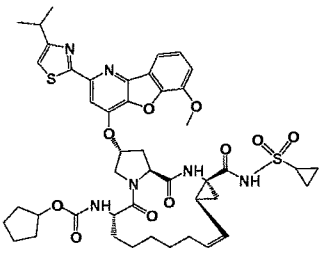
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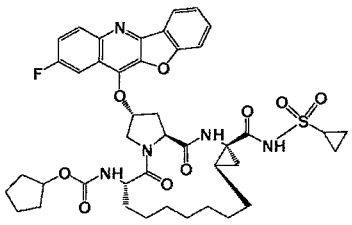
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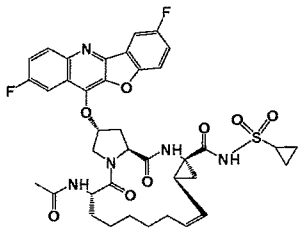
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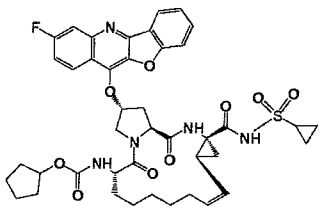
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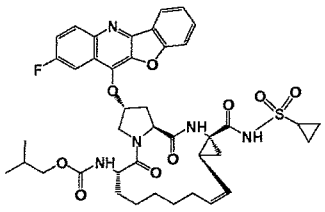
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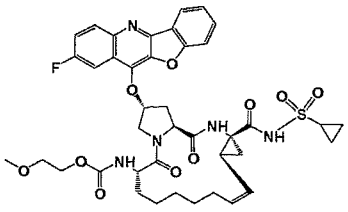
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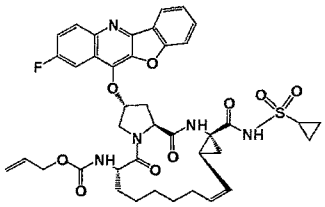
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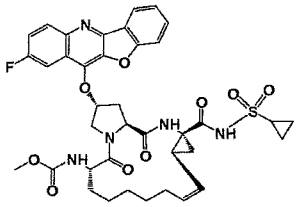
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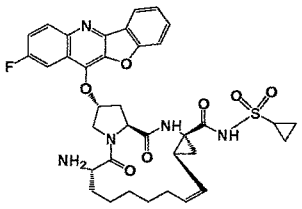
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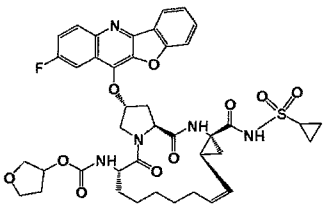
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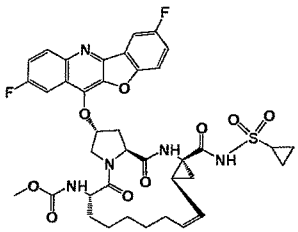
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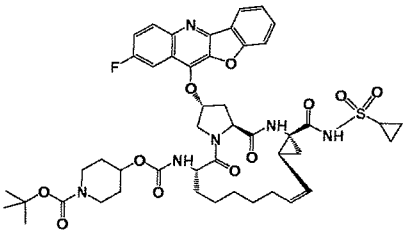
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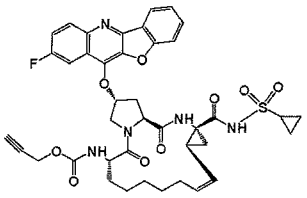
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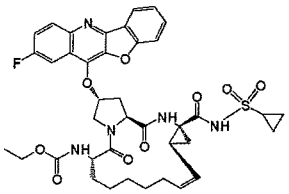
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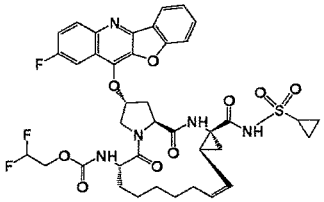
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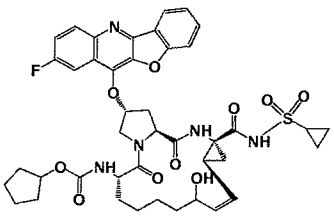
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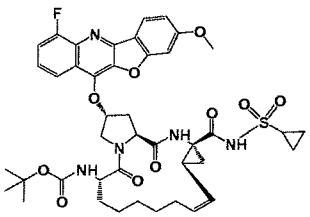
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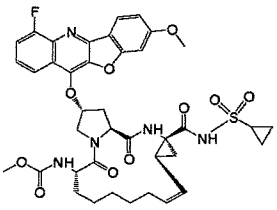
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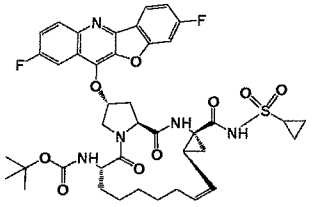
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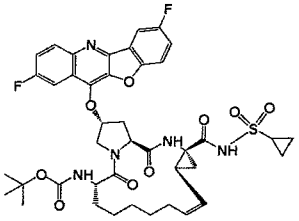
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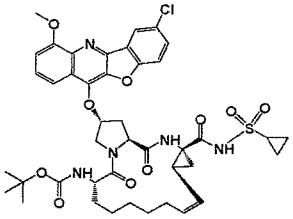
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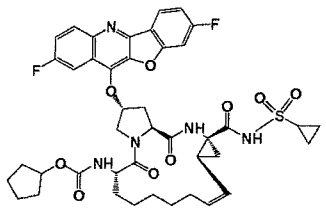
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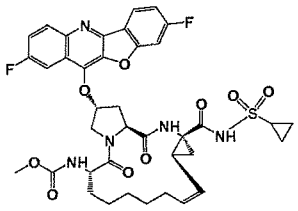
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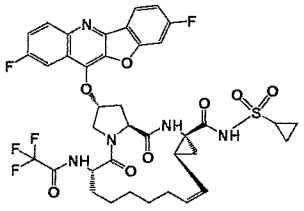
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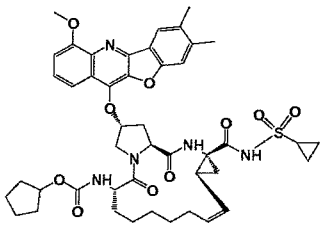
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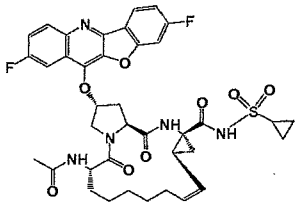
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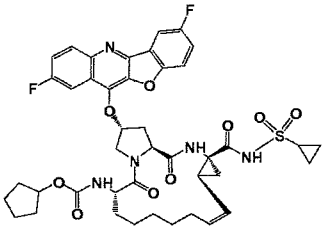
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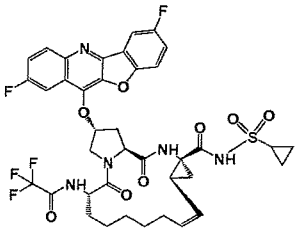
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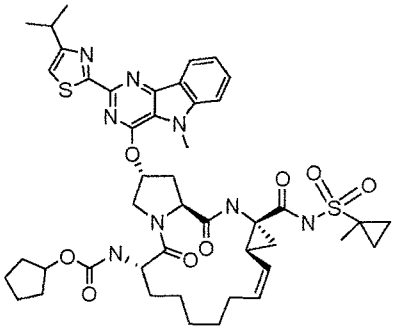
Compound 278



Compound 279



Compound 280



Compound 281

In another aspect, this invention relates to a method for treating hepatitis C virus infection. The method includes administering to a subject in need thereof an effective amount of compound of formula (I) shown above.

In still another aspect, this invention relates to a pharmaceutical composition for use in treating HCV infection. The composition contains an effective amount of at least one of the compounds of formula (I) and a pharmaceutically acceptable carrier. It may include an inhibitor of a target other than HCV NS3 protease in the HCV life cycle, e.g., NS5B polymerase, NS5A, NS4B, or p7.

Examples of such agents include, but are not limited to, N-[3-(1-cyclobutylmethyl-4-hydroxy-2-oxo-1,2-dihydro-quinolin-3-yl)-1,1-dioxo-1,4-dihydro-1l6-benzo[1,2,4]thiadiazin-7-yl]-methanesulfonamide (WO04041818), trans-1,2-di-4-

[(phenylacetyl-pyrrolidine-2-(S)-carbonyl) amino]-phenylethylene (WO0401413), and 1-aminoadamantane (Amentadine, Griffin, 2004, J. Gen. Virol. 85: p451). The pharmaceutical composition may also contain an immunomodulatory agent or a second antiviral agent. An immunomodulatory agent refers to an active agent that mediates the immune response. Examples of immunomodulatory agents include, but are not limited to, Nov-205 (Novelos Therapeutics Inc., WO02076490) and IMO-2125 (Idera Pharmaceuticals Inc., WO05001055). An antiviral agent refers to an active agent that kills a virus or suppresses its replication. Examples of antiviral agents include, but are not limited to, ribavirin, ribamidin, interferon-α, pegylated interferon, and HCV protease inhibitors, such as 2-(2-{2-cyclohexyl-2-[(pyrazine-2-carbonyl)-amino]-acetylamino}-3,3-dimethyl-butyryl)-octahydro-cyclopenta[c]pyrrole-1-carboxylic acid (1-cyclopropylaminooxalyl-butyl)-amide (Telaprevir, Vertex Pharmaceuticals Inc., WO02018369), 3-[2-(3-tert-butyl-ureido)-3,3-dimethyl-butyryl]-6,6-dimethyl-3-aza-bicyclo[3.1.0]hexane-2-carboxylic acid (2-carbamoyl-1-cyclobutylmethyl-2-oxo-ethyl)-amide (Boceprevir, Schering-Plough Research Institute, WO03062265), and 4-fluoro-1,3-dihydro-isoindole-2-carboxylic acid 14-tert-butoxycarbonylamino-4-cyclopropanesulfonylaminocarbonyl-2,15-dioxo-3,16-diaza-tricyclo[14.3.0.04,6]nonadec-7-en-18-yl ester (ITMN-191, InterMune Inc., US2005/0267018).

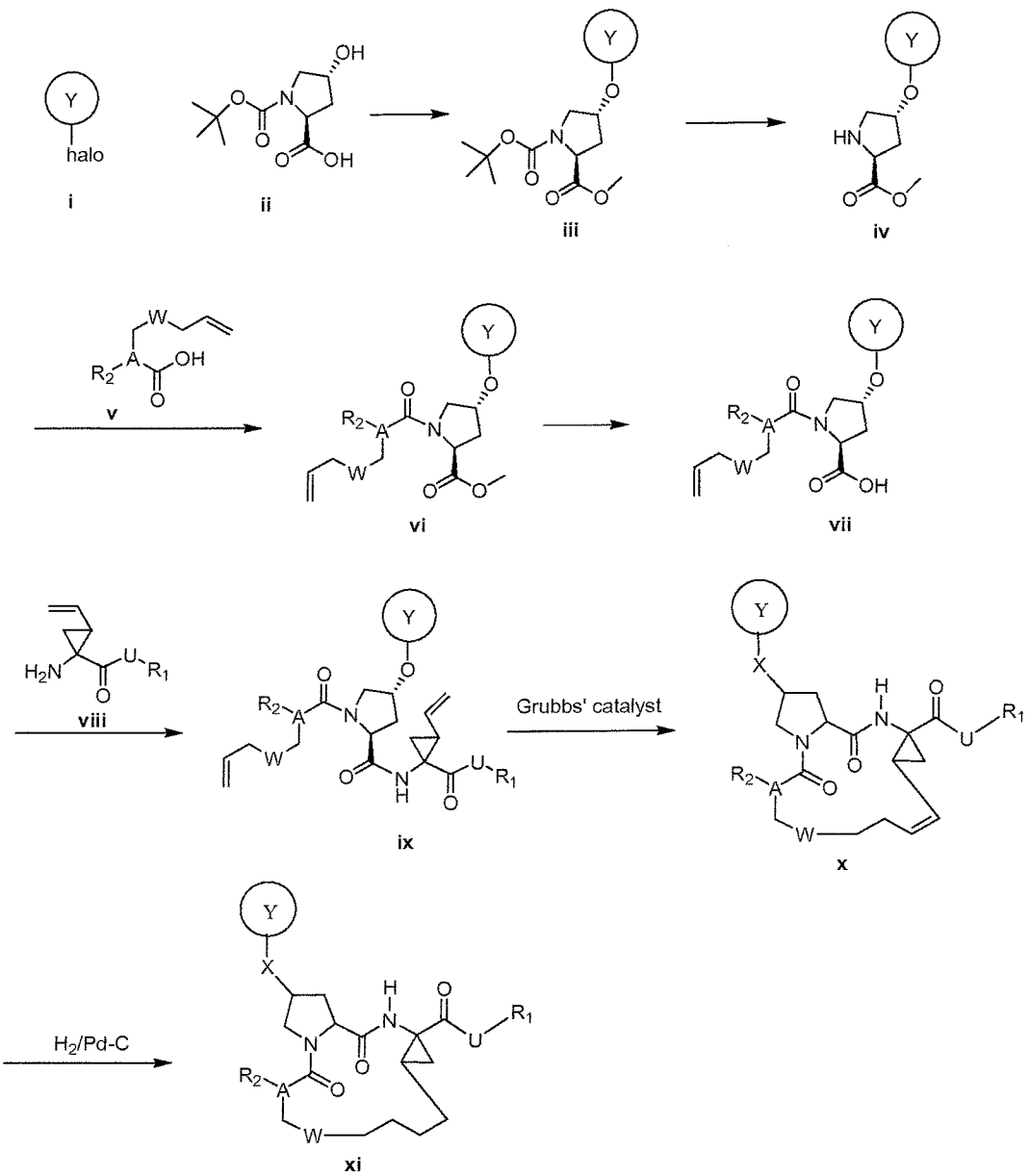
Also within the scope of this invention is the use of such a composition for treating HCV infection or for the manufacture of a medicament for the treatment.

The details of one or more embodiments of the invention are set forth in the description below. Other features, objects, and advantages of the invention will be apparent from the description and from the claims.

DETAILED DESCRIPTION

The compounds of this invention can be synthesized from commercially available starting materials by methods well known in the art. For example, one can prepare the compounds of this invention via the route shown in Scheme 1 below:

Scheme 1

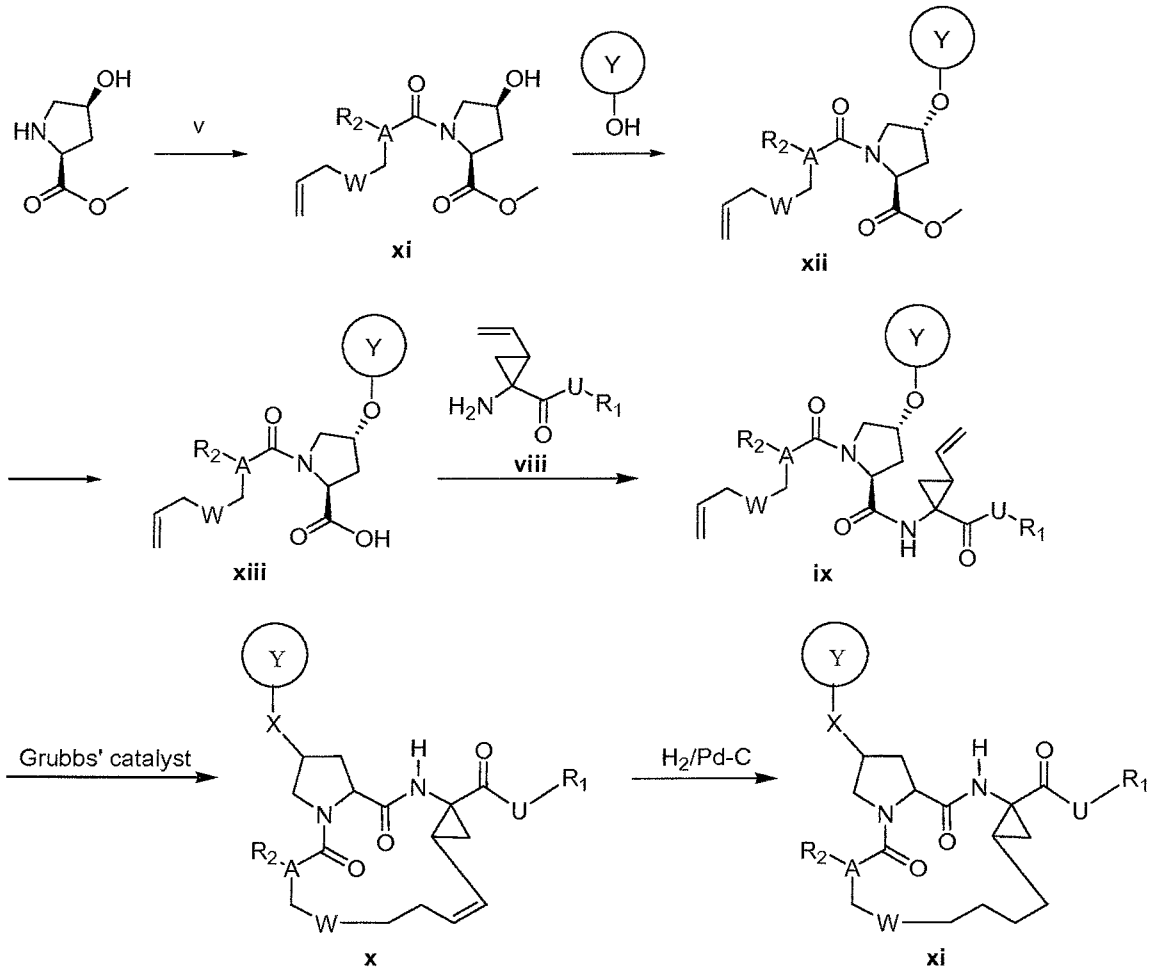


As illustrated in Scheme 1, multicyclic compound (**i**) is first coupled with N-(t-butoxycarbonyl)-L-proline (**ii**), followed by methylation, to form intermediate (**iii**). Intermediate (**iii**) is deprotected to remove the N-butoxycarbonyl group to produce N-free compound (**iv**), which is coupled with carboxylic acid (**v**) to afford intermediate (**vi**). Intermediate (**vi**) is hydrolyzed to give acid (**vii**), which is coupled with amine

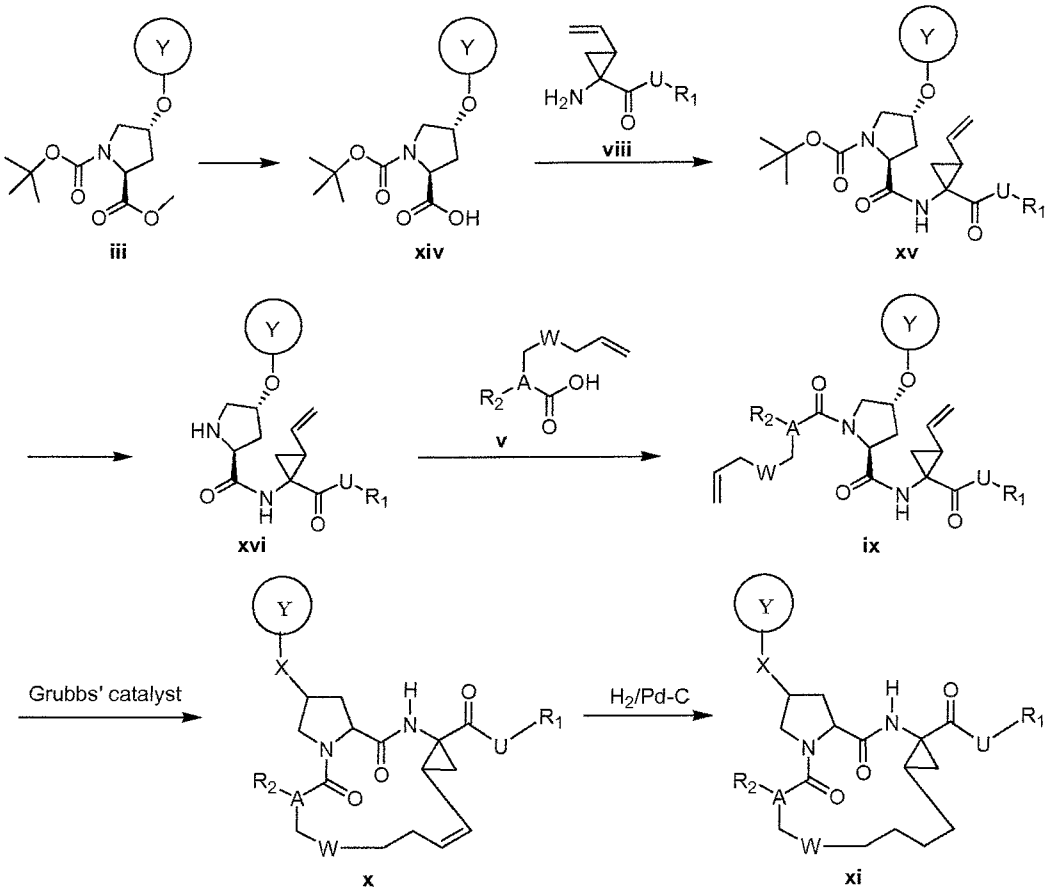
compound (**viii**) to provide pyrrolidine compound (**ix**) having two terminal alkenyl groups. Intermediate (**ix**) undergoes olefine metathesis in the presence of Grubbs' catalyst to afford desired macrocyclic compound (**x**). The double bond of macrocyclic analog (xi) can be further hydrogenation in the presence of Pd-C to obtain saturated-macrocyclic compound (**xi**).

Schemes 2 and 3 below illustrate two alternative synthetic routes to the compounds of this invention.

Scheme 2



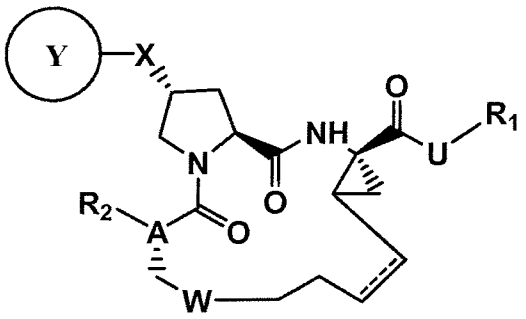
Scheme 3



The methods described above may also additionally include steps, either before or after the steps described specifically in Schemes 1-3, to add or remove suitable protecting groups in order to ultimately allow synthesis of the desired compounds. In addition, various synthetic steps may be performed in an alternate sequence or order to give the desired compounds. Synthetic chemistry transformations and protecting group methodologies (protection and deprotection) useful in synthesizing applicable compounds of formula (I) are known in the art and include, for example, those described in R. Larock, *Comprehensive Organic Transformations*, VCH Publishers (1989); T.W. Greene and P.G.M. Wuts, *Protective Groups in Organic Synthesis*, 2nd Ed., John Wiley and Sons (1991); L. Fieser and M. Fieser, *Fieser and Fieser's Reagents for Organic Synthesis*, John Wiley and Sons (1994); and L. Paquette, ed., *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons (1995) and subsequent editions thereof.

Examples 1-281 below provide detailed descriptions of how exemplary compounds 1-281 were actually prepared.

The compounds mentioned herein contain a non-aromatic double bond and asymmetric centers. Thus, they can occur as racemates and racemic mixtures, single enantiomers, individual diastereomers, diastereomeric mixtures, tautomers, and cis- or trans- isomeric forms. All such isomeric forms are contemplated. For example, the compounds of formulas (I) shown above may possess the following stereochemical configurations (II):



(II)

The compounds described above include the compounds themselves, as well as their salts, prodrugs, and solvates, if applicable. A salt, for example, can be formed between an anion and a positively charged group (e.g., amino) on a compound of formula (I). Suitable anions include chloride, bromide, iodide, sulfate, nitrate, phosphate, citrate, methanesulfonate, trifluoroacetate, acetate, malate, tosylate, tartrate, fumurate, glutamate, glucuronate, lactate, glutarate, and maleate. Likewise, a salt can also be formed between a cation and a negatively charged group (e.g., carboxylate) on a compound of formula (I). Suitable cations include sodium ion, potassium ion, magnesium ion, calcium ion, and an ammonium cation such as tetramethylammonium ion. The compounds of formula (I) also include those salts containing quaternary nitrogen atoms. Examples of prodrugs include esters and other pharmaceutically acceptable derivatives, which, upon administration to a subject, are capable of providing active compounds of formula (I). A solvate refers to a complex formed between an active compound of formula (I) and a pharmaceutically acceptable solvent. Examples of pharmaceutically acceptable solvents include water, ethanol, isopropanol, ethyl acetate, acetic acid, and ethanolamine.

Also within the scope of this invention is a method of treating HCV infection by administering an effective amount of one or more of the compounds of formula (I) to a patient. The term "treating" or "treatment" refers to administering the compounds to a subject, who has HCV infection, a symptom of it, or a predisposition toward it, with the purpose to confer a therapeutic effect, e.g., to cure, relieve, alter, affect, ameliorate, or prevent the HCV infection, the symptom of it, or the predisposition toward it. The term "an effective amount" refers to the amount of an active compound of this invention that is required to confer a therapeutic effect on the treated subject. Effective doses will vary, as recognized by those skilled in the art, depending on the types of diseases treated, route of administration, excipient usage, and the possibility of co-usage with other therapeutic treatment.

The compounds of this invention can remain in the blood system at an effective level for a prolonged period. Thus, these compounds can be administered at an effective amount once a day to confer the therapeutic effect.

To practice the method of the present invention, a composition having one or more compounds of this invention can be administered parenterally, orally, nasally, rectally, topically, or buccally. The term "parenteral" as used herein refers to subcutaneous, intracutaneous, intravenous, intrmuscular, intraarticular, intraarterial, intrasynovial, intrasternal, intrathecal, intralesional, or intracranial injection, as well as any suitable infusion technique.

A sterile injectable composition can be a solution or suspension in a non-toxic parenterally acceptable diluent or solvent, such as a solution in 1,3-butanediol. Among the acceptable vehicles and solvents that can be employed are mannitol, water, Ringer's solution, and isotonic sodium chloride solution. In addition, fixed oils are conventionally employed as a solvent or suspending medium (e.g., synthetic mono- or diglycerides). Fatty acid, such as oleic acid and its glyceride derivatives are useful in the preparation of injectables, as are natural pharmaceutically acceptable oils, such as olive oil or castor oil, especially in their polyoxyethylated versions. These oil solutions or suspensions can also contain a long chain alcohol diluent or dispersant, carboxymethyl cellulose, or similar dispersing agents. Other commonly used surfactants such as Tweens or Spans or other similar emulsifying agents or bioavailability enhancers which are commonly used in the

manufacture of pharmaceutically acceptable solid, liquid, or other dosage forms can also be used for the purpose of formulation.

A composition for oral administration can be any orally acceptable dosage form including capsules, tablets, emulsions and aqueous suspensions, dispersions, and solutions. In the case of tablets, commonly used carriers include lactose and corn starch. Lubricating agents, such as magnesium stearate, are also typically added. For oral administration in a capsule form, useful diluents include lactose and dried corn starch. When aqueous suspensions or emulsions are administered orally, the active ingredient can be suspended or dissolved in an oily phase combined with emulsifying or suspending agents. If desired, certain sweetening, flavoring, or coloring agents can be added.

A nasal aerosol or inhalation composition can be prepared according to techniques well known in the art of pharmaceutical formulation. For example, such a composition can be prepared as a solution in saline, employing benzyl alcohol or other suitable preservatives, absorption promoters to enhance bioavailability, fluorocarbons, and/or other solubilizing or dispersing agents known in the art.

A composition having one or more active compounds of this invention can also be administered in the form of suppositories for rectal administration.

The carrier in the pharmaceutical composition must be "acceptable" in the sense that it is compatible with the active ingredient of the composition (and preferably, capable of stabilizing the active ingredient) and not deleterious to the subject to be treated. One or more solubilizing agents can be utilized as pharmaceutical excipients for delivery of an active compound of this invention. Examples of other carriers include colloidal silicon oxide, magnesium stearate, cellulose, sodium lauryl sulfate, and D&C Yellow # 10.

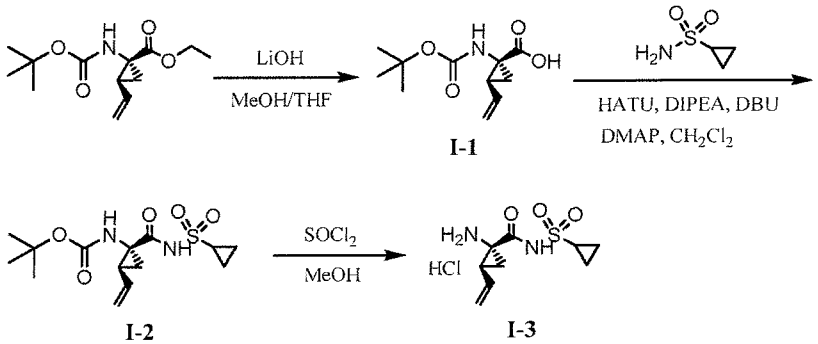
The compound of this invention can be used to treat HCV along with a second anti-HCV agent, such as an inhibitor of a target other than HCV NS3 protease in the HCV life cycle, an immunomodulatory agent, and another antiviral agent. The compound of this invention and the second anti-HCV agent can be administered concurrently or at different time. For concurrent administration, they may be admixed to form a single pill, or prepared as separate pills. These two agents can be each used at such an amount that the total of both is recognized by a skilled artisan as effective for treating HCV.

The compounds of this invention described above can be preliminarily screened for their efficacy in treating HCV infection by an *in vitro* assay (see Examples 282 and 283) and then confirmed by animal experiments and clinic trials. Other methods will also be apparent to those of ordinary skill in the art.

The specific examples below are to be construed as merely illustrative, and not limitative of the remainder of the disclosure in any way whatsoever. Without further elaboration, it is believed that one skilled in the art can, based on the description herein, utilize the present invention to its fullest extent. All publications cited herein are hereby incorporated by reference in their entirety.

Example 1: Synthesis of {4-Cyclopropanesulfonylaminocarbonyl-2,15-dioxo-18-[2-(4-trifluoromethyl-phenyl)-benzo[4,5]furo[3,2-d]pyrimidin-4-yloxy]-3,16-diaza-tricyclo[14.3.0.04,6]nonadec-14-yl}-carbamic acid cyclopentyl ester (Compound 1)

Compound I-3 was first prepared from commercially available 1-*t*-butoxycarbonylamino-2-vinyl-cyclopropanecarboxylic acid ethyl ester via the route shown below:

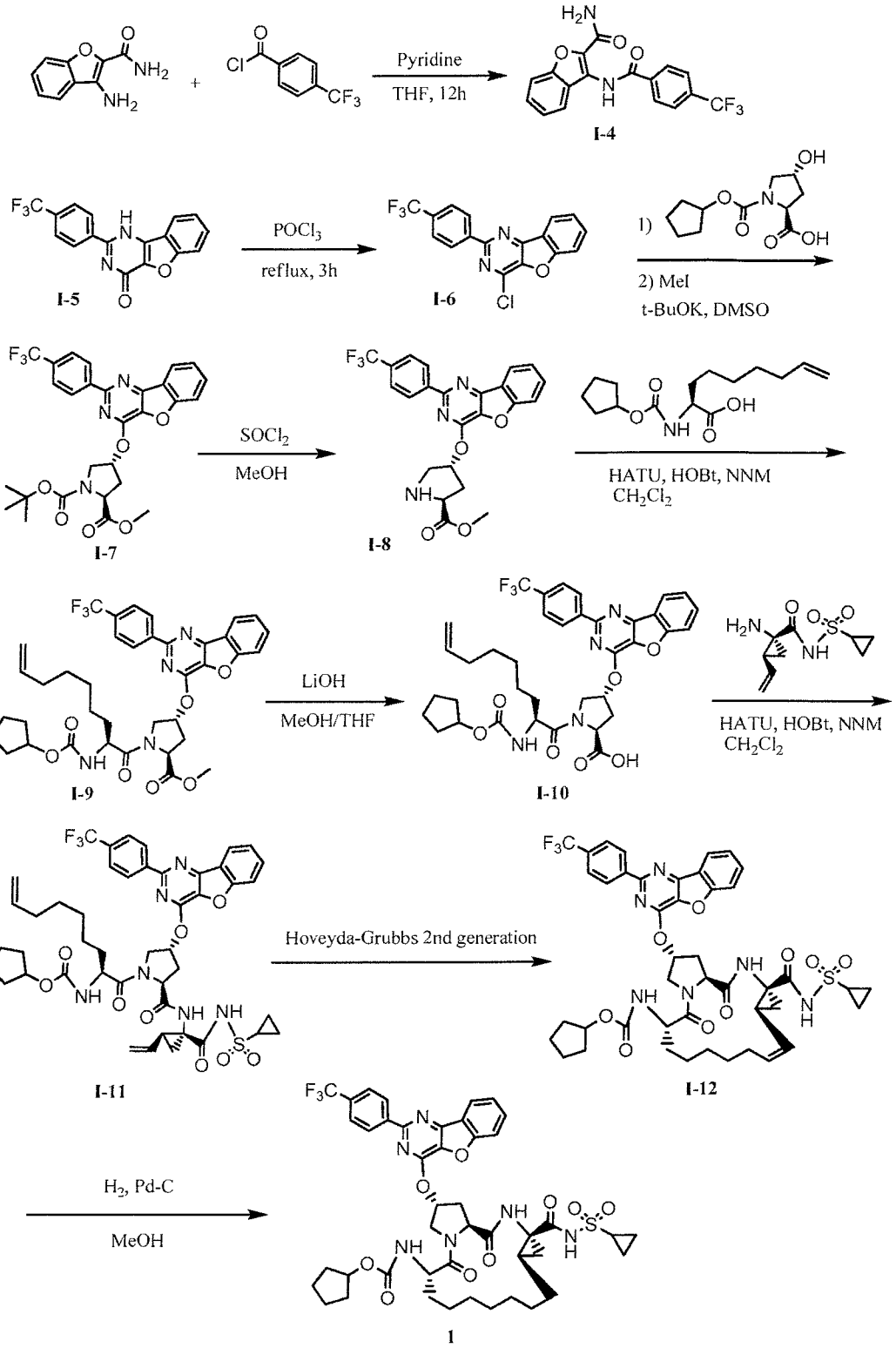


To a solution of 1-*t*-butoxycarbonylamino-2-vinyl-cyclopropanecarboxylic acid ethyl ester (0.34 g, 1.3 mmol) in THF (5 mL) and methanol (5 mL) was added a suspension of LiOH (0.13 g, 5.3 mmol) in water (1.4 mL). After being stirred overnight at room temperature, the reaction was quenched with 10% HCl (2 mL) and the solvent was removed under vacuum. The resultant solid powder was washed with water (10 mL) to give compound I-1 (0.27 g, 90%). MS m/z 249.9 (M^++23); ^{1}H NMR ($CDCl_3$) δ 10.35 (brs, 1H), 5.84-5.71 (m, 1H), 5.29 (d, J = 17.4 Hz, 1H), 5.12 (d, J = 10.2 Hz, 1H), 2.23-2.14 (m, 1H), 1.87-1.65 (m, 1H), 1.58-1.41 (m, 1H), 1.43 (s, 9H).

A solution of compound I-1 (0.52 g, 2.3 mmol), 2-(1H-7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyl uronium hexafluoro-phosphate methanaminium (HATU, 1.74 g, 4.6 mmol), and 4-dimethylaminopyridine (1.39 g, 11.6 mmol) in CH_2Cl_2 (40 mL) was stirred at room temperature for 1 hour, followed by slow addition of cyclopropanesulfonamide (0.57 g, 4.7 mmol), diisopropylethylamine (1.81 mL, 14.0 mmol), and 1,8-diazabicyclo[5,4,0]undec-7-ene (1.80 g, 11.7 mmol) over 15 minutes. After the reaction mixture was stirred at room temperature overnight, the solvent was removed under vacuum. The residue was purified by silica gel column chromatography to give compound I-2 (0.51 g, 66%). MS m/z 353.1 (M^++23); ^{1}H NMR ($CDCl_3$) δ 9.75 (brs, 1H), 5.64-5.51 (m, 1H), 5.30 (d, J = 17.4 H), 5.16 (d, J = 10.2 Hz, 1H), 2.95-2.89 (m, 1H), 2.19-2.10 (m, 1H), 1.93-1.88 (m, 1H), 1.47 (s, 9H), 1.46-1.38 (m, 1H), 1.32-1.23 (m, 2H), 1.15-1.00 (m, 2H).

To a solution of compound I-2 (0.50 g, 1.5 mmol) in MeOH (8 mL) was added $SOCl_2$ (0.26 g, 2.2 mmol) at room temperature. After the reaction mixture was refluxed for 1 hour, MeOH and $SOCl_2$ was removed under vacuum. The residue was triturated from pentane and filtered to give intermediate I-3 as an off-white solid (0.32 g, 91%). MS m/z (M^++1); ^{1}H NMR (CD_3COD) δ 5.77-5.65 (m, 1H), 5.43 (d, J = 17.4 Hz, 1H), 5.32 (d, J = 10.2 Hz, 1H), 3.06-2.97 (m, 1H), 2.45 (dd, J = 17.4 Hz, J = 7.8, 1H), 2.16 (dd, J = 8.0 Hz, J = 7.8 Hz, 1H), 1.75 (dd, J = 10.1 Hz, J = 7.8 Hz, 1H), 1.32-0.86 (m, 4H).

Compound 1 was prepared via the route shown below:



A solution of 3-amino-benzofuran-2-carboxylic acid amide (1.00 g, 5.7 mmol) and pyridine (1 mL, 12.26 mmol) in THF (25 mL) was stirred at 0°C for 10 min. To the resulting solution was slowly added 4-trifluoromethyl-benzoyl chloride (1.48 g, 7.1 mmol). Then the temperature was raised to room temperature and the mixture was stirred for 12 h. After the solvent was removed under reduced pressure, the resulting solid was collected, washed with water, and air-dried to yield I-4 (1.92 g, 96.0 %). MS: m/z 349.0 (M^++1).

To a suspension of I-4 (1.92 g, 5.5 mmol) and 2N NaOH (13 mL) in EtOH (25 mL) was heated at 85°C for 12h. After cooled, the mixture was acidified and then EtOH was removed. The resulting solid was collected, filtrated, washed with water, and dried to afford I-5 (1.71 g, 95.0%). MS m/z 331 (M^++1).

A solution of I-5 (1.71 g, 5.2 mmol) and excess phosphorus oxychloride ($POCl_3$) was refluxed for 2 hours. After cooled and thoroughly concentrated, the mixture was subjected to extraction with methylene chloride and 10% sodium hydroxide. The organic layer was dried over $MgSO_4$, concentrated, and crystallized from CH_2Cl_2 and *n*-hexane to give compound I-6 (1.49 g, 82%). MS m/z 348.8, 350.9 (M^++1); ^{1}H NMR ($CDCl_3$) δ 8.70 (d, 2H), 8.34 (d, 1H), 7.82-7.75 (m, 4H), 7.57 (ddd, 1H).

To a suspension of boc-trans-4-hydroxy-L-proline (0.53 g, 2.3 mmol) in DMSO (25 mL) was added *t*-BuOK (0.82 g, 5.1 mmol) at 0°C. After the mixture was allowed to warm to room temperature and stirred for 1 hour, compound I-6 (0.81 g, 2.3 mmol) was added slowly at 10°C. Stirring was continued overnight. Iodomethane (1.02 g, 6.9 mmol) was added and the reaction mixture was stirred at room temperature for additional 30 minutes. The reaction mixture was neutralized to pH 6~7 by 10% HCl aqueous solution and subjected to extraction with methylene chloride. The organic layer was dried over $MgSO_4$, evaporated under vacuum, and purified by silica gel column chromatography to give compound I-7 (1.12 g, 86%). MS m/z 557.8 (M^++1); ^{1}H NMR ($CDCl_3$) δ 8.63 (d, 2H), 8.28 (d, 1H), 7.80-7.74 (m, 2H), 7.70 (d, 2H), 7.51 (ddd, 1H).

