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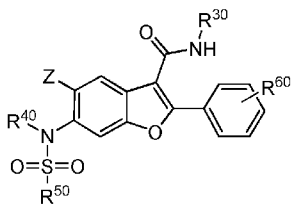
(54) **Title**: INHIBITORS OF HEPATITIS C VIRUS NS5B POLYMERASE



(I)

(57) **Abstract**: Compounds of formula (I) that are used as hepatitis C virus (HCV) NS5B polymerase inhibitors, the synthesis of such compounds, and the use of such compounds for inhibiting HCV NS5B polymerase activity, for treating or preventing HCV infections and for inhibiting HCV viral replication and /or viral production in a cell-based system. Wherein Z, R^{30}, R^{40}, R^{50} and R^{60} of compounds of formula (I) are herein defined as in the description.

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INHIBITORS OF HEPATITIS C VIRUS NS5B POLYMERASE

FIELD OF THE INVENTION

The present disclosure relates to antiviral compounds that are useful as inhibitors of the hepatitis C virus (HCV) NS5B (non-structural protein 5B) polymerase, compositions comprising such compounds, the use of such compounds for treating HCV infection and/or reducing the likelihood or severity of symptoms of HCV infection, methods for inhibiting the function of the NS5B polymerase, and methods for inhibiting HCV viral replication and/or viral production.

BACKGROUND OF THE INVENTION

Hepatitis C virus (HCV) infection is a major health problem that leads to chronic liver disease, such as cirrhosis and hepatocellular carcinoma, in a substantial number of infected individuals. Current treatments for HCV infection include immunotherapy with recombinant interferon-α alone or in combination with the nucleoside analog ribavirin.

Several virally-encoded enzymes are putative targets for therapeutic intervention, including a metalloprotease (NS2-3), a serine protease (NS3, amino acid residues 1-180), a helicase (NS3, full length), an NS3 protease cofactor (NS4A), a membrane protein (NS4B), a zinc metalloprotein (NS5A) and an RNA-dependent RNA polymerase (NS5B).

One identified target for therapeutic intervention is HCV NS5B polymerase. Sven-Erik Behrens *et al.*, *Identification and properties of the RNA-dependent RNA polymerase of heptatitis C virus*, 15(1) EMBO J. 12-22 (1996). Antagonists of NS5B activity are inhibitors of HCV replication. Steven S. Carroll *et al.*, *Inhibition of Hepatitis C Virus RNA Replication by 2'-Modified Nucleoside Analogs*, 278(14) J. BIOL. CHEM. 11979-84 (2003).

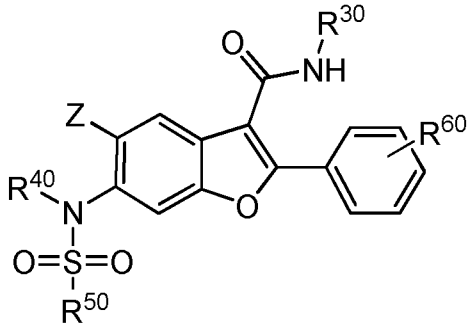
There is a clear and long-felt need to develop effective therapeutics for treatment of HCV infection. Specifically, there is a need to develop compounds that selectively inhibit HCV viral replication and that would be useful for treating HCV-infected patients.

SUMMARY OF THE INVENTION

The present disclosure relates to novel Compounds of Formula (I) and/or pharmaceutically acceptable salts thereof. These compounds are useful, either as compounds or their pharmaceutically acceptable salts (when appropriate), in the inhibition of HCV (hepatitis C

virus) NS5B (non-structural 5B) polymerase, the prevention or treatment of one or more of the symptoms of HCV infection, the inhibition of HCV viral replication and/or HCV viral production, and/or as pharmaceutical composition ingredients. As pharmaceutical composition ingredients, these compounds and their salts may be the primary active therapeutic agent, and, when appropriate, may be combined with other therapeutic agents including but not limited to other HCV antivirals, anti-infectives, immunomodulators, antibiotics or vaccines, as well as the present standard of care treatment options for HCV

More particularly, the present disclosure relates to Compounds of Formula (I)



(I)

and pharmaceutically acceptable salts thereof,

wherein:

Z is a phenyl group which is substituted with one R^{10} group and optionally further substituted with up to four R^{20} groups;

R^{10} is an 8- to 10-membered bicyclic heteroaryl group, wherein said 8- to 10-membered bicyclic heteroaryl group is optionally substituted with up to 4 groups, which can be the same or different, and are selected from halo, C_1-C_6 alkyl, -C(O)H, -$(CH_2)_t$-N(R^{70})$_2$, -$(CH_2)_t$-OH, -$(CH_2)_t$-O-(C_1-C_6 alkyl), -CF_3, -NHC(O)-heterocyclyl, -NHC(O)-(C_1-C_6 alkyl), -C(O)NH-(C_1-C_6 alkyl), -C(O)OH, -C(O)O-(C_1-C_6 alkyl), -NHC(O)-aryl, -$NHSO_2$-aryl, -$NHSO_2$-alkyl, -O-SO_2-alkyl, -O-(C_1-C_6 alkyl) and –CN, wherein the heterocyclyl moiety of said -NHC(O)-heterocyclyl group can be optionally substituted on a ring carbon or ring nitrogen atom with a –C(O)O-(C_1-C_6 alkyl) group;

R^{20} represents up to 4 optional substituents, which can be the same or different, and are selected from halo, 8- to 10-membered heteroaryl, C_1-C_6 alkyl, -O-(C_1-C_6 alkyl), -O-$(CH_2)_t$-OH, -O-$(CH_2)_t$-heterocyclyl, -O-(C_1-C_6 haloalkyl), -O-SO_2-(C_1-C_6 alkyl) and –CN;

R^{30} is H or C_1-C_6 alkyl;

R^{40} is selected from C_1-C_6 alkyl, C_1-C_6 haloalkyl, -$(CH_2)_t$-OH, -$(CH_2)_t$-heterocyclyl,-$(CH_2)_t$-$N(R^{70})_2$, -$(CH_2)_t$-CN, -$(CH_2)_t$-$NHC(O)OR^{30}$ and -$(CH_2)_t$-$NHC(O)R^{30}$;

R^{50} is C_1-C_6 alkyl, C_6-C_{10} aryl or C_3-C_7 cycloalkyl;

R^{60} represents up to 4 optional ring substituents, which can be the same or different, and are selected from halo, C_1-C_6 alkyl, -O-(C_1-C_6 alkyl), -O-(C_1-C_6 haloalkyl) and –CN;

each occurrence of R^{70} is independently H or C_1-C_6 alkyl; and

each occurrence of t is independently an integer ranging from 0 to 6.

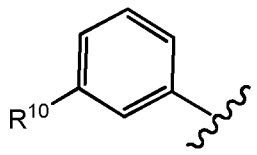
The present invention also includes pharmaceutical compositions containing a compound of the present invention and methods of preparing such pharmaceutical compositions. The present invention further includes methods of treating or reducing the likelihood or severity of HCV infection, methods for inhibiting the activity of the NS5B polymerase, and methods for inhibiting HCV viral replication and/or viral production.

Other embodiments, aspects and features of the present invention are either further described in or will be apparent from the ensuing description, examples and appended claims.

DETAILED DESCRIPTION OF THE INVENTION

The present invention includes Compounds of Formula (I) above, and pharmaceutically acceptable salts thereof. The Compounds of Formula (I) are HCV NS5B polymerase inhibitors.

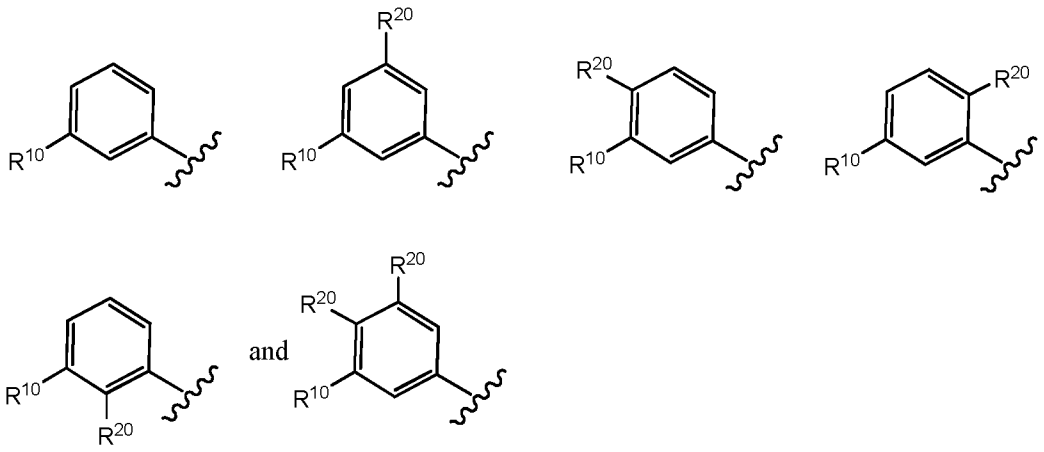
In a first embodiment of the present invention, Z is:



,

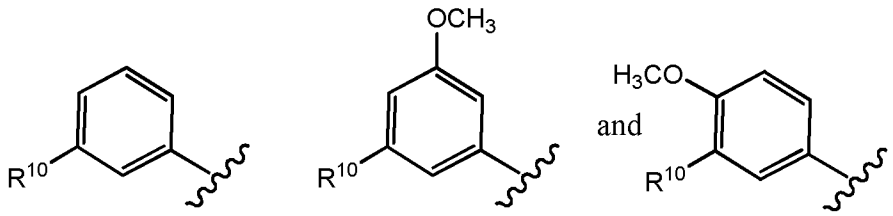
which can be optionally substituted on the depicted phenyl ring with one or two R^{20} groups, which can be the same or different.

In a first aspect of this first embodiment, Z is selected from:

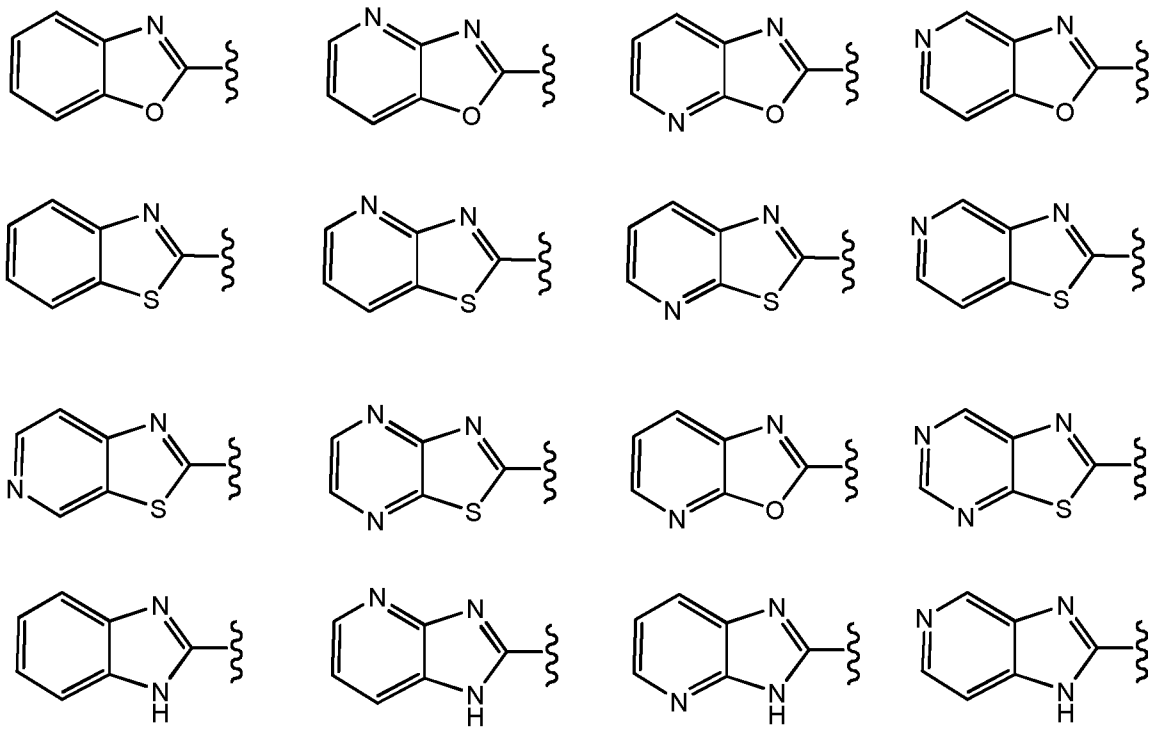


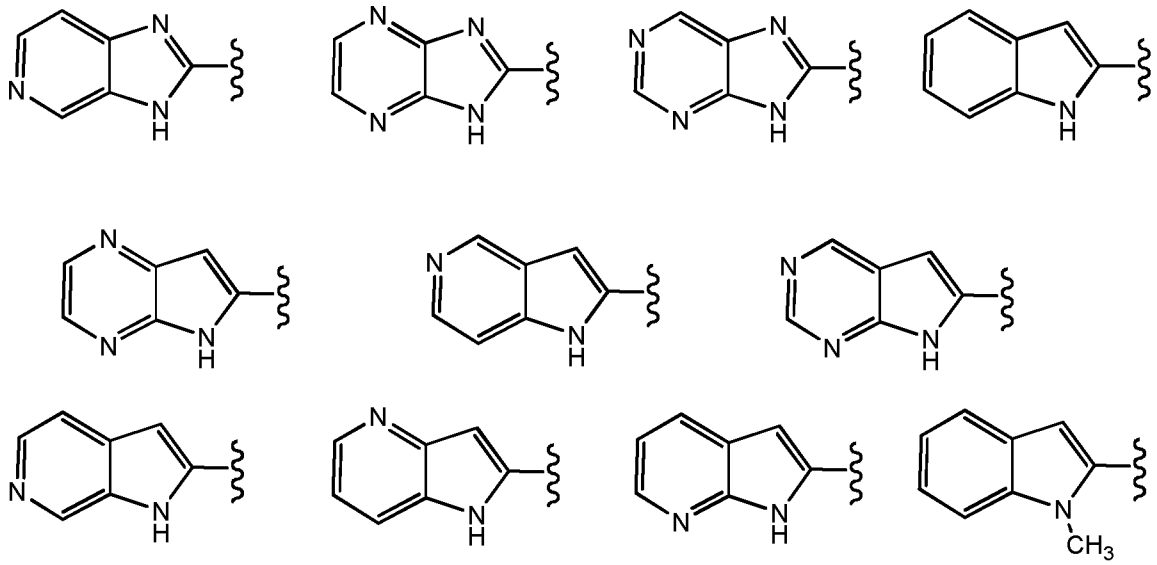
wherein each occurrence of R^{20} is independently Cl, F, CN, $-OCF_3$ or $-OCH_3$.