To a solution of compound I-7 (1.13 g, 2.0 mmol) in MeOH (20 mL) was added $SOCl_2$ (1.21 g, 9.8 mmol) at room temperature. The reaction mixture was refluxed for 1 hour, and MeOH and $SOCl_2$ were removed. The residue was triturated in pentane. The

suspension was filtered to give compound I-8 as an off-white solid (0.87 g, 95%). MS m/z 458.1 (M^++1).

To a solution of HATU (1.12 g, 3.0 mmol), 1-hydroxybenzotriazole (HOBT, 0.41 g, 3.0 mmol), I-8 (0.86 g, 1.9 mmol) and 2-*t*-butoxycarbonylamino-non-8-enoic acid (1.21 g, 1.9 mmol) in CH_2Cl_2 (40 mL) at room temperature was added N-methylmorpholine (NMM, 1.02 g, 9.9 mmol). After stirred overnight, the mixture was concentrated under vacuum. The residue was purified by silica gel column chromatography to give compound I-9 (1.03 g, 73%). MS m/z 711.3 (M^++1).

To a solution of compound I-9 (1.01 g, 1.4 mmol) in THF (20 mL) was added 0.5 M LiOH (5.7 mL, 2.9 mmol) at room temperature. After stirred overnight, the reaction mixture was neutralized by 10% HCl to pH < 7 and concentrated under vacuum. The resultant residue was filtered and washed by water to give compound I-10 (0.91 g, 92%). MS: m/z 697.3 (M^++1).

NMM (0.12 g, 1.2 mmol) was added to a solution of compound I-3 (0.28 g, 0.4 mmol), HATU(0.31 g, 0.8 mmol), HOBT (0.08 g, 0.6 mmol) and compound I-10 (0.09 g, 0.4 mmol) in CH_2Cl_2 (10 mL) at room temperature. After stirred overnight, the reaction mixture was concentrated under vacuum. The residue was purified by silica gel column chromatography to give compound I-11 (0.10 g, 85%). MS m/z 921.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.24 (s, 1H), 8.61 (d, 2H), 8.26 (d, 1H), 7.77 (d, 2H), 7.73-7.64 (m, 2H), 7.54-7.47 (m, 1H), 7.11 (s, 1H), 6.19 (d, 1H), 5.88-5.70 (m, 2H), 5.38-5.25 (m, 2H), 5.16 (d, 1H), 5.00-4.90 (m, 2H), 4.60 (dd, 1H), 4.88-4.34 (m, 2H), 4.18-4.10 (m, 1H), 2.98-2.89 (m, 1H), 2.68 (dd, 2H), 2.18-1.96 (m, 6H), 1.50-1.32 (m, 7H), 1.28 (s, 9H), 1.09-1.25 (m, 2H).

To a solution of compound I-11 (0.10 g, 0.11 mmol) in CH_2Cl_2 (10 mL) was added Hoveyda-Grubbs 2nd (35 mg, 0.056 mmol) at room temperature under N_2. Then, the reaction mixture was stirred at 40°C for 24 h to carry out metathesis cyclization. The reaction was quenched and the reaction mixture was purified by column chromatography to give compound I-12 (30 mg, 31%). MS: m/z 893.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.39 (s, 1H), 8.59 (d, 2H), 8.21 (d, 1H), 7.77 (d, 2H), 7.69-7.57 (m, 2H), 7.46 (dd, 1H), 7.20 (s, 1H), 6.12 (s, 1H), 5.69 (q, 1H), 5.12 (d, 1H), 4.97 (dd, 1H), 4.81-4.68 (m,

2H), 4.28-4.07 (m, 2H), 2.96-2.49 (m, 3H), 2.30 (q, 1H), 1.96-1.12 (m, 14H), 1.08 (s, 9H), 0.96-0.82 (m, 2H).

To a solution of compound I-12 (30 mg, 0.034 mmol) in MeOH (10 mL) was added 5% Pd-C (5 mg) at room temperature under N_2. Then, the reaction mixture was stirred under hydrogen at room temperature and a pressure of 60 psi for 4 h. The reaction mixture was filtrated and purified by column chromatography to give compound 1 (16.5 mg, 55%). MS: m/z 895.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.79 (s, 1H), 8.57 (d, 2H), 8.21 (d, 1H), 7.75 (d, 2H), 7.64 (m, 2H), 7.46 (d, 1H), 7.11 (s, 1H), 6.11 (s, 1H), 5.29 (d, 1H), 4.72 (m, 2H), 4.38 (m, 2H), 4.12 (m, 1H), 3.02-2.58 (m, 3H), 1.98-0.86 (m, 29H).

Example 2-141: Syntheses of Compound 2-141

Each of Compounds 2-141 was prepared in a manner similar to those described in Examples 1.

Compound 2: MS: m/z 883.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.51 (s, 1H), 8.53 (d, 2H), 8.16 (d, 1H), 7.73 (d, 2H), 7.62 (m, 2H), 7.22 (m, 2H), 6.07 (s, 1H), 5.23 (d, 1H), 4.77 (dd, 1H), 4.49 (d, 1H), 4.35 (m, 1H), 4.13 (m, 1H), 3.02-2.57 (m, 3H), 1.99-0.91 (m, 30H).

Compound 3: MS: m/z 823.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.38 (s, 1H), 8.53 (d, 2H), 8.16 (d, 1H), 7.73 (d, 2H), 7.61(m, 2H), 7.41 (m, 2H), 6.13 (m, 2H), 5.69 (q, 1H), 4.98 (dd, 1H), 4.78 (m, 1H), 4.55 (m, 1H), 4.42 (m, 1H), 4.19 (m, 1H), 2.89 (m, 1H), 2.78 (m, 2H), 2.52 (m, 1H), 2.23 (q, 1H), 1.96-0.84 (m, 15H), 1.90 (s, 3H).

Compound 4: MS: m/z 882.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.47 (s, 1H), 8.64 (d, 1H), 8.52 (m, 3H), 7.70 (d, 2H), 7.44 (dd, 1H), 6.07 (s, 1H), 5.63 (q, 1H), 5.01-4.73 (m, 3H), 4.07-4.01 (m, 2H), 2.90-2.22 (m, 4H), 1.97-1.09 (m, 17H), 0.94 (s, 9H), 0.90-0.88 (m, 1H).

Compound 5: MS: m/z 840.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.42 (s, 1H), 8.64-8.47 (m, 4H), 7.80 (d, 2H), 7.50-7.27 (m, 2H), 6.15 (s, 1H), 5.69 (q, 1H), 5.23 (d, 1H), 5.02 (dd, 1H), 4.84 (dd, 1H), 4.53 (d, 1H), 4.25-4.11 (m, 2H), 3.32 (s, 3H), 2.93-2.15 (m, 4H), 1.92-0.83 (m, 16H).

Compound 6: MS: m/z 824.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.48 (s, 1H), 8.63 (d, 1H), 8.62-8.48 (m, 3H), 7.78 (d, 2H), 7.44-7.40 (m, 1H), 6.16-6.14 (m, 2H), 5.73 (q, 1H), 5.04 (dd, 1H), 4.85 (dd, 1H), 4.55 (s, 1H), 4.51 (s, 1H), 4.15 (d, 1H), 2.93-2.89 (m, 2H), 2.77-2.22 (m, 3H), 1.95-1.85 (m, 1H), 1.79 (s, 3H), 1.76-0.83 (m,15H).

Compound 7: MS: m/z 839.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.39 (s, 1H), 8.46 (d, 2H), 8.15 (d, 1H), 7.71 (d, 2H), 7.62-7.37 (m, 3H), 7.16 (s, 1H), 6.08 (s, 1H), 5.71 (q, 1H), 5.25 (d, 1H), 4.96 (dd, 1H), 4.75 (dd, 1H), 4.44 (d, 1H), 4.35-4.09 (m, 2H), 3.34 (s, 3H), 2.96-2.71 (m, 2H), 2.57 (brs, 1H), 2.28 (q, 1H), 2.08-0.87 (m, 16H).

Compound 8: MS: m/z 849.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.54 (s, 1H), 8.45 (d, 2H), 8.06 (d, 1H), 7.71 (d, 2H), 7.57 (m, 3H), 7.35 (s, 1H), 6.28 (d, 1H), 6.04 (s, 1H), 5.71 (q, 1H), 4.96 (dd, 1H), 4.67 (dd, 1H), 4.47 (d, 1H), 4.45 (brs, 1H), 4.11 (m, 1H), 2.92-2.45 (m, 4H), 2.32 (q, 1H), 1.96-0.84 (m, 20H).

Compound 9: MS: m/z 880.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.45 (s, 1H), 8.40 (d, 2H), 8.14 (s, 1H), 7.97 (d, 1H), 7.64 (d, 2H), 7.48-7.41 (m, 2H), 7.25-7.20 (m, 1H), 5.96 (s, 1H), 5.63 (q, 1H), 4.92-4.86 (m, 2H), 4.77 (d, 1H), 4.44 (s, 1H), 4.20 (dd, 1H), 4.03 (dd, 1H), 2.90-2.84 (m, 2H), 2.80-2.63 (m, 1H), 2.38-2.32 (m, 1H), 1.98-1.02 (m, 15H), 0.91 (s, 9H), 0.90-.086 (m, 1H).

Compound 10: MS: m/z 911.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.23 (s, 1H), 8.54 (d, 2H), 7.87-7.80 (m, 1H), 7.71 (d, 2H), 7.56 (dd, 1H), 7.33-7.20 (m, 1H), 6.88 (s, 1H), 6.13 (s, 1H), 5.65 (q, 1H), 5.07-4.94 (m, 2H), 4.69 (dd, 1H), 4.57 (d, 1H), 4.43-4.38 (m, 1H), 4.24-4.01 (m, 2H), 2.91-2.80 (m, 2H), 2.74 (s, 3H), 2.65-2.63 (m, 1H), 2.60-2.41 (m, 1H), 2.22 (q, 1H), 1.98-0.86 (m, 20H).

Compound 11: MS: m/z 907.3 (M^++1).

Compound 12: MS: m/z 923.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.42 (s, 1H), 8.57 (d, 2H), 8.06 (d, 1H), 7.76 (d, 2H), 7.51 (s, 1H), 7.14-6.93 (m, 2H), 6.13 (s, 1H), 5.80-5.60 (m, 1H), 5.31 (d, 1H), 4.97-4.83 (m, 2H), 4.79 (dd, 1H), 4.64-4.04 (m, 3H), 3.88 (s, 3H), 2.94-2.43 (m, 3H), 2.36-0.86 (m, 25H).

Compound 13: MS: m/z 852.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.68 (s, 1H), 8.38 (d, 2H), 7.95 (d, 1H), 7.72-7.58 (m, 3H), 7.47 (d, 2H), 7.24-7.19 (m, 1H), 6.01 (s, 1H), 5.69 (q, 1H), 4.94 (dd, 1H), 4.78 (dd, 1H), 4.70 (d, 1H), 4.46 (d, 1H), 4.22-3.98 (m, 2H), 2.97-2.80 (m, 2H), 2.57 (s, 6H), 2.67-2.41 (m, 1H), 2.23 (q, 1H), 1.85-0.84 (m, 16H).

Compound 14: MS: m/z 766.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.30 (s, 1H), 8.62 (m, 2H), 8.24 (m, 1H), 7.77 (d, 2H), 7.67 (m, 2H), 7.48 (m, 1H), 6.90 (s, 1H), 6.18 (s, 1H), 5.72 (q, 1H), 4.98 (dd, 1H), 4.65 (dd, 1H), 4.24 (m, 1H), 4.05 (m, 1H), 2.92 (m, 1H), 2.76 (m, 2H), 2.58-2.28 (m, 4H), 1.94-1.05 (m, 13H), 0.97-0.86 (m, 2H).

Compound 15: MS: m/z 893.3(M^++1); ^{1}H NMR ($CDCl_3$) δ 10.33 (s, 1H), 8.88 (s, 1H), 8.68 (d, 1H), 8.26 (d, 1H), 7.80-7.65 (m, 4H), 7.35-7.26 (m, 1H), 6.98 (d, 1H), 6.20 (d, 1H), 5.71 (q, 1H), 5.18 (d, 1H), 5.00 (dd, 1H), 4.77 (dd, 1H), 4.64 (d, 1H), 4.46 (s, 1H), 4.25 (dd, 1H), 4.15 (dd, 1H), 2.92-2.28 (m, 4H), 2.17-0.82 (m, 24H).

Compound 16: MS: m/z 877.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.40 (s, 1H), 8.45 (d, 2H), 8.04 (d, 1H), 7.62 (d, 2H), 7.58-7.50 (m, 2H), 7.44 (s, 1H), 7.35 (dd, 1H), 6.02 (s, 1H), 5.95 (d, 1H), 5.63 (q, 1H), 4.81 (dd, 1H), 4.70 (dd, 1H), 4.49 (d, 1H), 4.42-4.38 (m, 1H), 4.04 (dd, 1H), 2.90-2.20 (m, 6H), 1.96-0.83 (m, 23H).

Compound 17: MS: m/z 907.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.42 (s, 1H), 8.73 (s, 1H), 8.62 (d, 1H), 7.96 (s, 1H), 7.71 (d, 1H), 7.64 (dd, 1H), 7.59-7.25 (m, 3H), 6.11 (s, 1H), 5.62 (q, 1H), 5.21 (d, 1H), 4.99 (dd, 1H), 4.79 (dd, 1H), 4.61 (d, 1H), 4.52 (s, 1H), 4.25-4.10 (m, 2H), 2.95-2.51 (m, 3H), 2.47 (s ,3H), 2.31 (q, 1H), 2.03-0.91 (m, 24H).

Compound 18: MS: m/z 767.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.38 (s, 1H), 8.49 (d, 2H), 8.15 (d, 1H), 7.77 (d, 2H), 7.64-7.58 (m, 2H), 7.41-7.32 (m, 1H), 7.29 (s, 1H), 6.08 (s, 1H), 5.78 (q, 1H), 5.08 (dd, 1H), 4.66 (dd, 1H), 4.42 (d, 1H), 4.09-4.06 (m, 1H), 3.85-3.62 (m, 4H), 2.93-2.45 (m, 4H), 2.04-0.87 (m, 13H).

Compound 19: MS: m/z 899.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.28 (s, 1H), 8.51 (d, 2H), 7.80 (dd, 1H), 7.70 (d, 2H), 7.51-7.42 (m, 1H), 7.37-7.23 (m, 1H), 6.97 (s, 1H), 6.06 (s, 1H), 5.63 (q, 1H), 4.96-4.85 (m, 2H), 4.75-4.63 (m, 2H), 4.09-4.02 (m, 2H), 2.93-2.43 (m, 4H), 2.21 (q, 1H), 1.96-0.76 (m, 24H).

Compound 20: MS: m/z 895.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.42 (s, 1H), 8.43 (d, 2H), 7.81 (s, 1H), 7.67 (d, 2H), 7.51 (s, 1H), 7.35-7.28 (m, 2H), 5.92 (s, 1H), 5.57 (q, 1H), 5.19 (d, 1H), 4.88-4.61 (m, 3H), 4.14-4.00 (m, 2H), 2.83-2.41 (m, 4H), 2.38 (s, 3H), 2.24 (q, 1H), 1.96-1.16 (m, 15H),1.05 (s, 9H), 0.97-0.78 (m, 1H).

Compound 21: MS: m/z 923.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.33 (s, 1H), 8.50 (d, 2H), 7.67 (d, 2H), 7.59 (s, 1H), 7.41 (d, 1H), 7.34 (s, 1H), 7.16 (d, 1H), 6.06 (s, 1H), 5.64 (q, 1H), 5.23 (d, 1H), 4.94 (dd, 1H), 4.87 (dd, 1H), 4.58-4.42 (m, 2H), 4.30-4.02 (m, 2H), 3.84 (s, 3H), 2.88-2.44 (m, 4H), 2.21 (q, 1H), 1.84-0.78 (m, 23H).

Compound 22: MS: m/z 752.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.76 (s, 1H), 8.61 (d, 2H), 8.25 (m, 1H), 7.79 (d, 2H), 7.67 (d, 2H), 7.52 (m, 1H), 6.70 (s, 1H), 6.19 (s, 1H), 5.69 (q, 1H), 5.08 (m, 1H), 4.65 (dd, 1H), 4.23 (dd, 1H), 4.02 (m, 1H), 3.05-1.98 (m, 7H), 1.96-0.82 (m, 13H).

Compound 23: MS: m/z 907.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.40 (s, 1H), 8.56 (d, 2H), 8.08 (d, 1H), 7.73 (d, 2H), 7.29 (s, 1H), 7.26-7.20 (m, 2H), 6.13 (s, 1H), 5.71 (q, 1H), 5.22 (d, 1H), 4.95 (dd, 1H), 4.82-4.73 (m, 1H), 4.63-4.51 (m, 1H), 4.33-4.06 (m, 2H), 2.96-2.51 (m, 4H), 2.53 (s, 3H), 2.24 (q, 1H), 1.96-0.94 (m, 24H).

Compound 24: MS: m/z 916.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.37 (s, 1H), 8.48 (d, 2H), 8.08 (s, 1H), 7.68 (d, 2H), 7.50-7.37 (m, 3H), 6.01 (s, 1H), 5.59 (q, 1H), 5.13 (d, 1H), 4.83 (dd, 1H), 4.74-4.63 (m, 2H), 4.15 (dd, 1H), 4.05 (d, 1H), 2.94-2.41 (m, 4H), 2.21 (q, 1H), 1.89-1.14 (m, 14H), 1.03 (s, 9H), 0.96-0.85 (m, 1H).

Compound 25: MS: m/z 923.3 (M^++1).

Compound 26: MS: m/z 923.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 1035 (s, 1H), 8.50 (d, 2H), 7.69 (d, 2H), 7.52 (dd, 1H), 7.40 (s, 1H), 7.12 (d, 1H), 6.75 (d, 1H), 6.05 (s, 1H), 5.63 (q, 1H), 5.27 (d, 1H), 4.97-4.83 (m, 1H), 4.75 (dd, 1H), 4.42 (brs, 1H), 4.28-4.08 (m, 2H), 4.08 (s, 3H), 2.91-2.38 (m, 4H), 2.23 (q, 1H), 1.96-0.82 (m, 24H).

Compound 27: MS: m/z 894.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.38 (s, 1H), 8.47 (d, 2H), 8.08 (d, 1H), 7.62 (d, 2H), 7.58-7.54 (m, 2H), 7.40-7.33 (m, 1H), 7.31 (s, 1H), 6.07 (s, 1H), 5.63 (q, 1H), 4.95 (dd, 1H), 4.83 (d, 1H), 4.87 (dd, 1H), 4.58 (d, 1H), 4.31-4.19 (m, 1H), 4.09 (dd, 1H), 3.40-3.32 (m, 4H), 3.01-2.41 (m, 8H), 2.19 (q, 1H), 1.92-0.83 (m, 15H).

Compound 28: MS: m/z 878.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.56 (s, 1H), 8.41 (d, 2H), 8.02 (d, 1H), 7.74 (s, 1H), 7.68 (d, 2H), 7.53-7.47 (m, 2H), 7.35-7.32 (m, 1H), 6.01 (s, 1H), 5.62 (q, 1H), 4.90 (dd, 1H), 4.78 (dd, 1H), 4.59-4.43 (m, 2H), 4.35-4.25 (m, 1H), 4.05 (dd, 1H), 3.61-3.49 (m, 1H), 3.01-2.45 (m, 8H), 2.21 (q, 1H), 1.85-0.83 (m, 18H).

Compound 29: MS: m/z 909.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.27 (s, 1H), 8.53 (d, 2H), 8.16 (d, 1H), 7.67 (d, 2H), 7.64-7.43 (m, 4H), 6.03 (s, 1H), 5.61 (q, 1H), 5.22-5.19 (m, 1H), 4.87 (dd, 1H), 4.66 (dd, 1H), 4.57 (d, 1H), 4.19-4.01 (m, 3H), 3.71-3.42 (m, 4H), 3.19-2.97 (m, 2H), 2.91-2.43 (m, 4H), 2.20 (q, 1H), 1.95-0.81 (m, 17H).

Compound 30: MS: m/z 906.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.18 (s, 1H), 8.62 (d, 2H), 8.25 (d, 1H), 7.78 (d, 2H), 7.70-7.61 (m, 2H), 7.55-7.46 (m, 1H), 7.01 (1H), 6.18 (1H), 5.71 (q, 1H), 5.12 (d, 1H), 5.02 (dd, 1H), 4.77 (dd, 1H), 4.64 (d, 1H), 4.53-4.43 (1H), 4.31-4.18 (m, 2H), , 2.83-2.44 (m, 3H), 2.28 (q, 1H), 1.95-1.22 (m, 23H), 0.83 (s, 3H).

Compound 31: MS: m/z 907.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.39 (s, 1H), 8.57 (d, 2H), 8.05 (d, 1H), 7.77 (d, 2H), 7.42-7.26 (m, 3H), 6.15 (s, 1H), 5.69 (q, 1H), 5.29 (d, 1H), 4.96 (dd, 1H), 4.78 (dd, 1H), 4.63-4.56 (m, 1H), 4.40-4.13 (m, 3H), 2.91-2.64 (m, 3H), 2.62 (s, 3H), 2.56-2.22 (m, 2H), 1.89-0.96 (m, 23H).

Compound 32: MS: m/z 895.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.45 (s, 1H), 8.60 (d, 2H), 8.22 (d, 1H), 7.55 (d, 2H), 7.67-7.60 (m, 2H), 7.45 (dd, 1H), 7.20 (s, 1H), 6.12 (s, 1H), 5.65 (q, 1H), 5.13 (d, 1H), 4.97 (dd, 1H), 4.81-4.71 (m, 2H), 4.14-4.10 (m, 2H), 2.82-2.45 (m, 3H), 2.27 (q, 1H), 1.97-1.21 (m, 14H), 1.08 (s, 9H), 0.89-0.80 (m, 4H).

Compound 33: MS: m/z 853.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.22 (s, 1H), 8.58 (s, 1H), 8.48 (d, 2H), 8.08 (d, 1H), 7.57 (d, 2H), 7.53-7.44 (m, 2H), 7.39-7.26 (m, 1H), 6.05 (s, 1H), 5.65 (q, 1H), 5.21 (d, 1H), 4.95 (dd, 1H), 4.82 (dd, 1H), 4.40 (d, 1H), 4.21-4.03 (m, 2H), 3.27 (s, 3H), 2.81-2.40 (m, 3H), 2.22 (q, 1H), 1.95-1.20 (m,15H), 0.81 (s, 3H).

Compound 34: MS: m/z 923.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.17 (s, 1H), 8.61 (d, 2H), 8.25 (d, 1H), 7.80 (d, 2H), 7.65-7.50 (m, 2H), 7.41 (dd, 1H), 6.97 (s, 1H), 6.18 (s, 1H), 5.72 (q, 1H), 5.15 (d, 1H), 5.05 (dd, 1H), 4.77 (dd, 1H), 4.65 (d, 1H), 4.29-4.10 (m, 2H), 3.78-3.52 (m, 2H), 3.23-3.03 (m, 2H), 2.79-2.85 (m, 2H), 2.56 (brs, 1H), 2.27 (q, 1H), 1.98-1.19 (m, 20H), 0.88 (s, 3H).

Compound 35: MS: m/z 894.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.45 (s, 1H), 8.47 (d, 2H), 8.12 (s, 1H), 8.05 (d, 1H), 7.70 (d, 2H), 7.53-7.46 (m, 2H), 7.31-7.22 (m, 1H), 6.03 (s, 1H), 5.70 (q, 1H), 5.03-4.84 (m, 4H), 4.24 (d, 1H), 2.95-2.47 (m, 3H), 2.38 (q, 1H), 1.94-1.11 (m, 25H), 0.85 (s, 3H).

Compound 36: MS: m/z 889.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.26 (s, 1H), 8.47 (d, 2H), 8.07 (d, 1H), 7.65 (d, 2H), 7.57 (s, 1H), 7.55-7.42 (m, 2H), 7.38-7.27 (m, 2H), 6.82 (d, 1H), 6.62 (d, 1H), 5.63 (dd, 1H), 6.15 (s, 1H), 5.63 (q, 1H), 4.92 (dd, 1H), 4.74-4.59 (m, 2H), 4.42 (d, 1H), 4.17 (dd, 1H), 2.79-2.42 (m, 3H), 2.23 (q, 1H), 1.95-1.05 (m, 15H), 0.76 (s, 3H).

Compound 37: MS: m/z 837.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.16 (s, 1H), 8.48 (d, 2H), 8.11 (d, 1H), 7.69 (d, 2H), 7.58 (d, 2H), 7.36 (dd, 1H), 7.17 (s, 1H), 6.15 (s, 1H), 6.04 (d, 1H), 5.64 (q, 1H), 4.94 (dd, 1H), 4.67 (dd, 1H), 4.47 (dd, 1H), 4.41 (d, 1H), 4.12 (dd, 1H), 2.78-2.68 (m, 1H), 2.43 (brs, 1H), 2.22 (q, 1H), 1.98-1.64 (m, 7H), 1.53-1.11 (m, 12H), 0.78 (s, 3H).

Compound 38: MS: m/z 863.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.52 (s, 1H), 8.38 (d, 2H), 7.92 (d, 1H), 7.88 (s, 1H), 7.65 (d, 2H), 7.58-7.52 (m, 2H), 7.35-7.21 (m, 1H), 6.19 (d, 1H), 5.92 (s, 1H), 5.71 (q, 1H), 5.01 (dd, 1H), 4.81 (dd, 1H), 4.62 (d, 1H), 4.37 (brs, 1H), 4.11-4.01 (m, 1H), 2.98-2.87 (m, 1H), 2.74-2.52 (m, 2H), 2.33 (q, 1H), 1.98-1.19 (m, 16H), 0.88 (s, 3H), 0.68-0.41 (m, 4H).

Compound 39: MS: m/z 908.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.26 (s, 1H), 8.48 (d, 2H), 8.15 (d, 1H), 7.67 (d, 2H), 7.57-7.46 (m, 2H), 7.39-7.35 (m, 2H), 6.07 (s, 1H), 5.62 (q, 1H), 4.98-4.86 (m, 2H), 4.77 (dd, 1H), 4.58 (d, 1H), 4.02 (dd, 1H), 3.38-3.24 (m, 4H), 2.99-2.81 (m, 4H), 2.82-2.42 (m, 3H), 2.19 (q, 1H), 1.88-1.04 (m, 15H), 0.92-0.72 (m, 4H).

Compound 40: MS: m/z 866.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.51 (s, 1H), 8.37 (d, 2H), 7.91 (d, 1H), 7.69 (s, 1H), 7.61 (d, 2H), 7.53-7.42 (m, 2H), 7.23-7.14 (m, 1H), 6.01 (s, 1H), 5.67 (q, 1H), 4.94 (dd, 1H), 4.72 (dd, 1H), 4.61 (d, 1H), 4.43 (d, 1H), 4.30-4.02 (m, 2H), 2.94-2.60 (m, 3H), 2.57 (s, 6H), 2.20 (q, 1H), 1.80-1.15 (m, 15H), 0.77 (s, 3H).

Compound 41: MS: m/z 892.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.40 (s, 1H), 8.51 (d, 2H), 8.16 (d, 1H), 7.85 (d, 2H), 7.65 (s, 1H), 7.58 (d, 1H), 7.41-7.37 (m, 1H), 6.14 (s, 1H), 5.59 (q, 1H), 4.99 (dd, 1H), 4.80 (dd, 1H), 4.62 (d, 1H), 4.57 (d, 1H), 4.45-4.37 (m, 1H), 4.17 (dd, 1H), 3.75-3.65 (m, 2H), 3.60-3.48 (m, 2H), 2.80-2.45 (m, 3H), 2.24 (q, 1H), 1.89-1.41 (m,20H), 0.8 (s, 3H).

Compound 42: MS: m/z 907.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.20 (s, 1H), 8.43 (d, 2H), 8.10 (d, 1H), 7.65 (d, 2H), 7.60-7.55 (m, 2H), 7.39-7.35 (m, 1H), 7.25 (s, 1H), 6.05

(s, 1H), 5.98 (d, 1H), 5.66 (q, 1H), 4.93 (dd, 1H), 4.72 (dd, 1H), 4.52-4.42 (m, 2H), 4.08 (dd, 1H), 3.78-3.60 (m, 2H), 3.21-3.11 (m, 2H), 3.81-2.43 (br, 3H), 2.19-2.05 (m, 2H), 1.85-1.09 (m, 19H), 0.77 (s, 3H).

Compound 43: MS: m/z 890.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.16 (s, 1H), 8.55 (d, 2H), 8.21 (d, 1H), 8.14 (s, 1H), 7.68 (d, 2H), 7.58-7.41 (m, 4H), 7.21 (s, 1H), 6.40 (s, 1H), 6.18 (s, 1H), 5.63 (q, 1H), 4.95 (dd, 1H), 4.78-4.62 (m, 2H), 4.44 (d, 1H), 4.16 (dd, 1H), 2.69-2.44 (m, 3H), 2.24 (q, 1H), 1.98-1.15 (m, 15H), 0.79 (s, 3H).

Compound 44: MS: m/z 879.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.22 (s, 1H), 8.59 (d, 2H), 8.22 (d, 1H), 7.76 (d, 2H), 7.75-7.60 (m, 2H), 7.48-7.42 (m, 1H), 7.17 (s, 1H), 6.20 (s, 1H), 6.16 (d, 1H), 5.71 (q, 1H), 5.02 (dd, 1H), 4.77 (dd, 1H), 4.60-4.52 (m, 2H), 4.20 (dd, 1H), 2.79-2.45 (m, 3H), 2.21 (q, 1H), 1.96-1.07 (m, 15H), 1.03 (s, 9H), 0.82 (s, 3H).

Compound 45: MS: m/z 933.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.22 (s, 1H), 8.56 (d, 2H), 8.19 (d, 1H), 7.88 (d, 2H), 7.69-7.42 (m, 3H), 7.19 (s, 1H), 6.81-6.62 (m, 4H), 6.11 (s, 1H), 5.68 (q, 1H), 5.00 (dd, 1H), 4.77 (dd, 1H), 4.55 (d, 2H), 4.41-4.12 (m, 2H), 2.82-2.42 (m, 3H), 2.28 (q, 1H), 2.01-1.11 (m, 15H), 0.83 (s, 1H).

Compound 46: MS: m/z 891.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.34 (s, 1H), 8.35 (d, 2H), 7.94 (d, 1H), 7.66 (s, 1H), 7.62 (d, 2H), 7.54-7.46 (m, 2H), 7.22 (dd, 1H), 5.93-5.84 (m, 2H), 5.61 (q, 1H), 4.92 (dd, 1H), 4.87 (dd, 1H), 4.58 (d, 1H), 4.41-4.36 (m, 1H), 4.04 (dd, 1H), 2.82-2.75 (m, 1H), 2.65-2.50 (m, 2H), 2.24 (q, 1H), 1.80-1.00 (m, 24H), 0.81 (s, 3H).

Compound 47: MS: m/z 867.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.35 (s, 1H), 8.54 (d, 2H), 8.18 (d, 1H), 7.86 (d, 1H), 7.66 (d, 2H), 7.61 (m, 2H), 7.46 (m, 2H), 6.13 (s, 1H), 5.67 (q, 1H), 4.94 (dd, 1H), 4.77 (m, 1H), 4.61 (m, 1H), 4.40 (d, 1H), 4.20 (m, 1H), 3.72 (s, 3H), 2.91 (m, 1H), 2.72-2.39 (m, 3H), 2.25 (q, 1H), 1.96-0.82 (m, 15H).

Compound 48: MS: m/z 908.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.28 (s, 1H), 8.44 (d, 1H), 8.23 (d, 1H), 7.67 (m, 3H), 7.52 (m, 1H), 7.07 (s, 1H), 6.04 (s, 1H), 5.68 (q, 1H), 5.12 (d, 1H), 4.98 (dd, 1H), 4.79-4.68 (m, 2H), 4.34 (s, 1H), 4.20 (dd, 1H), 4.00 (m, 1H), 2.95 (s, 3H), 2.93 (m, 1H), 2.72 (m, 2H), 2.52 (m, 1H), 2.26 (q, 1H), 1.94-0.82 (23H).

Compound 49: MS: m/z 920.2 (M^++1).

Compound 50: MS: m/z 806.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.47 (s, 1H), 8.77-8.53 (m, 2H), 8.19 (d, 1H), 8.13 (d, 1H), 7.73 (s, 1H), 7.53-7.30 (m, 2H), 7.26-7.18 (m, 1H), 6.07 (s, 1H), 5.70-5.40 (m, 2H), 4.98-4.61 (m, 2H), 4.40-4.03 (m, 3H), 3.47 (s, 3H), 2.95-2.90 (m, 1H), 2.87-2.50 (m, 3H), 2.20 (dd, 1H), 2.10-1.86 (m, 3H), 1.61-1.08 (m, 11H), 0.96 (m, 1H).

Compound 51: MS: m/z 822.3, 824.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.42 (s, 1H), 8.69-8.44 (m, 3H), 8.34 (d, 2H), 7.65 (s, 1H), 7.42-7.30 (m, 3H), 6.04 (s, 1H), 5.70-5.45 (m, 2H), 4.91-4.63 (m, 2H), 4.35-4.03 (m, 3H), 3.42 (s, 3H), 2.84 (s, 1H), 2.72-2.50 (m, 3H), 2.22 (dd, 1H), 2.19 (m, 3H), 1.54-0.78 (m, 11H).

Compound 52: MS: m/z 774.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.33 (s, 1H), 8.65-8.58 (m, 1H), 8.46 (d, 1H), 8.18 (d, 1H), 8.06 (d, 1H), 7.46-7.38 (m,3H), 7.19-7.11 (m, 1H), 6.13 (s, 1H), 6.04 (d, 1H), 5.66 (dd, 1H), 5.27-5.08 (m, 1H), 5.07-4.67 (m, 2H), 4.52-4.39 (m, 2H), 4.13-4.09 (m, 1H), 3.62-3.60 (m, 1H), 2.95-2.10 (m, 4H), 1.98 (s, 3H), 1.90-0.81 (m, 14H).

Compound 53: MS: m/z 825.3 (M^++1).

Compound 54: MS: m/z 805.3, 807.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.46 (s, 1H), 8.28-8.19 (m, 1H), 7.98 (s, 1H), 7.88-7.85 (m, 1H), 7.63-7.39 (m, 6H), 6.07 (s, 1H), 5.67-5.46 (m, 2H), 4.96-4.79 (m, 2H), 4.41-4.09 (m, 3H), 3.37 (s, 3H), 2.97-0.88 (m, 20H).

Compound 55: MS: m/z 789.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.61 (s, 1H), 8.49 (s, 1H), 8.39-8.24 (m, 2H), 8.05-7.94 (m, 2H), 7.56-7.04 (m, 5H), 5.90 (s, 1H), 5.47 (br, 1H), 4.93-4.69 (br, 2H), 4.40-4.07 (m, 3H), 3.46 (s, 1H), 3.23 (s, 3H), 2.91-2.07 (m, 11H), 1.99-1.54 (m, 4H), 1.32-0.81 (m, 5H).

Compound 56: MS: m/z 839.3, 843.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.27 (s, 1H), 8.24 (d, 1H), 7.89 (d, 1H), 7.63 (d, 1H), 7.56 (s, 1H), 7.52-7.40 (m, 2H), 7.14 (brs, 1H), 6.08 (s, 1H), 5.69 (q, 1H), 5.30 (brs, 1H), 4.97 (dd, 1H), 4.74 (dd, 1H), 4.46 (d, 1H), 4.40-4.22 (m, 1H), 4.13-4.08 (m, 1H), 3.36 (s, 3H), 2.99-2.05 (m, 5H), 1.90-1.10 (m, 15H), 0.99-0.88 (m, 1H).

Compound 57: MS: m/z 827.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.17 (s, 1H), 8.42 (d, 2H), 7.84 (d, 1H), 7.49-7.41 (m, 4H), 7.28 (m, 1H), 7.13 (brs, 1H), 6.16 (s, 1H), 5.63 (q, 1H), 4.95 (m, 1H), 4.70 (dd, 1H), 4.63 (m, 1H), 4.31-4.11 (m, 2H), 2.97-2.70 (m, 3H), 2.50-1.06 (m,17H), 0.91 (m,1H).

Compound 58: MS: m/z 803.3 (M^++1).

Compound 59: MS: m/z 789.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.39 (s, 1H), 8.53-8.41 (m, 3H), 7.81 (d, 1H), 7.59-7.42 (m, 4H), 7.26 (m, 1H), 7.18 (s, 1H), 6.17 (s, 1H), 5.17 (q, 1H), 5.28 (dd, 1H), 4.95 (dd, 1H), 4.75 (m, 1H), 4.43 (d, 1H), 4.38-4.04 (m, 2H), 3.40 (s, 3H), 2.96-2.67 (m, 3H), 2.60-2.41 (m, 1H), 2.37-2.22 (m, 1H), 1.99-0.85 (m, 14H).

Compound 60: MS: m/z 773.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.33 (s, 1H), 8.46 (d, 2H), 7.88-7.84 (m, 1H), 7.60-7.50 (m, 4H), 7.35-7.17 (m, 1H), 6.20 (s, 1H), 6.08 (d, 1H), 5.72 (q, 1H), 4.98 (dd, 1H), 4.72 (dd, 1H), 4.56 (m, 1H), 4.41 (d, 1H), 4.21 (m, 1H), 2.94-2.90 (m, 1H), 2.80-2.77 (m, 1H), 2.55-2.52 (m, 1H), 2.23 (q, 1H), 1.98-1.90 (m, 1H), 1.84 (s, 3H), 1.80-0.80 (m, 16H).

Compound 61: MS: m/z 845.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.41 (s, 1H), 8.34 (d, 2H), 7.84 (d, 1H), 7.53-7.44 (m, 1H), 7.40-7.33 (m, 3H), 7.19 (s, 1H), 6.14 (s, 1H), 5.71 (q, 1H), 5.15 (d, 1H), 4.98 (dd, 1H), 4.89-4.80 (m, 2H), 4.25-4.19 (m, 2H), 2.95-2.90 (m, 1H), 2.88-2.42 (m, 3H), 2.44 (s, 3H), 2.29 (m, 1H), 1.98-1.20 (m, 14H), 1.11 (s, 9H), 1.00-0.87 (1H).

Compound 62: MS: m/z 841.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.21 (s, 1H), 8.35 (d, 2H), 7.89 (d, 1H), 7.60-7.57 (m, 1H), 7.33 (d, 2H), 7.17 (d, 1H), 7.05 (s, 1H), 6.22 (s, 1H), 5.68 (q, 1H), 4.97 (dd, 1H), 4.77-4.64 (m, 2H), 4.33-4.17 (m, 2H), 2.93-2.74 (m, 3H), 2.44 (s, 3H), 2.21 (m, 1H), 1.95-0.91 (m, 17H).

Compound 63: MS: m/z 903.3; 905.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.18 (s, 1H), 8.45 (d, 2H), 8.23 (d, 1H), 7.64 (m, 2H), 7.49 (d, 3H), 7.01 (s, 1H), 6.17 (s, 1H), 5.72 (q, 1H), 5.13 (d, 1H), 4.99 (dd, 1H), 4.77 (dd, 1H), 4.58 (d, 1H), 4.53 (brs, 1H), 4.27 (m, 1H), 4.14 (m, 1H), 2.83-2.44 (m, 3H), 2.27 (q, 1H), 1.95-1.22 (m, 23H), 0.83 (s, 3H).

Compound 64: MS: m/z 787.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.45 (s, 1H), 8.25 (d, 2H), 7.75 (d, 1H), 7.67 (s, 1H), 7.53-7.52 (m, 1H), 7.26 (d, 2H), 6.29 (d, 1H), 6.19 (s, 1H), 5.67 (q, 1H), 4.94 (dd, 1H), 4.75 (dd, 1H), 4.52 (brs, 1H), 4.42 (d, 1H), 4.10-4.18 (m, 1H), 2.89-2.50 (m, 3H), 2.43 (s, 3H), 2.35-2.20 (m, 1H), 1.98-1.85 (m, 1H), 1.82 (s, 3H), 1.62-0.81 (m, 16H).

Compound 65: MS: m/z 803.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.46 (s, 1H), 8.30 (d, 1H), 8.17 (d, 2H), 7.63 (d, 1H), 7.55 (s, 1H), 7.45-7.41 (m, 1H), 7.25-7.20 (m, 2H), 5.97 (s, 1H), 5.65-5.59 (m, 1H), 5.36 (d, 1H), 4.91-4.87 (m, 1H), 4.73 (dd, 1H), 4.37-4.05 (m, 3H), 3.30 (s, 3H), 2.84-2.47 (m, 3H), 2.38 (s, 3H), 2.40-2.16 (m, 1H), 1.90-0.87 (m, 16H).

Compound 66: MS: m/z 871.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.42 (s, 1H), 8.19-8.02 (m, 2H), 7.93 (s, 1H), 7.67 (s, 1H), 7.47-7.26 (m, 3H), 6.05 (s, 1H), 5.62 (q, 1H), 5.34 (d, 1H), 4.96-4.42 (m, 4H), 4.36-4.10 (m, 2H), 2.95-2.90 (m, 1H), 2.77 (s, 3H), 2.76-2.48 (m, 3H), 2.35 (s, 3H), 2.30-0.87 (m, 24H).

Compound 67: MS: m/z 875.3 (M^++1).

Compound 68: TG-2379: MS: m/z 871.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.33 (s, 1H), 8.34 (d, 2H), 7.85 (d, 1H), 7.73 (s, 1H), 7.54-7.46 (m, 1H), 7.38-7.22 (m, 3H), 6.12 (s, 1H), 5.65 (q, 1H), 5.35 (d, 1H), 4.93 (dd, 1H), 4.78 (dd, 1H), 4.62-4.50 (m, 2H), 4.32-4.08 (m, 2H), 2.81-2.42 (m, 3H), 2.40 (s, 3H), 2.26 (q, 1H), 1.93-1.11 (m, 23H), 0.80 (s, 3H).

Compound 69: MS: m/z 861.3 (M^++1).

Compound 70: MS: m/z 857.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.23 (s, 1H), 8.09 (s, H), 8.05 (s, 1H), 7.96 (dd, 1H), 7.58 (dd, 1H), 7.47-7.19 (m, 3H), 7.06 (d, 1H), 6.21 (s, 1H), 5.69 (q, 1H), 4.95 (dd, 1H), 4.81-4.60 (m, 2H), 4.35-4.17 (m, 2H), 3.94 (s, 3H), 2.92-2.41 (m, 3H), 2.23 (q, 1H), 1.92-0.82 (m, 17H).

Compound 71: MS: m/z 819.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.36 (s, 1H), 8.01-7.81 (m, 3H), 7.71 (d, 1H), 7.34-7.22 (m, 3H), 6.96 (d, 1H), 6.01 (s, 1H), 5.61 (q, 1H), 5.27 (dd, 1H), 4.90 (dd, 1H), 4.69 (dd, 1H), 4.38 (d, 1H), 4.22-4.03 (m, 2H), 3.87 (s, 3H), 3.28 (s, 3H), 2.86-2.42 (m, 3H), 2.20 (q, 1H), 1.97-0.88 (m, 16H).

Compound 72: MS: m/z 861.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.38 (s, 1H), 8.10-7.98 (m, 2H), 7.86 (d, 1H), 7.54-7.22 (m, 3H), 7.20 (s, 1H), 7.06 (d, 1H), 6.10 (s, 1H), 5.70 (q, 1H), 5.29 (d, 1H), 4.97 (dd, 1H), 4.79-4.67 (m, 2H), 4.18-4.04 (m, 2H), 3.94 (s, 3H), 2.95-2.57 (m, 3H), 2.28 (q, 1H), 1.91-0.87 (m, 25H).

Compound 73: MS: m/z 803.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.37 (s, 1H), 8.12-8.96 (m, 2H), 7.85 (d, 1H), 7.56-7.26 (m, 4H), 7.05 (d, 1H), 6.19-6.15 (m, 2H), 5.71 (q,

1H), 4.96 (dd, 1H), 4.74 (s, 1H), 4.53-4.42 (m, 2H), 4.19 (d, 1H), 3.93 (s, 3H), 2.91-2.20 (m, 4H), 2.10-0.82 (m, 19H).

Compound 74: MS: m/z 861.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.42 (s, 1H), 8.39 (d, 2H), 7.81 (d, 1H), 7.50-7.26 (m, 3H), 7.00 (d, 2H), 6.05 (s, 1H), 5.65 (q, 1H), 5.21 (d, 1H), 4.95 (dd, 1H), 4.84 (dd, 1H), 4.68 (d, 1H), 4.21-4.07 (m, 2H), 3.90 (s, 3H), 2.90-2.45 (m, 4H), 2.22 (q, 1H), 1.98-1.20 (m, 14H), 1.13 (s, 9H), 0.99-0.84 (m, 1H).

Compound 75: MS: m/z 887.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.33 (s, 1H), 8.38 (d, 2H), 7.82 (d, 1H), 7.61 (s, 1H), 7.59-7.43 (m, 1H), 7.35-7.20 (m, 1H), 7.01 (d, 2H), 6.07 (s, 1H), 5.68 (q, 1H), 5.42 (d, 1H), 4.98 (dd, 1H), 4.75 (dd, 1H), 4.58 (s, 1H), 4.38-4.13 (m, 3H), 3.88 (s, 3H), 2.86 (br, 2H), 2.59-2.11 (m, 2H), 1.96-1.20 (m, 22H), 0.92-0.78 (m, 4H).

Compound 76: MS: m/z 903.3, 905.3 (M^++1).

Compound 77: MS: m/z 887.3 (M^++1).

Compound 78: MS: m/z 883.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.19 (s, 1H), 8.46 (d, 2H), 8.25 (d, 1H), 7.62 (m, 2H), 7.46 (m, 1H), 7.04 (d, 2H), 6.96 (s, 1H), 6.19 (s, 1H), 5.73 (q, 1H), 5.15 (d, 1H), 5.02 (dd, 1H), 4.77 (m, 1H), 4.58 (m, 2H), 4.30 (m, 1H), 4.15 (m, 3H), 2.79 (m, 2H), 2.54 (m, 1H), 2.26 (q, 1H), 1.92-0.83 (m, 26H), 0.83 (s, 3H).

Compound 79: MS: m/z 869.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.36 (s, 1H), 8.44 (d, 2H), 8.24 (d, 1H), 7.60 (m, 2H), 7.44 (m, 1H), 7.04 (s, 1H), 7.00 (d, 2H), 6.16 (s, 1H), 5.71 (q, 1H), 5.21 (d, 1H), 4.97 (dd, 1H), 4.74 (m, 1H), 4.57 (m, 2H), 4.30 (m, 1H), 4.15 (m, 3H), 2.91 (m, 1H), 2.75 (m, 2H), 2.56 (m, 1H), 2.26 (q, 1H), 1.92-0.83 (m, 26H).

Compound 80: MS: m/z 883.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.42 (s, 1H), 8.43 (d, 2H), 8.23 (d, 1H), 7.61-7.39 (m, 4H), 7.03 (d, 2H), 6.18 (s, 1H), 5.71 (q, 1H), 5.30 (d, 1H), 4.96 (dd, 1H), 4.79-4.57 (m, 4H), 4.41-4.22 (m, 1H), 4.15-4.08 (m, 1H), 2.96-2.67 (m, 3H), 2.57-2.42 (m, 1H), 2.25 (q, 1H), 1.98-0.87 (m, 29H).

Compound 81: MS: m/z 897.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.31 (s, 1H), 8.42 (d, 2H), 8.21 (d, 1H), 7.57-7.25 (m, 4H), 7.02 (d, 2H), 6.14 (s, 1H), 5.67-5.64 (m, 1H), 5.40 (d, 1H), 5.03-4.93 (m, 1H), 4.79-4.54 (m, 4H), 4.39-4.12 (m, 2H), 2.77-2.72 (m, 2H), 2.54 (br, 1H), 2.26 (q, 1H), 2.03-1.24 (m, 29H), 0.80 (s, 3H).

Compound 82: MS: m/z 915.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.29 (s, 1H), 8.38 (d, 2H), 7.74 (d, 1H), 7.57-7.24 (m, 3H), 7.27 (d, 2H), 6.14 (s, 1H), 5.66 (q, 1H), 5.32 (d,

1H), 4.98 (dd, 1H), 4.76 (dd, 1H), 4.71-4.48 (m, 3H), 4.39-4.08 (m, 2H), 2.85-2.42 (m, 3H), 2.31 (q, 1H), 2.03-1.24 (m, 29H), 0.80 (s, 3H).

Compound 83: MS: m/z 901.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.42 (s, 1H), 8.46 (d, 2H), 7.82 (d, 1H), 7.54 (dd, 1H), 7.42 (s, 1H), 7.32 (m, 1H), 6.98 (d, 2H), 6.14 (s, 1H), 5.65 (q, 1H), 5.33 (d, 1H), 4.97 (dd, 1H), 4.76 (dd, 1H), 4.71-4.50 (m, 3H), 4.41-4.08 (m, 2H), 2.93-2.42 (m, 4H), 2.31 (q, 1H), 2.03-0.80 (m, 29H).

Compound 84: MS: m/z 885.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.26 (s, 1H), 8.42 (d, 2H), 8.23 (d, 1H), 7.58 (m, 2H), 7.44 (dd, 1H), 7.22 (s, 1H), 7.01 (d, 2H), 6.17 (s, 1H), 5.67 (q, 1H), 5.16 (d, 1H), 4.98 (dd, 1H), 4.75 (dd, 1H), 4.62 (m, 2H), 4.38-4.08 (m, 2H), 2.80-2.42 (m, 3H), 2.32 (q, 1H), 1.96-1.20 (m, 21H), 1.13 (s, 9H), 0.81 (m, 3H).

Compound 85: MS: m/z 923.2 (M^++1).

Compound 86: MS: m/z 883.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.41 (s, 1H), 8.19 (d, 1H), 8.06 (d, 1H), 7.95 (s, 1H), 7.61-7.41 (m, 4H), 6.92 (d, 1H), 6.12 (s, 1H), 6.04 (s, 2H), 5.67 (q, 1H), 5.35 (d, 1H), 4.97 (dd, 1H), 4.77 (dd, 1H), 4.58 (d, 1H), 4.36-4.11 (m, 2H), 2.85-2.43 (m, 3H), 2.27 (q, 1H), 1.98-1.21 (m, 24H), 0.81 (s, 3H).

Compound 87: MS: m/z 869.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.36 (s, 1H), 8.17 (d, 1H), 7.97 (d, 1H), 7.88 (s, 1H), 7.58-7.32 (m, 4H), 6.85 (d, 1H), 6.02 (s, 1H), 5.98 (s, 2H), 5.59 (q, 1H), 5.37 (d, 1H), 4.87 (d, 1H), 4.68 (dd, 1H), 4.52-4.02 (m, 3H), 2.90-2.38 (m, 4H), 2.23 (q, 1H), 1.91-0.88 (m, 24H).

Compound 88: MS: m/z 868.5 (M^++1).

Compound 89: MS: m/z 882.5 (M^++1).

Compound 90: MS: m/z 910.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.32 (s, 1H), 8.34 (d, 2H), 8.22 (d, 1H), 7.61-7.43 (m, 3H), 7.44 (dd, 1H), 6.76 (d, 2H), 6.14 (s, 1H), 5.62 (q, 1H), 5.39 (d, 1H), 4.96 (dd, 1H), 4.72 (dd, 1H), 4.63 (brs, 1H), 4.55 (d, 1H), 4.41-4.04 (m, 2H), 3.42 (q, 4H), 2.80-2.42 (m, 3H), 2.32 (q, 1H), 1.98-1.17 (m, 29H), 0.83 (s, 3H).

Compound 91: MS: m/z 896.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.46 (s, 1H), 8.33 (d, 2H), 8.21 (d, 1H), 7.62-7.43 (m, 3H), 7.43 (dd, 1H), 6.77 (d, 2H), 6.13 (s, 1H), 5.65 (q, 1H), 5.39 (d, 1H), 4.93 (dd, 1H), 4.73 (dd, 1H), 4.64 (brs, 1H), 4.53 (d, 1H), 4.43-4.05 (m, 2H), 3.43 (q, 4H), 2.94-2.42 (m, 4H), 2.29 (q, 1H), 2.14-0.83 (m, 29H).

Compound 92: MS: m/z 901.4, 903.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.40 (s, 1H), 8.36 (d, 2H), 8.23 (s, 1H), 7.58-7.26 (m, 5H), 6.15 (s, 1H), 5.65 (q, 1H), 5.19 (d, 1H),

4.96 (dd, 1H), 4.77 (dd, 1H), 4.62-4.52 (m, 2H), 4.33-4.08 (m, 2H), 3.01-2.42 (m, 5H), 2.25 (q, 1H), 1.96-0.89 (m, 29H).

Compound 93: MS: m/z 915.4, 917.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.27 (s, 1H), 8.38 (d, 2H), 8.22 (s, 1H), 7.59-7.34 (m, 5H), 6.13 (s, 1H), 5.70 (q, 1H), 5.29 (d, 1H), 4.98 (dd, 1H), 4.78 (dd, 1H), 4.62-4.55 (m, 2H), 4.35-4.08 (m, 2H), 3.04-2.96 (m, 1H), 2.80-2.43 (m, 3H), 2.25 (q, 1H), 1.97-1.20 (m, 29H), 0.81 (s, 3H).

Compound 94: MS: m/z 867.4 (M^++1).

Compound 95: MS: m/z 881.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.31 (s, 1H), 8.41 (d, 2H), 8.22 (d, 1H), 7.63-7.21 (m, 4H), 7.20 (d, 2H), 6.16 (s, 1H), 5.65 (q, 1H), 5.38 (d, 1H), 4.94 (dd, 1H), 4.80 (dd, 1H), 4.65-4.56 (m, 2H), 4.38-4.12 (m, 2H), 3.08-2.92 (m, 1H), 2.83-2.67 (m, 2H), 2.59-2.41 (m, 1H), 2.25 (q, 1H), 1.98-1.08 (,m, 28H), 0.95-0.86 (m, 4H).

Compound 96: MS: m/z 881.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.47 (s, 1H), 8.40 (d, 2H), 8.23 (d, 1H), 7.76 (s, 1H), 7.62-7.41 (m, 5H), 6.13 (s, 1H), 5.65 (q, 1H), 5.33 (d, 1H), 5.03-4.87 (m, 2H), 4.78 (dd, 1H), 4.57 (d, 1H), 4.38-4.04 (m, 2H), 2.95-2.43 (m, 4H), 2.21 (q, 1H), 2.01-1.37 (m, 20H), 1.33 (s, 9H), 1.21-0.86 (m, 3H).

Compound 97: MS: m/z 895.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.30 (s, 1H), 8.40 (d, 2H), 8.23 (d, 1H), 7.59-7.43 (m, 5H), 6.98 (d, 1H), 6.16 (s, 1H), 5.65 (q, 1H), 5.41 (d, 1H), 4.98 (dd, 1H), 4.79 (q, 1H), 4.62-4.52 (m, 1H), 4.36-4.09 (m, 3H), 2.75 (brs, 2H), 2.59-2.56 (m, 1H), 2.28 (q, 1H), 1.91-1.18 (m, 31H), 0.89-0.78 (m, 4H).

Compound 98: MS: m/z 869.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.41 (s, 1H), 8.42 (d, 2H), 8.23 (d, 1H), 7.62-7.43 (m, 5H), 7.44 (dd, 1H), 6.17 (s, 1H), 5.64 (q, 1H), 5.17 (d, 1H), 4.97 (dd, 1H), 4.77-4.63 (m, 2H), 4.21-4.10 (m, 2H), 2.94-2.55 (m, 4H), 2.27 (q, 1H), 1.891.15 (m, 23H), 1.10 (s, 9H), 0.98-0.87 (m, 1H).

Compound 99: MS: m/z 925.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.28 (s, 1H), 8.37 (d, 2H), 8.03 (d, 1H), 7.50 (d, 2H), 7.48 (s, 1H), 7.01-6.92 (m, 2H), 6.13 (s, 1H), 5.65 (q, 1H), 5.39 (d, 1H), 4.98 (dd, 1H), 4.88 (dd, 1H), 4.64 (s, 1H), 4.53 (d, 1H), 4.41-4.23 (m, 1H), 4.19-4.11 (m, 1H), 3.88 (s, 3H), 2.78-2.42 (m, 3H), 2.26 (q, 1H), 2.04-1.18 (m, 31H), 0.89-0.78 (m, 4H).

Compound 100: MS: m/z 925.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.23 (s, 1H), 8.35 (d, 2H), 7.77 (d, 1H), 7.48 (d, 2H), 7.38-7.22 (m, 1H), 7.04-6.81 (m, 2H), 6.16 (s, 1H),

5.68 (q, 1H), 5.21 (d, 1H), 4.99 (dd, 1H), 4.78 (dd, 1H), 4.57 (d, 1H), 4.22-4.03 (m, 3H), 4.00 (s, 3H), 2.80-2.43 (m, 3H), 2.31 (q, 1H), 1.96-1.20 (m, 31H), 0.95-0.78 (m, 4H).

Compound 101: MS: m/z 827.3 (M^++1).

Compound 102: MS: m/z 897.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.30 (s, 1H), 8.39 (d, 2H), 8.20 (d, 1H), 7.59-7.37 (m, 5H), 7.14 (s, 1H), 6.04 (s, 1H), 5.61 (q, 1H), 5.21 (d, 1H), 4.87 (dd, 1H), 4.77 (dd, 1H), 4.57 (d, 1H), 4.19-4.07 (m, 4H), 3.67-3.42 (m, 2H), 3.17-2.40 (m, 6H), 2.20 (q, 1H), 1.93-0.78 (m, 27H).

Compound 103: MS: m/z 866.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.45 (s, 1H), 8.31 (d, 2H), 8.12 (d, 1H), 7.51-7.42 (m, 5H), 7.32-7.25 (m, 1H), 6.09 (s, 1H), 5.61 (q, 1H), 4.90 (dd, 1H), 4.81 (dd, 1H), 4.59 (d, 1H), 4.50-4.36 (m, 2H), 4.13 (dd, 1H), 3.69-3.27 (m, 3H), 3.10 (brs, 4H), 2.90-2.41 (m, 4H), 2.19 (q, 1H), 1.98-0.78 (m, 25H).

Compound 104: MS: m/z 811.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.38 (s, 1H), 8.38 (d, 2H), 8.19 (d, 1H), 7.60-7.31 (m, 5H), 7.32-7.25 (m, 1H), 6.15 (s, 1H), 5.65 (q, 1H), 4.88 (dd, 1H), 4.70 (dd, 1H), 4.57 (dd, 1H), 4.40 (d, 1H), 4.21-4.05 (m, 2H), 2.95-2.41 (m, 4H), 2.22 (q, 1H), 2.01 (s, 3H), 1.98-0.79 (m, 24H).

Compound 105: MS: m/z 868.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.57 (s, 1H), 8.37 (d, 2H), 8.15 (d, 1H), 8.09 (s, 1H), 7.58-7.51 (m, 4H), 7.27 (dd, 1H), 6.09 (s, 1H), 5.61 (q, 1H), 4.98-4.79 (m, 4H), 4.44 (s, 1H), 4.10 (dd, 1H), 3.79-3.68 (m, 2H), 2.92-2.45 (m, 4H), 2.24 (q, 1H), 1.98-0.88 (m, 32H).

Compound 106: MS: m/z 882.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.37 (s, 1H), 8.35 (d, 2H), 8.16 (d, 1H), 7.56-7.48 (m, 2H), 7.42 (d, 2H), 7.36-7.33 (m, 1H), 7.30 (s, 1H), 6.09 (s, 1H), 5.63 (q, 1H), 4.97-4.86 (m, 2H), 4.76 (dd, 1H), 4.58 (d, 1H), 4.28-4.11 (m, 2H), 3.39-3.25 (m, 4H), 3.01-2.82 (m, 5H), 2.75-2.44 (m, 2H), 2.16 (q, 1H), 1.95-0.76 (m, 25H).

Compound 107: MS: m/z 863.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.34 (s, 1H), 8.33 (d, 2H), 8.32 (d, 1H), 7.59-7.40 (m, 6H), 7.37 (s, 1H), 6.81 (d, 1H), 6.65 (d, 1H), 6.25 (s, 1H), 6.13 (s, 1H), 5.62 (q, 1H), 4.87 (dd, 1H), 4.69-4.52 (m, 2H), 4.42 (d, 1H), 4.18 (dd, 1H), 2.95-2.40 (m, 4H), 2.24-0.78 (m, 25H).

Compound 108: MS: m/z 840.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.67 (s, 1H), 8.32 (d, 2H), 8.19 (d, 1H), 7.77 (s, 1H), 7.58-7.44 (m, 4H), 7.34-7.25 (m, 1H), 6.14 (s, 1H),

5.77 (q, 1H), 4.98 (dd, 1H), 4.78-4.71 (m, 2H), 4.44 (d, 1H), 4.29 (brs, 1H), 4.11-4.05 (m, 1H), 2.96-2.72 (m, 2H), 2.64 (s, 6H), 2.41 (br, 1H), 2.20 (q, 1H), 1.96-0.78 (m, 25H).

Compound 109: MS: m/z 837.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.49 (s, 1H), 8.35-8.25 (m, 3H), 7.71 (s, 1H), 7.55-7.41 (m, 4H), 7.26 (s, 1H), 6.19 (d, 1H), 6.01 (s, 1H), 5.63 (q, 1H), 4.88 (dd, 1H), 4.71 (brs, 1H), 4.56 (d, 1H), 4.39 (brs, 1H), 4.06 (d, 1H), 2.81-2.45 (m, 4H), 2.23 (q, 1H), 1.99-1.64 (m, 4H), 1.58-0.77 (m, 21H), 0.51 (brs, 4H).

Compound 110: MS: m/z 865.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.39 (s, 1H), 8.29 (d, 2H), 8.15 (d, 1H), 7.56-7.42 (m, 5H), 7.36-7.24 (m, 1H), 6.05 (s, 1H), 5.98 (d, 1H), 5.64 (q, 1H), 4.87 (dd, 1H), 4.69 (dd, 1H), 4.55 (d, 1H), 4.42 (dd, 1H), 4.04 (dd, 1H), 2.81-2.05 (m, 5H), 1.95-1.71 (m, 4H), 1.57-0.76 (m, 29H).

Compound 111: MS: m/z 881.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.29 (s, 1H), 8.33 (d, 2H), 8.30 (s, 1H), 7.58-7.41 (m, 4H), 7.39 (dd, 1H), 7.22 (s, 1H), 6.10 (s, 1H), 5.98 (d, 1H), 5.62 (q, 1H), 4.91 (dd, 1H), 4.68 (dd, 1H), 4.46-4.40 (m, 2H), 4.05 (dd, 1H), 3.79-3.62 (m, 2H), 3.21-3.09 (m, 2H), 2.88-2.40 (m, 3H), 2.22-1.72 (m, 6H), 1.47-0.78 (m, 25H).

Compound 112: MS: m/z 864.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.29 (s, 1H), 8.38 (d, 2H), 8.23 (d, 1H), 8.09 (s, 1H), 7.57-7.45 (m, 5H), 7.41 (dd, 1H), 7.28 (s, 1H), 6.42 (s, 1H), 6.15 (s, 1H), 5.62 (q, 1H), 4.86 (dd, 1H), 4.75-4.66 (m, 2H), 4.49 (d, 1H), 4.17 (dd, 1H), 2.83-2.43 (m, 3H), 2.25 (q, 1H), 1.99-0.78 (m, 25H).

Compound 113: MS: m/z 853.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.34 (s, 1H), 8.36 (d, 2H), 8.30 (d, 1H), 7.62-7.46 (m, 4H), 7.41-7.36 (m, 1H), 7.17 (s, 1H), 6.19 (s, 1H), 6.17 (d, 1H), 5.68 (q, 1H), 4.92 (dd, 1H), 4.73 (dd, 1H), 4.58-4.43 (m, 2H), 4.19 (dd, 1H), 2.89-2.43 (m, 3H), 2.22 (q, 1H), 1.99-1.82 (m, 6H), 1.59-0.83 (m, 28H).

Compound 114: MS: m/z 907.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.30 (s, 1H), 8.39 (d, 2H), 8.21 (d, 1H), 7.56 (dd, 1H), 7.48 (d, 2H), 7.40 (dd, 1H), 7.24 (s, 1H), 7.18 (d, 2H), 7.03 (d, 2H), 6.92 (s, 1H), 6.06 (s, 1H), 5.74 (d, 1H), 5.61 (q, 1H), 4.87 (dd, 1H), 4.70 (dd, 1H), 4.42 (d, 1H), 4.31 (dd, 1H), 4.08 (dd, 1H), 2.84-2.79 (m, 1H), 2.65-2.43 (m, 2H), 2.23 (q, 1H), 1.88-1.62 (m, 6H), 1.49-0.78 (m, 19H).

Compound 115: MS: m/z 895.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.42 (s, 1H), 8.40 (d, 2H), 8.01 (s, 1H), 7.55 (d, 2H), 7.46-7.32 (m, 3H), 6.13 (s, 1H), 5.61 (q, 1H), 5.32

(brs, 1H), 5.01-4.87 (m, 1H), 4.89 (dd, 1H), 4.62-4.55 (m, 2H), 4.34-4.08 (m, 2H), 2.94-2.55 (m, 4H), 2.50 (s, 3H), 2.23 (q, 1H), 1.95-1.10 (m, 32H).

Compound 116: MS: m/z 909.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.29 (s, 1H), 8.40 (d, 2H), 8.01 (s, 1H), 7.55 (d, 2H), 7.47-7.26 (m, 3H), 6.14 (s, 1H), 5.69 (q, 1H), 5.37 (d, 1H), 4.99 (dd, 1H), 4.78 (dd, 1H), 4.60 (d, 1H), 4.40-4.05 (m, 3H), 2.80-2.51 (m, 3H), 2.50 (s, 3H), 2.29 (q, 1H), 1.98-1.12 (m, 32H), 0.82 (s, 3H).

Compound 117: MS: m/z 855.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.08 (s, 1H), 8.22 (d, 2H), 8.03 (d, 2H), 7.44-7.18 (m, 3H), 7.26-7.17 (m, 1H), 7.13 (d, 1H), 6.12 (s, 1H), 5.65 (q, 1H), 4.89 (dd, 1H), 4.77 (dd, 1H), 4.49 (d, 1H), 4.42-4.36 (m, 1H), 4.13 (dd, 1H), 3.16 (s, 1H), 2.84-2.46 (m, 4H), 2.16 (q, 1H), 1.95-0.77 (m, 31H).

Compound 118: MS: m/z 895.4 (M^++1).

Compound 119: MS: m/z 895.4 (M^++1).

Compound 120: MS: m/z 840.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.26 (s, 1H), 8.38 (d, 2H), 8.20 (d, 1H), 8.00 (d, 1H), 7.61-7.54 (m, 2H), 7.50 (d, 2H), 7.41-7.35 (m, 1H), 7.15 (s, 1H), 6.72 (d, 1H), 6.10 (d, 1H), 5.63 (q, 1H), 5.27 (d, 1H), 4.89 (dd, 1H), 4.68 (dd, 1H), 4.51-4.42 (m, 2H), 4.12 (dd, 1H), 2.84-2.43 (m, 4H), 2.22 (q, 1H), 1.98-0.84 (m, 24H).

Compound 121: MS: m/z 829.3 (M^++1).

Compound 122: MS: m/z 833.3 (M^++1).

Compound 123: MS: m/z 821.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.27 (s, 1H), 7.90 (dd, 1H), 7.60 (s, 1H), 7.27 (dd, 1H), 7.32-7.20 (m, 2H), 6.91 (s, 1H), 6.53 (dd, 1H), 6.03 (s, 1H), 5.64 (q, 1H), 4.98-4.89 (m, 2H), 4.71-4.58 (m, 2H), 4.14-4.03 (m, 2H), 2.86-2.80 (m, 1H), 2.67-2.40 (m, 2H), 2.22 (q, 1H), 1.98-1.10 (m, 15H), 1.05 (s, 9H), 0.98-0.82 (m, 1H).

Compound 124: MS: m/z 779.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.31 (s, 1H), 7.93 (dd, 1H), 7.70 (s, 1H), 7.65-7.55 (dd, 1H), 7.41-7.26 (m, 2H), 7.04 (s, 1H), 6.61 (s, 1H), 6.15 (s, 1H), 5.72 (q, 1H), 5.37 (d, 1H), 5.01-4.91 (m, 1H), 4.77 (dd, 1H), 4.46 (d, 1H), 4.37-4.09 (m, 2H), 3.36 (s, 3H), 2.92-2.53 (m, 3H), 2.23 (q, 1H), 1.99-0.86 (m, 16H).

Compound 125: MS: m/z 817.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.28 (s, 1H), 7.98 (d, 1H), 7.66 (s, 1H), 7.60 (dd, 1H), 7.40-7.09 (m, 3H), 6.11 (s, 1H), 6.60 (s, 1H), 6.17 (s,

1H), 5.72 (q, 1H), 4.99 (dd, 1H), 4.76-4.67 (m, 2H), 4.31-4.18 (m, 2H), 2.91-2.75 (m, 2H), 2.45 (br, 1H), 2.22-0.84 (m, 17H).

Compound 126: MS: m/z 763.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.29 (s, 1H), 7.81 (dd, 1H), 7.60 (s, 1H), 7.52 (dd, 1H), 7.35-7.18 (m, 3H), 6.52 (d, 1H), 6.13-6.01(m, 2H), 5.61 (q, 1H), 4.83 (dd, 1H), 4.62 (dd, 1H), 4.45 (dd, 1H), 4.38 (d, 1H), 4.17 (dd, 1H), 2.85-2.79 (m, 1H), 2.67 (d, 1H), 2.41 (m, 1H), 2.21-0.84 (m, 20H).

Compound 127: MS: m/z 821.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.37 (s, 1H), 8.15 (s, 1H), 7.79 (d, 1H), 7.45-7.42 (m, 3H), 7.35-7.25 (m, 1H), 7.01 (s, 1H), 5.89 (s, 1H), 5.54 (q, 1H), 5.19 (d, 1H), 4.85 (dd, 1H), 4.67 (dd, 1H), 4.54 (d, 1H), 4.20 (dd, 1H), 4.04 (d, 1H), 2.91-2.44 (m, 3H), 2.24 (q, 1H), 2.01-1.11 (m, 15H), 1.06 (s, 9H), 0.83-0.78 (m, 1H).

Compound 128: MS: m/z 833.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.37 (s, 1H), 8.07 (d, 1H), 7.56-7.22 (m, 5H), 6.89 (d, 1H), 5.96 (s, 1H), 5.57-5.49 (m, 1H), 5.21-5.17 (m, 1H), 4.96-4.83 (m, 1H), 4.72 (dd, 1H), 4.67 (d, 1H), 4.18-4.03 (m, 2H), 2.90-2.79 (m, 1H), 2.69 (s, 3H), 2.64-2.46 (m, 2H), 2.22 (q, 1H), 1.97-1.04 (m, 15H), 1.04 (s, 9H), 0.96-0.87 (m, 1H).

Compound 129: MS: m/z 836.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.29 (s, 1H), 7.88 (d, 1H), 7.53-7.50 (m, 1H), 7.49 (dd, 1H), 7.19 (s, 1H), 6.65 (s, 1H), 6.04 (s, 1H), 5.70-5.50 (m, 1H), 5.12-4.48 (m, 4H), 4.19-3.98 (m, 2H), 2.95-2.58 (m, 3H), 2.48 (s, 3H), 2.32-2.12 (m, 1H), 1.97-1.18 (m, 15H), 1.00 (s, 9H), 0.98-0.86 (m, 1H).

Compound 130: MS: m/z 832.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.20 (s, 1H), 7.84 (dd, 1H), 7.52 (dd, 1H), 7.39 (, 1H), 7.38-7.26 (m, 2H), 6.62 (s, 1H), 6.05 (s, 1H), 5.60 (q, 1H), 4.83 (dd, 1H), 4.67 (dd, 1H), 4.55 (dd, 1H), 4.36 (d, 1H), 4.08 (dd, 1H), 2.81-2.50 (m, 3H), 2.48 (s, 3H), 2.45-2.37 (m, 1H), 2.18 (q, 1H), 1.99-0.87 (m, 15H).

Compound 131: MS: m/z 888.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.36 (s, 1H), 8.23 (d, 1H), 7.41 (s, 1H), 7.30 (m, 2H), 7.11 (s, 1H), 6.16 (s, 1H), 5.68 (q, 1H), 5.23 (d, 1H), 4.98 (dd, 1H), 4.75 (brs, 1H), 4.54 (d, 1H), 4.36-4.11 (m, 3H), 3.39-3.27 (m, 1H), 2.96-2.63 (m, 3H), 2.54 (s, 3H), 2.25 (q, 1H), 1.89-0.93 (m, 30H).

Compound 132: MS: m/z 888.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.24 (s, 1H), 8.37 (d, 1H), 7.74-7.51 (m, 2H), 7.48-7.42 (m, 1H), 7.22 (s, 1H), 7.12 (s, 1H), 6.17 (s, 1H), 5.70 (q, 1H), 5.28 (d, 1H), 4.99 (dd, 1H), 4.76 (dd, 1H), 4.58 (d, 1H), 4.52 (brs, 1H),

4.35-4.16 (m, 2H), 3.40-3.35 (m, 1H), 2.79-2.43 (m, 3H), 2.25 (q, 1H), 1.95-1.23 (m, 29H),0.87-0.76 (m, 3H).

Compound 133: MS: m/z 887.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.37 (s, 1H), 8.59 (s, 1H), 8.22 (d, 1H), 7.81 (d, 1H), 7.58-7.42 (m, 3H), 6.95-6.89 (m, 2H), 6.09 (s, 1H), 5.68 (q, 1H), 5.32 (d, 1H), 4.99 (m, 1H), 4.74 (m, 1H), 4.54 (d, 1H), 4.39-4.22 (m, 1H), 4.14-4.11 (m, 1H), 2.90 (m, 1H), 2.78 (m, 2H), 2.55 (m, 1H), 2.27 (q, 1H), 1.90-1.10 (m, 21H), 1.45 (s, 9H), 0.94-0.83 (m, 2H).

Compound 134: MS: m/z 901.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.21 (s, 1H), 8.8.51 (s, 1H), 8.23 (d, 1H), 7.81 (d, 1H), 7.59-7.43 (m, 3H), 7.13 (s, 1H), 6.90 (d, 1H), 6.09 (s, 1H), 5.68 (q, 1H), 5.22 (d, 1H), 4.99 (dd, 1H), 4.76 (m, 1H), 4.55 (d, 1H), 4.39-4.22 (m, 1H), 4.14-4.11 (m, 1H), 2.78 (m, 2H), 2.55 (m, 1H), 2.27 (q, 1H), 1.90-0.83 (m, 23H), 1.46 (s, 9H).

Compound 135: MS: m/z 888.3 (M^++1).

Compound 136: MS: m/z 902.3 (M^++1).

Compound 137: MS: m/z 899.4 (M^++1).

Compound 138: MS: m/z 885.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.36 (s, 1H), 8.17 (d, 1H), 7.58 (m, 2H), 7.42-7.33 (m, 2H), 6.63 (m, 1H), 6.07 (s, 1H), 5.67 (q, 1H), 5.29 (d, 1H), 4.97 (dd, 1H), 4.77 (m, 1H), 4.57 (m, 1H), 4.42-4.03 (m, 3H), 2.89 (m, 1H), 2.75 (m, 5H), 2.52 (m, 1H), 2.27 (q, 1H), 1.91-0.82 (m, 32H).

Compound 139: MS: m/z 803.3 (M^++1).

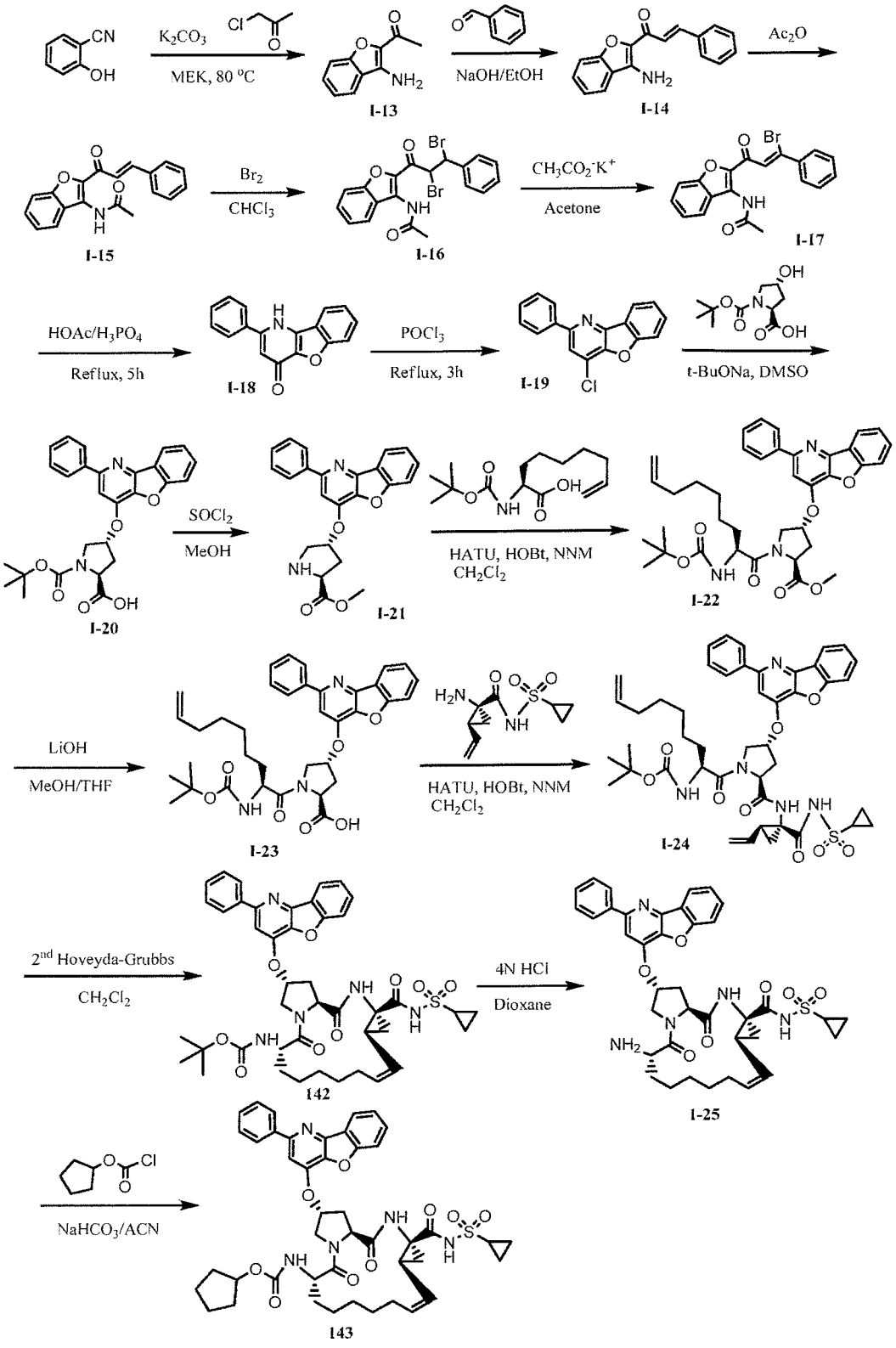
Compound 140: MS: m/z 817.3 (M^++1).

Compound 141: MS: m/z 831.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.33 (s, 1H), 8.05 (s, 1H), 7.56-7.48 (m, 3H), 6.06 (s, 1H), 5.62 (q, 1H), 5.15 (dd, 1H), 4.91 (dd, 1H), 4.75 (dd, 1H), 4.59 (d, 1H), 4.35-4.02 (m, 3H), 2.96-2.88 (m, 1H), 2.74-2.65 (m, 2H), 2.53 (s, 3H), 2.24 (q, 1H), 1.96-0.89 (m, 24H).