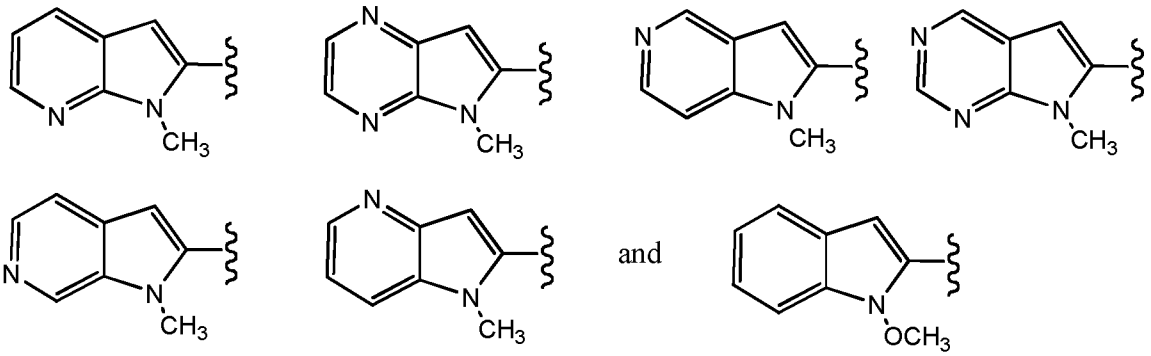
In a second aspect of this first embodiment, Z is selected from:



In a second embodiment of the present invention, R^{10} is selected from:



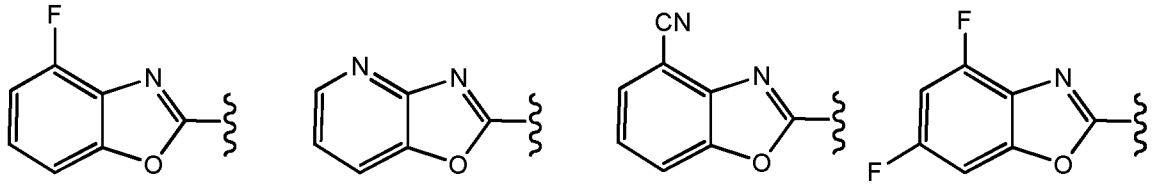




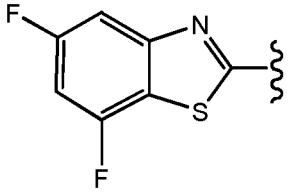
and

each of which can be optionally substituted as set forth above for the Compounds of Formula (I).

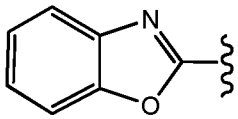
In a first aspect of this second embodiment, R^{10} is selected from:



and

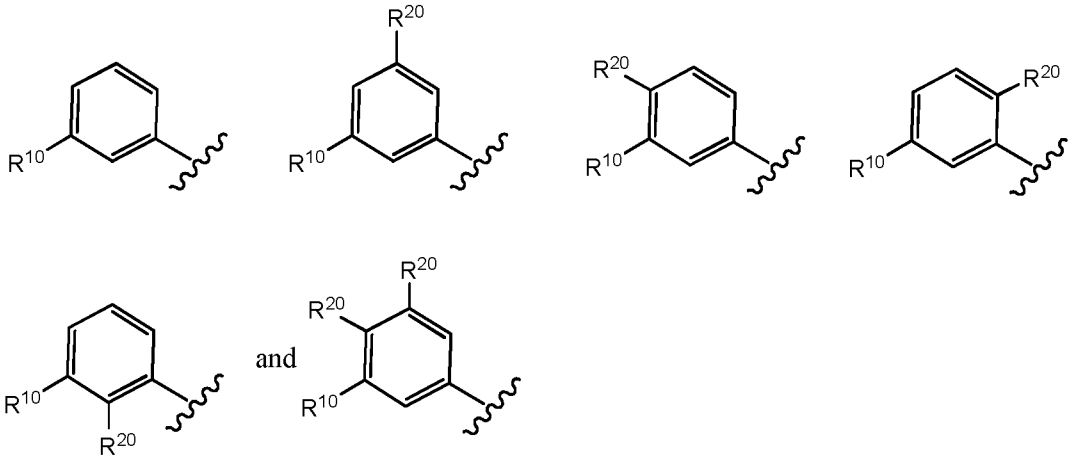


In a second aspect of this second embodiment, R^{10} is:



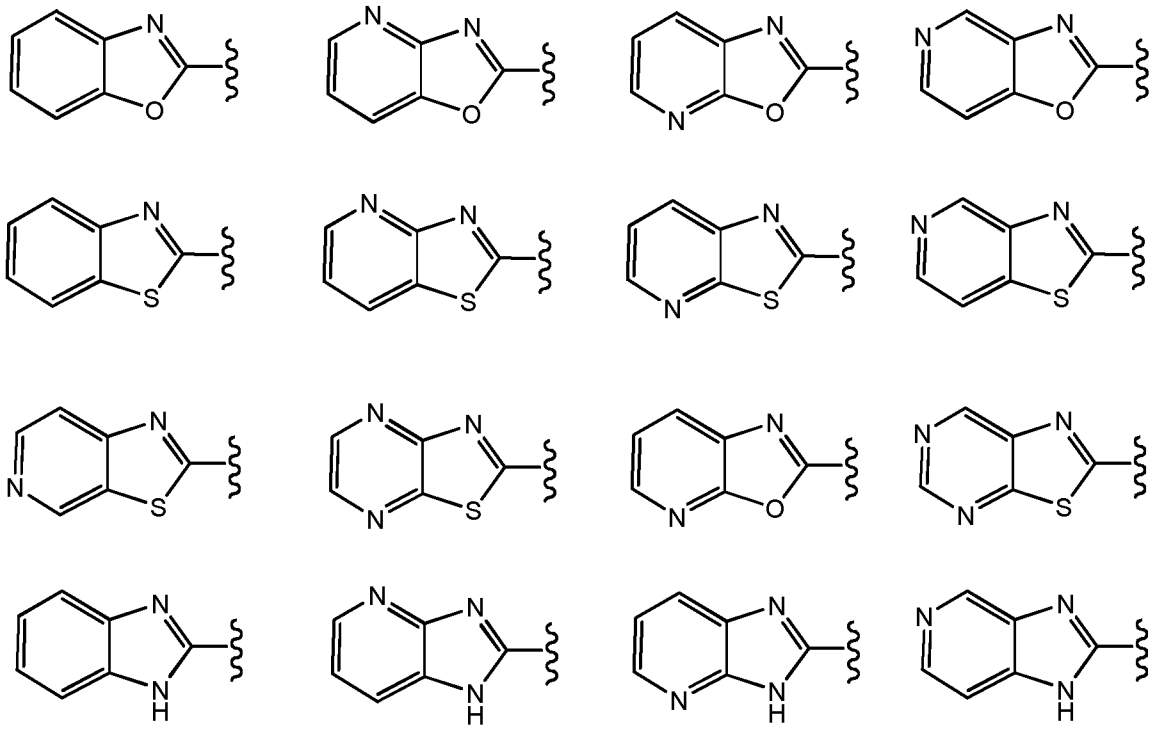
which can be optionally substituted as set forth above for the Compounds of Formula (I).

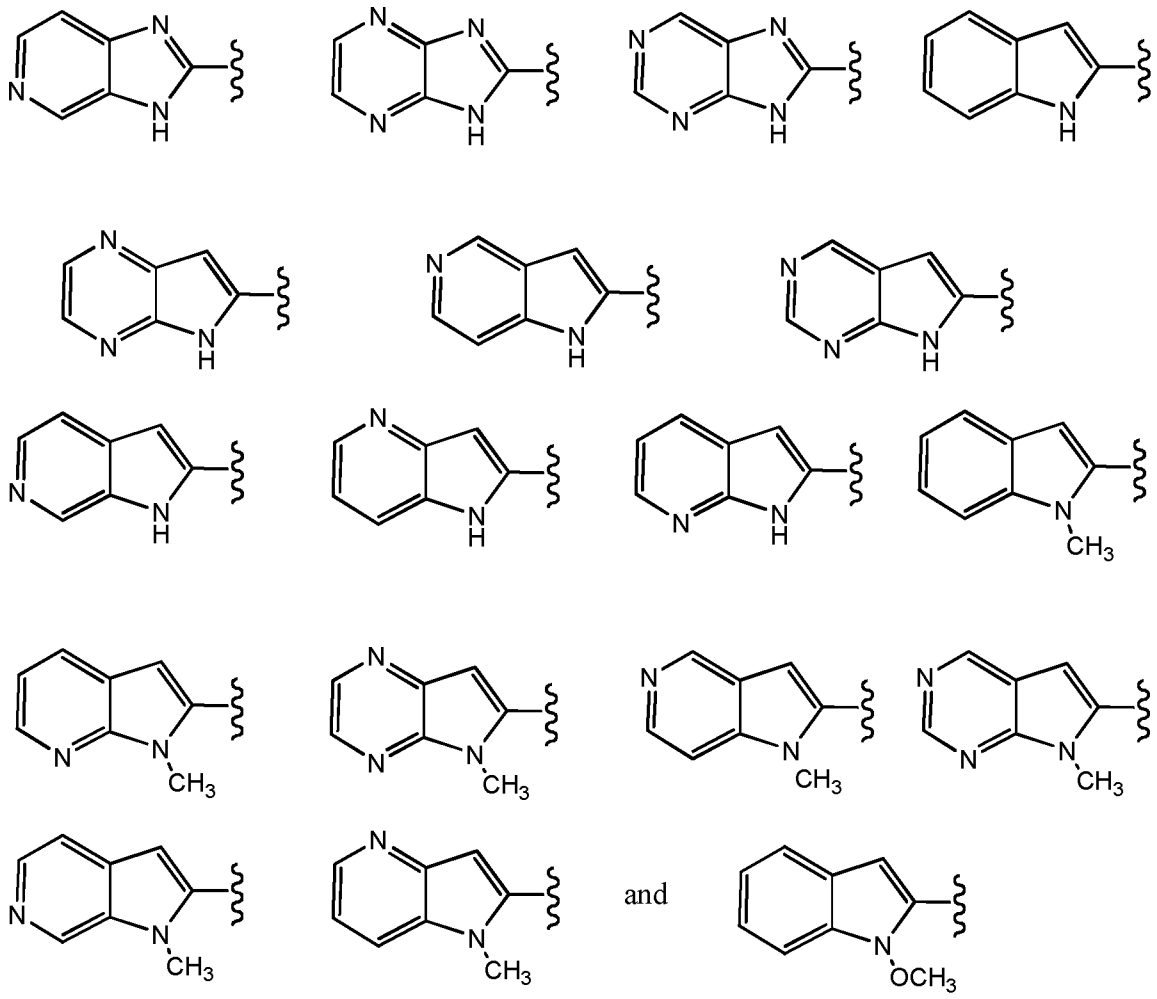
In a third embodiment of the present invention, Z is selected from:



wherein each occurrence of R^{20} is independently Cl, F, CN, $-OCF_3$ or $-OCH_3$; and

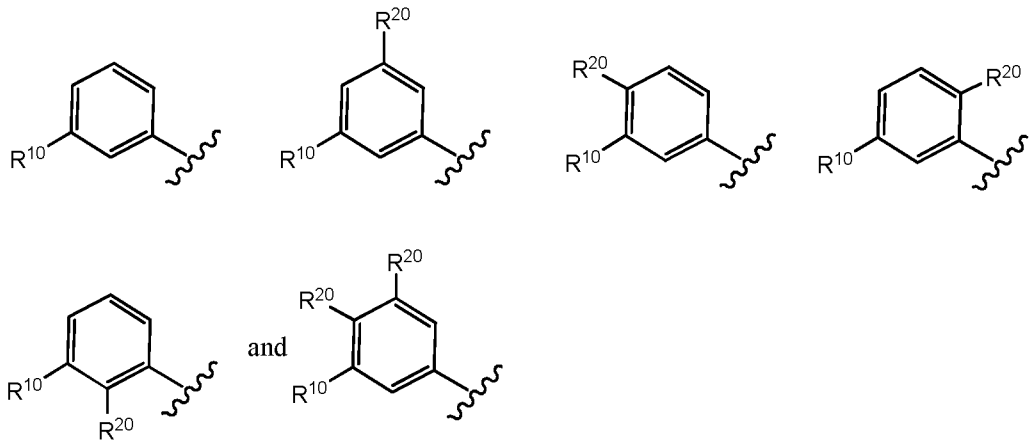
R^{10} is selected from:



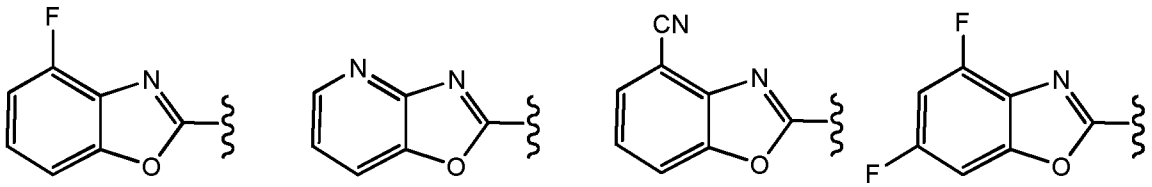


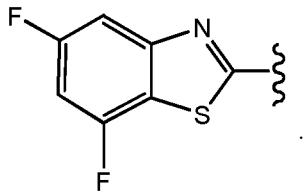
each of which can be optionally substituted as set forth above for the Compounds of Formula (I).