Example 142 and 143: Synthesis of [4-Cyclopropanesulfonylaminocarbonyl-2,15-dioxo-18-(2-phenyl-benzo[4,5]furo[3,2-b]pyridin-4-yloxy)-3,16-diaza-tricyclo[14.3.0.04,6]nonadec-7-en-14-yl]-carbamic acid tert-butyl ester (Compound 142) and [4-Cyclopropanesulfonylaminocarbonyl-2,15-dioxo-18-(2-phenyl-

benzo[4,5]furo[3,2-b]pyridin-4-yloxy)-3,16-diaza-tricyclo[14.3.0.04,6]nonadec-7-en-14-yl]-carbamic acid cyclopentyl ester (Compound 143)

Compounds 142 and 143 were prepared via the route shown below:


K2CO3
MEK, 80 °C
NaOH/EtOH
Ac2O
I-13
I-14
Br2
CHCl3
CH3CO2-K+
Acetone
I-15
I-16
I-17
HOAc/H3PO4
Reflux, 5h
POCl3
Reflux, 3h
I-18
I-19
t-BuONa, DMSO
SOCl2
MeOH
I-20
I-21
HATU, HOBt, NNM
CH2Cl2
I-22
LiOH
MeOH/THF
I-23
HATU, HOBt, NNM
CH2Cl2
I-24
2nd Hoveyda-Grubbs
CH2Cl2
142
4N HCl
Dioxane
I-25
NaHCO3/ACN
143

To a solution of 2-hydroxybenzonitrile (30 g, 251.6 mmol) in ethyl methyl ketone (320 mL) was added potassium carbonate (69.6 g, 755.5 mmol). After stirred at room temperature for 30 min, chloroacetone (34.95 g, 377.8 mmol) was added to the resulting mixture and then the solution was heated at 100°C for overnight. Finally, the reaction solvent was removed under reduced pressure and the resulting solid was washed with water and ethyl ether to give I-13 (31 g, 70.3% yield) MS: m/z 176.0 (M^++1); ^{1}H NMR ($CDCl_3$) δ 7.59 (d, 1H), 7.46 (dd, 1H), 7.41 (d, 1H), 7.24 (dd, 1H), 2.50 (s, 3H).

To a solution of 2-acetyl-3-aminobenzofuran I-13 (2.17 g, 12.38 mmol) and benzaldehyde (1.31 g, 12.38 mmol) in ethanol (30 mL) at 5~10°C was added an aqueous solution of sodium hydroxide (70%, 5 mL) dropwise under constant stirring. After stirred for overnight, a bright yellow solid of crude product was suspended in the reaction solution. The solid was filtrated, collected, and re-crystallized from ethanol to afford a silky needles I-14 (2.7 g, 90%). MS: m/z 264.0 (M^++1); ^{1}H NMR ($CDCl_3$) δ 7.83 (d, 1H), 7.71 (dd, 2H), 7.64 (d, 1H), 7.62 (d, 1H), 7.58-7.39 (m, 5H), 7.29-7.24 (m, 1H), 5.83 (broad, 2H).

Intermediate I-14 (1.32 g, 5.0 mmol) was suspended in acetic anhydride (10 mL) and stirred on a warmed water-bath. After stirred overnight, the reaction mixture was poured into ice-water. The suspended crude product was separated and collected, and then re-crystallized from ethanol to give I-15 (1.52g, 90%). MS: m/z 306.0 (M^++1); ^{1}H NMR ($CDCl_3$) δ 8.58 (d, 1H), 7.91 (d, 1H), 7.72 (m, 3H), 7.54-7.44 (m, 5H), 7.34-7.7.28 (m, 1H), 2.35 (s, 3H).

A solution of intermediate I-15 (1.22 g, 4.0 mmol) in $CHCl_3$ (20 mL) was added dropwise to a solution of bromine (0.72 g 4.5 mmol) in $CHCl_3$ (15mL) slowly. After stirred overnight, the reaction mixture was quenched with ice water. The suspended solid was separated, collected, and re-crystallized from ethanol/H2O to afford I-16 (1.12 g, 60%). MS: m/z 465.9 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.22 (brs, 1H), 8.63 (d, 1H), 7.61-7.25 (m, 8H), 5.92 (d, 1H), 5.62 (d, 1H), 2.37 (s, 3H).

To a solution of I-16 (0.93 g, 2.0 mmol) in acetone (25 mL) was added anhydrous potassium acetate (0.2 g, 2.0 mmol). After stirred overnight, the reaction mixture was poured into cold water. A suspended solid was separated, collected, and re-crystallized from ethanol to give monobromide-compound I-17 (0.46 g, 60%). MS: m/z 385.9

(M^++1); ^{1}H NMR ($CDCl_3$) δ 10.50 (brs, 1H), 8.54 (d, 1H), 8.48 (s, 1H), 7.93 (m, 2H), 7.56-7.46 (m, 5H), 7.36-7.31 (m,1H), 2.35 (s, 3H).

Compound I-17 (0.35 g, 1.0 mmol) in acetic acid (5 mL) and orthophosphoric acid (5 mL) was refluxed for 5 hr. The reaction mixture was cooled to room temperature, poured into an ice water and stirred for additional 30 min. A suspended solid was separated, collected, and re-crystallized from DMF to give I-18 (0.2 g, 80%). MS: m/z 262.0 (M^++1).

A solution of I-18 (1.0 g, 3.8 mmol) and phosphorus oxychloride ($POCl_3$) (10 mL) was refluxed for 2 hours. After the solution was cooled and thoroughly concentrated, the resulting residue was quenched with 10% sodium hydroxide and extracted with methylene chloride (20 mL x 3). The organic layer was collected, dried over sodium sulfate, and concentrated. The crude product was recrystallized from CH_2Cl_2 and *n*-hexane to afford I-19 (0.7 g, 75%). MS: m/z 279.9 (M^++1); ^{1}H NMR ($CDCl_3$) δ 8.45 (d, 1H), 8.09 (d, 2H), 7.84 (s, 1H), 7.71-7.64 (m, 2H), 7.56-7.47 (m, 4H).

To a suspension of Boc-trans-4-hydroxy-L-proline (0.53 g, 2.3 mmol) in DMSO (10 mL) was added *t*-BuONa (0.49 g, 5.08 mmol) at 0°C. After warmed to room temperature and stirred for 1 h, intermediate I-19 (0.64 g, 2.3 mmol) was added slowly at 10°C. The reaction mixture was stirred for 4 h and then quenched with 10% HCl aqueous solution to pH 6~7. The crude solid was filtrated, washed with water, and dried under vaccum to give I-20 (0.94g, 86.3%). MS: m/z 475.1 (M^++1); ^{1}H NMR ($CDCl_3$) δ 8.27 (d, 1H), 7.97 (m, 2H), 7.86-7.76 (m,3H), 7.66-7.44 (m, 4H), 5.81 (s, 1H), 4.47 (m, 1H), 4.03-3.89 (m, 2H), 2.81 (m,1H), 2.50 (q, 1H).

To a solution of I-20 (1.1 g, 2.3 mmol) in MeOH (20 mL) was added $SOCl_2$ (1.17 g, 9.9 mmol) at room temperature. After refluxed for 1 hour, the reaction solvent was removed under vaccum to give crude compound I-21 which was used in the next step without further purification. MS: m/z 389.1 (M^++1).

To a solution of I-21 (0.78g, 2.0 mmol), 2-(1H-7-Azabenzotriazol-1-yl)-1,1,3,3-tetramethyl uronium hexafluoro-phosphate methanaminium (HATU, 1.12 g, 3.0 mmol), N-Hydroxybenzotriazole (HOBT, 0.4 g, 3.0 mmol), and 2-tert-butoxycarbonylamino-non-8-enoic acid (1.19 g, 5.2 mmol) in CH_2Cl_2 (20 mL) was added NMM (1.0 g, 9.9 mmol) at room temperature. After the mixture was stirred overnight, it was

concentrated under vacuum. The residue was purified by silica gel column chromatography to give compound I-22 (1.02 g, 80.7%). MS: m/z 642.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 8.24 (d, 1H), 8.05 (d, 2H), 7.58 (m, 2H), 7.56-7.41 (m, 4H), 7.28 (d, 1H), 5.83-5.76 (q, 1H), 5.71 (s, 1H), 5.24 (d, 1H), 5.01-4.82 (m, 2H), 4.76 (dd, 1H), 4.75-4.34 (m, 2H), 4.03 (m, 1H), 3.77 (s, 3H), 2.78 (m, 1H), 2.36 (q, 1H), 2.01 (m, 2H), 1.75 (m, 1H), 1.54 (m, 1H), 1.42 (m, 6H), 1.31 (s, 9H).

To a solution of I-22 (1.0 g, 1.6 mmol) in THF (20 mL) was added 0.5 M LiOH (5.7 mL, 2.9 mmol) at room temperature. After the reaction mixture was stirred overnight, it was acidified by 10% HCl to pH < 7 and concentrated under vacuum to give a solid product, which was filtered and washed with water to give I-23. MS: m/z 628.1 (M^++1); ^{1}H NMR ($CDCl_3$) δ 8.34 (brs, 1H), 8.04 (d, 2H), 7.62 (m, 2H), 7.60-7.41 (m, 4H), 7.28 (m, 2H), 5.81-5.72 (q, 1H), 5.70 (s, 1H), 5.29 (d, 1H), 5.00-4.87 (m, 3H), 4.48 (m, 2H), 4.01 (m, 1H), 2.77 (m, 2H), 1.98 (m, 2H), 1.72 (m, 1H), 1.61 (m, 1H), 1.44 (m, 6H), 1.33 (s, 9H).

NMM (0.12 g, 1.2 mmol) was added to a solution of compound I-23 (0.26 g, 0.41 mmol), HATU (0.31 g, 0.81 mmol), HOBT (0.084 g, 0.61 mmol), and cyclopropanesulfonic acid (1-amino-2-vinyl-cyclopropanecarbonyl)-amide (0.094 g, 0.41 mmol) in CH_2Cl_2 (10 mL) at room temperature. After the reaction mixture was stirred overnight, it was concentrated under vacuum. The residue was purified by silica gel column chromatography to give compound I-24 (0.15g, 45%). MS: m/z 804.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.22 (s, 1H), 8.35 (d, 1H), 8.01 (d, 2H), 7.59 (d, 2H), 7.48-7.30 (m, 5H), 7.04 (s, 1H), 5.78 (m, 3H), 5.35 (d, 1H), 5.23 (d, 1H), 5.15 (d, 1H), 4.93 (m, 2H), 4.53 (dd, 1H), 4.41-4.30 (m, 2H), 4.05 (m, 1H), 2.91 (m, 1H), 2.61 (m, 2H), 2.14 (dd, 1H), 2.04 (m, 3H), 1.91-1.52 (m,3H), 1.45-1.22 (18H), 1.21 (m, 2H).

To a solution of compound I-24 (100 mg, 0.12 mmol) in CH_2Cl_2 was added Hoveyda-Grubbs 2nd generation catalyst (35mg, 0.056 mmol) under N_2 at room temperature, and then the reaction mixture was heated to 40°C and stirred for 24 hours. The reaction mixture was concentrated and purified by column to give compound 142 (30 mg, 31%). MS: m/z 812.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.29 (s, 1H), 8.28 (d,1H), 8.04 (d, 2H), 7.61-7.41 (m, 7H), 7.00 (s, 1H), 5.69 (m, 2H), 5.19 (d, 1H), 4.97 (dd, 1H),

4.67 (m, 2H), 4.31 (m, 1H), 4.05 (m, 1H), 2.89 (m, 1H), 2.70 (m, 2H), 2.55 (m, 1H), 2.29 (q, 1H), 1.89-1.11 (m, 13H), 1.19 (s, 9H), 0.97-0.86 (m, 2H).

To a solution of compound 142 (0.1 g, 0.14 mmol) in CH_2Cl_2 (5 mL) was added an excessive amount of 4 N HCl solution in dioxane (2 mL) at room temperature. After stirred for 4 hr, HCl, dioxane and CH_2Cl_2 was removed by evaporated to give crude compound I-25 which was used in the next step without further purification. MS: m/z 712.3 (M^++1).

I-25 was dissolved in acetonitrile (2 mL) and then saturated $NaHCO_3$ (1 mL) was added. The reaction mixture was stirred for 10 min. Cyclepentyl chloroformate (0.02 g, 0.15 mmol) was added to the reaction mixture at room temperature. After stirrred for additional 2 hours, the reaction mixture was quenched by saturated $NaHCO_3$ and extracted by CH_2Cl_2. The residue was purified by silica gel column chromatography to give compound 143 (0.1 g, 87%). MS: m/z 824.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.26 (s, 1H), 8.29 (d,1H), 8.07 (d, 2H), 7.62-7.32 (m, 7H), 7.00 (s, 1H), 5.75 (s, 1H), 5.70 (q, 1H), 5.22 (d, 1H), 4.99 (dd, 1H), 4.75 (m, 2H), 4.56 (d, 1H), 4.32 (m, 1H), 4.05 (m, 1H), 2.89 (m, 1H), 2.70 (m, 2H), 2.52 (m, 1H), 2.29 (q, 1H), 1.91-0.85 (m, 23H).

Example 144-253: Syntheses of Compound 144-253

Each of Compounds 144-253 was prepared in a manner similar to those described in Examples 142 and 143.

Compound 144: MS: m/z 7887.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.36 (s, 1H), 8.40 (s, 1H), 8.21 (d,1H), 8.08 (dd, 1H), 7.56-7.11 (m, 7H), 6.80 (s, 1H), 5.63 (m, 2H), 4.93 (m, 1H), 4.79 (m, 1H), 4.31 (m, 2H), 4.05 (m, 1H), 3.45 (s, 3H), 2.87 (m, 1H), 2.70 (m, 2H), 2.52 (m, 1H), 2.25 (q, 1H), 1.91-0.84 (m, 15H).

Compound 145: MS: m/z 872.3 (M^++1).

Compound 146: MS: m/z 770.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.35 (s, 1H), 8.25 (d,1H), 8.00 (d, 2H), 7.56-7.25 (m, 7H), 6.66 (s, 1H), 5.69 (m, 2H), 5.45 (d, 1H), 4.95 (dd, 1H), 4.70 (m, 1H), 4.40-4.28 (m, 2H), 4.05 (m, 1H), 3.52 (s, 3H), 2.88 (m, 1H), 2.70 (m, 2H), 2.51 (m, 1H), 2.30 (q, 1H), 1.87-1.09 (m, 13H), 0.97-0.84 (m, 2H).

Compound 147: MS: m/z 697.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.37 (s, 1H), 8.24 (d, 1H), 8.04 (d, 2H), 7.56-7.31 (m, 8H), 5.63 (m, 2H), 4.97 (dd, 1H), 4.63 (m, 1H), 4.09 (m, 1H), 3.96 (m, 1H), 2.84 (m,1H), 2.62 (m, 2H), 2.6-2.03 (m, 4H), 1.95-0.84 (m, 15H).

Compound 148: MS: m/z 872.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.29 (s, 1H), 8.09 (dd, 1H), 7.69 (d, 1H), 7.48-7.14 (m, 7H), 5.71 (m, 2H), 5.31 (d,1H), 4.98 (dd, 1H), 4.74 (m, 1H), 4.55 (d, 1H), 4.36 (m, 1H), 4.05 (m, 2H), 3.96 (s, 3H), 2.89 (m, 1H), 2.68 (m, 2H), 2.52 (m, 1H), 2.28 (q, 1H), 2.00-0.88 (m, 23H).

Compound 149: MS: m/z 818.2 (M^++1).

Compound 150: MS: m/z 802.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.23 (s, 1H), 8.08 (dd, 1H), 7.68 (d, 1H), 7.49 (d, 1H), 7.39-7.13 (m, 6H), 6.10 (d, 1H), 5.72 (m, 2H), 4.95 (dd, 1H), 4.63 (m, 2H), 4.17 (d, 1H), 4.06 (m, 1H), 3.92 (s, 3H), 2.89 (m, 1H), 2.69 (m, 2H), 2.46 (m, 1H), 2.26 (q, 1H), 1.94-0.86 (m, 15H), 1.91 (s, 3H).

Compound 151: MS: m/z 854.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.26 (s, 1H), 8.27 (d, 1H), 8.03 (d, 2H), 7.59 (m, 3H), 7.45 (dd, 1H), 7.01 (d, 2H), 6.88 (m, 1H), 5.74 (m, 2H), 5.19 (d, 1H), 4.96 (m, 2H), 4.75 (s, 1H), 4.53 (d, 1H), 4.32 (m, 1H), 4.04 (m, 1H), 3.87 (s, 3H), 2.89 (m, 1H), 2.69 (m, 2H), 2.46 (m, 1H), 2.27 (q, 1H), 1.90-1.12 (m,21H), 0.92-0.87(m,2H).

Compound 152: MS: m/z 842.3 (M^++1).

Compound 153: MS: m/z 854.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.31 (s, 1H), 8.58 (s, 1H), 8.43 (m,1H), 7.85 (d, 1H), 7.59 (m, 2H), 7.37 (m, 3H), 7.12 (dd, 1H), 7.01 (d, 1H), 5.65 (m, 2H), 5.31 (d, 1H), 4.94 (dd, 1H), 4.72 (m, 2H), 4.53 (d, 1H), 4.37 (m, 1H), 4.07 (m, 1H), 3.87 (s, 3H), 2.88 (m,1H), 2.66 (m, 2H), 2.50 (m, 1H), 2.28 (q, 1H), 1.88-0.82 (m, 23H).

Compound 154: MS: m/z 854.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.29 (s, 1H), 8.50 (s, 1H), 8.29 (d, 1H), 7.63 (s, 1H), 7.56 (m, 3H), 7.43 (m, 2H), 7.28 (m, 1H), 7.11 (s, 1H), 6.98 (dd,1H), 5.74 (s, 1H), 5.69 (q, 1H), 5.29 (d, 1H), 4.94 (dd, 1H), 4.73 (m, 1H), 4.57 (d, 1H), 4.34 (m, 1H), 4.04 (m, 1H), 3.92 (s, 3H), 2.88 (m, 1H), 2.68 (m,2H), 2.51 (m, 1H), 2.29 (q, 1H), 1.87-0.84 (m, 23H).

Compound 155: MS: m/z 842.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.28 (s, 1H), 8.28 (d,1H), 7.85 (d, 1H), 7.57 (m, 2H), 7.40 (m, 3H), 7.14 (dd, 1H), 7.01 (d, 2H), 5.68 (q, 1H), 5.58 (s, 1H), 5.19 (d, 1H), 4.92 (dd, 1H), 4.67 (m, 2H), 4.33 (m, 1H), 4.03 (m, 1H),

3.87 (s, 3H), 2.89 (m,1H), 2.68 (m, 2H), 2.54 (m, 1H), 2.28 (q, 1H), 1.90-1.11 (m, 13H), 1.21 (s, 9H), 0.97-0.87 (m, 2H).

Compound 156: MS: m/z 854.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.24 (s, 1H), 8.59 (s, 1H), 8.04 (m, 2H), 7.84 (d, 1H), 7.49-7.28 (m, 4H), 7.08 (d, 1H), 6.91 (s, 1H), 5.72 (s, 1H), 5.68 (q, 1H), 5.21 (d, 1H), 4.97 (dd, 1H), 4.71-4.67 (m, 2H), 4.56 (d, 1H), 4.36 (m, 1H), 4.05 (s, 3H), 4.04 (m, 1H), 2.90 (m, 1H), 2.69 (m, 2H), 2.54 (m, 1H), 2.31 (q, 1H), 1.96-1.06 (m, 21H), 0.95-0.83 (m, 2H).

Compound 157: MS: m/z 838.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.30 (s, 1H), 8.59 (s, 1H), 8.27 (d, 1H), 7.92 (d, 2H), 7.57 (m, 2H), 7.44 (m, 1H), 7.26-7.17 (m, 3H), 5.68 (s, 1H), 5.64 (q, 1H), 5.37 (d, 1H), 4.96 (m, 1H), 4.76 (m, 1H), 4.67 (m, 1H), 4.56 (d, 1H), 4.36 (m, 1H), 4.04 (m, 1H), 2.89 (m, 1H), 2.69 (m, 2H), 2.53 (m, 1H), 2.40 (s, 3H), 2.31 (q, 1H), 1.94-1.07 (m, 21H), 0.95-0.83 (m, 2H).

Compound 158: MS: m/z 842.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.31 (s, 1H), 8.26 (d, 1H), 8.05 (m, 2H), 7.58 (m, 2H), 7.43 (m, 1H), 7.25-7.19 (m, 4H), 5.72 (s, 1H), 5.68 (q, 1H), 5.35 (d, 1H), 4.96 (dd, 1H), 4.75-4.69 (m, 2H), 4.56 (d, 1H), 4.36 (m, 1H), 4.04 (m, 1H), 2.87 (m, 1H), 2.67 (m, 2H), 2.50 (m, 1H), 2.28 (q, 1H), 1.91-1.07 (m, 21H), 0.97-0.84 (m, 2H).

Compound 159: MS: m/z 872.3 (M^++1).

Compound 160: MS: m/z 872.1 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.48 (s, 1H), 8.02 (m, 2H), 7.68 (d, 1H), 7.47 (d, 1H), 7.23-7.17 (m, 4H), 5.74 (m, 2H), 5.68 (q, 1H), 5.23 (d, 1H), 4.97 (dd, 1H), 4.76 (s, 1H), 4.67 (m, 1H), 4.54 (d, 1H), 4.33 (m, 1H), 4.04 (m, 1H), 3.93 (s, 3H), 2.89 (m, 1H), 2.67 (m, 2H), 2.52 (m, 1H), 2.27 (q, 1H), 1.92-1.06 (m, 21H), 0.97-0.84 (m, 2H).

Compound 161: MS: m/z 860.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.34 (s, 1H), 8.01 (m, 2H), 7.67 (d, 1H), 7.47 (d, 1H), 7.29-7.16 (m, 5H), 5.68 (m, 2H), 5.23 (d, 1H), 4.95 (dd, 1H), 4.69-4.63 (m, 2H), 4.31 (m, 1H), 4.04 (m, 1H), 3.92 (s, 3H), 2.88 (m, 1H), 2.67 (m, 2H), 2.54 (m, 1H), 2.27 (q, 1H), 1.92-0.83 (m, 15H), 1.20 (s, 9H).

Compound 162: MS: m/z 856.1 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.23 (s, 1H), 8.03 (m, 2H), 7.66 (d, 1H), 7.48 (d, 1H), 7.32 (s, 1H), 7.29-7.15 (m, 5H), 5.73 (m, 2H), 4.92 (dd, 1H), 4.69 (m, 2H), 4.31 (d, 1H), 4.06 (m, 1H), 3.91 (s, 3H), 2.85 (m, 1H), 2.68 (m, 2H), 2.44 (m, 1H), 2.20 (q, 1H), 1.93-0.83 (m, 15H).

Compound 163: MS: m/z 854.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.30 (s, 1H), 8.60 (s, 1H), 8.01 (m, 2H), 7.68 (d, 1H), 7.46 (m, 4H), 7.15 (m, 2H), 5.71 (s, 1H), 5.68 (q, 1H), 5.37 (d, 1H), 4.96 (dd, 1H), 4.67 (s, 1H), 4.64 (m, 1H), 4.55 (d, 1H), 4.36 (m, 1H), 4.03 (m, 1H), 3.93 (s, 3H), 2.88 (m, 1H), 2.68 (m, 2H), 2.52 (m, 1H), 2.28 (q, 1H), 1.94-1.07 (m, 21H), 0.97-0.84 (m, 2H).

Compound 164: MS: m/z 830.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.33 (s, 1H), 8.25 (d, 1H), 8.04 (m, 2H), 7.57 (m, 2H), 7.42 (m, 1H), 7.25-7.14 (m, 4H), 5.68 (m, 2H), 5.25 (d, 1H), 4.92 (dd, 1H), 4.66 (m, 2H), 4.32 (m, 1H), 4.05 (m, 1H), 2.87 (m, 1H), 2.68 (m, 2H), 2.55 (m, 1H), 2.28 (q, 1H), 1.91-1.06 (m, 13H), 1.20 (s,9H), 0.97-0.84 (m, 2H).

Compound 165: MS: m/z 868.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.29 (s, 1H), 8.53 (s, 1H), 8.13 (d, 1H), 7.91 (m, 2H), 7.58 (m, 1H), 7.19 (m, 1H), 7.00 (m, 3H), 5.72 (s, 1H), 5.68 (q, 1H), 5.28 (d, 1H), 4.95 (dd, 1H), 4.79 (s, 1H), 4.68 (m, 1H), 4.53 (d, 1H), 4.37 (m, 1H), 4.05 (m, 1H), 3.91 (s, 3H), 2.88 (m, 1H), 2.66 (m, 2H), 2.50 (m, 1H), 2.40 (s, 3H), 2.25 (q, 1H), 1.90-1.06 (m, 21H), 0.97-0.83 (m, 2H).

Compound 166: MS: m/z 868.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.30 (s, 1H), 8.59 (s, 1H), 7.98 (m, 2H), 7.71 (s, 1H), 7.46 (d, 1H), 7.27 (m, 2H), 7.15 (m, 2H), 5.71 (s, 1H), 5.68 (q, 1H), 5.29 (d, 1H), 4.94 (dd, 1H), 4.78 (s, 1H), 4.67 (m, 1H), 4.54 (d, 1H), 4.36 (m, 1H), 4.04 (m, 1H), 3.93 (s, 3H), 2.88 (m, 1H), 2.68 (m, 2H), 2.53 (m, 1H), 2.40 (s, 3H), 2.28 (q, 1H), 1.92-1.08 (m, 21H), 0.97-0.83 (m, 2H).

Compound 167: MS: m/z 872.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.29 (s, 1H), 8.51 (s, 1H), 8.08 (d, 1H), 8.01 (m, 2H), 7.15 (d, 2H), 7.04 (m, 3H), 5.73 (s, 1H), 5.69 (q, 1H), 5.30 (d, 1H), 4.95 (dd, 1H), 4.79 (s, 1H), 4.65 (m, 1H), 4.53 (d, 1H), 4.37 (m, 1H), 4.04 (m, 1H), 3.91 (s, 3H), 2.88 (m, 1H), 2.66 (m, 2H), 2.50 (m, 1H), 2.28 (q, 1H), 1.90-1.05 (m, 21H), 0.97-0.83 (m, 2H).

Compound 168: MS: m/z 826.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.23 (s, 1H), 8.28 (d, 1H), 7.94 (d, 2H), 7.56 (m, 2H), 7.42 (m, 1H), 7.28 (m, 3H), 7.03 (s, 1H), 5.68 (m, 2H), 5.21 (d, 1H), 4.94 (dd, 1H), 4.67 (m, 2H), 4.32 (m, 1H), 4.05 (m, 1H), 2.89 (m, 1H), 2.68 (m, 2H), 2.55 (m, 1H), 2.55 (s, 3H), 2.35 (q, 1H), 1.94-1.07 (m, 13H), 1.20 (s, 9H), 0.97-0.84 (m, 2H).

Compound 169: MS: m/z 858.3, 859.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.35 (s, 1H), 8.58 (s, 1H), 8.24 (d, 1H), 8.00 (d, 2H), 7.57 (m, 2H), 7.45 (m, 3H), 7.25 (s, 1H), 5.71 (s, 1H), 5.66 (q, 1H), 5.41 (d, 1H), 4.96 (dd, 1H), 4.75 (m, 2H), 4.55 (d, 1H), 4.35 (m, 1H), 4.04 (m, 1H), 2.87 (m, 1H), 2.69 (m, 2H), 2.57 (m, 1H), 2.28 (q, 1H), 1.92-0.83 (m, 23H).

Compound 170: MS: m/z 772.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.31 (s, 1H), 8.22 (d, 1H), 8.00 (m, 2H), 7.59 (m, 2H), 7.41 (m, 1H), 7.20-7.10 (m, 4H), 6.12 (d, 1H), 5.72 (m, 2H), 4.96 (dd, 1H), 4.64 (m, 1H), 4.55 (m, 1H), 4.40 (d, 1H), 4.01 (m, 1H), 2.88 (m, 1H), 2.66 (m, 2H), 2.50 (m, 1H), 2.26 (q, 1H), 1.92-1.05 (m, 13H), 1.91 (s,3H), 0.97-0.85 (m, 2H).

Compound 171: MS: m/z 768.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.29 (s, 1H), 8.26 (d, 1H), 7.93 (d, 2H), 7.57 (m, 2H), 7.42 (m, 1H), 7.27 (m, 4H), 6.16 (d, 1H), 5.69 (m, 2H), 4.94 (dd, 1H), 4.67 (m, 1H), 4.57 (m, 1H), 4.40 (d, 1H), 4.05 (m, 1H), 2.89 (m, 1H), 2.68 (m, 2H), 2.51 (m, 1H), 2.39 (s, 3H),2.30 (q, 1H), 1.94-1.05 (m, 13H), 1.92 (s, 3H), 0.97-0.84 (m, 2H).

Compound 172: MS: m/z 788.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.32 (s, 1H), 8.22 (d, 1H), 8.01 (m, 2H), 7.57 (m, 2H), 7.42 (m, 1H), 7.22-7.11 (m, 4H), 5.72 (m, 2H), 5.39 (d, 1H), 4.96 (dd, 1H), 4.71 (m, 1H), 4.39 (m, 2H), 4.04 (m, 1H), 3.54 (s, 3H), 2.89 (m, 1H), 2.71 (m, 2H), 2.54 (m, 1H), 2.25 (q, 1H), 1.91-1.06 (m, 13H), 0.93-0.83 (m, 2H).

Compound 173: MS: m/z 822.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.15 (s, 1H), 8.27 (d, 1H), 7.91 (d, 2H), 7.59 (m, 2H), 7.44 (m, 1H), 7.27 (m, 3H), 7.15 (d, 1H), 7.07 (s, 1H), 5.75 (s, 1H), 5.69 (q, 1H), 4.91 (dd, 1H), 4.68 (m, 2H), 4.32 (d, 1H), 4.06 (m, 1H), 2.89 (m, 1H), 2.68 (m, 2H), 2.41 (m, 1H), 2.39 (s, 3H), 2.21 (q, 1H), 1.96-1.08 (m, 13H), 0.96-0.83 (m, 2H).

Compound 174: MS: m/z 826.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.21 (s, 1H), 8.22 (d, 1H), 8.02 (m, 2H), 7.59 (m, 2H), 7.41 (m, 1H), 7.24-7.13 (m, 5H), 5.73 (s, 1H), 5.67 (q, 1H), 4.89 (dd, 1H), 4.72 (m, 2H), 4.31 (d, 1H), 4.05 (m, 1H), 2.87 (m, 1H), 2.69 (m, 2H), 2.47 (m, 1H), 2.24 (q, 1H), 1.93-1.04 (m, 13H), 0.93-0.82 (m, 2H).

Compound 175: MS: m/z 842.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.30 (s, 1H), 8.58 (s, 1H), 8.26 (d,1H), 8.10 (dd, 1H), 7.61-7.14 (m, 7H), 6.91 (s, 1H), 5.67 (m, 2H), 5.38

(d, 1H), 4.96 (dd, 1H), 4.70 (m, 1H), 4.56 (d, 1H), 4.36 (m, 1H), 4.06 (m, 1H), 2.88 (m, 1H), 2.69 (m, 2H), 2.51 (m, 1H), 2.28 (q, 1H), 1.87-0.88 (m, 23H).

Compound 176: MS: m/z 844.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.28 (s, 1H), 8.00 (m, 3H), 7.42 (d, 1H), 7.37 (d, 1H), 7.19 (m, 3H), 6.98 (s, 1H), 5.68 (m, 2H), 5.19 (d, 1H), 4.96 (dd, 1H), 4.66 (m, 2H), 4.30 (m, 1H), 4.04 (m, 1H), 2.89 (m, 1H), 2.67 (m, 2H), 2.52 (s, 3H), 2.51 (m, 1H), 2.26 (q, 1H), 1.94-1.05 (m, 13H), 1.20 (s, 9H), 0.98-0.83 (m, 2H).

Compound 177: MS: m/z 840.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.25 (s, 1H), 8.00 (m, 3H), 7.42 (d, 1H), 7.35-7.11 (m, 6H), 5.73 (s, 1H), 5.69 (q, 1H), 4.93 (dd, 1H), 4.66 (m, 2H), 4.32 (d, 1H), 4.04 (m, 1H), 2.89 (m, 1H), 2.70 (m, 2H), 2.51 (s, 3H), 2.48 (m, 1H), 2.23 (q, 1H), 1.95-1.04 (m, 13H), 0.96-0.82 (m, 2H).

Compound 178: MS: m/z 784.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.33 (s, 1H), 8.27 (d, 1H), 7.92 (d, 2H), 7.55 (m, 2H), 7.41 (m, 1H), 7.27 (m, 4H), 5.70 (m, 2H), 5.45 (d, 1H), 4.95 (dd, 1H), 4.67 (m, 1H), 4.36 (m, 2H), 4.06 (m, 1H), 3.49 (s, 3H), 2.89 (m, 1H), 2.69 (m, 2H), 2.51 (m, 1H), 2.39 (s, 3H),2.26 (q, 1H), 1.96-1.06 (m, 13H), 0.97-0.83 (m, 2H).

Compound 179: MS: m/z 856.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.28 (s, 1H), 7.92 (d, 2H), 7.69 (d, 1H), 7.44 (d, 1H), 7.29 (d, 2H), 7.15 (s, 1H), 7.05 (dd, 1H), 6.97 (s, 1H), 5.68 (m, 2H), 5.22 (d, 1H), 4.95 (dd, 1H), 4.62 (m, 2H), 4.30 (m, 1H), 4.03 (m, 1H), 3.93 (s, 3H), 2.87 (m, 1H), 2.66 (m, 2H), 2.54 (m, 1H), 2.41 (s, 3H), , 2.29 (q, 1H), 1.94-0.82 (m, 15H), 1.21 (s, 9H).

Compound 180: MS: m/z 814.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.35 (s, 1H), 7.92 (d, 2H), 7.63 (d, 1H), 7.42 (d, 1H), 7.33-7.21 (m, 4H), 7.10 (dd, 1H), 5.66 (m, 2H), 5.41 (d, 1H), 4.94 (dd, 1H), 4.65 (m, 1H), 4.37 (m, 2H), 4.03 (m, 1H), 3.91 (s, 3H), 3.50 (s, 3H), 2.87 (m, 1H), 2.66 (m, 2H), 2.51 (m, 1H), 2.41 (s, 3H), 2.25 (q, 1H), 1.94-1.07 (m, 13H), 0.93-0.83 (m, 2H).

Compound 181: MS: m/z 852.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.19 (s, 1H), 7.91 (d, 2H), 7.71 (d, 1H), 7.48 (d, 1H), 7.30-7.15 (m, 5H), 7.13 (dd, 1H), 5.66 (s, 1H), 5.64 (q, 1H), 4.94 (dd, 1H), 4.65 (m, 2H), 4.30 (d, 1H), 4.03 (m, 1H), 3.93 (s, 3H), 2.84 (m, 1H), 2.67 (m, 2H), 2.46 (m, 1H), 2.40 (s, 3H), 2.22 (q, 1H), 1.95-0.84 (m, 15H).

Compound 182: MS: m/z 798.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.33 (s, 1H), 7.92 (d, 2H), 7.72 (d, 1H), 7.43 (d, 1H), 7.39 (s, 1H), 7.21 (m, 3H), 7.11 (dd, 1H), 6.18 (d, 1H), 5.70 (q, 1H), 5.64 (s, 1H), 4.94 (dd, 1H), 4.66 (dd, 1H), 4.56 (m, 1H), 4.39 (d, 1H), 4.02 (m, 1H), 3.93 (s, 3H), 2.84 (m, 1H), 2.68 (m, 2H), 2.47 (m, 1H), 2.39 (s, 3H), 2.25 (q, 1H), 1.95-0.83 (m, 15H), 1.91 (s, 3H).

Compound 183: MS: m/z 802.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.39 (s, 1H), 7.96 (m, 3H), 7.44 (m, 2H), 7.35 (m, 1H), 7.14 (m, 3H), 5.66 (m, 2H), 5.41 (d, 1H), 4.92 (dd, 1H), 4.61 (m, 1H), 4.30 (m, 2H), 4.00 (m, 1H), 3.50 (s, 3H), 2.89 (m, 1H), 2.72 (m, 2H), 2.51 (s, 3H), 2.50 (m, 1H), 2.26 (q, 1H), 1.93-1.06 (m, 13H), 0.97-0.83 (m, 2H).

Compound 184: MS: m/z 786.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.36 (s, 1H), 7.96 (m, 3H), 7.42 (m, 2H), 7.32 (m, 1H), 7.15 (m, 3H), 6.12 (d, 1H), 5.69 (q, 1H), 5.65 (s, 1H), 4.94 (dd, 1H), 4.64 (m, 1H), 4.54 (m, 1H), 4.38 (d, 1H), 3.98 (m, 1H), 2.88 (m, 1H), 2.71 (m, 2H), 2.50 (m, 1H), 2.49 (s, 3H), 2.27 (q, 1H), 1.92-0.82 (m, 15H), 1.91 (s, 3H).

Compound 185: MS: m/z 812.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.37 (s, 1H), 7.96 (m, 3H), 7.41 (d, 1H), 7.36 (d, 1H), 7.25 (m, 1H), 7.10 (m, 3H), 6.19 (d, 1H), 5.71 (q, 1H), 5.64 (s, 1H), 4.95 (dd, 1H), 4.66 (m, 1H), 4.48 (m, 2H), 3.99 (m, 1H), 2.89 (m, 1H), 2.70 (m, 2H), 2.51 (m, 1H), 2.50 (s, 3H), 2.27 (q, 1H), 1.91-1.10 (m, 14H), 0.97-0.80 (m, 2H), 0.80-0.68 (m, 4H).

Compound 186: MS: m/z 856.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.28 (s, 1H), 8.00 (m, 3H), 7.42 (d, 1H), 7.37 (d, 1H), 7.25-7.13 (m, 3H), 7.04 (s, 1H), 5.72 (s, 1H), 5.69 (q, 1H), 5.23 (d, 1H), 4.97 (dd, 1H), 4.77 (s, 1H), 4.67 (m, 1H), 4.55 (d, 1H), 4.35 (m, 1H), 4.04 (m, 1H), 2.89(m, 1H), 2.68 (m, 2H), 2.52 (s, 3H), 2.51 (m, 1H), 2.25 (q, 1H), 1.93-1.06 (m, 21H), 0.97-0.83 (m, 2H).

Compound 187: MS: m/z 830.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.29 (s, 1H), 8.01 (d, 2H), 7.93 (d, 1H), 7.50 (m, 4H), 7.29 (m, 2H), 7.07 (s, 1H), 5.67 (m, 2H), 5.19 (d, 1H), 4.94 (dd, 1H), 4.67 (m, 2H), 4.30 (m, 1H), 4.04 (m, 1H), 2.89 (m, 1H), 2.69 (m, 2H), 2.52 (m, 1H), 2.28 (q, 1H), 1.94-1.05 (m, 13H), 1.19 (s, 9H), 0.97-0.84 (m, 2H).

Compound 188: MS: m/z 842.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.27 (s, 1H), 8.02 (d, 2H), 7.93 (d, 1H), 7.52 (m, 4H), 7.32 (s, 1H), 7.26 (m, 1H), 7.08 (s, 1H), 5.68 (s, 1H), 5.66 (q, 1H), 5.22 (d, 1H), 4.92 (dd, 1H), 4.71 (m, 2H), 4.57 (d, 1H), 4.33 (m, 1H), 4.05 (m, 1H), 2.89(m, 1H), 2.68 (m, 2H), 2.53 (m, 1H), 2.28 (q, 1H), 1.95-0.83 (m, 23H).

Compound 189: MS: m/z 882.4 (M^++1).

Compound 190: MS: m/z 884.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.29 (s, 1H), 7.96 (m, 3H), 7.54 (m, 1H), 7.36-7.26 (m, 5H), 5.70 (m, 2H), 5.27 (d, 1H), 4.95 (dd, 1H), 4.74 (m, 1H), 4.53 (d, 1H), 4.32 (m, 1H), 4.05 (m, 2H), 2.95 (m, 2H), 2.69 (m, 2H), 2.52 (m, 1H), 2.28 (q, 1H), 1.94-0.83 (m, 23H), 1.29 (d, 6H).