In a first aspect of this third embodiment, Z is selected from:

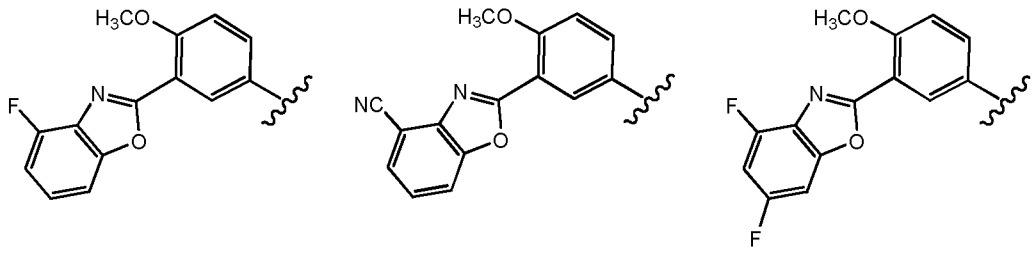


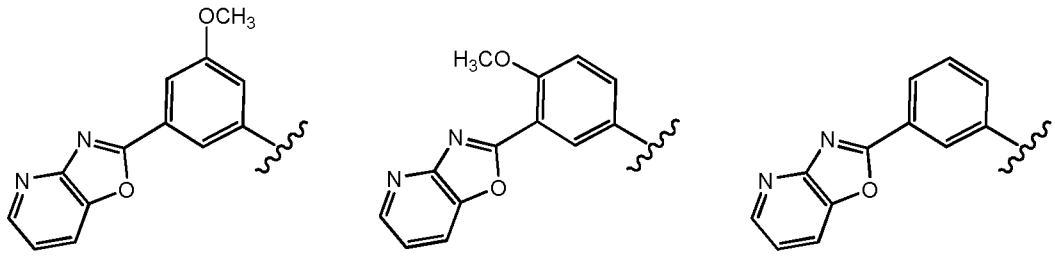
wherein each occurrence of R^{20} is independently Cl, F, CN, $-OCF_3$ or $-OCH_3$; and R^{10} is selected from:

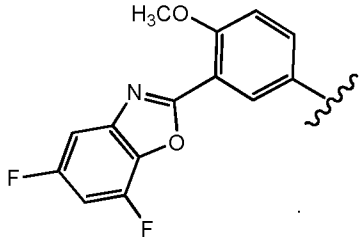


and 

In a second aspect of this third embodiment, Z is selected from:





and 

In a fourth embodiment of the present invention, R^{30} is $-CH_3$.

In a fifth embodiment of the present invention, R^{40} is C_1-C_6 alkyl, C_1-C_6 haloalkyl, $-(CH_2)_t$-OH or $-(CH_2)_t$-CN, wherein t is an integer ranging from 0 to 6. In a first aspect of this fifth embodiment, R^{40} is C_1-C_6 alkyl. In a second aspect of this fifth embodiment, R^{40} is $-CH_3$, $-(CH_2)_3$-CN, $-CH_2CH_2F$, or $-CH_2CH_2C(CH_3)_2$-OH. In a third aspect of this fifth embodiment, R^{40} is $-CH_3$.

In a sixth embodiment of the present invention, R^{50} is C_1-C_6 alkyl. In a first aspect of this sixth embodiment, R^{50} is C_6-C_{10} aryl. In a second aspect of this sixth embodiment, R^{50} is C_3-C_7 cycloalkyl. In a third aspect of this sixth embodiment, R^{50} is -CH_3, phenyl or cyclopropyl. In a fourth aspect of this sixth embodiment, R^{50} is -CH_3.

In a seventh embodiment of the present invention, only one R^{60} group is present. In a first aspect of this seventh embodiment, R^{60} represents a single halo group. In a second aspect of this seventh embodiment, R^{60} represents a single F group. In a third aspect of this seventh embodiment, R^{60} represents a single F group at the para position of the phenyl ring to which it is attached.

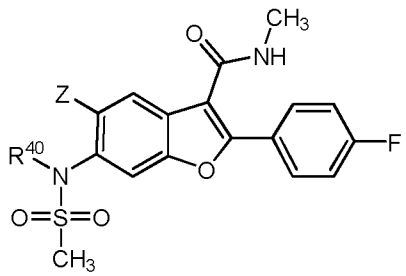
In an eighth embodiment of the present invention, R^{40} is -CH_3, –$(CH_2)_3$-CN, -CH_2CH_2F or -$CH_2CH_2C(CH_3)_2$-OH, and R^{50} is -CH_3. In a first aspect of this eighth embodiment, R^{40} and R^{50} are each -CH_3.

In a ninth embodiment of the present invention, R^{30}, R^{40} and R^{50} are each -CH_3.

In a tenth embodiment of the present invention, R^{40} is -CH_3, –$(CH_2)_3$-CN, -CH_2CH_2F or -$CH_2CH_2C(CH_3)_2$-OH; R^{50} is -CH_3; and R^{60} represents a single F group at the para position of the phenyl ring to which it is attached.

In an eleventh embodiment of the present invention, R^{30} is -CH_3; R^{40} is -CH_3, –$(CH_2)_3$-CN, -CH_2CH_2F or -$CH_2CH_2C(CH_3)_2$-OH; R^{50} is -CH_3; and R^{60} represents a single F group at the para position of the phenyl ring to which it is attached. In a first aspect of this eleventh embodiment, R^{30}, R^{40} and R^{50} are each -CH_3 and R^{60} represents a single F group at the para position of the phenyl ring to which it is attached.

In a twelfth embodiment of the present invention, the Compounds of Formula (I) have the formula (Ia):

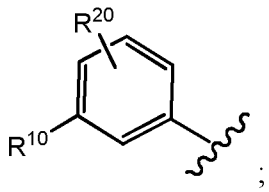


(Ia)

or a pharmaceutically acceptable salt thereof,

wherein:

Z is:



;

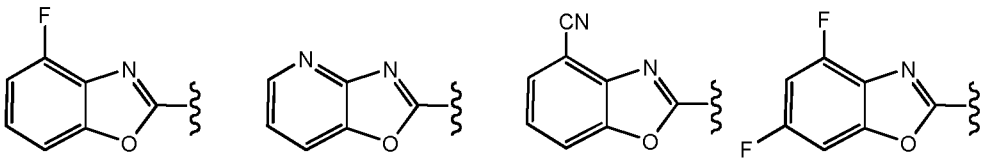
R^{10} is a 9-membered bicyclic heteroaryl group, wherein said 9-membered bicyclic heteroaryl group is optionally substituted with up to 2 groups, which can be the same or different, and are selected from halo, C_1-C_6 alkyl, -$(CH_2)_t$-$N(R^{70})_2$, -$(CH_2)_t$-OH, -$(CH_2)_t$-O-(C_1-C_6 alkyl), -CF_3, -NHC(O)-heterocyclyl, -NHC(O)-(C_1-C_6 alkyl), -C(O)NH-(C_1-C_6 alkyl), -C(O)OH, -C(O)O-(C_1-C_6 alkyl), -NHC(O)-aryl, -$NHSO_2$-aryl, -$NHSO_2$-alkyl, -O-SO_2-alkyl,-O-(C_1-C_6 alkyl) and –CN, wherein the heterocyclyl moiety of said -NHC(O)-heterocyclyl group can be optionally substituted on a ring carbon or ring nitrogen atom with a –C(O)O-(C_1-C_6 alkyl) group;

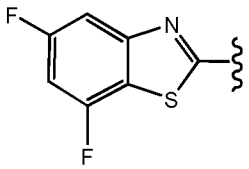
R^{20} represents up to 2 optional substituents, which can be the same or different, and are selected from halo, C_1-C_6 alkyl, -O-(C_1-C_6 alkyl), -O-$(CH_2)_t$-OH, -O-$(CH_2)_t$-heterocyclyl, -O-(C_1-C_6 haloalkyl), -O-SO_2-(C_1-C_6 alkyl) and –CN;

R^{40} is C_1-C_6 alkyl, C_1-C_6 haloalkyl, -$(CH_2)_t$-OH or -$(CH_2)_t$-CN; and

each occurrence of t is independently an integer ranging from 0 to 6.

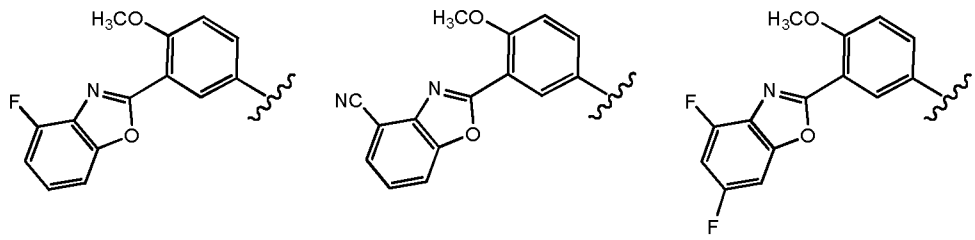
In a first aspect of this twelfth embodiment, R^{10} is selected from:

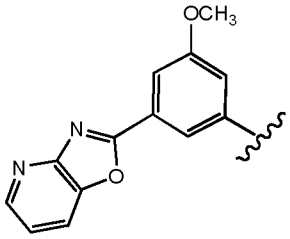
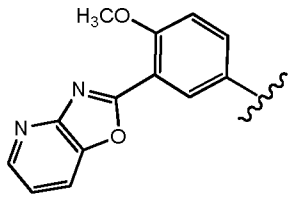
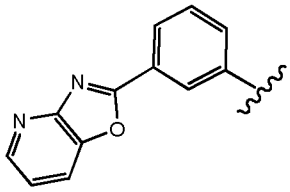


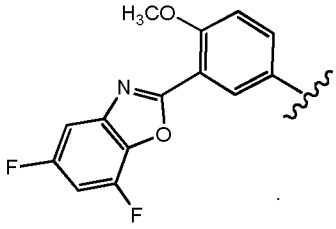
and 

.

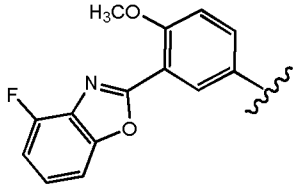
In a second aspect of this twelfth embodiment, Z is selected from:



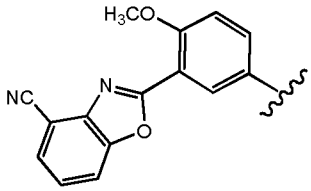




and 

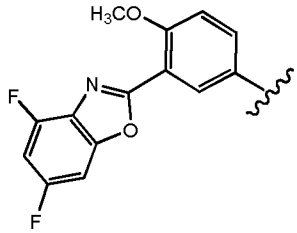
In a third aspect of this twelfth embodiment, Z is:



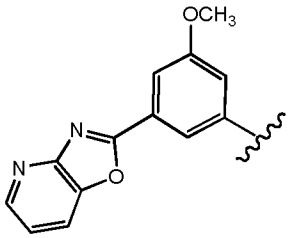
In a fourth aspect of this twelfth embodiment, Z is:



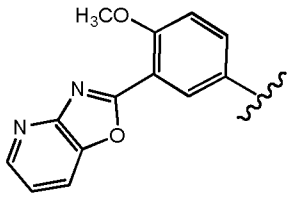
In a fifth aspect of this twelfth embodiment, Z is:



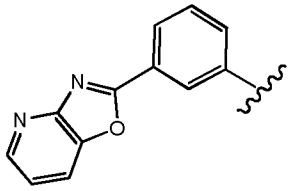
In a sixth aspect of this twelfth embodiment, Z is:



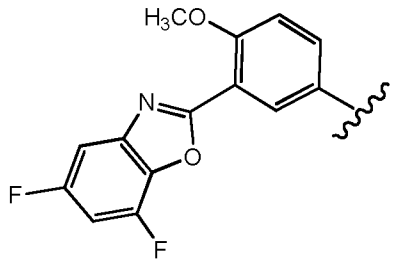
In a seventh aspect of this twelfth embodiment, Z is:



In a eighth aspect of this twelfth embodiment, Z is:



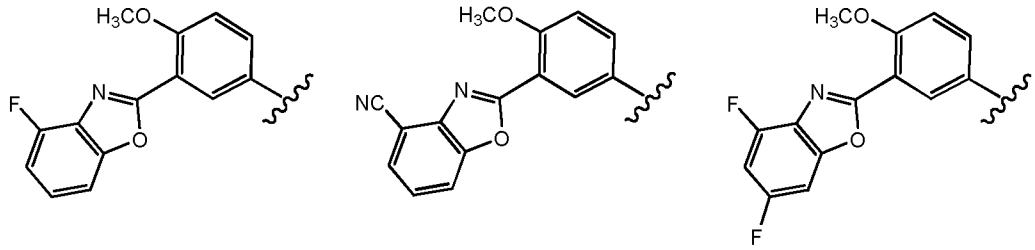
In an ninth aspect of this twelfth embodiment, Z is:

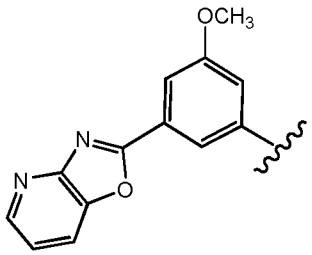
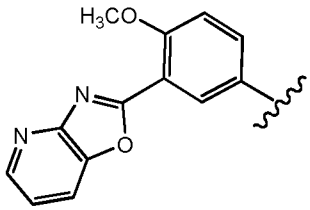
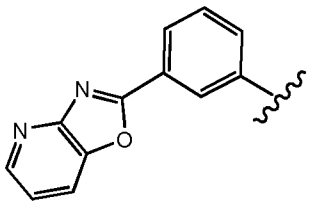


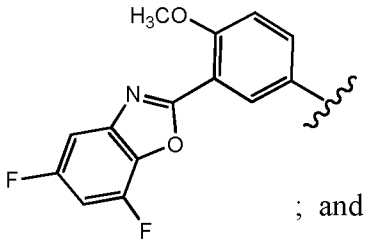
In a tenth aspect of this twelfth embodiment, R^{40} is C_1-C_6 alkyl.