Compound 191: MS: m/z 898.2 (M^++1).

Compound 192: MS: m/z 880.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.31 (s, 1H), 8.28 (d, 1H), 7.95 (d, 2H), 7.50 (m, 4H), 7.42 (dd, 1H), 7.27 (s, 1H), 7.21 (s, 1H), 5.68 (s, 1H), 5.65 (q, 1H), 5.35 (d, 1H), 4.94 (dd, 1H), 4.72 (m, 2H), 4.57 (d, 1H), 4.35 (m, 1H), 4.04 (m, 1H), 2.88 (m, 1H), 2.68 (m, 2H), 2.53 (m, 1H), 2.28 (q, 1H), 1.93-1.05 (m, 21H), 1.36 (s, 9H), 0.97-0.82 (m, 2H).

Compound 193: MS: m/z 894.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.21 (s, 1H), 8.28 (d, 1H), 7.95 (d, 2H), 7.52 (m, 4H), 7.41 (dd, 1H), 7.34 (s, 1H), 7.26 (s, 1H), 5.70 (s, 1H), 5.65 (q, 1H), 5.41 (d, 1H), 4.95 (dd, 1H), 4.75 (m, 2H), 4.57 (d, 1H), 4.36 (m, 1H), 4.05 (m, 1H), 2.70 (m, 2H), 2.50 (m, 1H), 2.29 (q, 1H), 1.93-0.82 (m, 23H), 1.46 (s, 3H), 1.36 (s, 9H).

Compound 194: MS: m/z 857.3 (M^++1).

Compound 195: MS: m/z 857.3 (M^++1).

Compound 196: MS: m/z 784.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.20 (s, 1H), 8.27 (d,1H), 7.88 (d, 1H), 7.57 (m, 2H), 7.39 (m, 3H), 7.13 (dd, 1H), 7.01 (d, 2H), 6.14 (d, 1H), 5.68 (q, 1H), 5.62 (s, 1H), 4.97 (dd, 1H), 4.64 (m, 2H), 4.41 (d, 1H), 4.07 (m, 1H), 3.87 (s, 3H), 2.87 (m,1H), 2.67 (m, 2H), 2.45 (m, 1H), 2.25 (q, 1H), 1.93-0.85 (m, 15H), 1.92 (s, 3H).

Compound 197: MS: m/z 856.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.34 (s, 1H), 8.03 (s, 1H), 8.00 (d, 2H), 7.45 (d, 1H), 7.35 (d, 1H), 7.16 (m, 2H), 7.00 (d, 2H), 5.71 (s, 1H), 5.69 (q, 1H), 5.23 (d, 1H), 4.95 (dd, 1H), 4.62 (m, 2H), 4.30 (m, 1H), 4.03 (m, 1H), 3.86 (s, 3H), 2.88 (m, 1H), 2.66 (m, 2H), 2.51 (s, 3H), 2.50 (m, 1H), 2.31 (q, 1H), 1.91-0.82 (m, 15H), 1.22 (s, 9H).

Compound 198: MS: m/z 784.2 (M^++1).

Compound 199: MS: m/z 798.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.37 (s, 1H), 7.96 (m, 3H), 7.58 (s, 1H), 7.43 (d, 1H), 7.32 (d, 1H), 7.16 (s, 1H), 6.97 (d, 2H), 6.24 (d, 1H),

5.69 (q, 1H), 5.64 (s, 1H), 4.96 (dd, 1H), 4.66 (m, 1H), 4.55 (m, 1H), 4.40 (d, 1H), 4.02 (m, 1H), 3.84 (s, 3H), 2.87 (m, 1H), 2.68 (m, 2H), 2.49 (s, 3H), 2.50 (m, 1H), 2.28 (q, 1H), 1.91-0.83 (m, 15H), 1.91 (s, 3H).

Compound 200: MS: m/z 852.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.26 (s, 1H), 8.03 (s, 1H), 7.96 (d, 2H), 7.52 (s, 1H), 7.45 (d, 1H), 7.34 (d, 1H), 7.23 (s, 1H), 6.98 (d, 2H), 5.67 (s, 1H), 5.64 (q, 1H), 5.21 (m, 1H), 4.93 (dd, 1H), 4.67 (m, 2H), 4.30 (d, 1H), 4.04 (m, 1H), 3.85 (s, 3H), 2.87 (m, 1H), 2.66-2.40 (m, 3H), 2.51 (s, 3H), 2.22 (q, 1H), 1.95-0.82 (m, 15H).

Compound 201: MS: m/z 814.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.41 (s, 1H), 7.98 (m, 3H), 7.60 (s, 1H), 7.43 (d, 1H), 7.33 (d, 1H), 7.16 (s, 1H), 6.98 (d, 2H), 5.64 (m, 2H), 5.29 (m, 2H), 4.93 (dd, 1H), 4.69 (m, 1H), 4.36 (m, 1H), 4.01 (m, 1H), 3.84 (s, 3H), 3.42 (s, 3H), 2.87 (m, 1H), 2.66 (m, 2H), 2.50 (m, 1H), 2.49 (s, 3H), 2.25 (q, 1H), 1.94-0.82 (m, 15H).

Compound 202: MS: m/z 838.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.23 (s, 1H), 8.26 (d, 1H), 8.00 (d, 2H), 7.60 (m, 2H), 7.44 (m, 2H), 7.23 (m, 2H), 7.01 (d, 2H), 5.73 (s, 1H), 5.67 (q, 1H), 4.94 (dd, 1H), 4.68 (m, 2H), 4.32 (d, 1H), 4.07 (m, 1H), 3.86 (s, 3H), 2.86 (m, 1H), 2.67 (m, 2H), 2.41 (m, 1H), 2.23 (q, 1H), 1.94-1.08 (m,13H), 0.94-0.87 (m,2H).

Compound 203: MS: m/z 842.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.30 (s, 1H), 8.28 (d, 1H), 7.63 (s, 1H), 7.57 (m, 3H), 7.42 (m, 2H), 7.25 (m, 1H), 7.08 (s, 1H), 6.97 (dd,1H), 5.71 (m, 2H), 5.22 (d, 1H), 4.92 (dd, 1H), 4.64 (m, 2H), 4.31 (m, 1H), 4.00 (m, 1H), 3.91 (s, 3H), 2.89 (m, 1H), 2.69 (m,2H), 2.55 (m, 1H), 2.29 (q, 1H), 1.85-0.83 (m, 15H), 1.19 (s, 9H).

Compound 204: MS: m/z 784.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.28 (s, 1H), 8.26 (d, 1H), 7.62 (s, 1H), 7.58 (m, 3H), 7.41 (m, 2H), 7.25 (m, 2H), 6.96 (dd,1H), 6.13 (d, 1H), 5.71 (q, 1H), 5.68 (s, 1H), 4.95 (dd, 1H), 4.63 (t, 1H), 4.59 (m, 1H), 4.41 (d, 1H), 4.04 (m, 1H), 3.90 (s, 3H), 2.88 (m, 1H), 2.71 (m,2H), 2.52 (m, 1H), 2.29 (q, 1H), 1.92-1.1.05 (m, 13H), 1.91 (s, 3H), 0.97-0.84 (m, 2H).

Compound 205: MS: m/z 801.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.34 (s, 1H), 8.25 (d, 1H), 7.61 (s, 1H), 7.57 (m, 3H), 7.39-7.25 (m, 4H), 6.93 (dd,1H), 5.70 (m, 2H), 5.44 (d, 1H), 4.94 (dd, 1H), 4.70 (m, 1H), 4.39 (d, 1H), 4.32 (m, 1H), 4.03 (m, 1H), 3.90 (s,

3H), 3.48 (s, 3H), 2.88 (m, 1H), 2.70 (m,2H), 2.52 (m, 1H), 2.26 (q, 1H), 1.89-0.82 (m, 15H).

Compound 206: MS: m/z 838.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.19 (s, 1H), 8.27 (d, 1H), 7.62 (s, 1H), 7.58 (m, 3H), 7.41 (m, 2H), 7.25 (m, 3H), 6.97 (dd,1H), 5.71 (s, 1H), 5.63 (q,1H), 4.92 (dd, 1H), 4.64 (m, 2H), 4.33 (d, 1H), 4.05 (m, 1H), 3.90 (s, 3H), 2.88 (m, 1H), 2.69 (m,2H), 2.46 (m, 1H), 2.23 (q, 1H), 1.94-1.1.03 (m, 13H), 0.95-0.84 (m, 2H).

Compound 207: MS: m/z 800.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.24 (s, 1H), 8.27 (d,1H), 7.86 (d, 1H), 7.55 (m, 2H), 7.42 (m, 3H), 7.12 (m, 2H), 7.00 (d, 1H), 5.68 (q, 1H), 5.62 (s, 1H), 5.47 (d, 1H), 4.92 (dd, 1H), 4.68 (m, 1H), 4.40 (m, 2H), 4.04 (m, 1H), 3.87 (s, 3H), 3.50 (s, 3H), 2.89 (m,1H), 2.68 (m, 2H), 2.50 (m, 1H), 2.25 (q, 1H), 1.91-1.03 (m, 13H), 0.98-0.82 (m, 2H).

Compound 208: MS: m/z 838.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.19 (s, 1H), 8.27 (d,1H), 7.82 (d, 1H), 7.57 (m, 2H), 7.39 (m, 5H), 7.12 (dd, 1H), 7.02 (d, 1H), 5.63 (q, 1H), 5.60 (s, 1H), 4.90 (dd, 1H), 4.70 (m, 2H), 4.32 (d, 1H), 4.03 (m, 1H), 3.85 (s, 3H), 2.86 (m,1H), 2.71-2.52 (m, 2H), 2.39 (m, 1H), 2.20 (q, 1H), 1.94-0.84 (m, 15H).

Compound 209: MS: m/z 896.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.20 (s, 1H), 8.31 (d, 1H), 7.99 (d, 2H), 7.58 (m, 2H), 7.42 (m, 1H), 7.30-7.22 (m, 2H), 7.01 (d, 2H), 5.68 (s, 1H), 5.66 (q, 1H), 5.37 (d, 1H), 4.96 (dd, 1H), 4.78-4.51 (m, 4H), 4.37 (m, 1H), 4.06 (m, 1H), 2.69 (m, 2H), 2.51 (m, 1H), 2.28 (q, 1H), 1.94-0.83 (m, 23H), 1.46 (s, 3H), 1.37 (d, 6H).

Compound 210: MS: m/z 882.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.24 (s, 1H), 8.27 (d, 1H), 7.98 (d, 2H), 7.58 (m, 2H), 7.42 (m, 1H), 7.24 (m, 1H), 7.01 (d, 2H), 6.89 (s, 1H), 5.68 (s, 1H), 5.66 (q, 1H), 5.22 (d, 1H), 4.97 (dd, 1H), 4.78-4.52 (m, 4H), 4.36 (m, 1H), 4.04 (m, 1H), 2.88 (m, 1H), 2.68 (m, 2H), 2.54 (m, 1H), 2.29 (q, 1H), 1.94-1.05 (m, 21H), 1.37 (d, 6H), 0.97-0.83 (m, 2H)

Compound 211: MS: m/z 922.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.13(s, 1H), 8.26(d, 1H), 8.10(d, 2H), 7.59(m, 2H), 7.42(m, 1H), 7.35-7.25(m, 3H), 7.03(s, 1H), 5.77(s, 1H), 5.66(q, 1H), 5.20(d, 1H), 4.99(dd, 1H), 4.71(m, 2H), 4.56(d, 1H), 4.35(m, 1H), 4.03(m, 1H), 2.70(m, 2H), 2.50(m, 1H), 2.29(q, 1H), 1.90-0.84(m, 23H), 0.85 (s, 3H).

Compound 212: MS: m/z 892.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.36 (s, 1H), 8.59 (s, 1H), 8.25 (d, 1H), 8.18 (d, 2H), 7.73 (d, 2H), 7.58 (m, 2H), 7.45 (m, 1H), 7.34 (s, 1H), 5.74 (s, 1H), 5.68 (q, 1H), 5.39 (d, 1H), 4.94 (dd, 1H), 4.72 (m, 2H), 4.55 (d, 1H), 4.31 (m, 1H), 4.04 (m, 1H), 2.86 (m, 1H), 2.67 (m, 2H), 2.49 (m, 1H), 2.26 (q, 1H), 1.91-1.05 (m, 23H).

Compound 213: MS: m/z 880.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.36 (s, 1H), 8.26 (d, 1H), 8.16 (d, 2H), 7.74 (d, 2H), 7.59 (m, 2H), 7.45 (m, 1H), 7.30 (m, 2H), 5.71 (s, 1H), 5.66 (q, 1H), 5.25 (d, 1H), 4.95 (dd, 1H), 4.71 (m, 1H), 4.65 (d, 1H), 4.28 (m, 1H), 4.03 (m, 1H), 2.87 (m, 1H), 2.70 (m, 2H), 2.51 (m, 1H), 2.27 (q, 1H), 1.92-1.06 (m, 13H), 1.19 (s, 9H), 0.97-0.82 (m, 2H).

Compound 214: MS: m/z 780.2 (M^++1).

Compound 215: MS: m/z 822.2 (M^++1).

Compound 216: MS: m/z 910.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.30 (s, 1H), 8.15 (d, 2H), 7.75 (d, 2H), 7.61 (s, 1H), 7.47 (d, 1H), 7.25-7.15 (m, 3H), 5.72 (s, 1H), 5.68 (q, 1H), 5.18 (d, 1H), 4.98 (dd, 1H), 4.67 (m, 2H), 4.28 (m, 1H), 4.04 (m, 1H), 3.93 (s, 3H), 2.89 (m, 1H), 2.69 (m, 2H), 2.52 (m, 1H), 2.28 (q, 1H), 1.91-0.85 (m, 15H), 1.20 (s, 9H).

Compound 217: MS: m/z 922.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.28 (s, 1H), 8.17 (m, 3H), 7.74 (d, 2H), 7.26 (m, 1H), 7.17 (s, 1H), 7.02 (m, 2H), 5.77 (s, 1H), 5.69 (q, 1H), 5.20 (d, 1H), 4.96 (dd, 1H), 4.77 (s, 1H), 4.69 (m, 1H), 4.54 (d, 1H), 4.33 (m, 1H), 4.04 (m, 1H), 3.92 (s, 3H), 2.89 (m, 1H), 2.71 (m, 2H), 2.52 (m, 1H), 2.28 (q, 1H), 1.90-1.05 (m, 21H), 0.97-0.83 (m, 2H).

Compound 218: MS: m/z 892.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.29 (s, 1H), 8.35 (s, 1H), 8.28 (d, 1H), 8.24 (d, 1H), 7.59 (m, 4H), 7.44 (m, 1H), 7.33 (s, 1H), 7.15 (s, 1H), 5.80 (s, 1H), 5.67 (q, 1H), 5.27 (d, 1H), 4.95 (dd, 1H), 4.70 (m, 2H), 4.58 (d, 1H), 4.30 (m, 1H), 4.06 (m, 1H), 2.88 (m, 1H), 2.70 (m, 2H), 2.54 (m, 1H), 2.28 (q, 1H), 1.92-0.83 (m, 23H).

Compound 219: MS: m/z 880.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.31 (s, 1H), 8.34 (s, 1H), 8.28 (d, 1H), 8.20 (d, 1H), 7.60 (m, 4H), 7.45 (m, 1H), 7.29 (s, 1H), 7.13 (s, 1H), 5.77 (s, 1H), 5.67 (q, 1H), 5.19 (m, 1H), 4.94 (dd, 1H), 4.67 (m, 2H), 4.26 (m, 1H), 4.05 (m, 1H), 2.88 (m, 1H), 2.71 (m, 2H), 2.53 (m, 1H), 2.29 (q, 1H), 1.90-0.83 (m, 15H), 1.18 (s, 9H).

Compound 220: MS: m/z 892.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.29 (s, 1H), 8.39 (d, 1H), 8.06 (d, 2H), 7.88 (s, 1H), 7.71 (d, 1H), 7.45 (m, 3H), 7.36 (s, 1H), 7.18 (s, 1H), 5.68 (s, 1H), 5.65 (q, 1H), 5.33 (d, 1H), 4.93 (dd, 1H), 4.72 (m, 2H), 4.67 (d, 1H), 4.36 (m, 1H), 4.05 (m, 1H), 2.88 (m, 1H), 2.70 (m, 2H), 2.53 (m, 1H), 2.28 (q, 1H), 1.92-0.84 (m, 23H).

Compound 221: MS: m/z 880.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.30 (s, 1H), 8.39 (d, 1H), 8.04 (d, 2H), 7.87 (s, 1H), 7.69 (d, 1H), 7.48 (m, 3H), 7.33 (s, 1H), 7.25 (s, 1H), 5.67 (m, 2H), 5.21 (d, 1H), 4.94 (dd, 1H), 4.68 (m, 2H), 4.30 (m, 1H), 4.04 (m, 1H), 2.88 (m, 1H), 2.69 (m, 2H), 2.52 (m, 1H), 2.28 (q, 1H), 1.93-0.84 (m, 15H), 1.17 (s, 9H).

Compound 222: MS: m/z 814.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.29 (s, 1H), 8.46 (s, 1H), 8.27 (d,1H), 7.47 (m, 3H), 7.41 (m, 1H), 7.33 (s, 1H), 7.16 (d, 1H), 7.05 (s, 1H), 6.56 (d, 1H), 5.69 (m, 2H), 5.24 (d, 1H), 4.95 (dd, 1H), 4.66 (m, 1H), 4.58 (d, 1H), 4.38 (m, 1H), 4.05 (m, 1H), 2.89 (m, 1H), 2.70 (m, 2H), 2.34 (m, 1H), 2.29 (q, 1H), 1.90-1.06 (m, 21H), 0.96-0.83 (m, 2H).

Compound 223: MS: m/z 802.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.30 (s, 1H), 8.28 (d,1H), 7.54 (m, 3H), 7.42 (m, 1H), 7.29 (s, 1H), 7.20 (d, 1H), 7.08 (s, 1H), 6.56 (d, 1H), 5.66 (m, 2H), 5.15 (d, 1H), 4.95 (dd, 1H), 4.69 (m, 2H), 4.30 (m, 1H), 4.05 (m, 1H), 2.89 (m, 1H), 2.68 (m, 2H), 2.35 (m, 1H), 2.29 (q, 1H), 1.89-1.04 (m, 13H), 1.19 (s, 9H), 0.97-0.83 (m, 2H).

Compound 224: MS: m/z 848.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.30 (s, 1H), 8.08 (d,1H), 7.58 (d, 1H), 7.39 (d, 1H), 7.14 (s, 1H), 7.12-6.95 (m, 4H), 5.70 (m, 2H), 5.20 (d, 1H), 4.95 (dd, 1H), 4.66 (m, 1H), 4.59 (d, 1H), 4.33 (m, 1H), 4.03 (m, 1H), 3.91 (s, 3H), 2.90 (m, 1H), 2.66 (m, 2H), 2.52 (m, 1H), 2.28 (q, 1H), 1.89-1.06 (m, 13H), 1.24 (s, 9H), 0.94-0.83 (m, 2H).

Compound 225: MS: m/z 760.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.35 (s, 1H), 8.25 (d,1H), 7.55 (m, 3H), 7.40 (m, 1H), 7.27 (m, 2H), 7.16 (d, 1H), 6.54 (d, 1H), 5.66 (m, 2H), 5.42 (d, 1H), 4.94 (dd, 1H), 4.67 (m, 1H), 4.46 (d, 1H), 4.35 (m, 1H), 4.04 (m, 1H), 3.50 (s, 3H), 2.89 (m, 1H), 2.66 (m, 2H), 2.33 (m, 1H), 2.26 (q, 1H), 1.92-0.83 (m, 15H).

Compound 226: MS: m/z 798.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.20 (s, 1H), 8.25 (d, 1H), 7.55 (m, 3H), 7.41 (m, 1H), 7.27 (m, 3H), 7.16 (d, 1H), 6.56 (d, 1H), 5.66 (m,

2H), 4.94 (dd, 1H), 4.67 (m, 2H), 4.35 (d, 1H), 4.05 (m, 1H), 2.88 (m, 1H), 2.66 (m, 2H), 2.43 (m, 1H), 2.26 (q, 1H), 1.96-0.83 (m, 15H).

Compound 227: MS: m/z 744.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.31 (s, 1H), 8.21 (d,1H), 7.55 (m, 3H), 7.39 (m, 1H), 7.33-7.25 (m, 2H), 7.12 (d, 1H), 6.56 (d, 1H), 6.16 (d, 1H), 5.66 (q, 1H), 5.62 (s, 1H), 4.94 (dd, 1H), 4.62 (m, 1H), 4.59 (m, 1H), 4.41 (d, 1H), 4.06 (m, 1H), 2.87 (m, 1H), 2.68 (m, 2H), 2.50 (m, 1H), 2.26 (q, 1H), 1.95-0.83 (m, 15H), 1.90 (s, 3H).

Compound 228: MS: m/z 857.3 (M^++1).

Compound 229: MS: m/z 830.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.25 (s, 1H), 8.26 (d,1H), 7.59 (m, 2H), 7.43 (m, 2H), 7.25 (m, 2H), 7.19 (m, 1H), 7.06 (m, 1H), 5.76 (s, 1H), 5.72 (q, 1H), 5.18 (m, 1H), 4.97 (dd, 1H), 4.68 (m, 2H), 4.56 (d, 1H), 4.30 (m, 1H), 4.04 (m, 1H), 2.90 (m, 1H), 2.70 (m, 2H), 2.39 (m, 1H), 2.27 (q, 1H), 1.90-0.80 (m, 23H).

Compound 230: MS: m/z 860.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.28 (s, 1H), 8.10 (d,1H), 7.58 (d, 1H), 7.39 (d, 1H), 7.18 (s, 1H), 7.09-6.97 (m, 4H), 5.72 (s, 1H), 5.68 (q, 1H), 5.24 (d, 1H), 4.95 (dd, 1H), 4.80 (s, 1H), 4.65 (m, 1H), 4.54 (d, 1H), 4.32 (m, 1H), 4.03 (m, 1H), 3.91(s, 3H), 2.94 (m, 1H), 2.68 (m, 2H), 2.54 (m, 1H), 2.28 (q, 1H), 1.90-1.05 (m, 21H), 0.95-0.84 (m, 2H).

Compound 231: MS: m/z 848.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.26 (s, 1H), 7.64 (d,1H), 7.60 (d, 1H), 7.48 (d, 1H), 7.40 (d, 1H), 7.20 (s, 1H), 7.15 (m, 2H), 6.88 (s, 1H), 5.65 (m, 2H), 5.10 (d, 1H), 4.96 (dd, 1H), 4.63 (m, 2H), 4.31 (m, 1H), 4.04 (m, 1H), 3.94 (s, 3H), 2.86 (m, 1H), 2.68 (m, 2H), 2.56 (m, 1H), 2.29 (q, 1H), 1.94-0.83 (m, 15H), 1.22 (s, 9H).

Compound 232: MS: m/z 836.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.29 (s, 1H), 7.89 (dd,1H), 7.60 (d, 1H), 7.50 (dd, 1H), 7.40 (d, 1H), 7.22 (m, 2H), 7.10 (m, 1H), 7.00 (s, 1H), 5.68 (m, 2H), 5.18 (d, 1H), 4.95 (dd, 1H), 4.66 (m, 2H), 4.29 (m, 1H), 4.04 (m, 1H), 2.88 (m, 1H), 2.67 (m, 2H), 2.53 (m, 1H), 2.26 (q, 1H), 1.92-0.83 (m, 15H), 1.20 (s, 9H).

Compound 233: MS: m/z 806.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.36 (s, 1H), 8.05 (d,1H), 7.59 (d, 1H), 7.38 (m, 2H), 7.14-6.97 (m, 4H), 5.70 (m, 2H), 5.64 (d, 1H), 4.96 (dd, 1H), 4.65 (m, 1H), 4.58 (m, 2H), 4.04 (m, 1H), 3.90 (s, 3H), 3.58 (s, 3H), 2.89 (m, 1H), 2.68 (m, 2H), 2.53 (m, 1H), 2.25 (q, 1H), 1.88-0.82 (m, 15H).

Compound 234: MS: m/z 860.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.31 (s, 1H), 7.63 (d,1H), 7.60 (d, 1H), 7.45 (d, 1H), 7.40 (d, 1H), 7.20 (m, 2H), 7.10 (m, 2H), 5.69 (s, 1H), 5.67 (q, 1H), 5.30 (d, 1H), 4.94 (dd, 1H), 4.78 (s, 1H), 4.64 (m, 1H), 4.55 (d, 1H), 4.36 (m, 1H), 4.04 (m, 1H), 3.94 (s, 3H), 2.89 (m, 1H), 2.68 (m, 2H), 2.53 (m, 1H), 2.26 (q, 1H), 1.93-1.04 (m, 21H), 0.97-0.82 (m, 2H).

Compound 235: MS: m/z 844.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.24 (s, 1H), 8.04 (d,1H), 7.58 (d, 1H), 7.39 (d, 1H),7.31 (m, 2H), 7.18 (s, 1H), 7.08 (m, 3H), 5.70 (s, 1H), 5.67 (q, 1H), 4.86 (dd, 1H), 4.64 (m, 2H), 4.26 (d, 1H), 4.02 (m, 1H), 3.90 (s, 3H), 2.84 (m, 1H), 2.65 (m, 2H), 2.44 (m, 1H), 2.20 (q, 1H), 1.91-0.83 (m, 15H).

Compound 236: MS: m/z 832.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.27 (s, 1H), 8.22 (d,1H), 7.58 (m, 2H), 7.44 (m, 1H), 7.29 (m, 1H), 7.10 (s, 1H), 6.94 (d, 1H), 6.90 (s, 1H), 5.69 (m, 2H), 5.18 (d, 1H), 4.93 (dd, 1H), 4.67 (m, 2H), 4.28 (m, 1H), 4.05 (m, 1H), 2.85 (m, 1H), 2.68 (m, 2H), 2.55 (s, 3H), 2.54 (m, 1H), 2.28 (q, 1H), 1.91-0.83 (m, 15H), 1.19 (s, 9H).

Compound 237: MS: m/z 844.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.23 (s, 1H), 8.22 (d,1H), 7.58 (m, 2H), 7.40 (m, 1H), 7.29 (m, 2H), 6.96 (d, 1H), 6.84 (s, 1H), 5.69 (s, 1H), 5.66 (q, 1H), 5.20 (d, 1H), 4.94 (dd, 1H), 4.73 (s, 1H), 4.67 (m, 1H), 4.58 (d, 1H), 4.35 (m, 1H), 4.05 (m, 1H), 2.89 (m, 1H), 2.68 (m, 2H), 2.56 (s, 3H), 2.54 (m, 1H), 2.26 (q, 1H), 1.91-0.83 (m, 23H).

Compound 238: MS: m/z 844.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.26 (s, 1H), 8.22 (d,1H), 7.55 (m, 2H), 7.43 (m, 2H), 7.18 (m, 1H), 6.93 (s, 1H), 6.75 (s, 1H), 5.70 (m, 2H), 5.21 (d, 1H), 4.94 (dd, 1H), 4.78 (s, 1H), 4.63 (m, 1H), 4.53 (d, 1H), 4.35 (m, 1H), 4.05 (m, 1H), 2.89 (m, 1H), 2.67 (m, 2H), 2.53 (s, 3H), 2.52 (m, 1H), 2.26 (q, 1H), 1.92-1.04 (m, 21H), 0.95-0.83 (m, 2H).

Compound 239: MS: m/z 790.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.34 (s, 1H), 8.20 (d,1H), 7.54 (m, 2H), 7.38 (m, 2H), 7.28 (s, 1H), 7.14 (s, 1H), 6.73 (s, 1H), 5.68 (m, 2H), 5.43 (d, 1H), 4.94 (dd, 1H), 4.65 (m, 1H), 4.39 (m, 2H), 4.04 (m, 1H), 3.58 (s, 3H), 2.89 (m, 1H), 2.68 (m, 2H), 2.51 (s, 3H), 2.50 (m, 1H), 2.28 (q, 1H), 1.93-1.06 (m, 13H), 0.94-0.82 (m, 2H).

Compound 240: MS: m/z 828.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.18 (s, 1H), 8.22 (d,1H), 7.56 (m, 2H), 7.40 (m, 2H), 7.20 (s, 2H), 7.08 (s, 1H), 6.76 (d, 1H), 5.71 (s, 1H),

5.66 (q, 1H), 4.94 (dd, 1H), 4.66 (m, 2H), 4.29 (d, 1H), 4.04 (m, 1H), 2.88 (m, 1H), 2.65 (m, 2H), 2.53 (s, 3H), 2.45 (m, 1H), 2.23 (q, 1H), 1.96-1.05 (m, 13H), 0.95-0.83 (m, 2H).

Compound 241: MS: m/z 778.1 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.38 (s, 1H), 7.89 (dd,1H), 7.58 (d, 2H), 7.44 (dd, 1H), 7.35 (d, 1H), 7.24 (m, 2H), 7.05 (m, 1H), 6.18(d, 1H), 5.71 (q, 1H), 5.62 (s, 1H), 4.95 (dd, 1H), 4.63 (m, 1H), 4.50 (m, 1H), 4.40 (d, 1H), 4.00 (m, 1H), 2.88 (m, 1H), 2.66 (m, 2H), 2.53 (m, 1H), 2.22 (q, 1H), 1.96-0.82 (m, 15H), 1.91 (s, 3H).

Compound 242: MS: m/z 846.4 (M^++1).

Compound 243: MS: m/z 858.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.28 (s, 1H), 8.24 (d, 1H), 7.57 (m, 2H), 7.42 (m, 2H), 7.19 (s, 1H), 7.08 (s, 1H), 6.79 (d, 1H), 5.66 (m, 2H), 5.24 (d, 1H), 4.96 (m, 1H), 4.78 (s, 1H), 4.67 (m, 1H), 4.55 (d, 1H), 4.35 (m, 1H), 4.03 (m, 1H), 2.85 (m, 3H), 2.67 (m, 2H), 2.53 (m, 1H), 2.28 (q, 1H), 1.94-0.84 (m, 26H).

Compound 244: MS: m/z 872.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.13(s, 1H), 8.24(d, 1H), 7.53(m, 2H), 7.41(m, 2H), 7.19(s, 1H), 6.99(s, 1H), 6.79(d, 1H), 5.69(m, 2H), 5.23(d, 1H), 4.98(dd, 1H), 4.77(s, 1H), 4.65(m, 1H), 4.55(d, 1H), 4.35(m, 1H), 4.04(m, 1H), 2.87(q, 2H), 2.68(m, 2H), 2.53(m, 1H), 2.29(q, 1H), 1.94-0.84(m, 26H), 0.83 (s, 3H).

Compound 245: MS: m/z 831.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.21 (s, 1H), 8.26 (d,1H), 7.90 (d, 2H), 7.58 (m, 2H), 7.46 (d, 2H), 7.00 (s, 1H), 5.69 (m, 2H), 5.09 (d, 1H), 4.99 (dd, 1H), 4.62 (m, 3H), 4.27 (m, 1H), 4.05 (m, 1H), 2.89 (m, 1H), 2.70 (m, 2H), 2.56 (m, 1H), 2.29 (q, 1H), 1.94-0.84 (m, 23H).

Compound 246: MS: m/z 761.4 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.21 (s, 1H), 8.17 (d,1H), 7.80 (d, 3H), 7.56 (m, 2H), 7.41 (d, 2H), 6.58 (s, 1H), 5.61 (m, 2H), 5.21 (d, 1H), 4.65 (m, 2H), 4.24 (m, 1H), 4.05 (m, 1H), 2.89 (m, 1H), 2.70 (m, 2H), 2.56-2.21 (m, 2H), 1.94-0.84 (m, 15H), 1.87 (s, 3H).

Compound 247: MS: m/z 803.4 (M^++1).

Compound 248: MS: m/z 845.3 (M^++1).

Compound 249: MS: m/z 917.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.22 (s, 1H), 8.08 (d,1H), 7.78 (s, 1H), 7.40 (s, 1H), 7.06 (s, 1H), 6.97 (m, 2H), 5.64 (m, 2H), 5.32 (d, 1H),

4.94 (dd, 1H), 4.70 (m, 2H), 4.54 (d, 1H), 4.34 (dd, 1H), 4.08 (m, 1H), 3.83 (s, 3H), 3.18 (m, 1H), 2.73-2.43 (m, 2H), 2.33 (q, 1H), 2.15-1.20 (m, 30H), 0.83 (s, 3H).

Compound 250: MS: m/z 905.4 (M^++1).

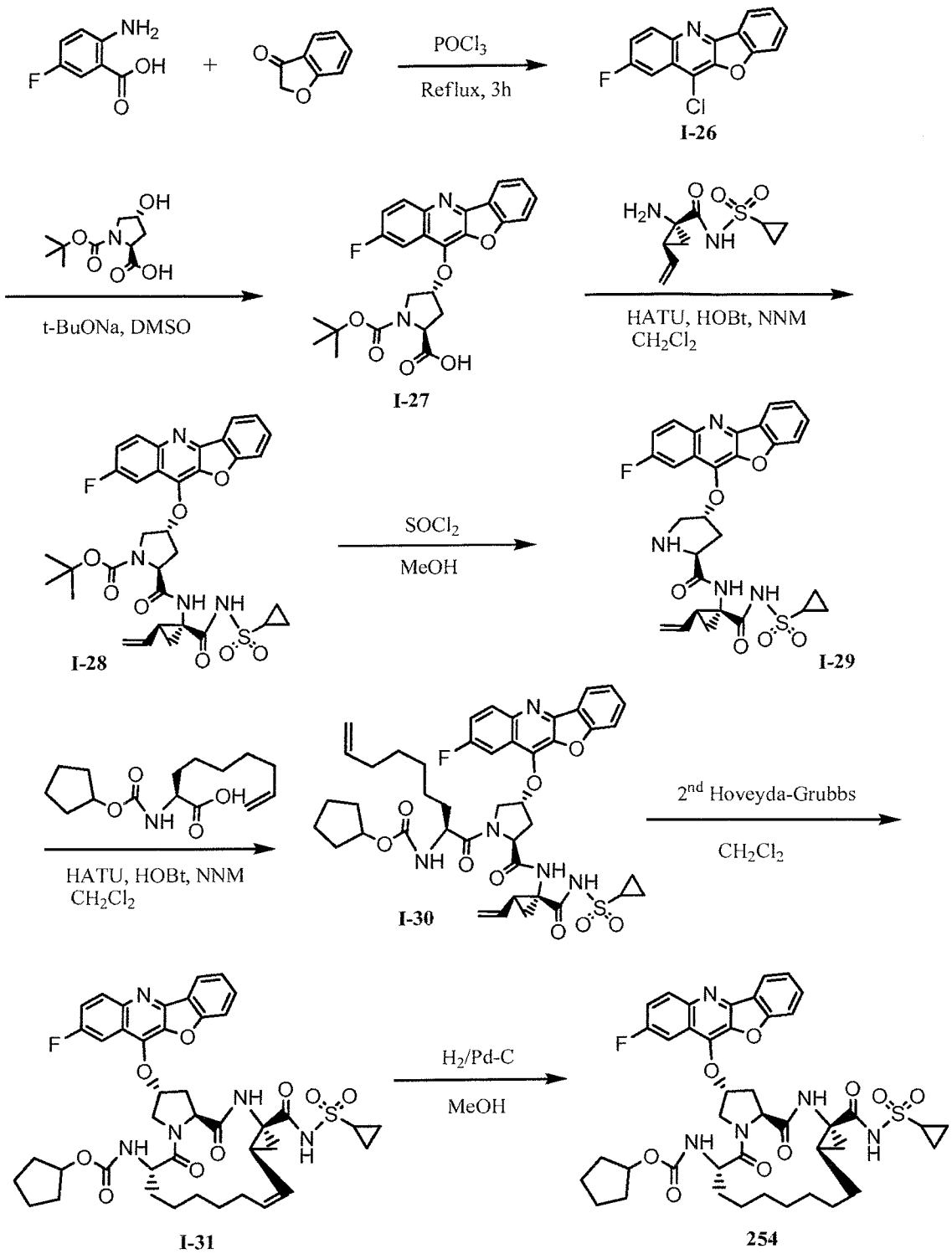
Compound 251: MS: m/z 901.3 (M^++1).

Compound 252: MS: m/z 917.4 (M^++1).

Compound 253: MS: m/z 903.3 (M^++1).

Example 254: Synthesis of [4-Cyclopropanesulfonylaminocarbonyl-18-(2-fluoro-benzo[4,5]furo[3,2-b]quinolin-11-yloxy)-2,15-dioxo-3,16-diaza-tricyclo[14.3.0.04,6]nonadec-14-yl]-carbamic acid cyclopentyl ester (Compound 254)

Compound 254 was prepared via the route shown below.



To a suspension of Boc-trans-4-hydroxy-L-proline (0.53 g, 2.30 mmol) in DMSO (10 mL) was added *t*-BuONa (0.49 g, 5.08 mmol) at 0°C. After warmed to room

temperature and stirred for additional 1 hour, intermediate I-26 (0.62 g, 2.31 mmol) was added slowly at 10°C. The reaction mixture was stirred for 4 h and then quenched with 10% HCl aqueous solution to pH 6~7. The crude suspension solid was filtrated, washed with water and dried under vaccum to give I-27 (0.92 g, 86%). MS: m/z 467.1 (M^++1).

To a solution of I-27 (0.90 g, 1.93 mmol), HATU (58.9 g, 1.55 mmol), HOBt (7.0 g, 0.52 mmol) and NMM (38.3 g, 3.86 mmol) in CH_2Cl_2 (10 mL) was dropwisely added a mixture of cyclopropanesulfonic acid (1-amino-2-vinyl-cyclopropanecarbonyl)-amide (54.0 g, 2.03 mmol) and NMM (0.19 g, 1.93 mmol) dissolved in CH_2Cl_2 at 5°C. After wamed to room temperature and stirred for another 16 h, the reaction mixture was filtrated, concentrated and purified by silica gel column chromatography to afford a crude product I-28 (0.89 g, 80% yield). MS: m/z 679.1 (M^++1).

Compound I-28 (1.20 g, 1.77 mmol) was dissolved in MeOH (18 mL) at room temperature and then cooled the solution using an ice bath. To the reaction mixture was added thionyl chloride (0.39 mL, 5.30 mmol) dropwisely. After removal of the ice-bath, the reaction mixture was heated at 65°C for 1 h. The resulting solution was cooled to 40°C, filtrated, and washed with cold MeOH and ether to afford light yellow powder to give white powder I-29 without further purification used at next reaction step. MS: m/z 579.1 (M^++1).

To a solution of 2-cyclopentyloxycarbonylamino-non-8-enoic acid (0.87 g, 2.34 mmol), HATU (1.16 g, 3.05 mmol) and HOBt (0.14 g, 1.02 mmol) in CH_2Cl_2 (10 mL) was dropwisely added a mixture of I-29 (1.18 g, 2.03 mmol) and NMM (0.49 g, 4.87 mmol) dissolved in DMF (10 mL) at 5°C. After warmed to room temperature and stirred for additional 16 h, 10% HCl (1 mL) was added and the reaction mixture was concentrated. The residue was cooled to 5°C and washed with 5% HCl (aq) (10 mL x 2) and $NaHCO_3$(aq) (10 ml x 2) sequentially to give a light yellow solid. The solid was dissolved in MeOH (10 mL) and further precipitated by added small portion ether slowly to afford I-30 (1.51 g, 88% yield). MS: m/z 844.3 (M^++1).

A solution of compound I-30 (0.50 g, 0.59 mmol) in CH_2Cl_2 (120 mL) was degassed by bubbling nitrogen for 1 h. Hoveyda-Grubb's 2nd generation catalyst (48 mg, 0.076 mmol) was added, and then the reaction mixture was heated at 40°C for 16h. After completion of the reaction indicated by HPLC, the reaction mixture was cooled to 30°C,

concentrated and purified by silica gel column chromatography to give product I-31 (0.30 g, 62% yield). MS: m/z 816.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.33 (s, 1H), 8.30 (d, 1H), 8.11 (dd, 1H), 7.88 (dd, 1H), 7.67-7.56 (m, 2H), 7.46 (dd, 1H), 7.43-7.30 (m, 2H), 6.12 (s, 1H), 5.64 (q, 1H), 5.22 (d, 1H), 4.92 (dd, 1H), 4.77 (d, 1H), 4.66 (dd, 1H), 4.32-4.22 (m, 1H), 4.04 (dd, 1H), 2.93-2.46 (m, 3H), 2.31 (q, 1H), 1.92-0.80 (m, 25H).

To a solution of compound I-31 (50 mg, 0.061 mmol) in MeOH (10 mL) was added 5% Pd-C (5 mg) at room temperature under N_2. Then, the reaction mixture was stirred in the atmosphere of hydrogen under 60 psi pressure at room temperature for 4 h. The reaction mixture was filtrated and purified by column chromatography to give compound 254 (27.6 mg, 55%). MS: m/z 818.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.50 (s, 1H), 8.28 (d, 1H), 8.13 (dd, 1H), 7.80 (dd, 1H), 7.65-7.57 (m, 2H), 7.45 (dd, 1H), 7.39-7.30 (m, 2H), 6.11 (s, 1H), 5.25 (d, 1H), 4.96 (brs, 1H), 4.68 (dd, 1H), 4.60 (d, 1H), 4.37 (dd, 1H), 4.14 (dd, 1H), 3.02-2.57 (m, 3H), 1.92-0.80 (m, 29H).

Example 255-281: Syntheses of Compound 255-281

Each of Compounds 255-281 was prepared in a manner similar to that described in Examples 254.

Compound 255: MS: m/z 764.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.47 (s, 1H), 7.88-7.84 (m, 3H), 7.70 (s, 1H), 7.56 (dd, 1H), 7.37 (m, 1H), 7.18 (m, 1H), 6.20 (d, 1H), 5.97 (s, 1H), 5.64 (q, 1H), 4.94 (dd, 1H), 4.68 (m, 1H), 4.61 (d, 1H), 4.44 (m, 1H), 4.02 (m, 1H), 2.85 (m, 2H), 2.70 (m, 1H), 2.58 (m, 1H), 2.25 (q, 1H), 1.92 (s, 3H), 1.90-1.03 (m, 15H).

Compound 256: MS: m/z 815.6 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.31 (s, 1H), 8.32 (d, 1H), 8.25 (m, 1H), 7.81 (dd, 1H), 7.64 (m, 2H), 7.46 (dd, 1H), 7.23-7.12 (m, 2H), 6.20 (s, 1H), 5.66 (q, 1H), 5.16 (d, 1H), 4.98 (dd, 1H), 4.75-4.64 (m, 3H), 4.31 (m, 1H), 4.08 (m, 1H), 2.88 (m, 1H), 2.78 (m, 2H), 2.55 (m, 1H), 2.29 (q, 1H), 1.92-0.84 (m, 23H).

Compound 257: MS: m/z 804.1 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.52 (s, 1H), 8.29 (d, 1H), 8.03-7.97 (m, 2H), 7.82 (dd, 1H), 7.63-7.42 (m, 3H), 7.21 (m, 1H), 5.97 (s, 1H), 5.60 (q, 1H), 5.44 (d, 1H), 4.85 (dd, 1H), 4.66 (m, 2H), 4.29 (m, 1H), 4.02 (m, 1H), 3.88-3.62 (m, 2H), 2.87-2.58 (m, 5H), 2.33 (q, 1H), 1.90-0.78 (m, 15H), 0.97 (s, 6H).

Compound 258: MS: m/z 806.1 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.36 (s, 1H), 8.28 (d, 1H), 8.07 (m, 1H), 7.84 (s, 1H), 7.62 (m, 3H), 7.44 (m, 2H), 7.18 (m, 1H), 6.06 (s, 1H), 5.67 (q, 1H), 4.96 (dd, 1H), 4.80 (d, 1H), 4.60 (m, 1H), 4.41 (m, 1H), 4.10 (m, 2H), 3.66 (m, 1H), 3.39 (m, 2H), 3.22 (s, 3H), 2.91-2.58 (m, 4H), 2.20 (q, 1H), 1.90-0.86 (m, 15H).

Compound 259: MS: m/z 788.1 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.51 (s, 1H), 8.28 (d, 1H), 7.94 (m, 1H), 7.86 (s, 1H), 7.64 (d, 1H), 7.60-7.43 (m, 4H), 7.16 (m, 1H), 6.00 (s, 1H), 5.85 (m, 1H), 5.62 (m, 2H), 5.30-5.19 (m, 2H), 4.93 (dd, 1H), 4.66 (m, 1H), 4.58-4.36 (m, 3H), 4.02 (m, 1H), 2.87-2.56 (m, 4H), 2.26 (q, 1H), 1.86-0.86 (m, 15H).

Compound 260: MS: m/z 762.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.63 (s, 1H), 8.26 (d, 1H), 8.10 (s, 1H), 7.88 (d, 1H), 7.67-7.44 (m, 4H), 6.84 (s, 1H), 5.89 (s, 1H), 5.68 (q, 1H), 5.38 (d, 1H), 4.97 (dd, 1H), 4.76 (m, 1H), 4.58 (d, 1H), 4.21 (m, 1H), 3.96 (m, 1H), 3.66 (s, 3H), 2.91-2.60 (m, 4H), 2.25 (q, 1H), 1.89-0.89 (m, 15H).

Compound 261: MS: m/z 704.2 (M^++1); ^{1}H NMR (CD_3OD) δ 9.26 (s, 1H), 8.47 (d, 1H), 8.26 (m, 1H), 8.15 (dd, 1H), 7.97-7.82 (m, 3H), 7.66 (m, 1H), 6.54 (s, 1H), 5.74 (q, 1H), 5.13 (dd, 1H), 4.60 (d, 1H), 4.35 (m, 2H), 3.72-3.58 (m, 2H), 2.97-2.81 (m, 3H), 2.51 (m, 1H), 2.33 (q, 1H), 1.99-1.06 (m, 15H).

Compound 262: MS: m/z 818.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.42 (s, 1H), 8.30 (d, 1H), 8.12 (m, 1H), 7.86 (m, 1H), 7.49-7.33 (m, 5H), 6.10 (s, 1H), 5.66 (m, 2H), 5.08-4.66 (m, 4H), 4.28 (m, 1H), 4.03 (m, 1H), 3.86-3.58 (m, 4H), 2.86-2.57 (m, 4H), 2.34 (q, 1H), 2.03-0.87 (m, 17H).

Compound 263: MS: m/z 780.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.60 (s, 1H), 8.04-7.92 (m, 3H), 7.78 (m, 1H), 7.56 (dd, 1H), 7.38 (m, 1H), 6.94 (m, 1H), 5.89 (s, 1H), 5.67 (q, 1H), 5.40 (d, 1H), 4.95 (dd, 1H), 4.76 (m, 1H), 4.57 (d, 1H), 4.20 (m, 1H), 3.97 (m, 1H), 3.64 (s, 3H), 2.94-2.63 (m, 4H), 2.23 (q, 1H), 1.88-1.09 (m, 15H).

Compound 264: MS: m/z 931.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.43 (s, 1H), 8.30 (d, 1H), 8.10 (m, 1H), 7.86 (d, 1H), 7.62-7.34 (m, 5H), 6.08 (s, 1H), 5.60 (q, 1H), 5.38 (s, 1H), 4.90-4.62 (m, 4H), 4.26 (m, 1H), 4.03 (m, 1H), 3.64 (m, 2H), 3.15 (m, 2H), 2.85-2.55 (m, 4H), 2.33 (q, 1H), 1.83-0.86 (m, 19H), 1.44 (s, 9H).

Compound 265: MS: m/z 780.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.45 (s, 1H), 8.29 (d, 1H), 8.05 (m, 1H), 7.78 (d, 1H), 7.63-7.25 (m, 4H), 6.04 (m, 2H), 5.63 (q, 1H), 4.91 (dd, 1H), 4.72-4.63 (m, 3H), 4.43-4.32 (m, 2H), 4.02 (m, 1H), 3.78-3.58 (m, 1H), 2.85-2.35 (m, 6H), 2.03-0.86 (m, 15H).

Compound 266: MS: m/z 776.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.56 (s, 1H), 8.24 (d, 1H), 8.00 (s, 1H), 7.87-7.79 (m, 2H), 7.61-7.42 (m, 4H), 7.06 (m, 1H), 5.93 (s, 1H), 5.61 (q, 1H), 5.44 (m, 1H), 4.91 (dd, 1H), 4.68 (m, 1H), 4.25-3.96 (m, 4H), 2.86-2.57 (m, 4H), 2.29 (q, 1H), 1.81-0.88 (m, 18H).

Compound 267: MS: m/z 812.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.47 (s, 1H), 8.27 (d, 1H), 7.90 (m, 1H), 7.81 (m, 2H), 7.76-7.43 (m, 4H), 7.17 (m, 1H), 6.03-5.85 (m, 2H), 5.61 (q, 1H), 4.88 (dd, 1H), 4.72-4.61 (m, 2H), 4.25-3.98 (m, 4H), 2.86-2.58 (m, 4H), 2.30 (q, 1H), 1.84-0.88 (m, 15H).

Compound 268: MS: m/z 832.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.50 (s, 1H), 8.35-8.29 (m, 1H), 8.15-8.01 (m, 1H), 7.84-7.32 (m, 5H), 7.13-7.03 (m, 1H), 6.10 (s, 1H), 5.54 (m, 1H), 5.36 (d, 1H), 5.05-4.83 (m, 2H), 4.74-4.65 (m, 1H), 4.36 (m, 1H), 4.14-4.05 (m, 1H), 2.88-2.51 (m, 4H), 2.12-0.88 (m, 24H).

Compound 269: MS: m/z 834.3 (M^++1).

Compound 270: MS: m/z 792.2 (M^++1).

Compound 271: MS: m/z 822.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.38 (s, 1H), 8.09 (m, 1H), 7.99 (dd, 1H), 7.83 (dd, 1H), 7.58 (dd, 1H), 7.41-7.25 (m, 3H), 6.15 (s, 1H), 5.59 (q, 1H), 5.16 (d, 1H), 4.89 (dd, 1H), 4.78-4.67 (m, 2H), 4.25 (m, 1H), 4.07 (m, 1H), 2.77-2.70 (m, 3H), 2.57 (m, 1H), 2.30 (q, 1H), 1.90-0.82 (m, 15H), 1.23 (s, 9H).

Compound 272: MS: m/z 822.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.37 (s, 1H), 8.10 (m, 1H), 7.98 (dd, 1H), 7.83 (dd, 1H), 7.58 (dd, 1H), 7.42-7.27 (m, 2H), 7.19 (s, 1H), 6.16 (s, 1H), 5.62 (q, 1H), 5.11 (d, 1H), 4.92 (dd, 1H), 4.78-4.67 (m, 2H), 4.24 (m, 1H), 4.07 (m, 1H), 2.86-2.77 (m, 3H), 2.56 (m, 1H), 2.32 (q, 1H), 1.90-0.82 (m, 15H), 1.23 (s, 9H).

Compound 273: MS: m/z 850.3, 852.3 (M^++1).

Compound 274: MS: m/z 834.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.43 (s, 1H), 8.08 (m, 1H), 7.95 (dd, 1H), 7.91 (dd, 1H), 7.56 (dd, 1H), 7.50 (s, 1H), 7.37-7.31 (m, 2H),

6.05 (s, 1H), 5.58 (q, 1H), 5.39 (d, 1H), 4.72-4.67 (m, 4H), 4.27 (m, 1H), 4.03 (m, 1H), 2.89-2.67 (m, 3H), 2.55 (m, 1H), 2.29 (q, 1H), 1.90-0.87 (m, 23H).

Compound 275: MS: m/z 780.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.61 (s, 1H), 8.06-7.92 (m, 3H), 7.75 (m, 1H), 7.55 (dd, 1H), 7.39 (m, 1H), 6.90 (m, 1H), 5.89 (s, 1H), 5.66 (q, 1H), 5.44 (d, 1H), 4.94 (dd, 1H), 4.77 (m, 1H), 4.58 (d, 1H), 4.20 (m, 1H), 3.96 (m, 1H), 3.65 (s, 3H), 2.93-2.67 (m, 4H), 2.24 (q, 1H), 1.87-1.09 (m, 15H).

Compound 276: MS: m/z 818.1 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.35 (s, 1H), 8.05 (m, 1H), 7.96 (dd, 1H), 7.75 (dd, 1H), 7.57-7.52 (m, 2H), 7.39-7.32 (m, 3H), 6.06 (s, 1H), 5.60 (q, 1H), 4.85-4.73 (m, 2H), 4.55-4.48 (m, 2H), 4.06 (m, 1H), 2.83 (m, 2H), 2.69 (m, 1H), 2.50 (m, 1H), 2.23 (q, 1H), 1.85-1.05 (m, 15H).

Compound 277: MS: m/z 856.3 (M^++1).

Compound 278: MS: m/z 764.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.49 (s, 1H), 7.94-7.82 (m, 3H), 7.72 (s, 1H), 7.55 (dd, 1H), 7.38 (m, 1H), 7.17 (m, 1H), 6.21 (d, 1H), 5.99 (s, 1H), 5.62 (q, 1H), 4.94 (dd, 1H), 4.68 (m, 1H), 4.61 (d, 1H), 4.45 (m, 1H), 4.02 (m, 1H), 2.85 (m, 2H), 2.71 (m, 1H), 2.56 (m, 1H), 2.27 (q, 1H), 1.92 (s, 3H), 1.90-1.03 (m, 15H).

Compound 279: MS: m/z 834.3 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.43 (s, 1H), 8.05 (m, 1H), 7.96 (dd, 1H), 7.91 (dd, 1H), 7.55 (dd, 1H), 7.48 (s, 1H), 7.37-7.32 (m, 2H), 6.05 (s, 1H), 5.57 (q, 1H), 5.39 (d, 1H), 4.79-4.67 (m, 4H), 4.28 (m, 1H), 4.03 (m, 1H), 2.87-2.67 (m, 3H), 2.54 (m, 1H), 2.29 (q, 1H), 1.90-0.87 (m, 23H).

Compound 280: MS: m/z 818.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.36 (s, 1H), 8.02 (m, 1H), 7.94 (dd, 1H), 7.71 (dd, 1H), 7.60 (s, 1H), 7.54-7.51 (dd, 1H), 7.42 (d, 1H), 7.36-7.30 (m, 2H), 6.03 (s, 1H), 5.60 (q, 1H), 4.86-4.72 (m, 2H), 4.56-4.48 (m, 2H), 4.05 (m, 1H), 2.84 (m, 2H), 2.68 (m, 1H), 2.48 (m, 1H), 2.23 (q, 1H), 1.88-1.05 (m, 15H).

Compound 281 was prepared similar to the procedure described in Example 1: Compound 281: MS: m/z 901.2 (M^++1); ^{1}H NMR ($CDCl_3$) δ 10.25 (s, 1H), 8.48 (d, 1H), 7.59 (dd, 1H), 7.39 (d, 1H), 7.32 (dd, 1H), 7.15 (s, 1H), 7.04 (s, 1H), 6.14 (s, 1H), 5.69 (ddd, 1H), 5.04 (m, 2H), 4.72 (m, 1H), 4.56 (m, 2H), 4.24-4.15 (m, 2H), 3.97 (s, 3H), 3.34 (tt, 1H), 2.55 (m, 1H), 2.24-2.26 (m, 1H), 2.01-0.69 (m, 34H).

Example 282: Inhibition of NS3/4A Protease

Protein expression and purification

A plasmid containing a gene encoding N-terminal His_6-tagged-$NS4A_{(21-32)}$-GSGS-$NS3_{(3-181)}$ was transformed into *E. coli* strain BL21(DE3) pLysS (Novagen) for protein over-expression. Single colony of transformed BL21 (DE3) pLysS was cultured in 200 mL of Lauria-Bertani (LB) medium with Kanamycin and Chloramphenicol at 37°C overnight. The bacterial culture was transferred into 6 L LB medium (Difco) containing antibiotics and incubated with shaking at 22°C. After the absorbance at 600 nm reached 0.6, the culture was induced with 1 mM isopropyl-1-thio-β-D-galactopyranoside (IPTG) at 22°C for 5 hours. The culture was subsequently harvested by centrifugation (6,000 xg for 15 minutes at 4°C). Cell pellets were resuspended in 150 mL buffer A (50 mM HEPES, pH 7.4, 0.3 M NaCl, 0.1% (w/v) CHAPS, 10 mM imidazol, 10% (v/v) glycerol). After the mixture was disrupted by four passes through a Microfluidizer operated at 30 psi, the cell debris was removed by centrifugation (58,250 × g for 30 minutes at 4°C). The cell lysate containing His_6-tagged proteins was charged at 3 mL/min onto a 25 mL Ni-NTA (Qiagen) column in the presence of 10 mM imidazole using a gradiFrac system (Pharmacia). The column was washed with 10 column volumes of the lysis buffer. The bound $NS4A_{(21-32)}$-GSGS-$NS3_{(3-181)}$ was eluted with 8 column volumes of buffer A supplemented with 300 mM imidazole. The pooled fractions were further purified by Q-Sepharose column equilibrated with buffer B (50 mM HEPES, pH 7.4, 0.1% (w/v) CHAPS, 10% (v/v) glycerol, 5 mM dithiothreitol (DTT), and 1 M NaCl). The eluant containing $NS4A_{(21-32)}$-GSGS-$NS3_{(3-181)}$ was collected and further purified by size-exclusion chromatography at a flow rate of 0.5 mL/min using the sephacryl-75 column (16 × 100 cm, Pharmacia) pre-equilibrated with buffer C (50 mM HEPES, pH 7.4, 0.1% (w/v) CHAPS, 5 mM DTT, 10% (v/v) glycerol). The purified protein was frozen and stored at -80°C before use.

HPLC Microbore assay

A solution containing 50 mM Tris, pH 7.4, 100 mM NaCl, 20% glycerol, 0.012% CHAPS, 10 mM DTT, 5 μM substrate Ac-Asp-Glu-Asp(EDANS)-Glu-Glu-Abu-ψ-[COOAla]-Ser-Lys(DABCYL)-NH_2 (RET S1, ANASPEC), and 10 μM test compound was prepared. 80 μL of the solution was added to each well of a 96-well plate. Reaction

was initiated by addition of 20 μL of 10 nM NS3/4A protease in a buffer containing 50 mM Tris buffer, pH 7.4, 100 mM NaCl, 20% glycerol, and 0.012% CHAPS. The final concentration of NS3/4A protease was 2 nM, which was lower than the Km of substrate RET S1.

The assay solution was incubated for 30 minutes at 30°C. The reaction was then quenched by addition of 100 μL of 1% TFA. 200 μL aliquot was transferred to each well of Agilent 96-well plates.

Reaction products were analyzed using reverse phase HPLC described below. The HPLC system included: Agilent 1100, Degasser G1379A, Binary pump G1312A, Autosampler G1367A, Column thermostated chamber G1316A, Diode array detector G1315B, Column: Agilent, ZORBAX Eclipse XDB-C18, 4.6 mm, 5 μm, P/N 993967-902, Column thermostat: room temperature, injection volume: 100 μL, Solvent A = HPLC grade water + 0.09% TFA, Solvent B = HPLC grade acetonitrile + 0.09% TFA. Total HPLC running time was 7.6 minutes with a linear gradient from 25 to 50% solvent B in 4 minutes, 50% solvent B for 30 seconds, and a gradient from 50 to 25% solvent B for additional 30 seconds. The column was re-equilibrated with 25% solvent B for 2.6 minutes before next sample was injected. The IC_{50} value (the concentration at which 50% inhibition of NS3/4A activity was observed) was calculated for each test compound based on the HPLC results.

Compounds 1-281 were tested in the above inhibition assay. The results showed that 274 compounds exhibited IC_{50} values lower than 20 nM and 7 compounds exhibited IC_{50} values in the range of 20-100 nM.

In addition, certain compounds of this invention were found to unexpectedly inhibit in an effective manner HCV protease mutants resistant to one or more other HCV drugs.

Example 283: HCV Replicon Cell Assay Protocol

Cells containing HCV replicon were maintained in DMEM containing 10% fetal bovine serum (FBS), 1.0 mg/ml of G418, and appropriate supplements (media A).

On day 1, the replicon cell monolayer was treated with a trypsin/EDTA mixture, removed, and was diluted with media A to a final concentration of 48,000 cells/ml. The

solution (1 ml) was added to each well of a 24-well tissue culture plate, and cultured overnight in a tissue culture incubator at 37°C with 5% CO_2.

On day 2, a test compound (in 100% DMSO) was serially diluted by DMEM containing 10% FBS and appropriate supplements (media B). The final concentration of DMSO was maintained at 0.2% throughout the dilution series.

The media on the replicon cell monolayer was removed, and then media B containing various concentrations of compounds was added. Media B without any compound was added to other wells as compound-free controls.

The cells were incubated with a compound or 0.2% DMSO in media B for 72 hours in a tissue culture incubator with 5% CO_2 at 37°C. Then, the media was removed and the replicon cell monolayer was washed once with PBS. RNA extraction reagents from RNeasy kits or TRIZOL reagents were added to the cells immediately to avoid degradation of RNA. Total RNA was extracted according to the instruction provided by manufacturer with modification to improve extraction efficiency and consistency. Finally, total cellular RNA, including HCV replicon RNA, was eluted and stored at -80°C until further processing.

A TaqMan® real-time RT-PCR quantification assay was set up with two sets of specific primers: one was for HCV and the other was for ACTB (beta-actin). The total RNA was added to the PCR reactions for quantification of both HCV and ACTB RNA in the same PCR well. Experimental failure was flagged and rejected based on the level of ACTB RNA in each well. The level of HCV RNA in each well was calculated according to a standard curve run in the same PCR plate. The percentage of inhibition of HCV RNA level by the compound treatment was calculated using the DMSO or compound-free control as 0% of inhibition. EC50 (concentration at which 50% inhibition of HCV RNA level was achieved) was calculated from the titration curve of any given compound.

Compounds 1-281 were tested in the HCV replicon cell assay. The results showed that 274 compounds exhibited EC_{50} values lower than 20 nM and 7 compound exhibited EC_{50} values in the range of 20-100 nM.

Example 284: Pharmacokinetic study

Male Sprague-Dawley rats (300-400 g) were surgically implanted with polyethylene cannula in the jugular vein for blood sampling while under pentobarbital

anesthesia the day before the in-life phase. They were fasted overnight with water ad libitum, and then dosed the next day with a test compound by oral gavage (PO). Serial blood samples were collected from animals until 48 hrs post-dose and heparinized plasma was recovered following centrifugation. The test compound in blood plasma was extracted and determined by liquid chromatography-mass spectrometry analysis (LC-MS/MS).

Standard pharmacokinetic parameters were assessed by non-compartmental analysis using WinNonlin (Version 4.0, Pharsight, CA, USA). The maximum in the curve of the test compound concentration in blood plasma vs. time is denoted C_{max}. The apparent terminal-phase elimination ($t_{1/2}$) were calculated as $\ln(2)/\lambda_z$, where λ_z is an elimination rate constant. The area under the concentration vs. time curve from the time of dosing to infinity ($AUC_{(0\text{-inf})}$) was calculated according to the linear trapezoidal rule.

Certain compounds of this invention showed prolonged half life and a large AUC vaues.

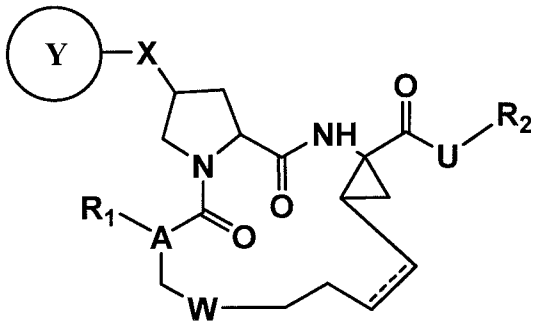
OTHER EMBODIMENTS

All of the features disclosed in this specification may be combined in any combination. Each feature disclosed in this specification may be replaced by an alternative feature serving the same, equivalent, or similar purpose. Thus, unless expressly stated otherwise, each feature disclosed is only an example of a generic series of equivalent or similar features.

From the above description, one skilled in the art can easily ascertain the essential characteristics of the present invention, and without departing from the spirit and scope thereof, can make various changes and modifications of the invention to adapt it to various usages and conditions. Thus, other embodiments are also within the scope of the following claims.

WHAT IS CLAIMED IS:

1. A compound of formula (I):



Formula (I)

wherein

R_1 is -H, -OH, C_{1-6} alkyl, C_{1-6} alkoxyl, C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, heteroaryl, -Z-R, or –NH-Z-R; in which R is H, or is a moiety selected from C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, and heteroaryl, each of which is optionally mono-, di- or tri-substituted with halo, nitro, cyano, amino, C_{1-6} alkyl, C_{1-6} alkoxyl, C_{2-6} alkenyl, C_{2-6} alkynyl, aryl, or heteroaryl; and Z is -C(O)-, -C(O)O-, -C(O)C(O)O-, -C(O)C(O)NH-, -C(O)NR'-, -OC(S)-, - C(S)NR'-, or -C(NH)O-, R' being H, C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, or heteroaryl;

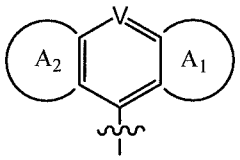
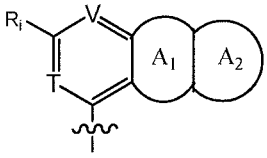
R_2 is H, or is a moiety selected from C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, and heteroaryl, each of which is optionally mono-, di-, or tri-substituted with halo, nitro, cyano, amino, C_{1-6} alkyl, C_{1-6} alkoxyl, C_{2-6} alkenyl, C_{2-6} alkynyl, aryl, or heteroaryl;

A is N or CH;

U is -O-, -NH-, -NH(CO)-, -NHSO-, or -$NHSO_2$-;

W is -$(CH_2)_m$-, -$NH(CH_2)_n$-, -$(CH_2)_nNH$-, -$O(CH_2)_n$-, -$(CH_2)_nO$-, -$S(CH_2)_n$-, -$(CH_2)_nS$-, -SO-, -$SO(CH_2)_n$-, -$(CH_2)_nSO$-, -$SO_2(CH_2)_n$-, or -$(CH_2)_nSO_2$-, m being 1, 2, or 3 and n being 0, 1, or 2;

X is -O-, -S-, or -NH-;

Y is  or , in which each of V and T, independently, is -CH- or -N-; each of A_1 and A_2, independently, is a moiety selected from C_{4-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, and heteroaryl, each of which is optionally mono-, di-, or tri-substituted with halo, nitro, cyano, amino, C_{1-6} alkyl, C_{1-6} alkoxyl, C_{2-6} alkenyl, C_{2-6} alkynyl, aryl, or heteroaryl, or optionally fused with C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, or heteroaryl; and R_i is H, halo, nitro, cyano, or amino, or is a moiety selected from C_{1-6} alkyl, C_{1-6} alkoxyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, and heteroaryl, each of C_{1-6} alkyl, C_{1-6} alkoxyl, C_{2-6} alkenyl, and C_{2-6} alkynyl being optionally mono-, di- or tri-substituted with halo, nitro, cyano, amino, C_{1-6} alkyl, C_{1-6} alkoxyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, or heteroaryl, and each of C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, and heteroaryl being optionally mono-, di- or tri-substituted with halo, nitro, cyano, amino, C_{1-6} alkyl, C_{1-6} alkoxyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, or heteroaryl, or optionally fused with C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, or heteroaryl; and

=== is a single bond or a double bond.

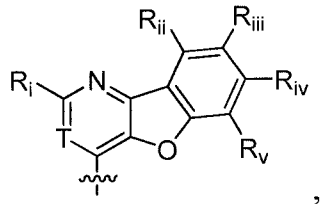
2. The compound of claim 1, wherein X is O.

3. The compound of claim 1, wherein A is CH and W is $-CH_2CH_2-$, $-OCH_2-$, $-SCH_2-$, or $-SOCH_2-$.

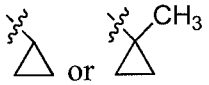
4. The compound of claim 1, wherein A is N and W is $-CH_2CH_2-$, $-OCH_2-$, $-SCH_2-$, or $-SOCH_2-$.

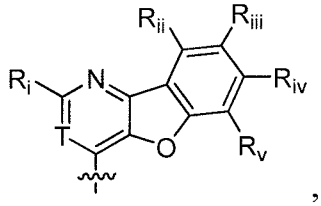
5. The compound of claim 1, wherein U is $-NHSO_2-$.

6. The compound of claim 1, wherein === is a double bond.

7. The compound of claim 1, wherein Y is , in which T is CH or N and each of R_i, R_{ii}, R_{iii}, R_{iv}, and R_v, independently, is H, halo, nitro, cyano, amino, C_{1-6} alkyl, C_{1-6} alkoxyl, C_{2-6} alkenyl, or C_{2-6} alkynyl, or is a moiety selected from C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, and heteroaryl, each of which is optionally mono-, di-, or tri-substituted with halo, nitro, cyano, amino, C_{1-6} alkyl, C_{1-6} alkoxyl, C_{2-6} alkenyl, C_{2-6} alkynyl, aryl, or heteroaryl, or optionally fused with C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, or heteroaryl.

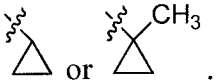
8. The compound of claim 7, wherein R_i is phenyl or thioazolyl optionally substituted with halo, amino, C_{1-6} alkyl, or C_{1-6} alkoxyl.

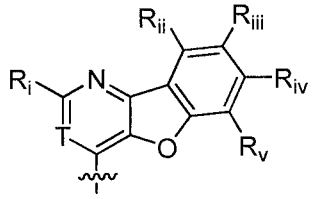
9. The compound of claim 1, wherein R_2 is  or .

10. The compound of claim 9, wherein Y is , in which T is CH or N; R_i is phenyl or thioazolyl optionally substituted with halo, amino, C_{1-6} alkyl, or C_{1-6} alkoxyl; and each of R_{ii}, R_{iii}, R_{iv}, and R_v, independently, is H, halo, nitro, cyano, amino, C_{1-6} alkyl, C_{1-6} alkoxyl, C_{2-6} alkenyl, or C_{2-6} alkynyl, or is a moiety selected from C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, and heteroaryl, each of which is optionally mono-, di-, or tri-substituted with halo, nitro, cyano, amino, C_{1-6} alkyl, C_{1-6} alkoxyl, C_{2-6} alkenyl, C_{2-6} alkynyl, aryl, or heteroaryl, or optionally fused with C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, or heteroaryl.

11. The compound of claim 1, wherein R_1 is –NH-Z-R, in which Z is -C(O)-, -C(O)O-, -C(O)C(O)O-, or -C(O)C(O)NH-.

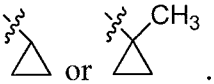
12. The compound of claim 11, wherein R_1 is –NH-C(O)O-t-Bu or –NH-C(O)O-cyclopentyl.

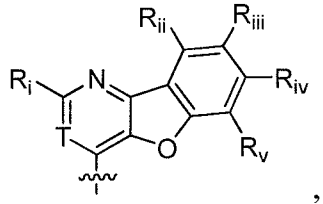
13. The compound of claim 12, wherein R_2 is  .

14. The compound of claim 13, wherein Y is  , in which T is CH or N; R_i is phenyl or thioazolyl optionally substituted with halo, amino, C_{1-6} alkyl, or C_{1-6} alkoxyl; and each of R_{ii}, R_{iii}, R_{iv}, and R_v, independently, is H, halo, nitro, cyano, amino, C_{1-6} alkyl, C_{1-6} alkoxyl, C_{2-6} alkenyl, or C_{2-6} alkynyl, or is a moiety selected from C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, and heteroaryl, each of which is optionally mono-, di-, or tri-substituted with halo, nitro, cyano, amino, C_{1-6} alkyl, C_{1-6} alkoxyl, C_{2-6} alkenyl, C_{2-6} alkynyl, aryl, or heteroaryl, or optionally fused with C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, or heteroaryl.

15. The compound of claim 14, wherein X is O; A is CH; W is $-CH_2CH_2-$, $-OCH_2-$, $-SCH_2-$, or $-SOCH_2-$; U is $-NHSO_2-$; and ≡ is a double bond.

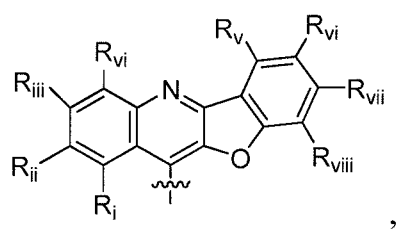
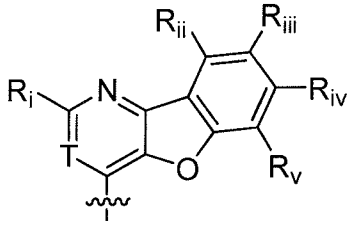
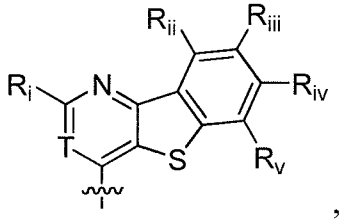
16. The compound of claim 11, wherein R_1 is –NH-C(O)-furyl.

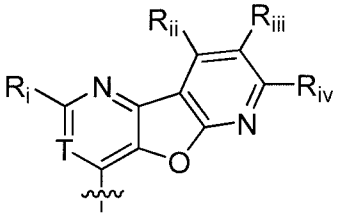
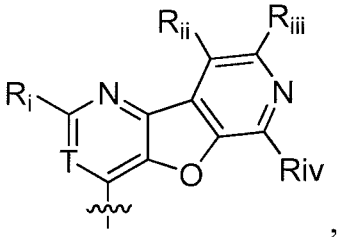
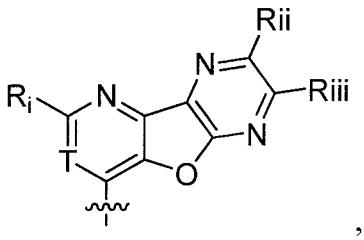
17. The compound of claim 16, wherein R_2 is  .

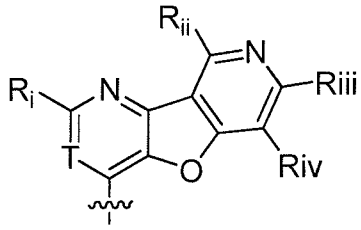
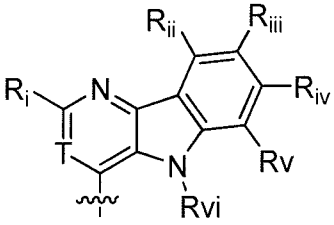
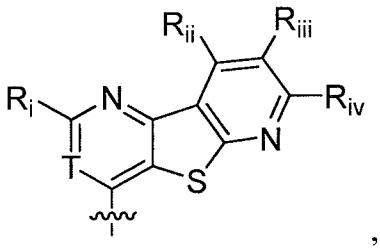
18. The compound of claim 17, wherein Y is , in which T is CH or N; R_i is phenyl or thioazolyl optionally substituted with halo, amino, C_{1-6} alkyl, or C_{1-6} alkoxyl; and each of R_{ii}, R_{iii}, R_{iv}, and R_v, independently, is H, halo, nitro, cyano, amino, C_{1-6} alkyl, C_{1-6} alkoxyl, C_{2-6} alkenyl, or C_{2-6} alkynyl, or is a moiety selected from C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, and heteroaryl, each of which is optionally mono-, di-, or tri-substituted with halo, nitro, cyano, amino, C_{1-6} alkyl, C_{1-6} alkoxyl, C_{2-6} alkenyl, C_{2-6} alkynyl, aryl, or heteroaryl, or optionally fused with C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, or heteroaryl.

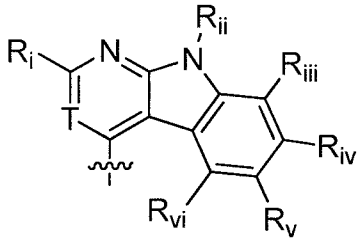
19. The compound of claim 18, wherein X is O; A is CH; W is $-CH_2CH_2-$, $-OCH_2-$, $-SCH_2-$, or $-SOCH_2-$; U is $-NHSO_2-$; and ⎓ is a double bond.

20. The compound of claim 1, wherein Y is

, , ,

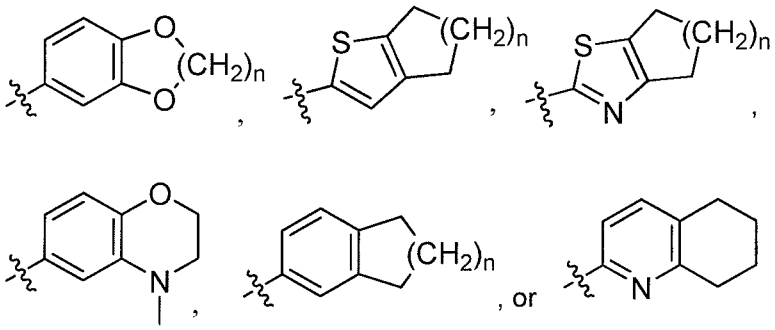
, , ,




, or


,

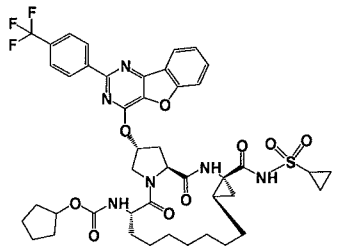
wherein each of R_i, R_{ii}, R_{iii}, R_{iv}, R_v, and R_{vi}, independently, is H, halo, nitro, cyano, amino, C_{1-6} alkyl, C_{1-6} alkoxyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, or heteroaryl, each of cycloalkyl, heterocycloalkyl, aryl, and heteroaryl being optionally mono-, di- or tri-substituted with halo, nitro, cyano, amino, C_{1-6} alkyl, C_{1-6} alkoxyl, C_{2-6} alkenyl, C_{2-6} alkynyl, aryl, or heteroaryl; and optionally fused with C_{3-10} cycloalkyl, C_{1-10} heterocycloalkyl, aryl, or heteroaryl.

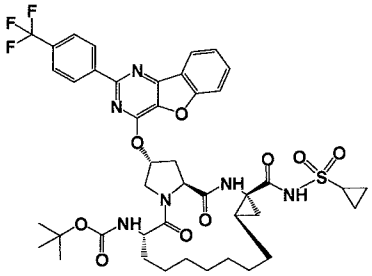
21. The compound of claim 20, wherein R_i is

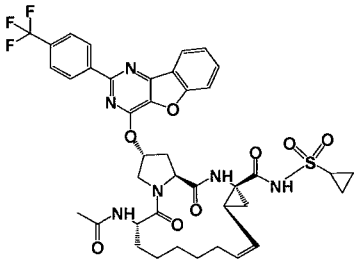

, or

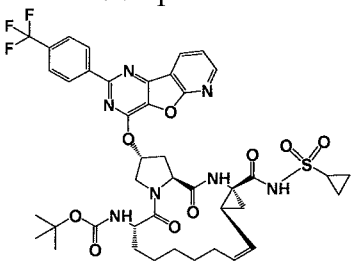
in which n is 1 or 2.