In an eleventh aspect of this twelfth embodiment, R^{40} is -CH_3, –$(CH_2)_3$-CN, -CH_2CH_2F, or -$CH_2CH_2C(CH_3)_2$-OH. In a fifth aspect of this twelfth embodiment, R^{40} is -CH_3.

In an twelfth aspect of this twelfth embodiment, Z is selected from:

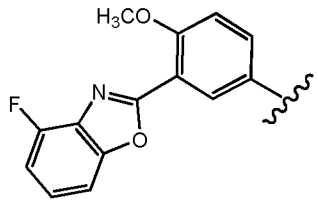
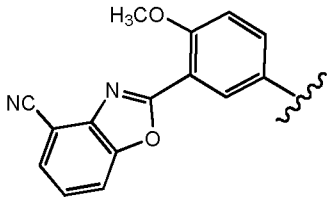
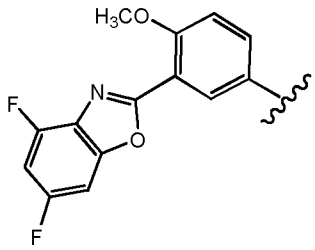


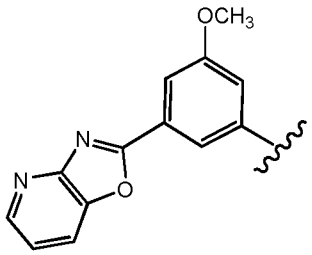
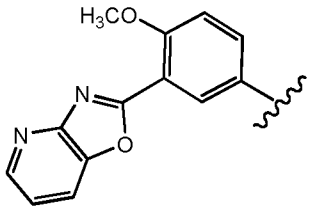
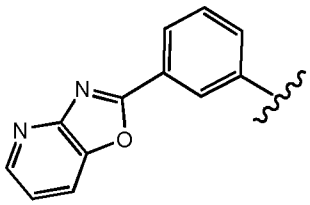




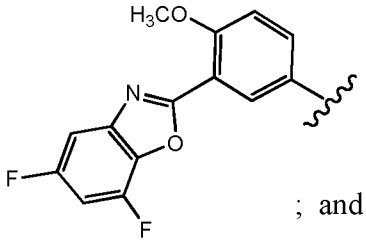
and  ; and

R^{40} is $-CH_3$, $-(CH_2)_3-CN$, $-CH_2CH_2F$, or $-CH_2CH_2C(CH_3)_2-OH$.

In a thirteenth aspect of this twelfth embodiment, Z is selected from:

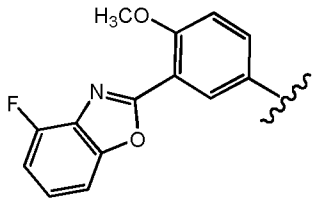




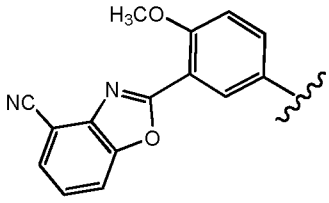
and  ; and

R^{40} is $-CH_3$.

In a fourteenth aspect of this twelfth embodiment, Z is:



or



, and

R^{40} is $-CH_3$.

In a thirteenth embodiment of the present invention, the compound of the invention is selected from Compounds **1-256** shown in the Examples below, and pharmaceutically acceptable salts thereof.

Other embodiments of the present invention include the following:

(a) A pharmaceutical composition comprising an effective amount of a Compound of Formula (I) and a pharmaceutically acceptable carrier.

(b) The pharmaceutical composition of (a), further comprising a second therapeutic agent selected from the group consisting of HCV antiviral agents, immunomodulators, and anti-infective agents.

(c) The pharmaceutical composition of (b), wherein the HCV antiviral agent is an antiviral selected from the group consisting of direct inhibitors of HCV, including but not limited to NS3 and NS3/4A protease inhibitors, NS5A inhibitors and HCV NS5B polymerase inhibitors.

(d) A pharmaceutical combination that is (i) a Compound of Formula (I) and (ii) a second therapeutic agent selected from the group consisting of HCV antiviral agents, immunomodulators, and anti-infective agents; wherein the Compound of Formula (I) and the second therapeutic agent are each employed in an amount that renders the combination effective for inhibiting HCV NS5B activity, or for inhibiting HCV viral replication, or for treating HCV infection and/or reducing the likelihood or severity of symptoms of HCV infection.

(e) The combination of (d), wherein the HCV antiviral agents are one or more antiviral agents selected from the group consisting of direct inhibitors of HCV, including but not limited to NS3 and NS3/4A protease inhibitors, NS5A inhibitors and HCV NS5B polymerase inhibitors.

(f) A use of a Compound of Formula (I) in the preparation of a medicament for inhibiting HCV NS5B activity in a subject in need thereof.

(g) A use of a Compound of Formula (I) in the preparation of a medicament for preventing and/or treating infection by HCV in a subject in need thereof.

(h) A method of treating HCV infection and/or reducing the likelihood or severity of symptoms of HCV infection in a subject in need thereof, which comprises administering to the subject an effective amount of a Compound of Formula (I).

(i) The method of (h), wherein the Compound of Formula (I) is administered in combination with an effective amount of at least one second therapeutic agent selected from the group consisting of HCV antiviral agents, immunomodulators, and anti-infective agents.

(j) The method of (i), wherein the HCV antiviral agent is an antiviral selected from the group consisting of direct inhibitors of HCV, including but not limited to NS3 and NS3/4A protease inhibitors, NS5A inhibitors and HCV NS5B polymerase inhibitors.

(k) A method of inhibiting HCV viral replication and/or HCV viral production in a cell-based system, which comprises administering to the subject an effective amount of a Compound of Formula (I) in combination with an effective amount of at least one second therapeutic agent selected from the group consisting of HCV antiviral agents, immunomodulators, and anti-infective agents.

(l) The method of (k), wherein the HCV antiviral agent is an antiviral selected from the group consisting of direct inhibitors of HCV, including but not limited to NS3 and NS3/4A protease inhibitors, NS5A inhibitors and HCV NS5B polymerase inhibitors.

(m) A method of inhibiting HCV NS5B activity in a subject in need thereof, which comprises administering to the subject the pharmaceutical composition of (a), (b), or (c) or the combination of (d) or (e).

(n) A method of treating HCV infection and/or reducing the likelihood or severity of symptoms of HCV infection in a subject in need thereof, which comprises administering to the subject the pharmaceutical composition of (a), (b), or (c) or the combination of (d) or (e).

In the embodiments of the compounds and salts provided above, it is to be understood that each embodiment may be combined with one or more other embodiments, to the extent that such a combination provides a stable compound or salt and is consistent with the description of the embodiments. It is further to be understood that the embodiments of compositions and methods provided as (a) through (n) above are understood to include all embodiments of the compounds and/or salts, including such embodiments as result from combinations of embodiments.

Additional embodiments of the invention include the pharmaceutical compositions, combinations, uses and methods set forth in (a) through (n) above, wherein the

compound of the present invention employed therein is a compound of one of the embodiments, aspects, classes, sub-classes, or features of the compounds described above. In all of these embodiments, the compound may optionally be used in the form of a pharmaceutically acceptable salt or hydrate as appropriate.

The present invention also includes a compound of the present invention for use (i) in, (ii) as a medicament for, or (iii) in the preparation of a medicament for: (a) inhibiting HCV NS5B activity, or (b) inhibiting HCV viral replication, or (c) treating HCV infection and/or reducing the likelihood or severity of symptoms of HCV infection, or (d) use in medicine. In these uses, the compounds of the present invention can optionally be employed in combination with one or more second therapeutic agents selected from HCV antiviral agents, anti-infective agents, and immunomodulators.

As used herein, all ranges are inclusive, and all sub-ranges are included within such ranges, although not necessarily explicitly set forth. In addition, the term "or," as used herein, denotes alternatives that may, where appropriate, be combined; that is, the term "or" includes each listed alternative separately as well as their combination.

As used herein, the term “alkyl” refers to any linear or branched chain alkyl group having a number of carbon atoms in the specified range. Thus, for example, “$C_{1\text{-}6}$ alkyl” (or “C_1-C_6 alkyl”) refers to all of the hexyl alkyl and pentyl alkyl isomers as well as n-, iso-, sec- and t-butyl, n- and isopropyl, ethyl and methyl. As another example, “$C_{1\text{-}4}$ alkyl” refers to n-, iso-, sec- and t-butyl, n- and isopropyl, ethyl and methyl. Alkyl groups may be substituted as indicated.

The term "halogenated" refers to a group or molecule in which a hydrogen atom has been replaced by a halogen. Similarly, the term “haloalkyl” refers to a halogenated alkyl group. The term "halogen" (or “halo”) refers to atoms of fluorine, chlorine, bromine and iodine (alternatively referred to as fluoro, chloro, bromo, and iodo).

The term “alkoxy” refers to an “alkyl-O-” group. Alkoxy groups may be substituted as indicated.

The term "cycloalkyl" refers to any cyclic ring of an alkane or alkene having a number of carbon atoms in the specified range. Thus, for example, “$C_{3\text{-}8}$ cycloalkyl” (or “C_3-C_8 cycloalkyl”) refers to cyclopropyl, cyclobutyl, cyclopentyl, cyclopentenyl, cyclohexyl, cyclohexenyl, cycloheptyl, cycloheptenyl, cyclooctyl, and cyclooctenyl. The term “cycloalkoxy” refers to a “cycloalkyl-O-” group. Cycloalkyl groups may be substituted as indicated.

The term "aryl" (or "aryl ring system") refers to aromatic mono- and poly-carbocyclic ring systems wherein the individual carbocyclic rings in the polyring systems are fused or attached to each other via a single bond. As used herein, the term aryl includes aromatic mono- and poly-carbocyclic ring systems that include from 0 to 4 heteroatoms (non-carbon atoms) that are independently chosen from N, O and S. Suitable aryl groups include phenyl, naphthyl, biphenylenyl, pyridinyl, pyrimidinyl and pyrrolyl, as well as those discussed below. Aryl groups may be substituted as indicated. Aryl ring systems may include, where appropriate, an indication of the variable to which a particular ring atom is attached. Illustrative examples of aryl groups include phenyl, naphthyl and anthracenyl. In one embodiment, an aryl group is phenyl. Unless otherwise indicated, substituents to the aryl ring systems can be attached to any ring atom, provided that such attachment results in formation of a stable ring system.

The term “carbocycle” (and variations thereof such as “carbocyclic”) as used herein, unless otherwise indicated, refers to (i) a C_5 to C_7 monocyclic, saturated or unsaturated ring, or (ii) a C_8 to C_{10} bicyclic saturated or unsaturated ring system. Each ring in (ii) is either independent of, or fused to, the other ring, and each ring is saturated or unsaturated. Carbocycle groups may be substituted as indicated. When the carbocycles contain one or more heteroatoms independently chosen from N, O and S, the carbocycles may also be referred to as "heterocycles," as defined below. The carbocycle may be attached to the rest of the molecule at any carbon or nitrogen atom that results in a stable compound. The fused bicyclic carbocycles are a subset of the carbocycles; *i.e.*, the term "fused bicyclic carbocycle" generally refers to a C_8 to C_{10} bicyclic ring system in which each ring is saturated or unsaturated and two adjacent carbon atoms are shared by each of the rings in the ring system. A fused bicyclic carbocycle in which both rings are saturated is a saturated bicyclic ring system. Saturated carbocyclic rings are also referred to as cycloalkyl rings, *e.g.*, cyclopropyl, cyclobutyl, *etc*. A fused bicyclic carbocycle in which one or both rings are unsaturated is an unsaturated bicyclic ring system. Carbocycle ring systems may include, where appropriate, an indication of the variable to which a particular ring atom is attached. Unless otherwise indicated, substituents to the ring systems can be attached to any ring atom, provided that such attachment results in formation of a stable ring system.

Unless indicated otherwise, the term “heterocycle” (and variations thereof such as “heterocyclic” or “heterocyclyl”) broadly refers to (i) a stable 5- to 7-membered, saturated or unsaturated monocyclic ring, or (ii) a stable 8- to 10-membered bicyclic ring system, wherein each ring in (ii) is independent of, or fused to, the other ring or rings and each ring is saturated or

unsaturated, and the monocyclic ring or bicyclic ring system contains one or more heteroatoms (*e.g.*, from 1 to 6 heteroatoms, or from 1 to 4 heteroatoms) independently selected from N, O and S and a balance of carbon atoms (the monocyclic ring typically contains at least one carbon atom and the bicyclic ring systems typically contain at least two carbon atoms); and wherein any one or more of the ring nitrogen and ring sulfur heteroatoms is optionally oxidized, for example to provide a ring N-oxide group or a ring $-S(O)_2-$ group, and any one or more of the nitrogen heteroatoms is optionally quaternized. Unless otherwise specified, the heterocyclic ring may be attached at any heteroatom or carbon atom, provided that attachment results in the creation of a stable structure. Heterocycle groups may be substituted as indicated, and unless otherwise specified, the substituents may be attached to any atom in the ring, whether a heteroatom or a carbon atom, provided that a stable chemical structure results. Representative examples include piperidinyl, piperazinyl, azepanyl, pyrrolidinyl, pyrazolidinyl, imidazolidinyl, oxazolidinyl, isoxazolidinyl, morpholinyl, thiomorpholinyl, thiazolidinyl, isothiazolidinyl, and tetrahydrofuryl (or tetrahydrofuranyl).