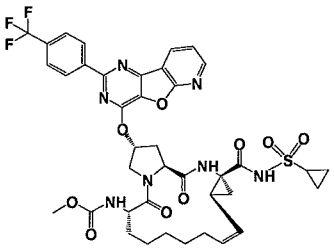
22. The compound of claim 1, wherein the compound is one of the following compounds:

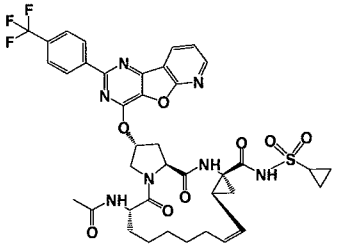

Compound 1

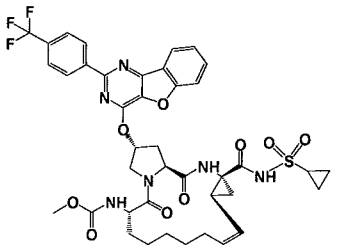

Compound 2

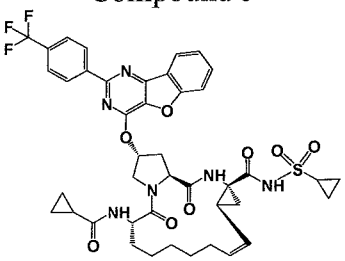

Compound 3

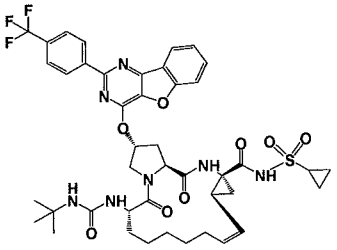

Compound 4

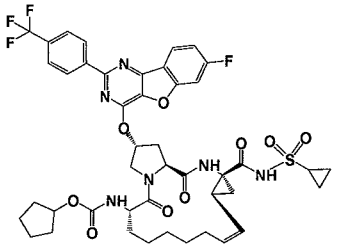

Compound 5

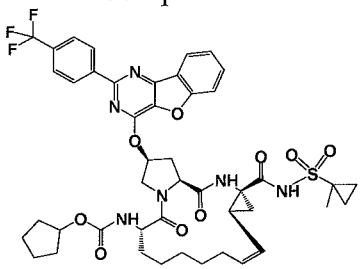

Compound 6

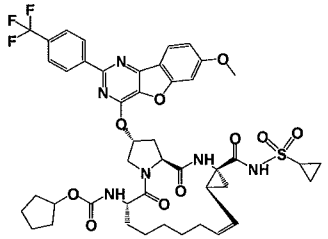

Compound 7

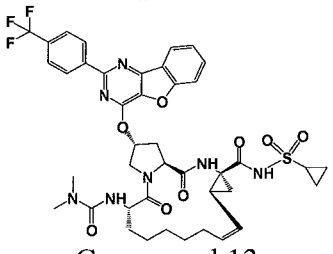

Compound 8

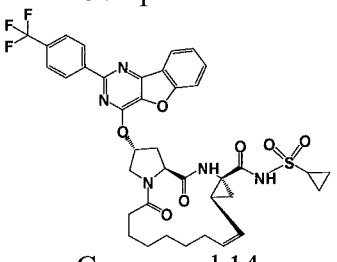

Compound 9

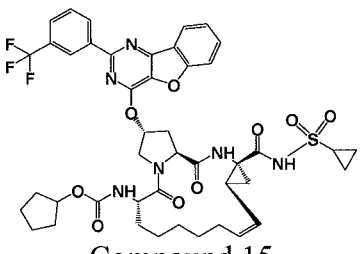

Compound 10

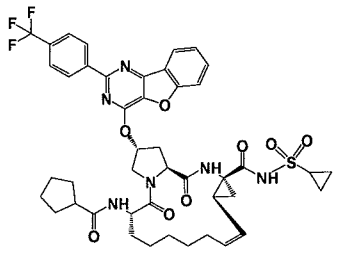

Compound 11


Compound 12

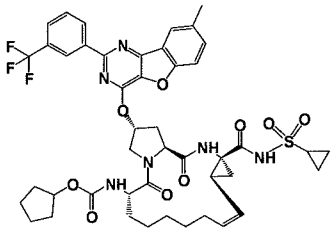

Compound 13


Compound 14

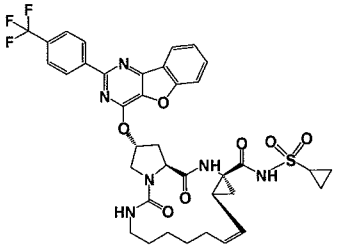

Compound 15



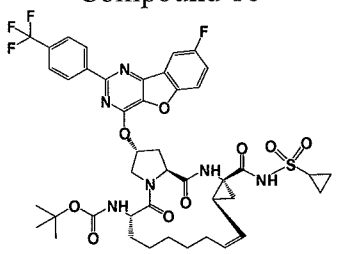
Compound 16



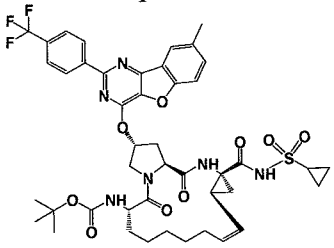
Compound 17



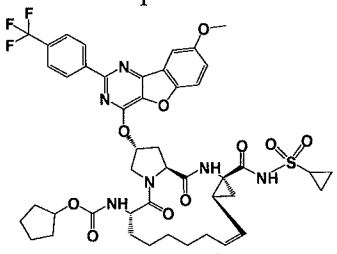
Compound 18



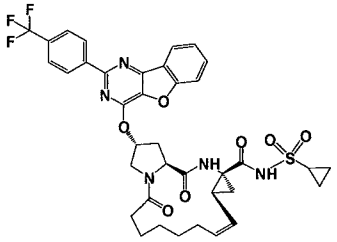
Compound 19



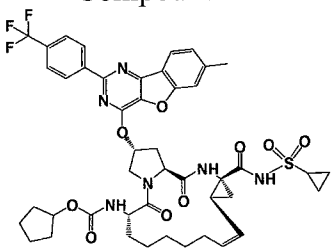
Compound 20



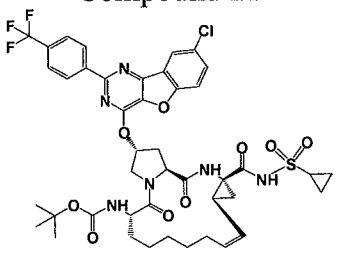
Compound 21



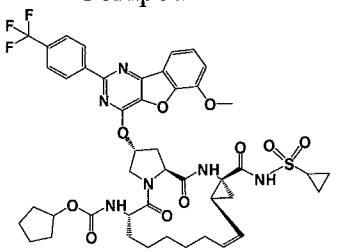
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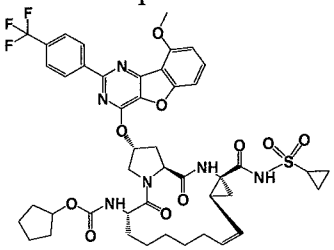
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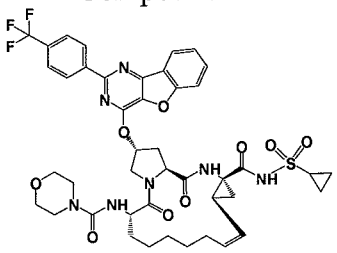
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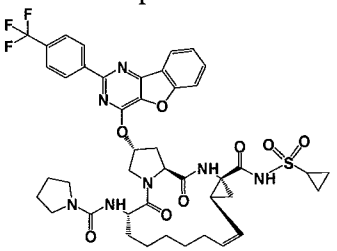
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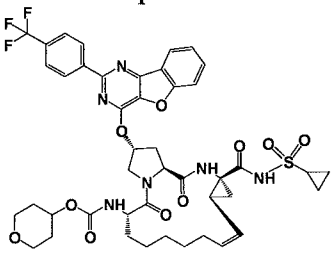
Compound 26



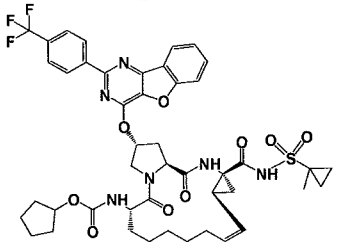
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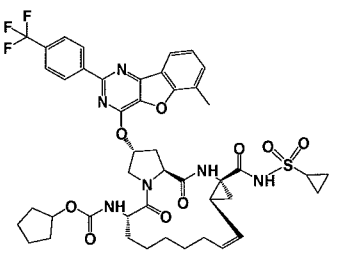
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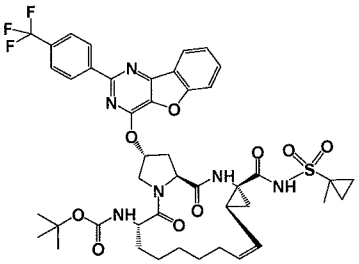


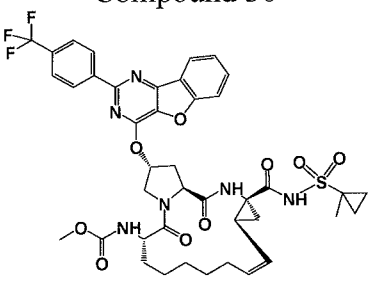
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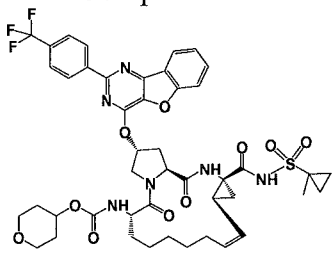
Compound 30



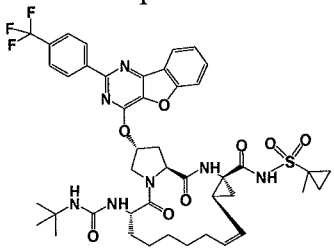




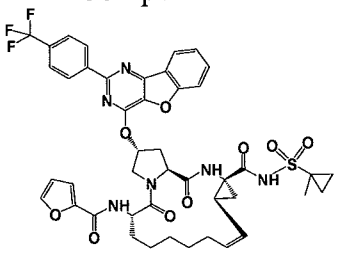
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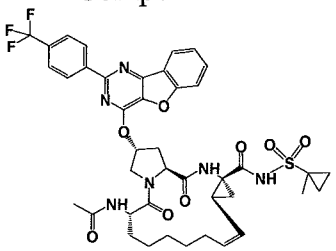
Compound 32



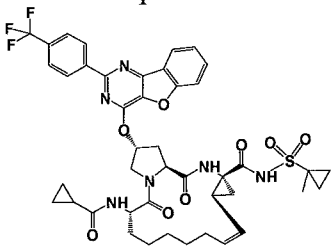
Compound 33



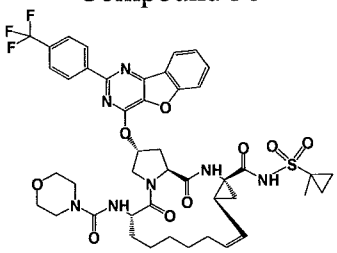
Compound 34



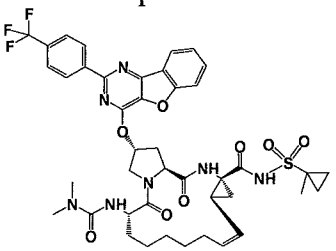
Compound 35



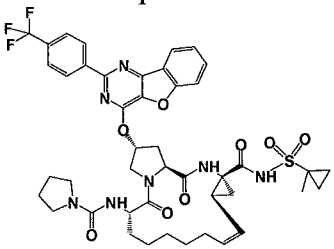
Compound 36



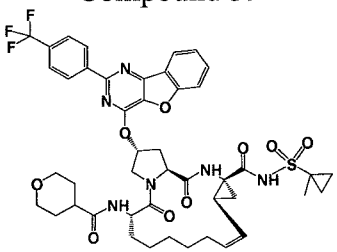
Compound 37



Compound 38



Compound 39

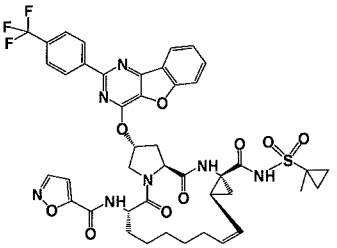


Compound 40

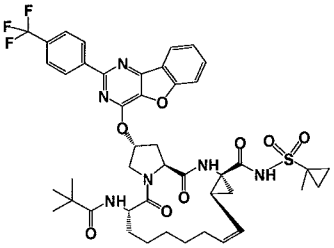
Compound 41

Compound 42

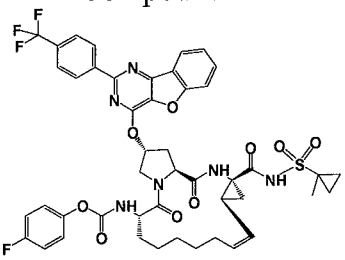
Compound 43



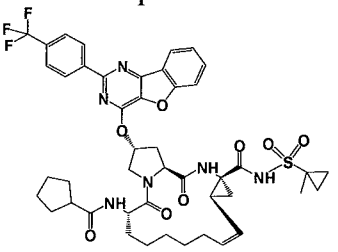
Compound 44



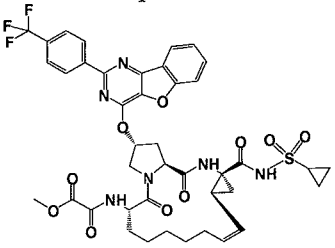
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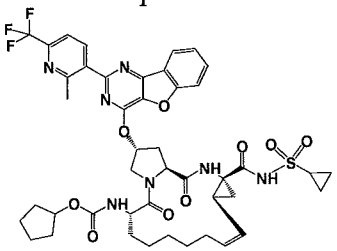
Compound 46



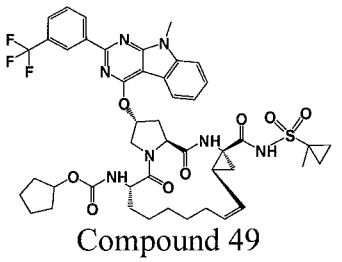
Compound 47



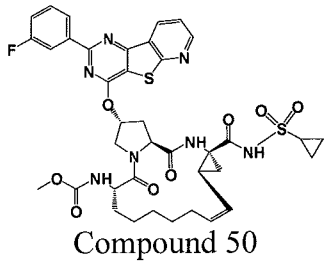
Compound 48



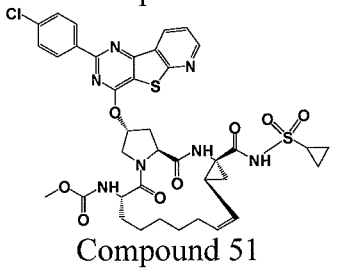
Compound 49

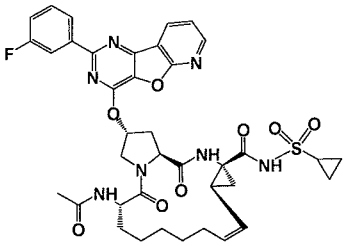


Compound 50

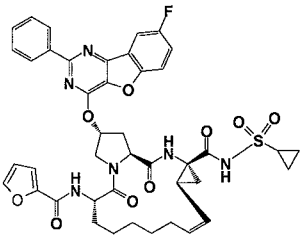


Compound 51

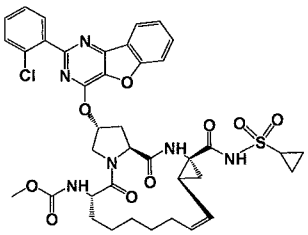




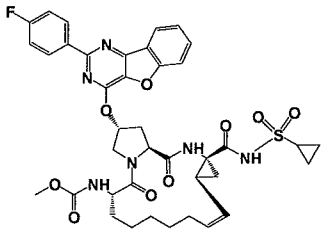
Compound 52



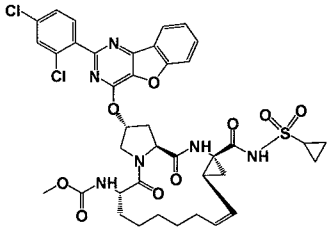
Compound 53



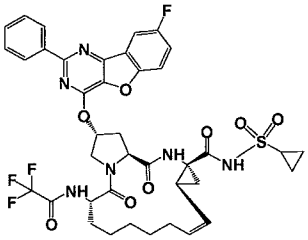
Compound 54



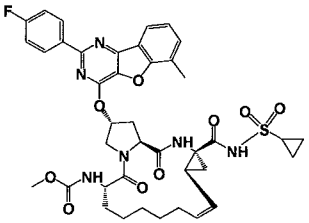
Compound 55



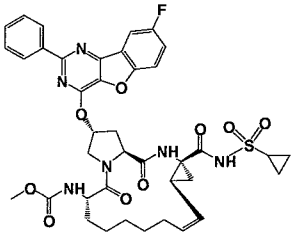
Compound 56



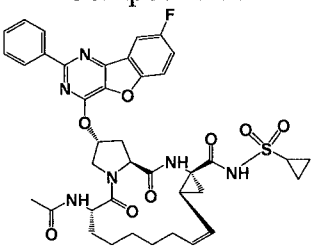
Compound 57



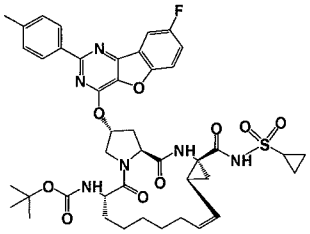
Compound 58



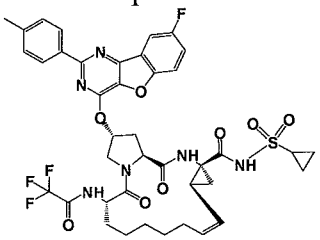
Compound 59



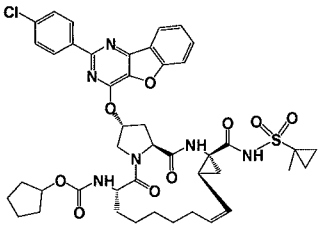
Compound 60



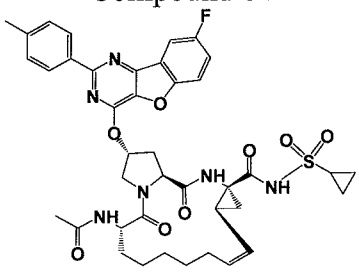
Compound 61



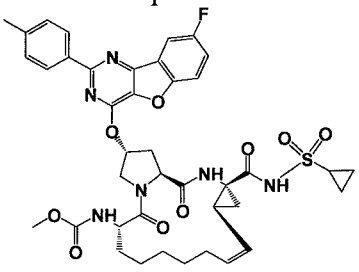
Compound 62



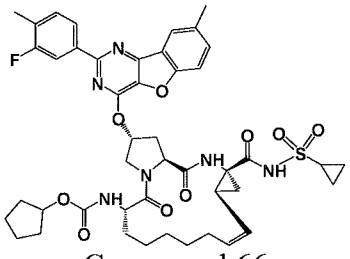
Compound 63



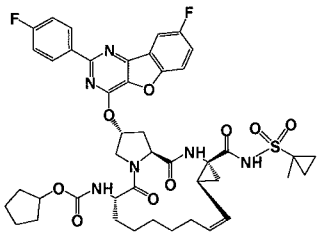
Compound 64

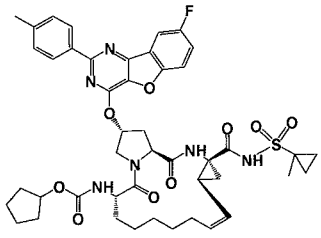


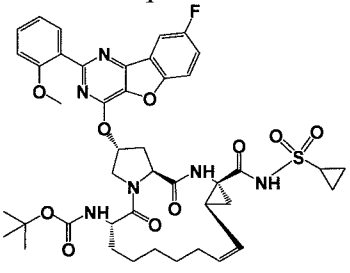
Compound 65



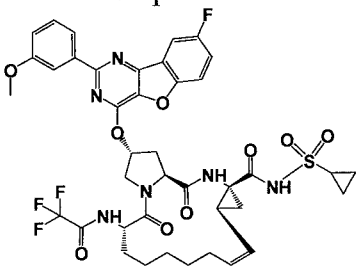
Compound 66



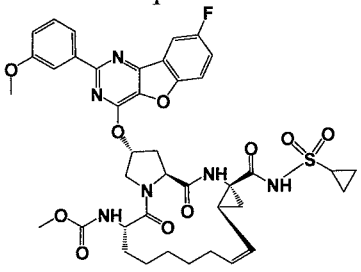




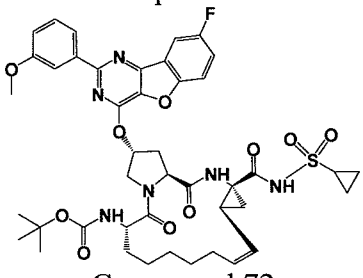
Compound 67



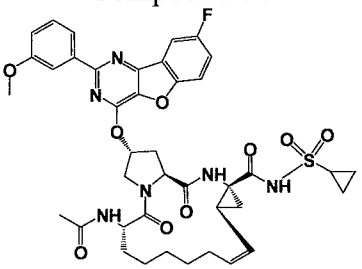
Compound 68



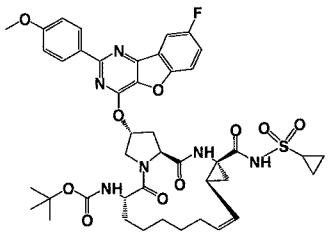
Compound 69



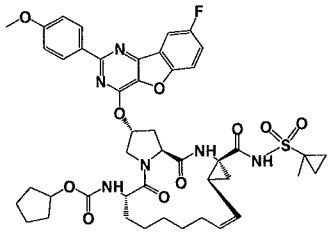
Compound 70



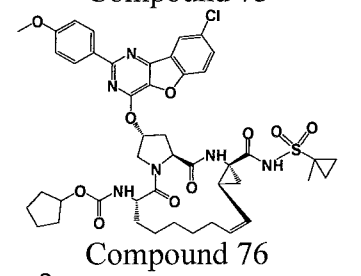
Compound 71



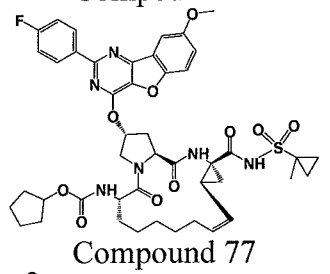
Compound 72



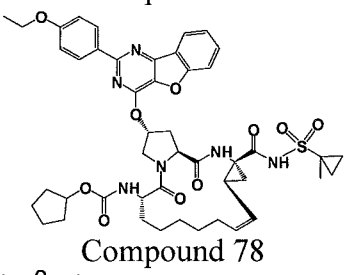
Compound 73



Compound 74



Compound 75

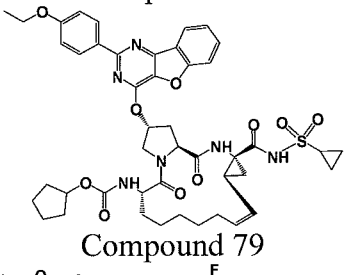


Compound 76

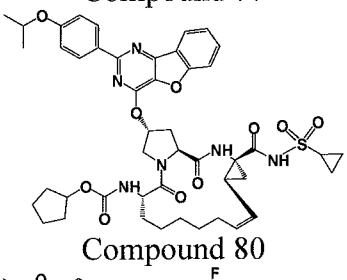
Compound 77

Compound 78

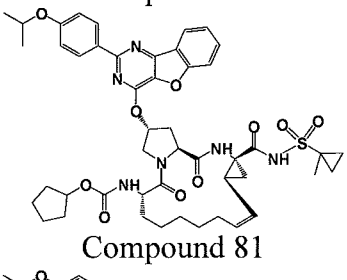
Compound 79



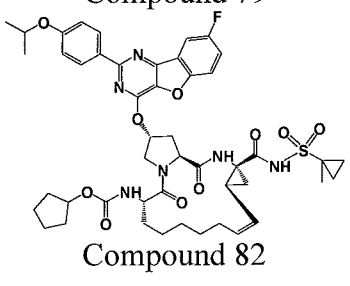
Compound 80



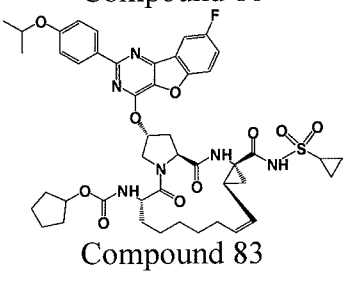
Compound 81



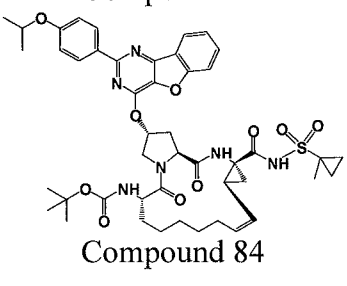
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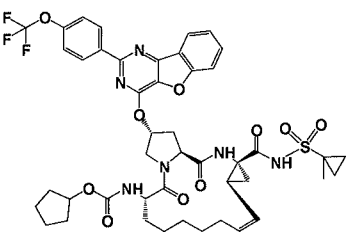


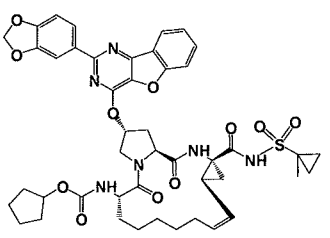
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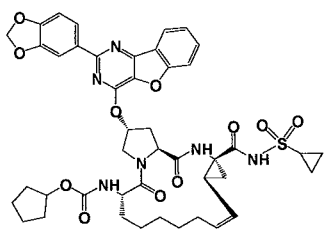


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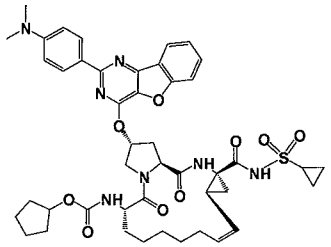




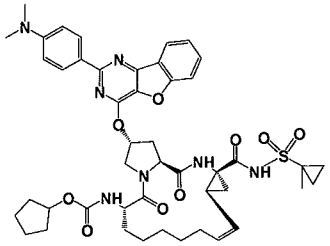




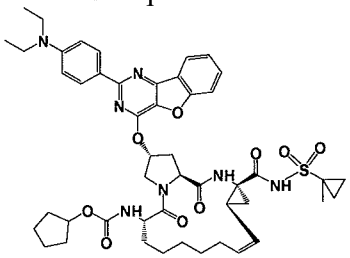
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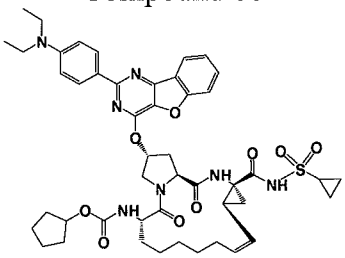
Compound 86



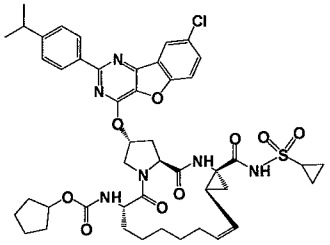
Compound 87



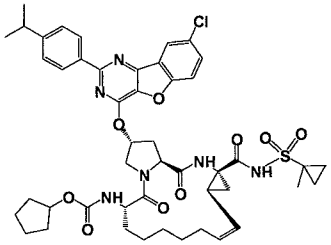
Compound 88



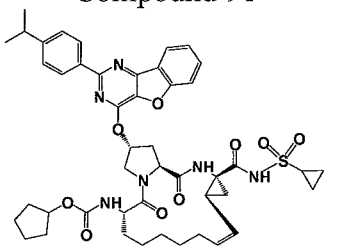
Compound 89



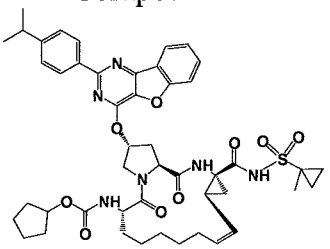
Compound 90



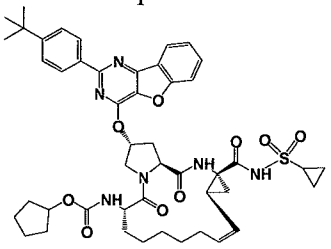
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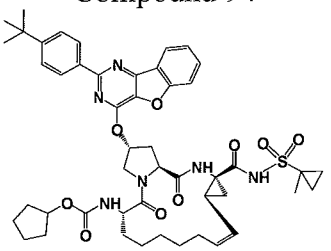
Compound 92



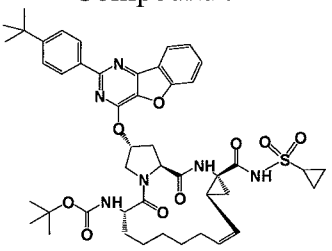
Compound 93



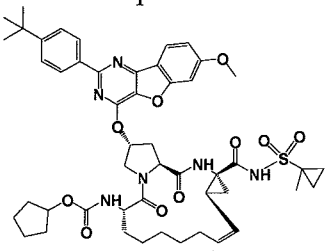
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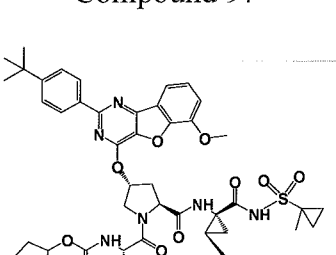
Compound 95



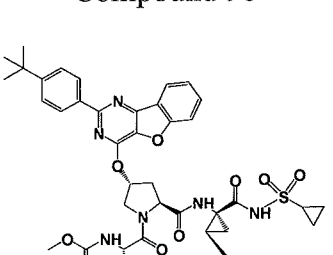
Compound 96



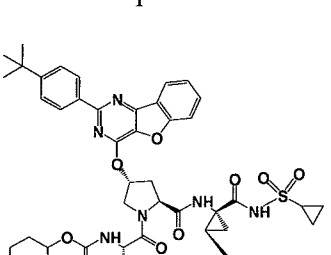
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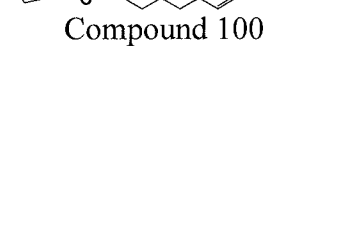
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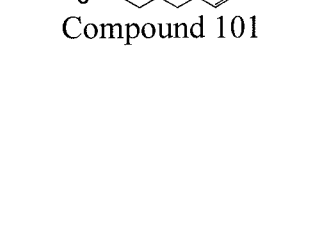
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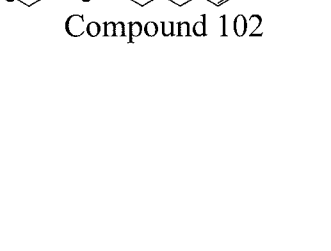
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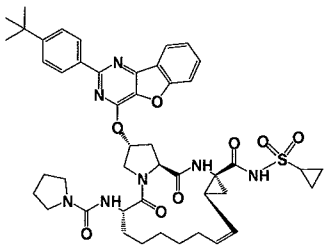


Compound 101

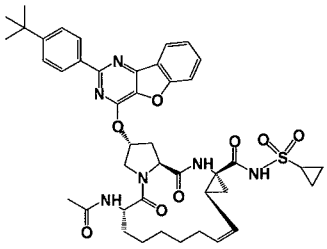


Compound 102

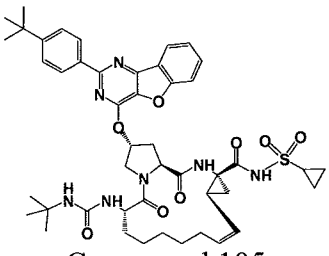




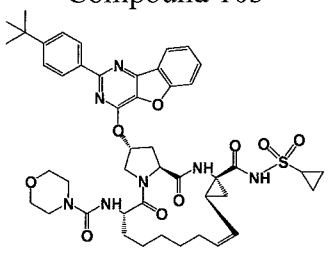
Compound 103



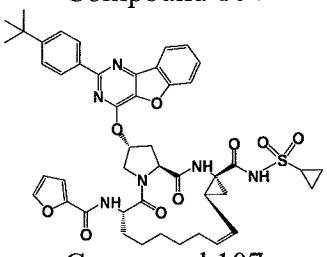
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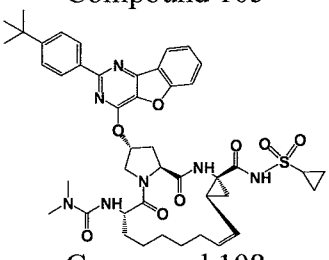
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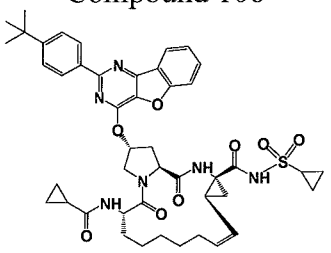
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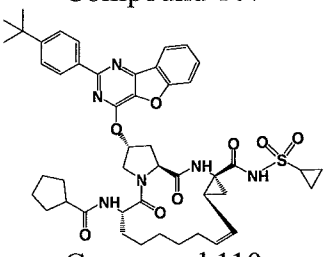
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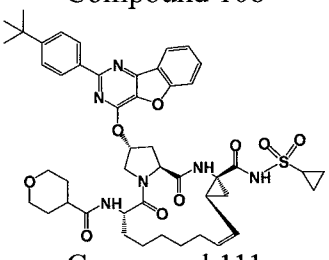
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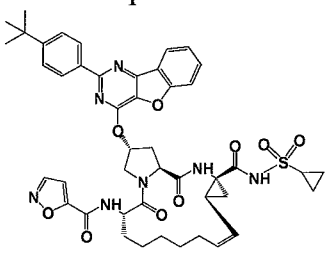
Compound 109



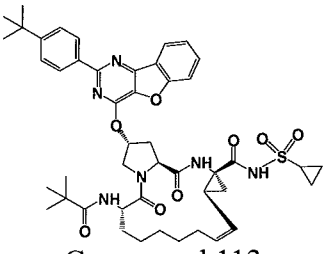
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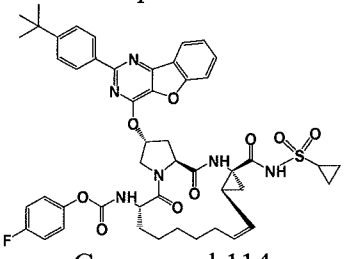
Compound 111



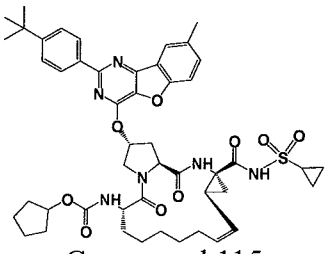
Compound 112



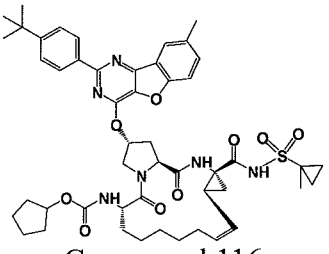
Compound 113



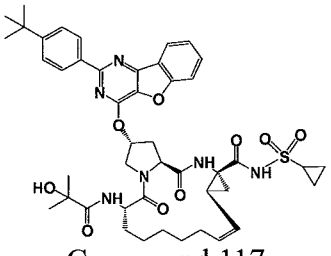
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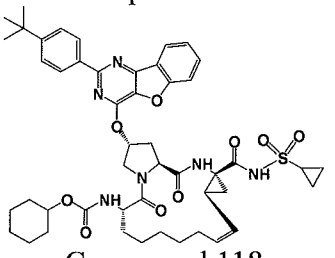
Compound 115



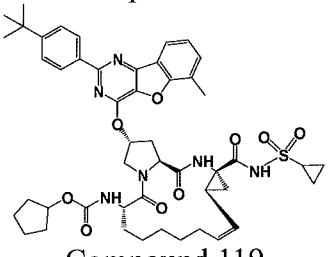
Compound 116



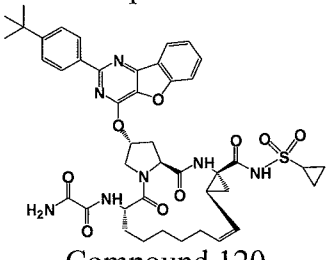
Compound 117



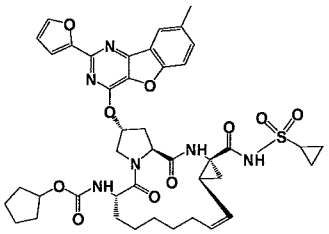
Compound 118



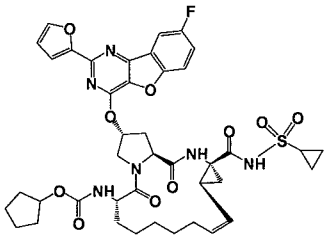
Compound 119



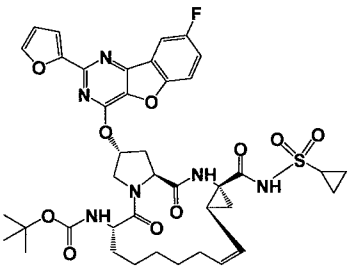
Compound 120



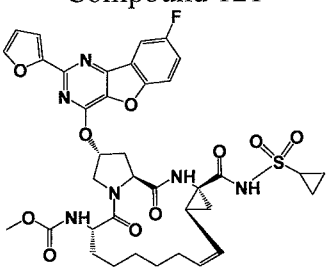
Compound 121



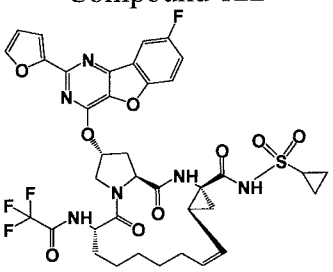
Compound 122



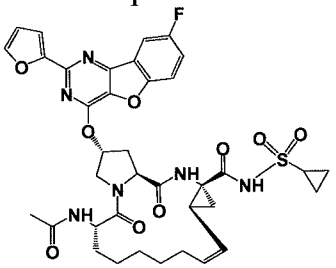
Compound 123



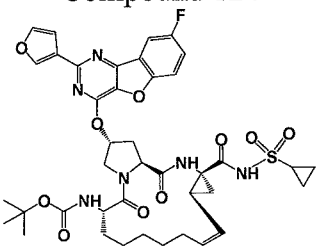
Compound 124



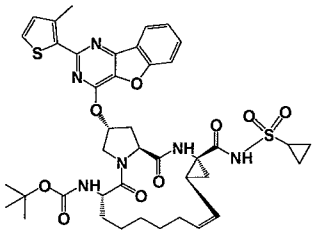
Compound 125



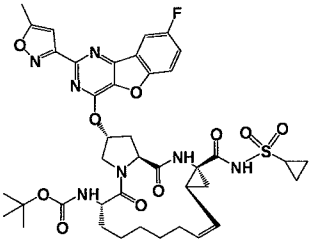
Compound 126



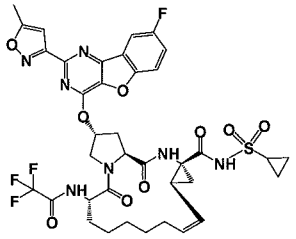
Compound 127



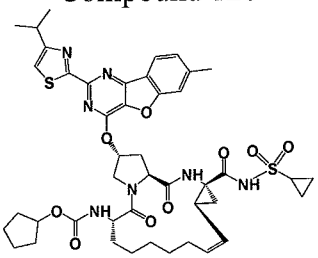
Compound 128



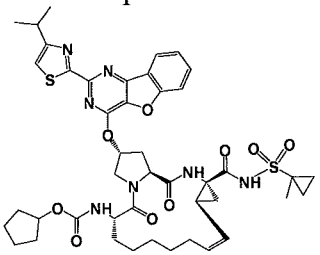
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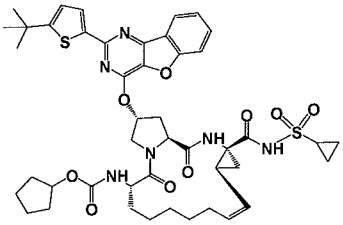
Compound 130



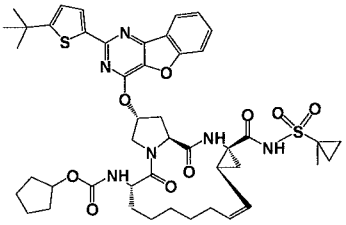
Compound 131



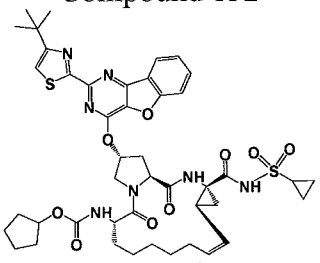
Compound 132



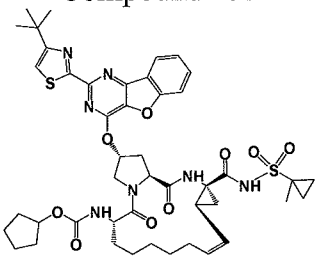
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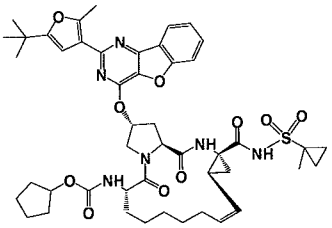