Unless expressly stated to the contrary, the term "heteroaryl ring system" refers to aryl ring systems, as defined above, that include from 1 to 4 heteroatoms (non-carbon atoms) that are independently chosen from N, O and S. In the case of substituted heteraromatic rings containing at least one nitrogen atom (*e.g.*, pyridine), such substitutions can be those resulting in N-oxide formation. Representative examples of heteroaromatic rings include pyridyl, pyrrolyl, pyrazinyl, pyrimidinyl, pyridazinyl, thienyl (or thiophenyl), thiazolyl, furanyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, oxazolyl, isooxazolyl, oxadiazolyl, thiazolyl, isothiazolyl, and thiadiazolyl. Representative examples of bicyclic heterocycles include benzotriazolyl, indolyl, isoindolyl, indazolyl, indolinyl, isoindolinyl, quinoxalinyl, quinazolinyl, cinnolinyl, chromanyl, isochromanyl, tetrahydroquinolinyl, quinolinyl, tetrahydroisoquinolinyl, isoquinolinyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzo-1,4-dioxinyl and benzo-1,3-dioxolyl.

Unless otherwise specifically noted as only “substituted”, alkyl, cycloalkyl, and aryl groups are not substituted. Preferably, the substituents are selected from the group which includes, but is not limited to, halo, C_1-C_{20} alkyl, $-CF_3$, $-NH_2$, $-N(C_1$-C_6 alkyl$)_2$, $-NO_2$, oxo, $-CN$, $-N_3$, $-OH$, $-O(C_1$-C_6 alkyl), C_3-C_{10} cycloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, (C_0-C_6 alkyl)$S(O)_{0\text{-}2}-$, aryl-$S(O)_{0\text{-}2}-$, (C_0-C_6 alkyl)$S(O)_{0\text{-}2}$(C_0-C_6 alkyl)-, (C_0-C_6 alkyl)C(O)NH-, H_2N-C(NH)-, $-O(C_1$-C_6 alkyl)CF_3, (C_0-C_6 alkyl)C(O)-, (C_0-C_6 alkyl)OC(O)-, (C_0-C_6alkyl)$O(C_1$-C_6 alkyl)-, (C_0-C_6 alkyl)$C(O)_{1\text{-}2}$(C_0-C_6 alkyl)-, (C_0-C_6 alkyl)OC(O)NH-, aryl, aralkyl, heteroaryl, heterocyclylalkyl, halo-aryl, halo-aralkyl, halo-heterocycle and halo-heterocyclylalkyl.

As used herein, the term "compound" is intended to encompass chemical agents described by generic Formula (I) in all forms, including hydrates and solvates of such chemical agents. In addition, the term "compound" is intended to encompass prodrugs of the chemical agents described by generic Formula (I).

In the Compounds of Formula (I), the atoms may exhibit their natural isotopic abundances, or one or more of the atoms may be artificially enriched in a particular isotope having the same atomic number, but an atomic mass or mass number different from the atomic mass or mass number predominantly found in nature. The present invention is meant to include all suitable isotopic variations of the Compounds of Formula (I). For example, different isotopic forms of hydrogen (H) include protium (^{1}H) and deuterium (^{2}H or D). Protium is the predominant hydrogen isotope found in nature. Enriching for deuterium may afford certain therapeutic advantages, such as increasing *in vivo* half-life or reducing dosage requirements, or may provide a compound useful as a standard for characterization of biological samples. Isotopically-enriched compounds within Formula (I) can be prepared without undue experimentation by conventional techniques well known to those skilled in the art or by processes analogous to those described in the Schemes and Examples herein using appropriate isotopically-enriched reagents and/or intermediates.

Unless expressly stated to the contrary, all ranges cited herein are inclusive. For example, a heteroaryl ring described as containing from "1 to 3 heteroatoms" means the ring can contain 1, 2, or 3 heteroatoms. It is also to be understood that any range cited herein includes within its scope all of the sub-ranges within that range. The oxidized forms of the heteroatoms N and S are also included within the scope of the present invention.

When any variable (for example, R^{20} or R^{60}) occurs more than one time in any constituent or in Formula (I) or in any other formula depicting and describing compounds of the invention, its definition on each occurrence is independent of its definition at every other occurrence. Also, combinations of substituents and/or variables are permissible only if such combinations result in stable compounds.

Unless expressly stated to the contrary, substitution by a named substituent is permitted on any atom provided such substitution is chemically allowed and results in a stable compound. A "stable" compound is a compound that can be prepared and isolated and whose structure and properties remain or can be caused to remain essentially unchanged for a period of time sufficient to allow use of the compound for the purposes described herein (*e.g.*, therapeutic or prophylactic administration to a subject).

As a result of the selection of substituents and substituent patterns, certain of the compounds of the present invention can have asymmetric centers and can occur as mixtures of stereoisomers, or as individual diastereomers, or enantiomers. All isomeric forms of these compounds, whether isolated or in mixtures, are within the scope of the present invention.

As would be recognized by one of ordinary skill in the art, certain of the compounds of the present invention can exist as tautomers. For the purposes of the present invention a reference to a Compound of Formula (I) is a reference to the compound *per se*, or to any one of its tautomers *per se*, or to mixtures of two or more tautomers.

The compounds of the present inventions are useful in the inhibition of HCV replication (*e.g.*, HCV NS5B activity), the treatment of HCV infection and/or reduction of the likelihood or severity of symptoms of HCV infection. For example, the compounds of this invention are useful in treating infection by HCV after suspected past exposure to HCV by such means as blood transfusion, exchange of body fluids, bites, accidental needle stick, or exposure to patient blood during surgery.

The compounds of this invention are useful in the preparation and execution of screening assays for antiviral compounds. For example, the compounds of this invention are useful for identifying resistant HCV replicon cell lines harboring mutations within NS5B, which are excellent screening tools for more powerful antiviral compounds. Furthermore, the compounds of this invention are useful in establishing or determining the binding site of other antivirals to the HCV replicase.

The compounds of the present invention may be administered in the form of pharmaceutically acceptable salts. The term "pharmaceutically acceptable salt" refers to a salt that possesses the effectiveness of the parent compound and that is not biologically or otherwise undesirable (*e.g.*, is neither toxic nor otherwise deleterious to the recipient thereof). Suitable salts include acid addition salts that may, for example, be formed by mixing a solution of the compound of the present invention with a solution of a pharmaceutically acceptable acid such as hydrochloric acid, sulfuric acid, acetic acid, trifluoroacetic acid, or benzoic acid. Many of the compounds of the invention carry an acidic moiety, in which case suitable pharmaceutically acceptable salts thereof can include alkali metal salts (*e.g.*, sodium or potassium salts), alkaline earth metal salts (*e.g.*, calcium or magnesium salts), and salts formed with suitable organic ligands such as quaternary ammonium salts. Also, in the case of an acid (-COOH) or alcohol group being present, pharmaceutically acceptable esters can be employed to modify the solubility or hydrolysis characteristics of the compound.

The term "administration" and variants thereof (*e.g.*, "administering" a compound) in reference to a compound of the invention mean providing the compound or a prodrug of the compound to the individual in need of treatment. When a compound of the invention is provided in combination with one or more other active agents (*e.g.*, antiviral agents useful for treating HCV infection), "administration" and its variants are each understood to include concurrent and sequential provision of the compound or salt and other agents.

As used herein, the term "composition" is intended to encompass a product comprising the specified ingredients, as well as any product which results, directly or indirectly, from combining the specified ingredients.

By "pharmaceutically acceptable" is meant that the ingredients of the pharmaceutical composition must be compatible with each other and not deleterious to the recipient thereof.

The term "subject" (alternatively referred to herein as "patient"), as used herein, refers to human or a chimpanzee. In one embodiment, the subject is a human.

The term "effective amount" as used herein means that amount of active compound or pharmaceutical agent that elicits the biological or medicinal response in a tissue, system, animal or human that is being sought by a researcher, veterinarian, medical doctor or other clinician. In one embodiment, the effective amount is a "therapeutically effective amount" for the alleviation of one or more symptoms of the disease or condition being treated. In another embodiment, the effective amount is a "prophylactically effective amount" for reduction of the severity or likelihood of one or more symptoms of the disease or condition. In another embodiment, the effective amount is a "therapeutically effective amount" for inhibition of HCV viral replication and/or HCV viral production. The term also includes herein the amount of active compound sufficient to inhibit HCV NS5B activity and thereby elicit the response being sought (*i.e.*, an "inhibition effective amount"). When the active compound (*i.e.*, active ingredient) is administered as the salt, references to the amount of active ingredient are to the free acid or free base form of the compound.

For the purposes of inhibiting HCV NS5B polymerase, treating HCV infection and/or reducing the likelihood or severity of symptoms of HCV infection and inhibiting HCV viral replication and/or HCV viral production, the compounds of the present invention, optionally in the form of a salt, can be administered by any means that produces contact of the active agent with the agent's site of action. They can be administered by one or more conventional means available for use in conjunction with pharmaceuticals, either as individual

therapeutic agents or in a combination of therapeutic agents. They can be administered alone, but typically are administered with a pharmaceutical carrier selected on the basis of the chosen route of administration and standard pharmaceutical practice. The compounds of the invention can, for example, be administered by one or more of the following: orally, parenterally (including subcutaneous injections, intravenous, intramuscular, intrasternal injection or infusion techniques), by inhalation (such as in a spray form), or rectally, in the form of a unit dosage of a pharmaceutical composition containing an effective amount of the compound and conventional non-toxic pharmaceutically-acceptable carriers, adjuvants and vehicles. Liquid preparations suitable for oral administration (*e.g.*, suspensions, syrups, elixirs and the like) can be prepared according to techniques known in the art and can employ any of the usual media such as water, glycols, oils, alcohols and the like. Solid preparations suitable for oral administration (*e.g.*, powders, pills, capsules and tablets) can be prepared according to techniques known in the art and can employ such solid excipients as starches, sugars, kaolin, lubricants, binders, disintegrating agents and the like. Parenteral compositions can be prepared according to techniques known in the art and typically employ sterile water as a carrier and optionally other ingredients, such as solubility aids. Injectable solutions can be prepared according to methods known in the art wherein the carrier comprises a saline solution, a glucose solution or a solution containing a mixture of saline and glucose. Further description of methods suitable for use in preparing pharmaceutical compositions of the present invention and of ingredients suitable for use in said compositions is provided in Remington: The Science and Practice of Pharmacy, 21st edition (ed. University of the Sciences in Philadelphia; Lippincott, Williams & Wilkins, 2005).

The compounds of this invention can be administered orally in a dosage range of 0.001 to 1000 mg/kg of mammal (*e.g.*, human) body weight per day in a single dose or in divided doses. One dosage range is 0.01 to 500 mg/kg body weight per day orally in a single dose or in divided doses. Another dosage range is 0.1 to 100 mg/kg body weight per day orally in single or divided doses. For oral administration, the compositions can be provided in the form of tablets or capsules containing 1.0 to 500 mg of the active ingredient, particularly 1, 5, 10, 15, 20, 25, 50, 75, 100, 150, 200, 250, 300, 400, and 500 mg of the active ingredient for the symptomatic adjustment of the dosage to the patient to be treated. The specific dose level and frequency of dosage for any particular patient may be varied and will depend upon a variety of factors including the activity of the specific compound employed, the metabolic stability and length of action of that compound, the age, body weight, general health, sex, diet, mode and time of

administration, rate of excretion, drug combination, the severity of the particular condition, HCV viral genotype, viral resistance, and the host undergoing therapy.

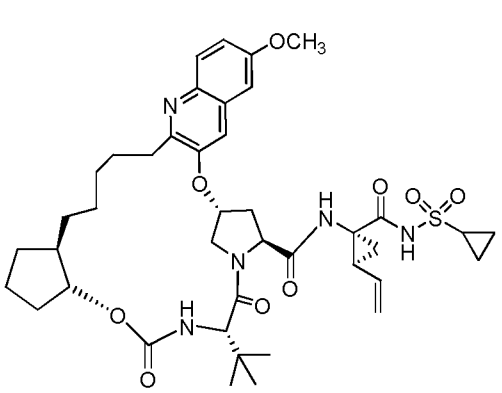
As noted above, the present invention also relates to a method of inhibiting HCV NS5B activity, inhibiting HCV viral replication and/or HCV viral production, treating HCV infection and/or reducing the likelihood or severity of symptoms of HCV infection with a compound of the present invention in combination with one or more therapeutic agents and a pharmaceutical composition comprising a compound of the present invention and one or more therapeutic agents selected from the group consisting of a HCV antiviral agent, an immunomodulator, and an anti-infective agent. Such therapeutic agents active against HCV include, but are not limited to, ribavirin, levovirin, viramidine, thymosin alpha-1, R7025 (an enhanced interferon (Roche)), interferon-β, interferon-α, pegylated interferon-α (peginterferon-α), a combination of interferon-α and ribavirin, a combination of peginterferon-α and ribavirin, a combination of interferon-α and levovirin, and a combination of peginterferon-α and levovirin. The combination of pegylated-interferon and ribaviron represents the current Standard of Care for HCV treatment. The combination of one or more compounds of the present invention with the Standard of Care for HCV treatment, pegylated-interferon and ribaviron is specifically contemplated as being encompassed by the present invention. Interferon-α includes, but is not limited to, recombinant interferon-α2a (such as ROFERON interferon available from Hoffmann-LaRoche, Nutley, NJ), pegylated interferon-α2a (PEGASYS), interferon-α2b (such as INTRON-A interferon available from Schering Corp., Kenilworth, NJ), pegylated interferon-α2b (PEGINTRON), a recombinant consensus interferon (such as interferon alphacon-1), albuferon (interferon-α bound to human serum albumin (Human Genome Sciences)), and a purified interferon-α product. Amgen's recombinant consensus interferon has the brand name INFERGEN. Levovirin is the L-enantiomer of ribavirin which has shown immunomodulatory activity similar to ribavirin. Viramidine represents an analog of ribavirin disclosed in International Patent Application Publication WO 01/60379. In accordance with the method of the present invention, the individual components of the combination can be administered separately at different times during the course of therapy or concurrently in divided or single combination forms.

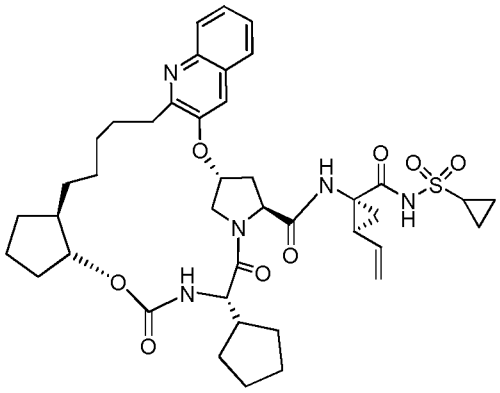
For the treatment of HCV infection, the compounds of the invention may also be administered in combination with an antiviral agent NS5B polymerase inhibitor, *e.g.*, R7128 (Roche), valopicitabine (NM-283; Idenix) and 2'-F-2'-beta-methylcytidine (*see also* WO 2005/003147).

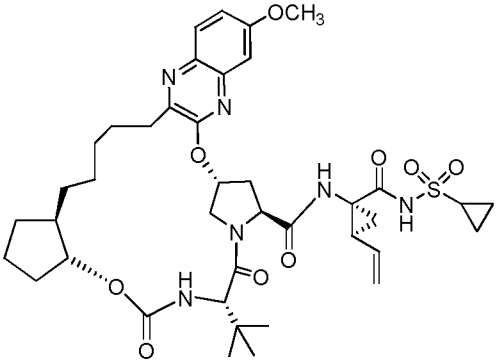
. The compounds of the present invention also may be combined for the treatment of HCV infection with antiviral 2'-*C*-branched ribonucleosides disclosed in Rogers E. Harry-O'Kuru *et al.*, *A Short, Flexible Route toward 2'-C-Branched Ribonucleosides*, 62 J. ORG. CHEM. 1754-59 (1997); Michael S. Wolfe & Rogers E. Harry-O'Kuru, *A Concise Synthesis of 2'-C-Methylribonucleosides*, 36(42) TETRAHEDRON LETTERS 7611-14 (1995); U.S. Patent No. 3,480,613; and International Patent Application Publications WO 01/90121, WO 01/92282, WO 02/32920, WO 04/002999, WO 04/003000 and WO 04/002422; the entire contents of each of which are incorporated by reference. Such 2'-*C*-branched ribonucleosides include, but are not limited to, 2'-*C*-methyl-cytidine, 2'-*C*-methyl-uridine, 2'-*C*-methyl-adenosine, 2'-*C*-methyl-guanosine, and 9-(2-*C*-methyl-β-D-ribofuranosyl)-2,6-diaminopurine, and the corresponding amino acid ester of the ribose C-2', C-3', and C-5' hydroxyls and the corresponding optionally substituted cyclic 1,3-propanediol esters of the 5'-phosphate derivatives.

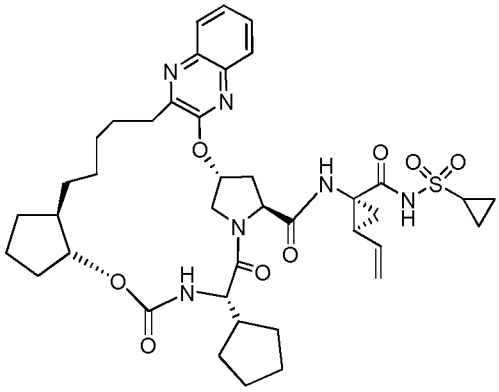
For the treatment of HCV infection, the compounds of the present invention may also be administered in combination with an agent that is an inhibitor of HCV NS3 serine protease. HCV NS3 serine protease is an essential viral enzyme and has been described to be an excellent target for inhibition of HCV replication. Exemplary substrate and non-substrate based inhibitors of HCV NS3 protease inhibitors are disclosed in International Patent Application Publications WO 98/22496, WO 98/46630, WO 99/07733, WO 99/07734, WO 99/38888, WO 99/50230, WO 99/64442, WO 00/09543, WO 00/59929, WO 02/48116, WO 02/48172, WO 2008/057208 and WO 2008/057209, in British Patent No. GB 2 337 262, and in U.S. Patent Nos. 6,323,180 and 7,470,664.

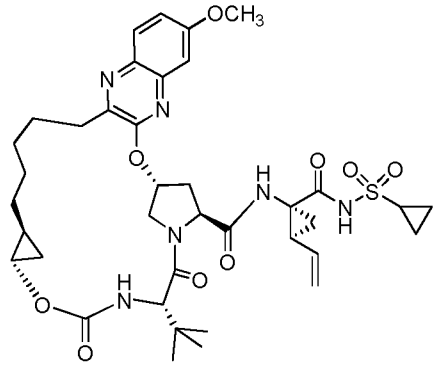
Further examples of HCV protease inhibitors useful in the present compositions and methods include, but are not limited to, the following compounds:

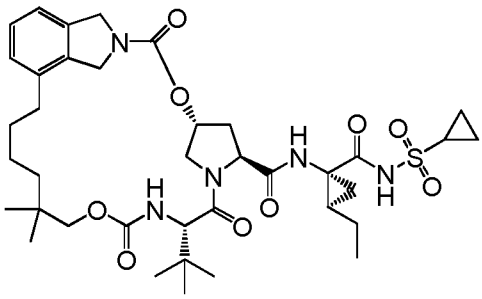


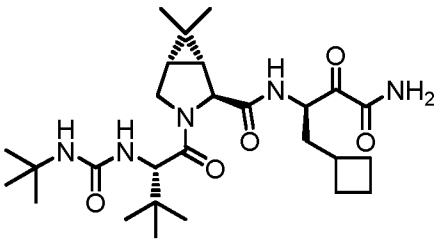


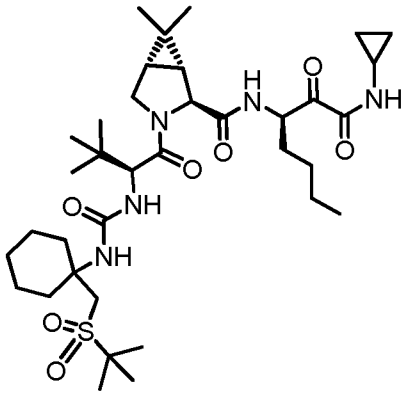












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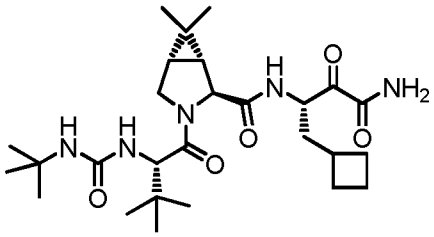
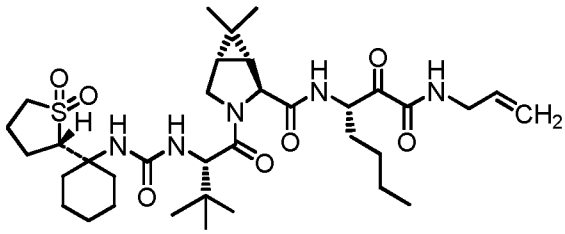
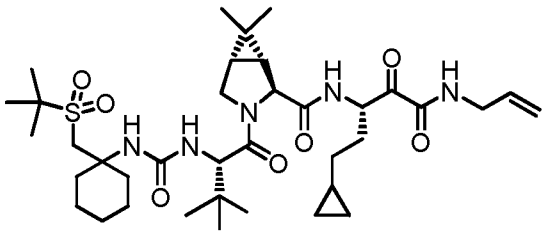
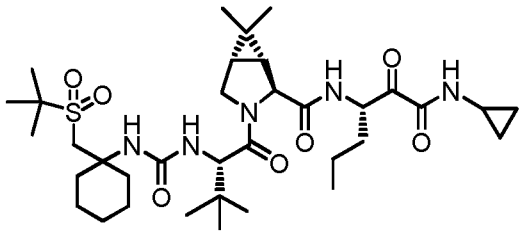
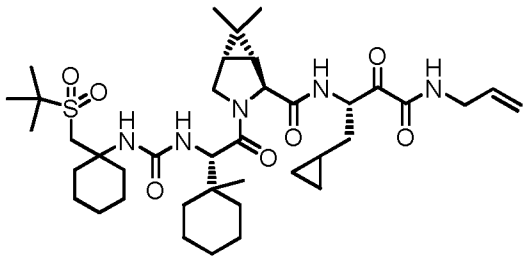
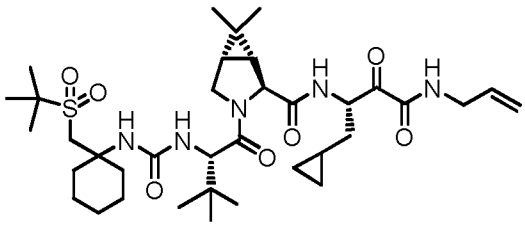


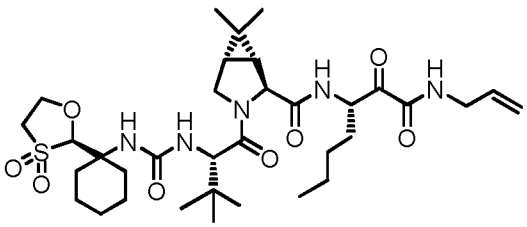


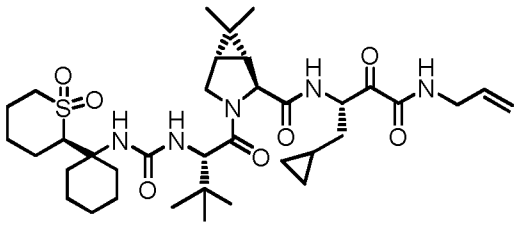


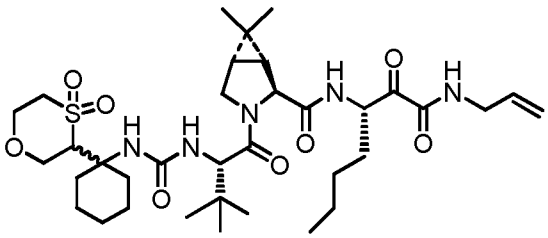


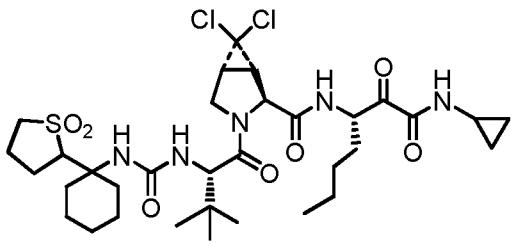


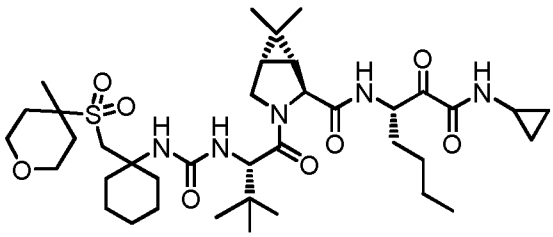


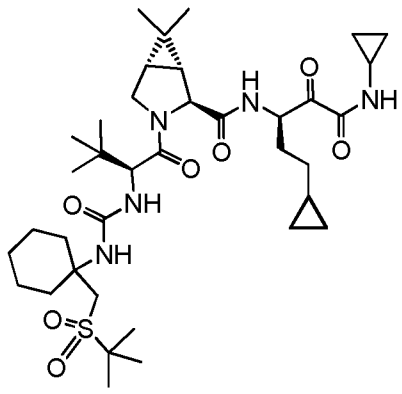


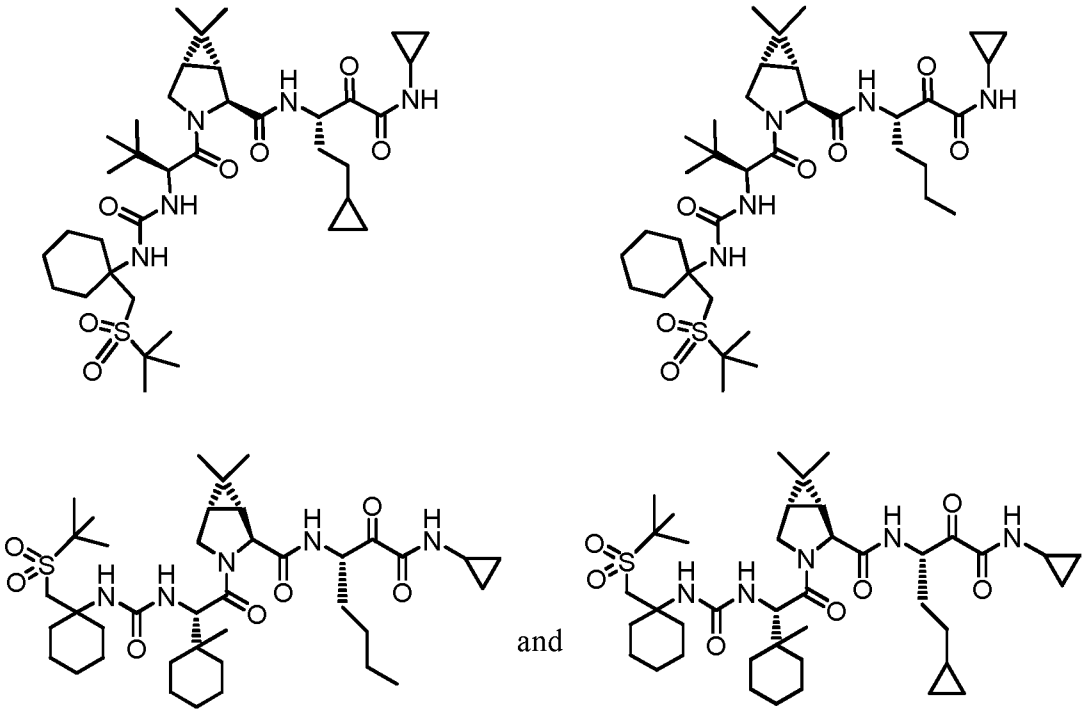












and pharmaceutically acceptable salts thereof.