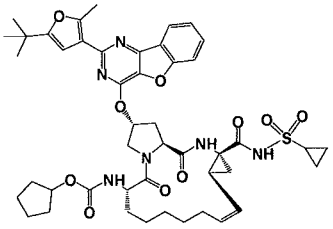
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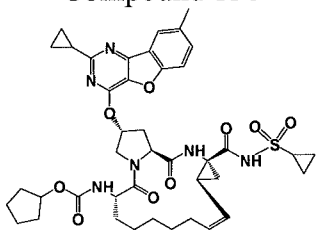
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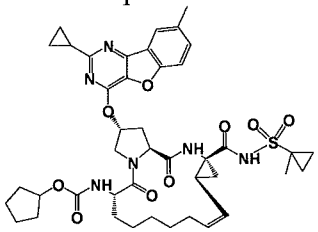




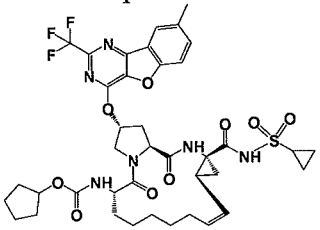
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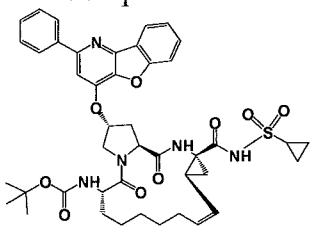
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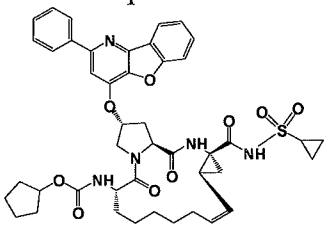
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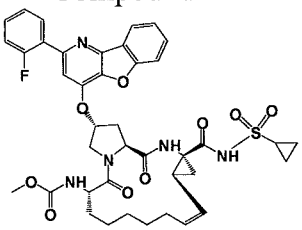
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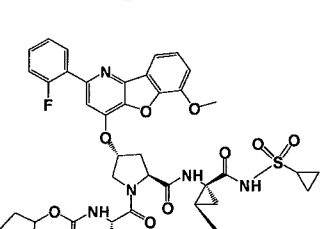
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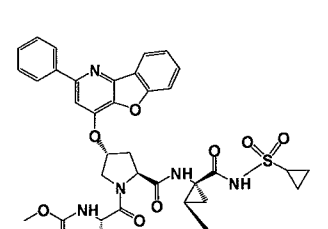
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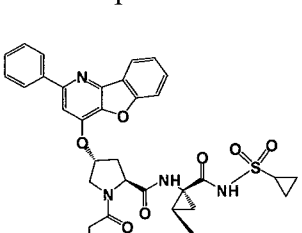
Compound 142



Compound 143



Compound 144

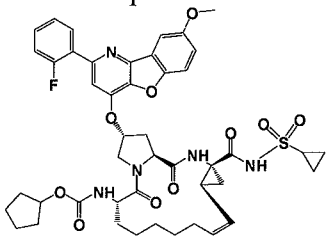


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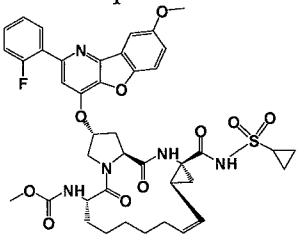
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Compound 147

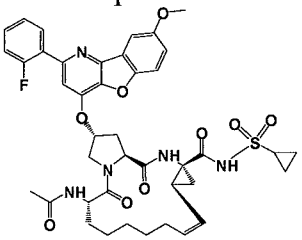
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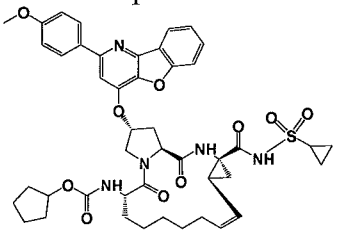
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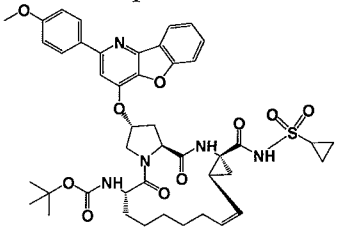
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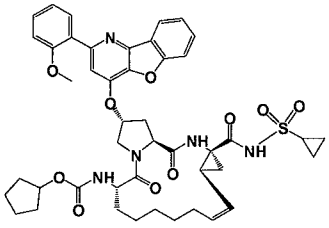
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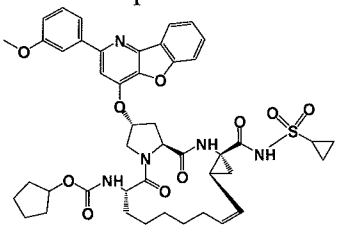
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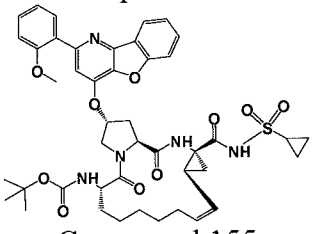
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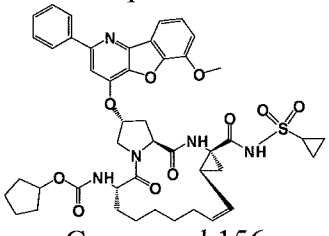
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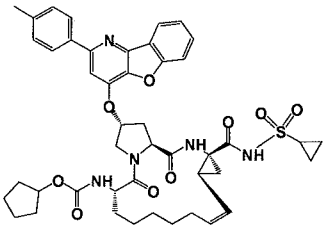


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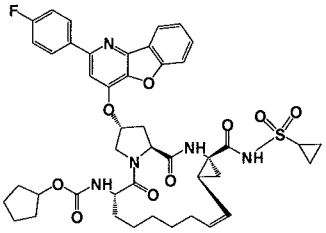


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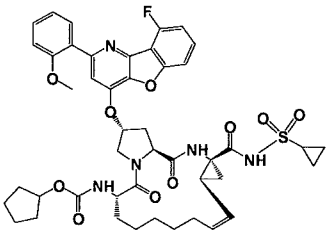




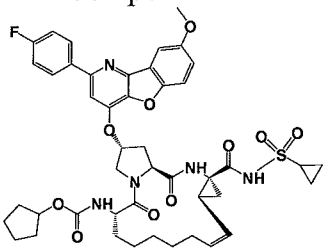
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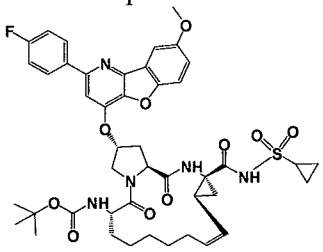
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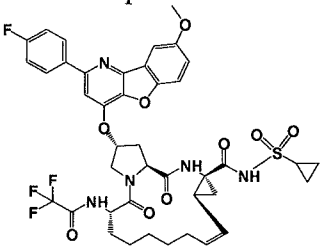
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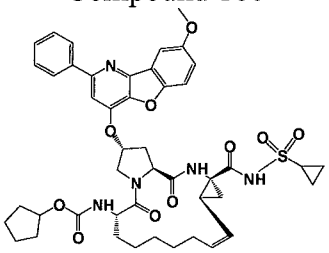
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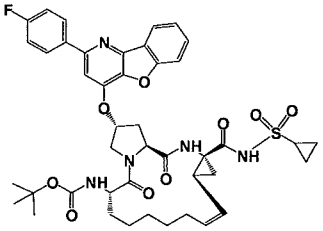
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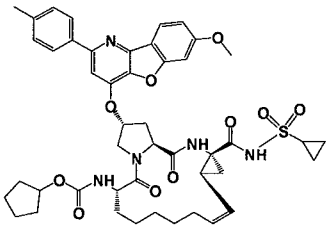
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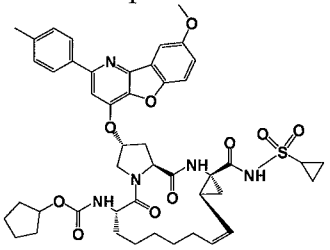
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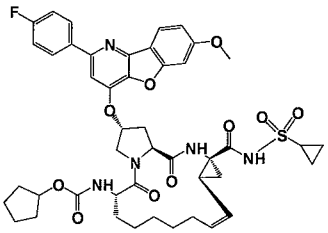
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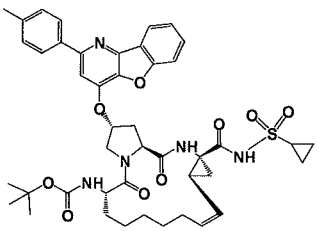
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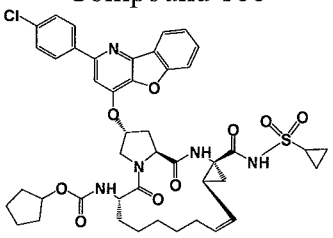
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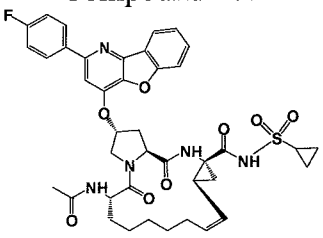
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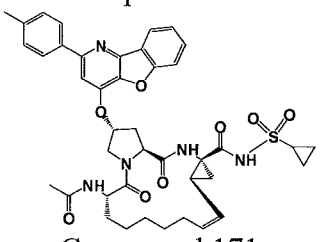
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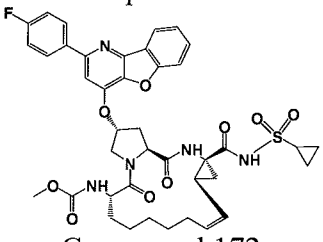
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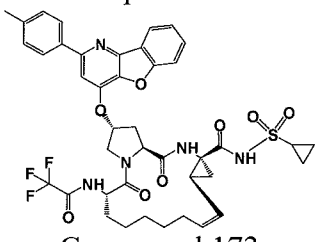
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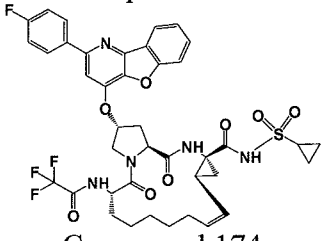
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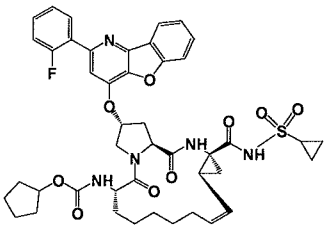
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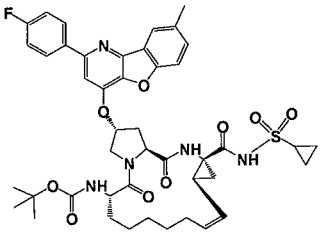
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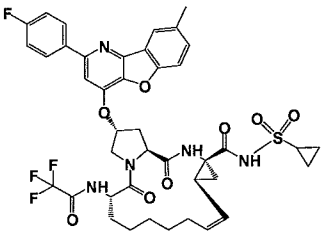
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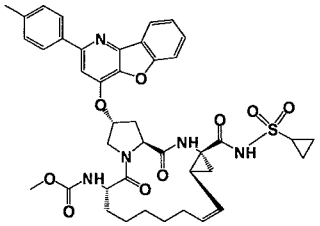
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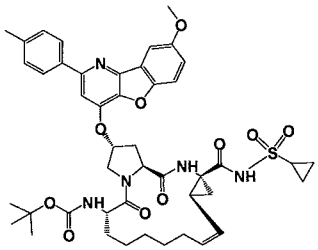
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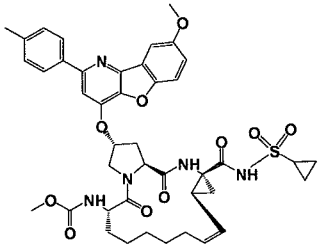
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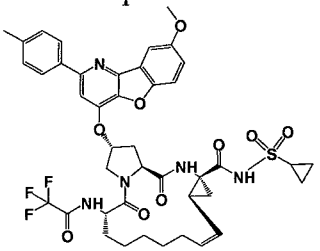
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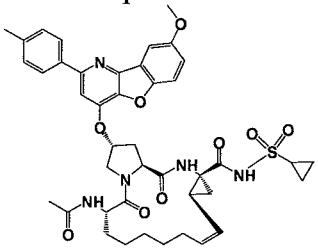
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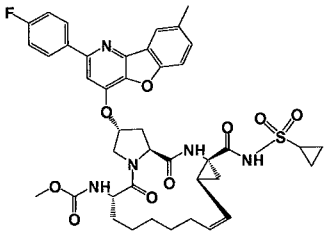
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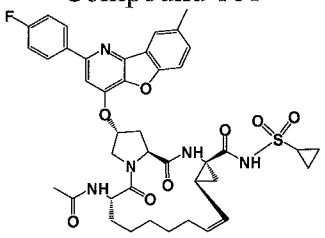
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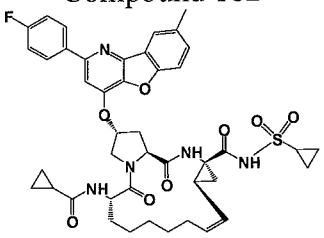
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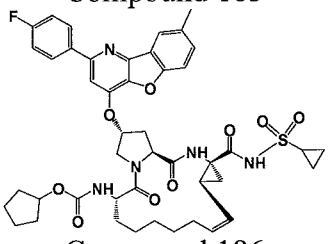
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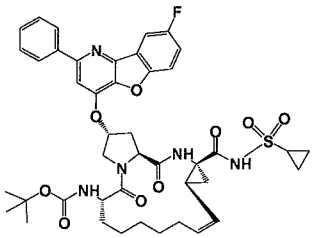
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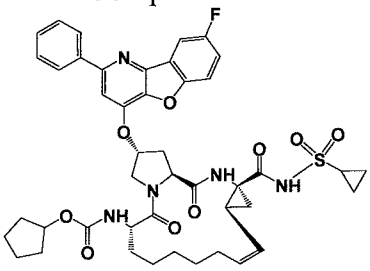
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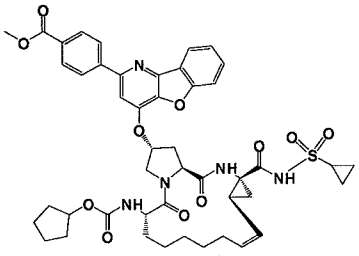
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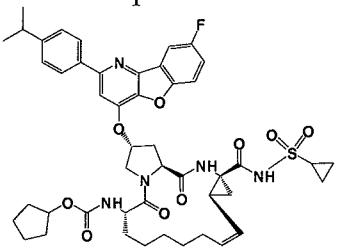
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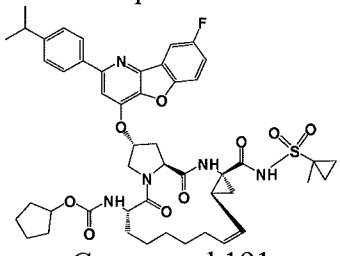
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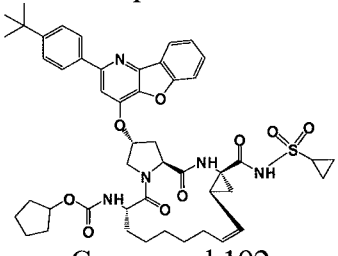
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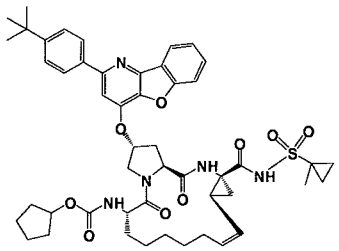
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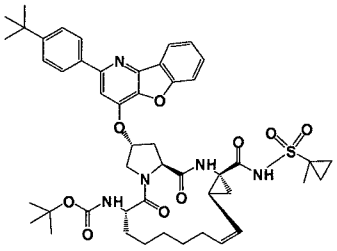
Compound 191



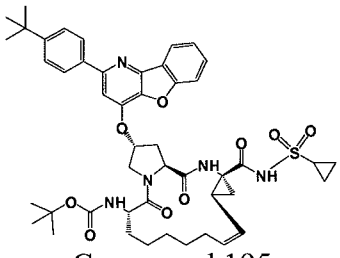
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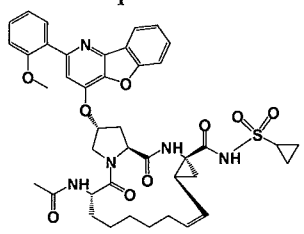
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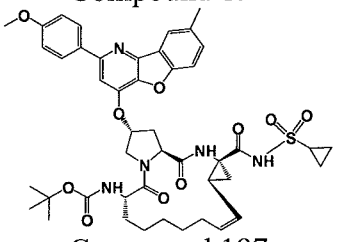
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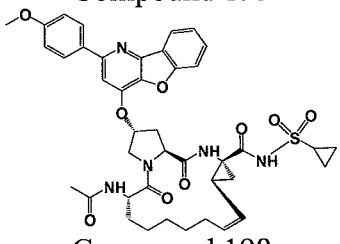
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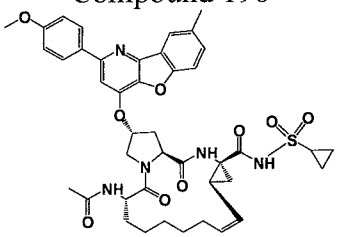
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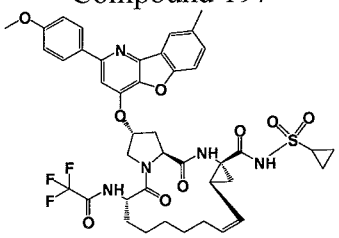
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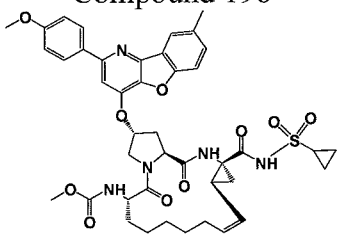
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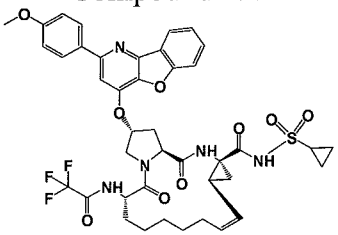
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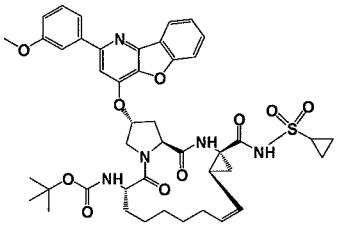
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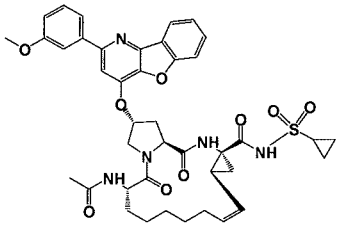
Compound 201



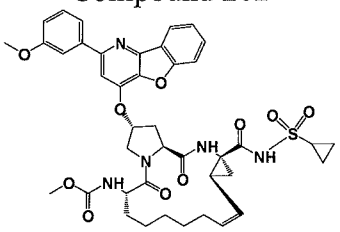
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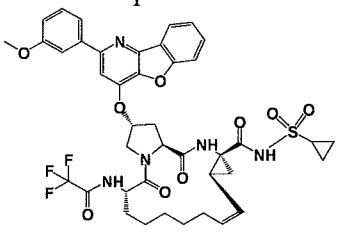
Compound 203



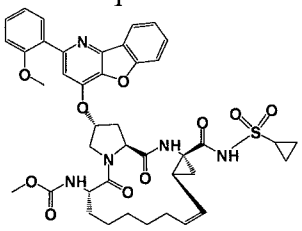
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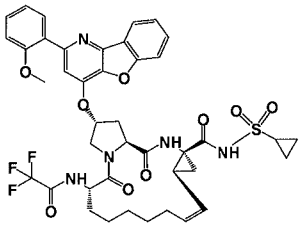
Compound 205



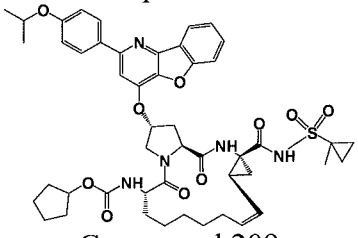
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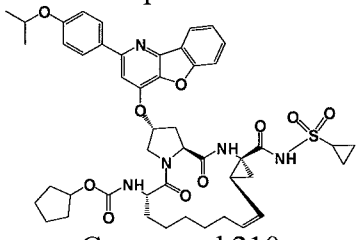
Compound 207



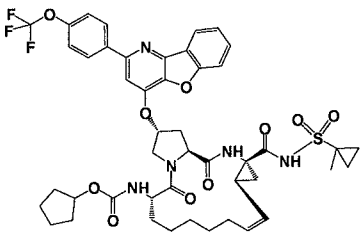
Compound 208



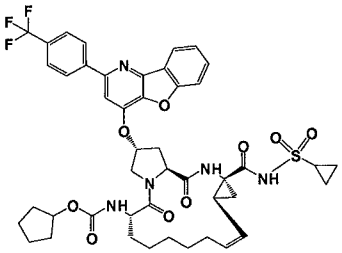
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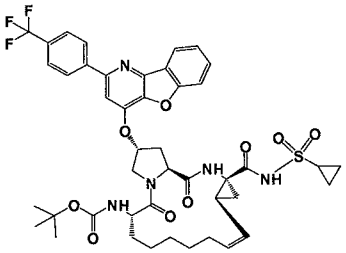
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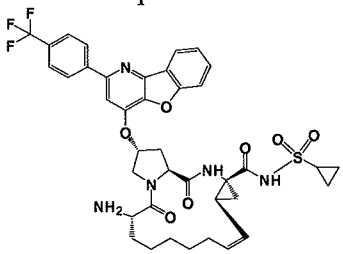
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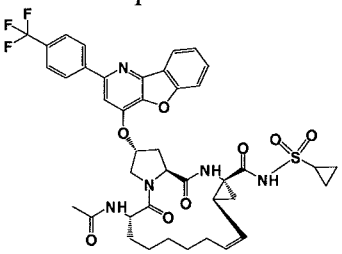
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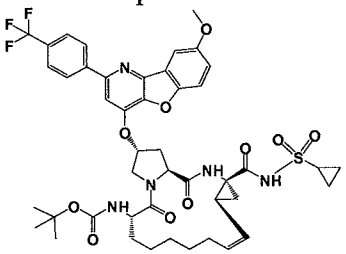
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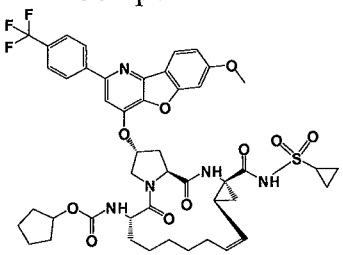
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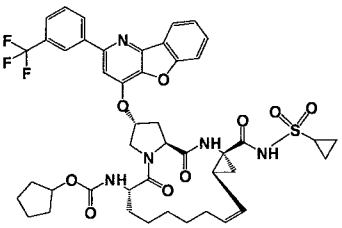
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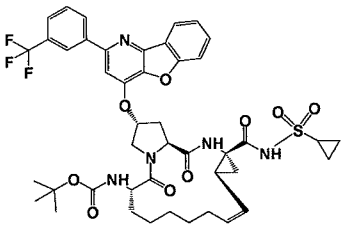
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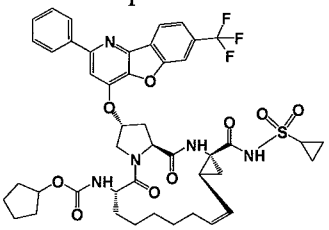
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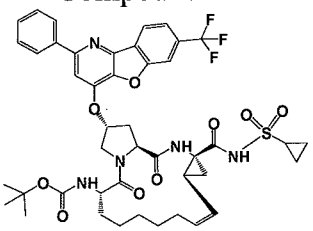
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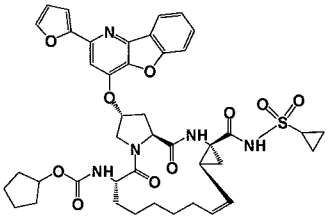
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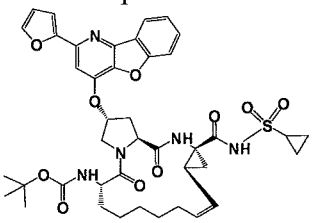
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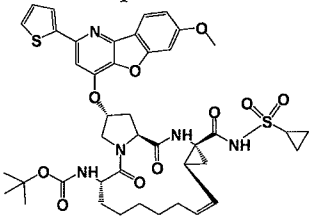
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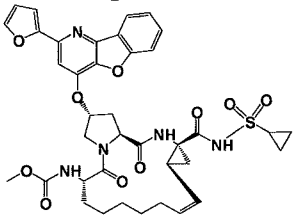
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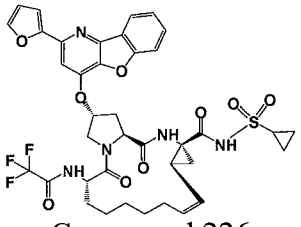
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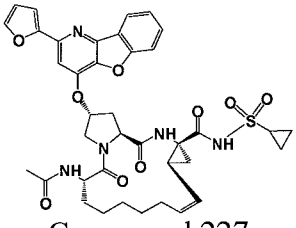
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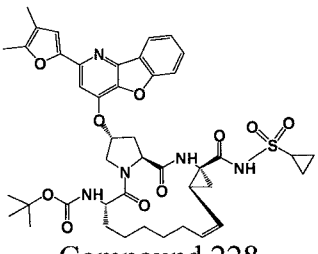
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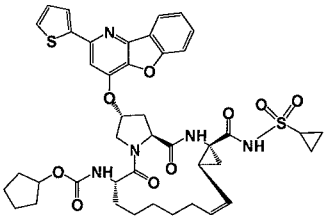
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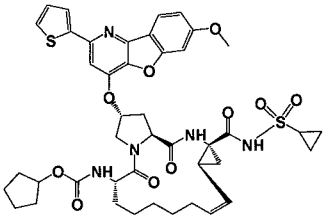
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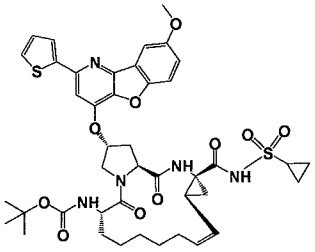
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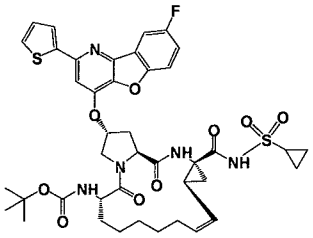
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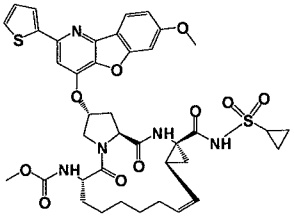
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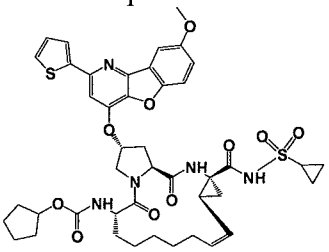
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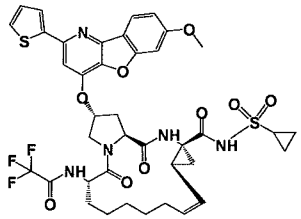
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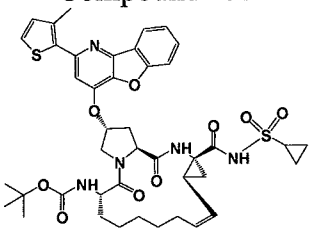
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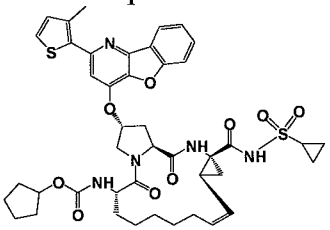
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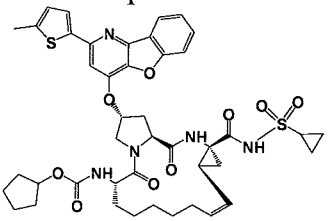
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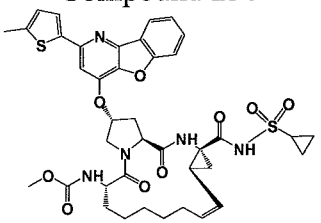
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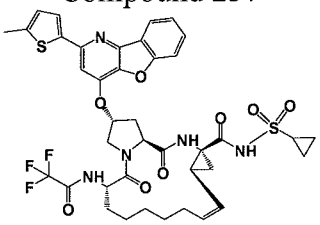
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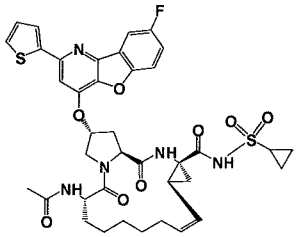
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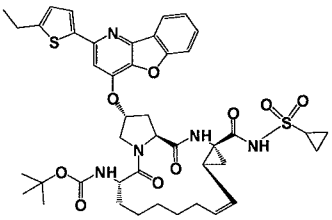
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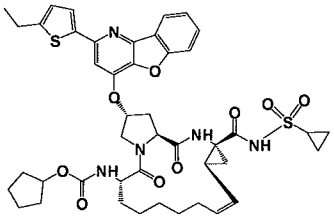
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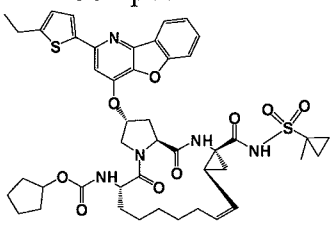
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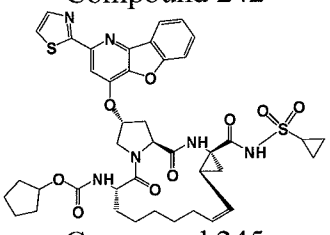
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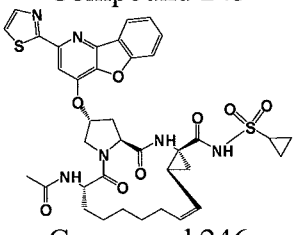
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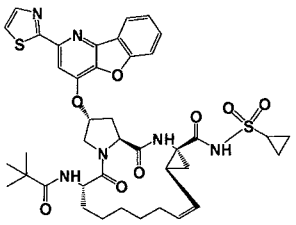
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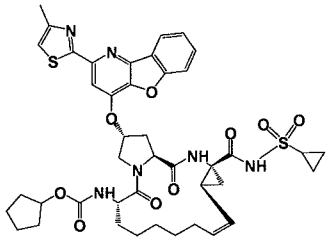
Compound 245



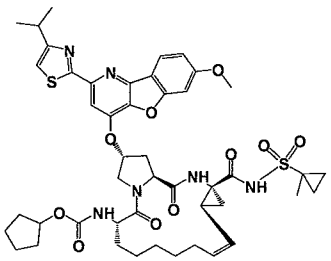
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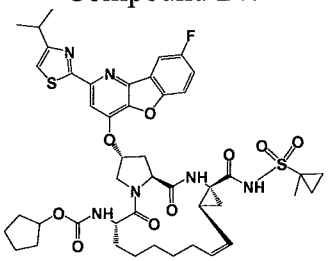
Compound 247



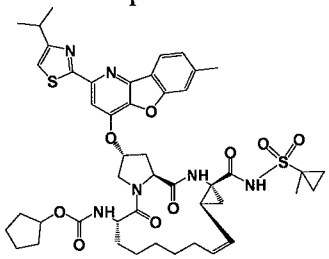
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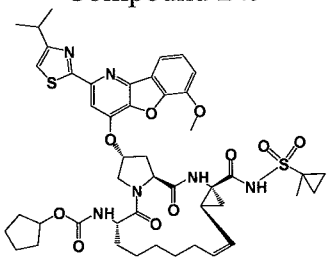
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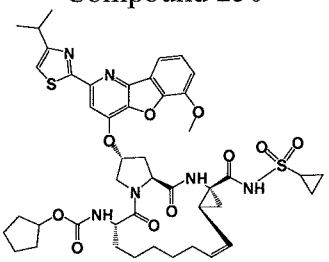
Compound 250



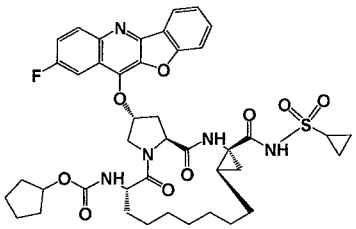
Compound 251



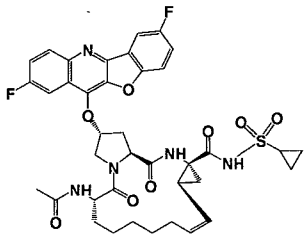
Compound 252



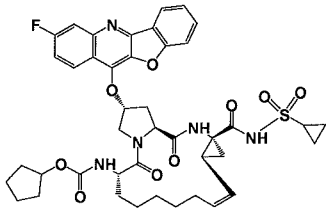
Compound 253



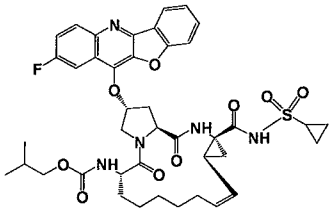
Compound 254



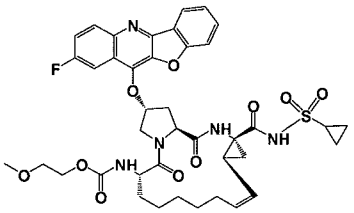
Compound 255



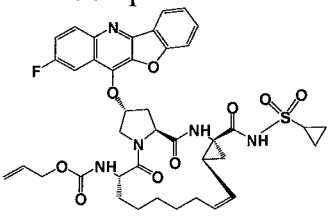
Compound 256



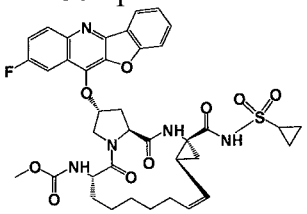
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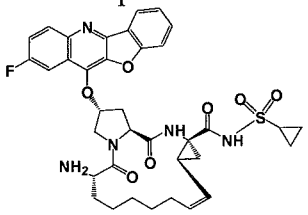
Compound 258



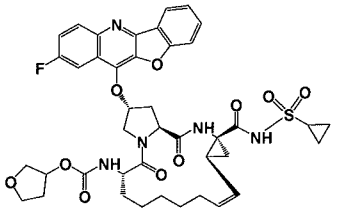
Compound 259



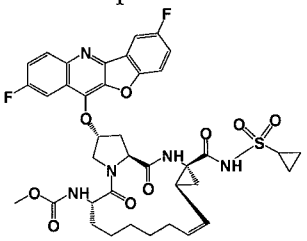
Compound 260



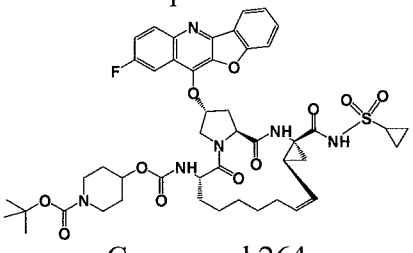
Compound 261



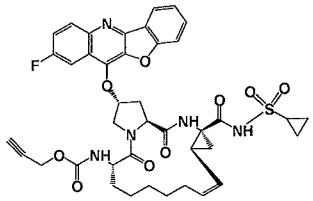
Compound 262



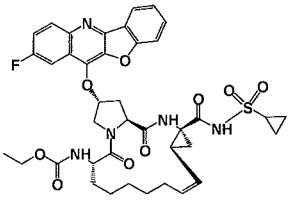
Compound 263



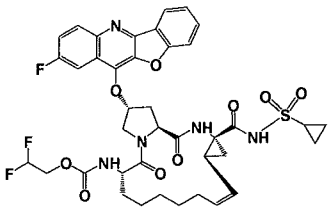
Compound 264



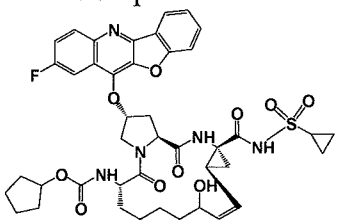
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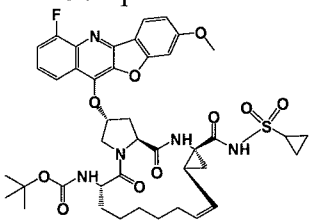
Compound 266



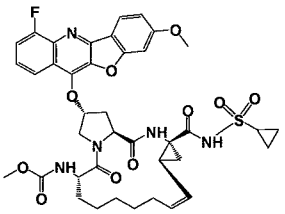
Compound 267



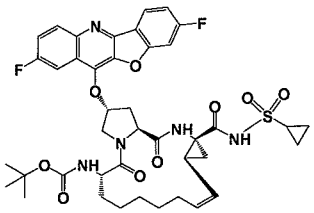
Compound 268



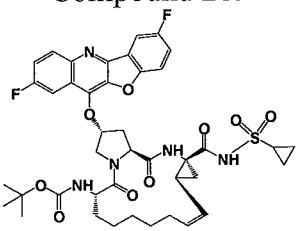
Compound 269



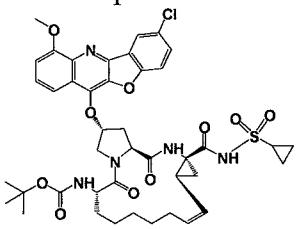
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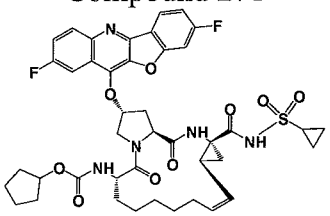
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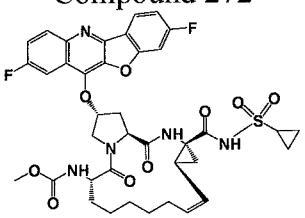
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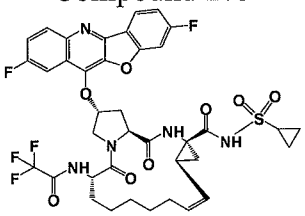
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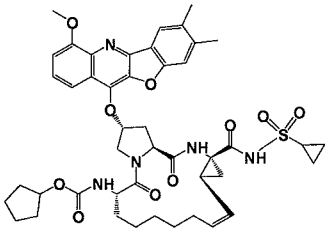
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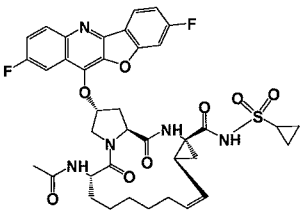
Compound 275



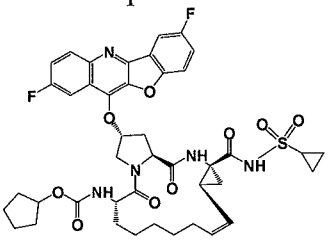
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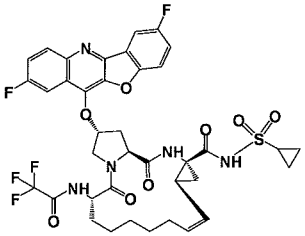
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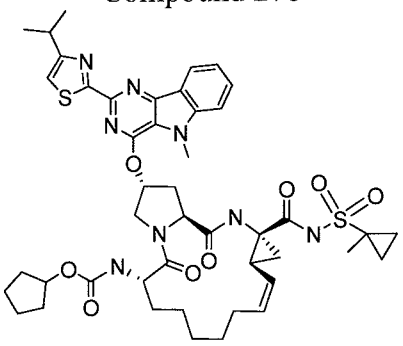
Compound 278



Compound 279



Compound 280



Compound 281.

23. A pharmaceutical composition comprising a compound of claim 1 and a pharmaceutically acceptable carrier.

24. The compound of claim 22, wherein the compound is one of Compounds 10, 16, 23, 25, 26, 30, 35, 36, 80, 81, 82, 84, 85, 86, 90, 95, 97, 100, 116, and 209.