The compounds of the present invention may also be combined for the treatment of HCV infection with nucleosides having anti-HCV properties, such as those disclosed in International Patent Application Publications WO 02/51425, WO 01/79246, WO 02/32920, WO 02/48165 and WO 2005/003147 (including R1656, (2'*R*)-2'-deoxy-2'-fluoro-2'-*C*-methylcytidine, shown as compounds 3-6 on page 77); WO 01/68663; WO 99/43691; WO 02/18404 and WO 2006/021341, and U.S. Patent Application Publication US 2005/0038240, including 4'-azido nucleosides such as R1626, 4'-azidocytidine; U.S. Patent Application Publications US 2002/0019363, US 2003/0236216, US 2004/0006007, US 2004/0063658 and US 2004/0110717; U.S. Patent Nos. 7,105,499, 7,125,855, 7,202,224; and International Patent Application Publications WO 02/100415, WO 03/026589, WO 03/026675, WO 03/093290, WO 04/011478, WO 04/013300 and WO 04/028481; the content of each is incorporated herein by reference in its entirety.

For the treatment of HCV infection, the compounds of the present invention may also be administered in combination with an agent that is an inhibitor of HCV NS5B polymerase. Such HCV NS5B polymerase inhibitors that may be used as combination therapy include, but are not limited to, those disclosed in International Patent Application Publications WO 02/057287, WO 02/057425, WO 03/068244, WO 2004/000858, WO 04/003138 and WO 2004/007512; U.S. Patent Nos. 6,777,392, 7,105,499, 7,125,855, 7,202,224 and U.S. Patent

Application Publications US 2004/0067901 and US 2004/0110717; the content of each is incorporated herein by reference in its entirety.

In one embodiment, additional nucleoside HCV NS5B polymerase inhibitors that are used in combination with the present HCV NS5B inhibitors are selected from the following compounds: 4-amino-7-(2-C-methyl-β-D-arabinofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine; 4-amino-7-(2-C-methyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine; 4-methylamino-7-(2-C-methyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine; 4-dimethylamino-7-(2-C-methyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine; 4-cyclopropylamino-7-(2-C-methyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine; 4-amino-7-(2-C-vinyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine; 4-amino-7-(2-C-hydroxymethyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine; 4-amino-7-(2-C-fluoromethyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine; 4-amino-5-methyl-7-(2-C-methyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine; 4-amino-7-(2-C-methyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine-5-carboxylic acid; 4-amino-5-bromo-7-(2-C-methyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine; 4-amino-5-chloro-7-(2-C-methyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine; 4-amino-5-fluoro-7-(2-C-methyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine; 2,4-diamino-7-(2-C-methyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine; 2-amino-7-(2-C-methyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine; 2-amino-4-cyclopropylamino-7-(2-C-methyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine; 2-amino-7-(2-C-methyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidin-4(3*H*)-one; 4-amino-7-(2-C-ethyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine; 4-amino-7-(2-C,2-O-dimethyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine; 7-(2-C-methyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidin-4(3*H*)-one; 2-amino-5-methyl-7-(2-C, 2-O-dimethyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidin-4(3*H*)-one; 4-amino-7-(3-deoxy-2-C-methyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine; 4-amino-7-(3-deoxy-2-C-methyl-β-D-arabinofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine; 4-amino-2-fluoro-7-(2-C-methyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine; 4-amino-7-(3-C-methyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine; 4-amino-7-(3-C-methyl-β-D-xylofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine; 4-amino-7-(2,4-di-C-methyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine; 4-amino-7-(3-deoxy-3-fluoro-2-C-methyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine; and the corresponding 5'-triphosphates; or a pharmaceutically acceptable salt thereof.

The compounds of the present invention may also be combined for the treatment of HCV infection with non-nucleoside inhibitors of HCV polymerase such as those disclosed in U.S. Patent Applciation Publications US 2006/0100262 and US 2009/0048239; International Patent Application Publications WO 01/77091, WO 01/47883, WO 02/04425, WO 02/06246, WO 02/20497, WO 2005/016927 (in particular JTK003), WO 2004/041201, WO 2006/066079, WO 2006/066080, WO 2008/075103, WO 2009/010783 and WO 2009/010785; the content of each is incorporated herein by reference in its entirety.

In one embodiment, additional non-nucleoside HCV NS5B polymerase inhibitors that are used in combination with the present HCV NS5B inhibitors are selected from the following compounds: 14-cyclohexyl-6-[2-(dimethylamino)ethyl]-7-oxo-5,6,7,8-tetrahydroindolo[2,1-*a*][2,5]benzodiazocine-11-carboxylic acid; 14-cyclohexyl-6-(2-morpholin-4-ylethyl)-5,6,7,8-tetrahydroindolo[2,1-*a*][2,5]benzodiazocine-11-carboxylic acid; 14-cyclohexyl-6-[2-(dimethylamino)ethyl]-3-methoxy-5,6,7,8-tetrahydroindolo[2,1-*a*][2,5]benzodiazocine-11-carboxylic acid; 14-cyclohexyl-3-methoxy-6-methyl-5,6,7,8-tetrahydroindolo[2,1-*a*][2,5]benzodiazocine-11-carboxylic acid; methyl ({[(14-cyclohexyl-3-methoxy-6-methyl-5,6,7,8-tetrahydroindolo[2,1-*a*][2,5]benzodiazocin-11-yl)carbonyl]amino}sulfonyl)acetate; ({[(14-cyclohexyl-3-methoxy-6-methyl-5,6,7,8-tetrahydroindolo[2,1-*a*][2,5]benzodiazocin-11-yl)carbonyl]amino}sulfonyl)acetic acid; 14-cyclohexyl-*N*-[(dimethylamino)sulfonyl]-3-methoxy-6-methyl-5,6,7,8-tetrahydroindolo[2,1-*a*][2,5]benzodiazocine-11-carboxamide; 3-chloro-14-cyclohexyl-6-[2-(dimethylamino)ethyl]-7-oxo-5,6,7,8-tetrahydroindolo[2,1-*a*][2,5]benzodiazocine 11-carboxylic acid; *N*'-(11-carboxy-14-cyclohexyl-7,8-dihydro-6*H*-indolo[1,2-*e*][1,5]benzoxazocin-7-yl)-*N*,*N*-dimethylethane-1,2-diaminium bis(trifluoroacetate); 14-cyclohexyl-7,8-dihydro-6*H*-indolo[1,2-*e*][1,5]benzoxazocine-11-carboxylic acid; 14-cyclohexyl-6-methyl-7-oxo-5,6,7,8-tetrahydroindolo[2,1-*a*][2,5]benzodiazocine-11-carboxylic acid; 14-cyclohexyl-3-methoxy-6-methyl-7-oxo-5,6,7,8-tetrahydroindolo[2,1-*a*][2,5]benzodiazocine-11-carboxylic acid; 14-cyclohexyl-6-[2-(dimethylamino)ethyl]-3-methoxy-7-oxo-5,6,7,8-tetrahydroindolo[2,1-*a*][2,5]benzodiazocine-11-carboxylic acid; 14-cyclohexyl-6-[3-(dimethylamino)propyl]-7-oxo-5,6,7,8-tetrahydroindolo[2,1-*a*][2,5]benzodiazocine-11-carboxylic acid; 14-cyclohexyl-7-oxo-6-(2-piperidin-1-ylethyl)-5,6,7,8-tetrahydroindolo[2,1-*a*][2,5]benzodiazocine-11-carboxylic acid; 14-cyclohexyl-6-(2-morpholin-4-ylethyl)-7-oxo-5,6,7,8-tetrahydroindolo[2,1-*a*][2,5]benzodiazocine-11-carboxylic acid; 14-cyclohexyl-6-[2-(diethylamino)ethyl]-7-oxo-5,6,7,8-tetrahydroindolo[2,1-*a*][2,5]benzodiazocine-11-carboxylic acid; 14-cyclohexyl-6-(1-methylpiperidin-4-yl)-7-oxo-

5,6,7,8-tetrahydroindolo[2,1-*a*][2,5]benzodiazocine-11-carboxylic acid; 14-cyclohexyl-*N*-[(dimethylamino)sulfonyl]-7-oxo-6-(2-piperidin-1-ylethyl)-5,6,7,8-tetrahydroindolo[2,1-*a*][2,5]benzodiazocine-11-carboxamide; 14-cyclohexyl-6-[2-(dimethylamino)ethyl]-*N*-[(dimethylamino)sulfonyl]-7-oxo-5,6,7,8-tetrahydroindolo[2,1-*a*][2,5]benzodiazocine-11-carboxamide; 14-cyclopentyl-6-[2-(dimethylamino)ethyl]-7-oxo-5,6,7,8-tetrahydroindolo[2,1-*a*][2,5]benzodiazocine-11-carboxylic acid; 14-cyclohexyl-5,6,7,8-tetrahydroindolo[2,1-*a*][2,5]benzodiazocine-11-carboxylic acid; 6-allyl-14-cyclohexyl-3-methoxy-5,6,7,8-tetrahydroindolo[2,1-*a*][2,5]benzodiazocine-11-carboxylic acid; 14-cyclopentyl-6-[2-(dimethylamino)ethyl]-5,6,7,8-tetrahydroindolo[2,1-*a*][2,5]benzodiazocine-11-carboxylic acid; 14-cyclohexyl-6-[2-(dimethylamino)ethyl]-5,6,7,8-tetrahydroindolo[2,1-*a*][2,5]benzodiazocine-11-carboxylic acid; 13-cyclohexyl-5-methyl-4,5,6,7-tetrahydrofuro[3',2':6,7][1,4]diazocino[1,8-*a*]indole-10-carboxylic acid; 15-cyclohexyl-6-[2-(dimethylamino)ethyl]-7-oxo-6,7,8,9-tetrahydro-5*H*-indolo[2,1-*a*][2,6]benzodiazonine-12-carboxylic acid; 15-cyclohexyl-8-oxo-6,7,8,9-tetrahydro-5*H*-indolo[2,1-*a*][2,5]benzodiazonine-12-carboxylic acid; 13-cyclohexyl-6-oxo-6,7-dihydro-5*H*-indolo[1,2-*d*][1,4]benzodiazepine-10-carboxylic acid; and pharmaceutically acceptable salts thereof.

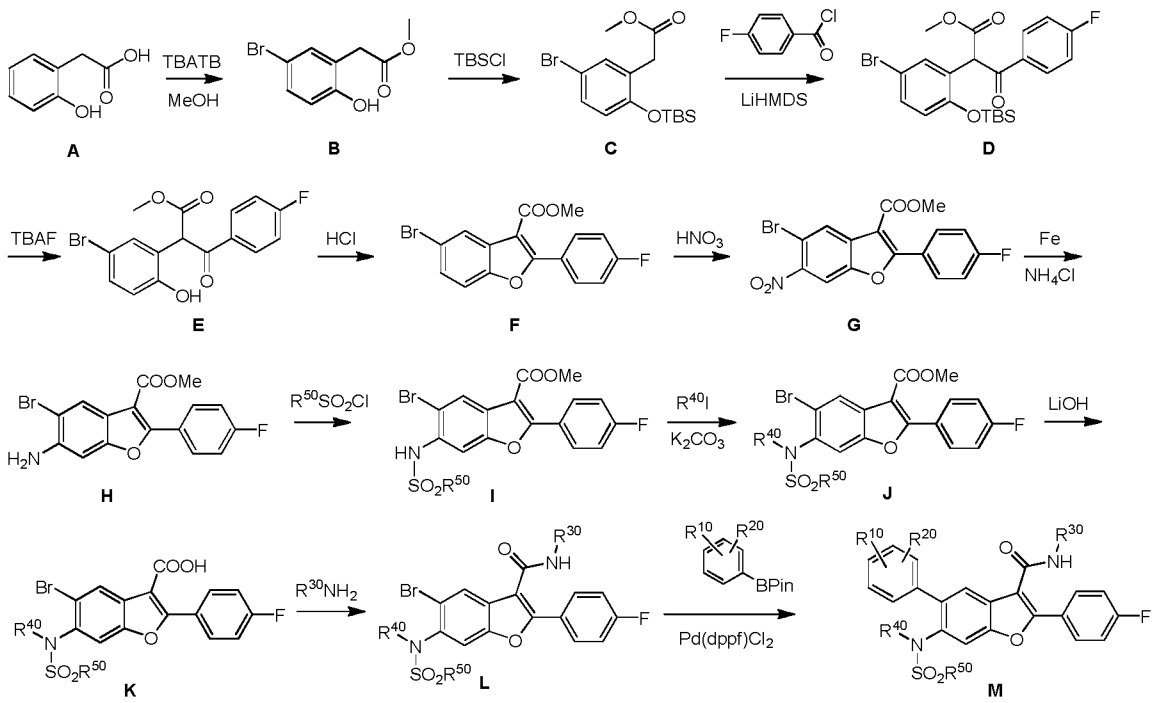
In another embodiment, the present HCV NS5B polymerase inhibitors are used in combination with non-nucleoside HCV NS5A inhibitors and pharmaceutically acceptable salts thereof.

The HCV NS5B inhibitory activity of the present compounds may be tested using assays known in the art. The HCV NS5B polymerase inhibitors described herein have activities in a genotype 1b replicon assay as described in the Examples. The assay is performed by incubating a replicon harboring cell-line in the presence of inhibitor for a set period of time and measuring the effect of the inhibitor on HCV replicon replication either directly by quantifying replicon RNA level, or indirectly by measuring enzymatic activity of a co-encoded reporter enzyme such as luciferase or β-lactamase. By performing a series of such measurements at different inhibitor concentrations, the effective inhibitory concentration of the inhibitor (EC_{50} or EC_{90}) is determined. *See* Jan M. Vrolijk *et al.*, *A replicons-based bioassay for the measurement of interferons in patients with chronic hepatitis C*, 110 J. VIROLOGICAL METHODS 201 (2003). Such assays may also be run in an automated format for high through-put screening. *See* Paul Zuck *et al.*, *A cell-based β-lactamase reporter gene assay for the identification of inhibitors of hepatitis C virus replication*, 334 ANALYTICAL BIOCHEMISTRY 344 (2004).

The present invention also includes processes for making Compounds of Formula (I). The compounds of the present invention can be readily prepared according to the following reaction schemes and examples, or modifications thereof, using readily available starting materials, reagents and conventional synthesis procedures. In these reactions, it is also possible to make use of variants which are themselves known to those of ordinary skill in this art, but are not mentioned in greater detail. Furthermore, other methods for preparing compounds of the invention will be readily apparent to the person of ordinary skill in the art in light of the following reaction schemes and examples. Unless otherwise indicated, all variables are as defined above. The following reaction schemes and examples serve only to illustrate the invention and its practice.

General Schemes

Scheme 1

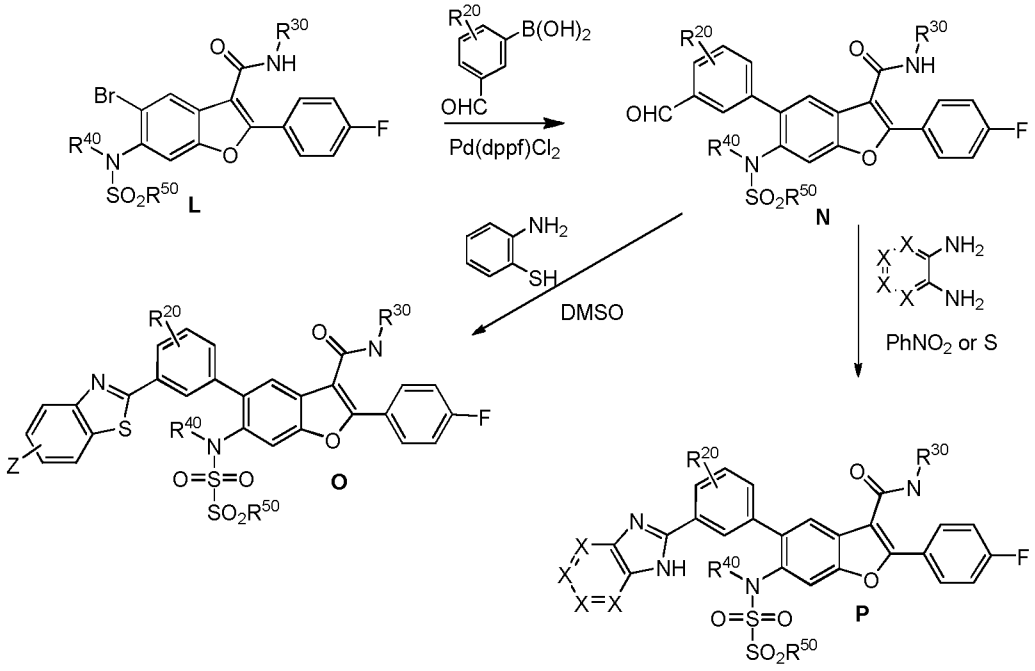


This scheme describes a method useful for making the compounds of formula **M**, which correspond to the Compounds of Formula (I) wherein BPin is pinacoldiborane; R^{60} is para-F; and R^{10}, R^{20}, R^{30}, R^{40} and R^{50} are defined above for the Compounds of Formula (I).

A compound of formula **A** can be brominated, then esterified using TBATB in MeOH to provide compounds of formula **B**. The phenol group of **B** can then be protected as its TBS derivative to provide compounds of formula **C**, which can be acylated using 4-fluorobenzoyl chloride to provide compounds of formula **D**. The phenol hydroxyl group of **D**

can then be deproteced using TBAF, followed by an intramolecular acid-mediated cycliczation to provide compounds of formulas **E** and **F** sequentially. A compound of formula **F** can subsequently be converted to a compound of formula **G** upon treatment with fuming HNO_3. Compounds of formula **H** can be obtained from compounds of formula **G** via reduction of the nitro group in **G**, and the resulting amino group in compouns of formula **H** can then be sulfonylated using a reagent of formula $R^{50}SO_2Cl$ to provide sulfonamide compounds of formula **I**. A compound of formula **I** can then be coupled with $R^{40}I$ in the presence of potassium carbonate to provide compounds of formula **J**, followed by base-catalyzed hydrolysis of the ester group in **J** to provide compounds of formula **K**. The carboxylic acid group of **K** can then be condensed with an amine of formula $R^{30}NH_2$ in the presence of an amide-forming reagent, such as EDCI or HOBT, to provide compounds of formula **L**. Transition-metal mediated coupling of the bromo moiety of **L** with a substituted phenyl boronic ester (alternatively boronic acid, alkyl tin, silicon, or other types of coupling partners may be used) finally provides the target compounds of formula **M**.

Scheme 2

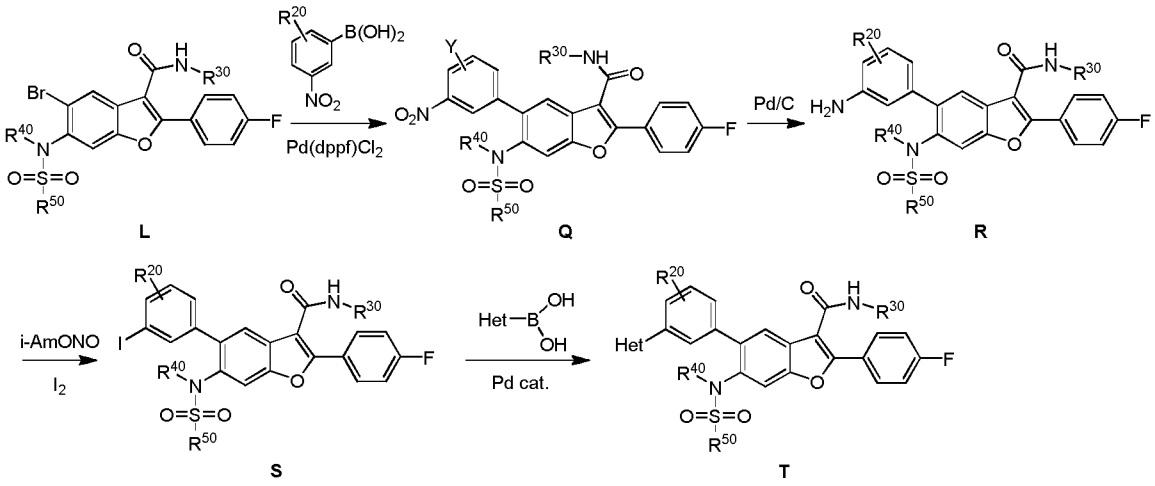


This scheme describes methods useful for making: (a) compounds of formula **O**, which correspond to the Compounds of Formula (I) wherein R^{10} is benzthiazolyl; R^{60} is para-F; and R^{20}, R^{30}, R^{40} and R^{50} are defined above for the Compounds of Formula (I), and (b) compounds of formula **P**, which correspond to the Compounds of Formula (I) wherein R^{10} is

benzimidazole or other bicyclic imidazole derivative; R^{60} is para-F; and R^{20}, R^{30}, R^{40} and R^{50} are defined above for the Compounds of Formula (I).

A compound of formula **L** can be coupled with a substituted or unsubstituted 3-formylphenylboronic acid using a transition metal catalyst, such as $Pd(dppf)Cl_2$, to provide compounds of the formula **N**. Compounds of formula **N** are then cyclized with ortho amino thiophenols or ortho di-amino compounds to provide the target compounds of formulas **O** and **P**, respectively.

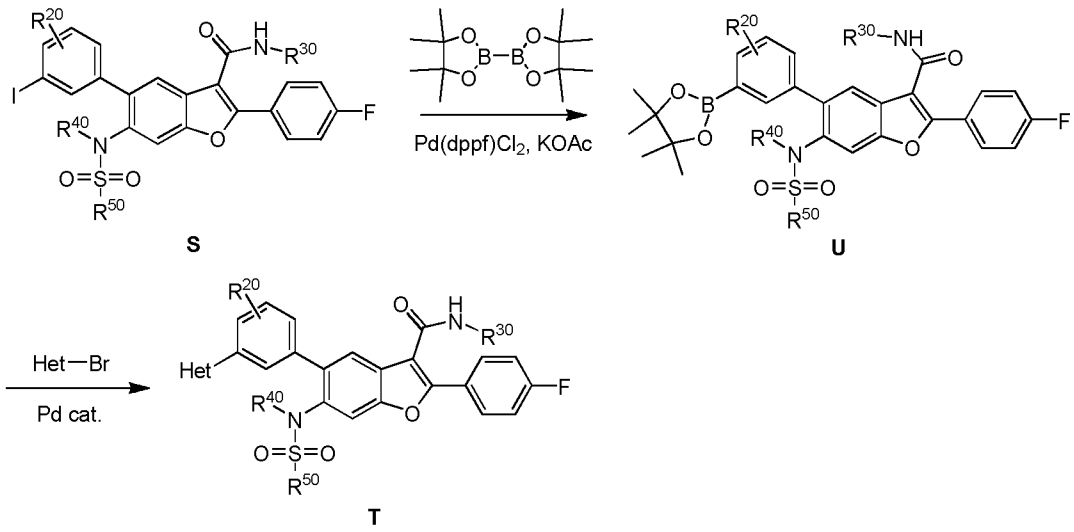
Scheme 3



This scheme describes a method useful for making the compounds of formula **T**, which correspond to the Compounds of Formula (I) wherein Het is a heterocyclyl or heteroaryl group; R^{60} is para-F; and R^{20}, R^{30}, R^{40} and R^{50} are defined above for the Compounds of Formula (I).

A compound of formula **L** can be coupled with a substituted or unsubstituted 3-nitrophenylboronic acid catalyzed by a transition metal, in this case $Pd(dppf)Cl_2$, to provide the compounds of formula **Q**. Compounds of formula **Q** can then be hydrogenated to provide the amino compounds of formula **R**, which are reacted with i-AmONO / I_2, to provide the iodo compounds of formula **S**. Transition metal mediated coupling of **S** with a heterocyclic boronic acid (alternatively boronic ester, alkyl tin, silicon, or other types of coupling partners may be used) provides the target compounds of formula **T**.

Scheme 4

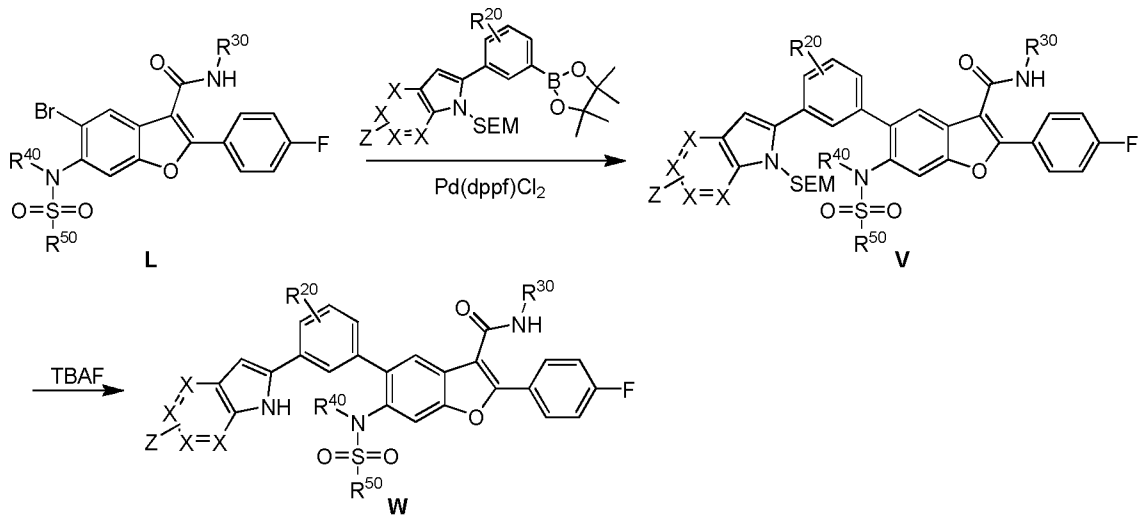


S U T

This scheme describes an alternate useful for making the compounds of formula **T**, which correspond to the Compounds of Formula (I) wherein Het is a heterocyclyl or heteroaryl group; R^{60} is para-F; and R^{20}, R^{30}, R^{40} and R^{50} are defined above for the Compounds of Formula (I).

An iodo compound of formuls **S** can be converted to boronic ester compounds of formula **U** in the presence of $Pd(dppf)Cl_2$. A compound of formula **U** can then be coupled with and aryl bromide or heterocyclic bromide to provide the compounds of formula **T**.

Scheme 5

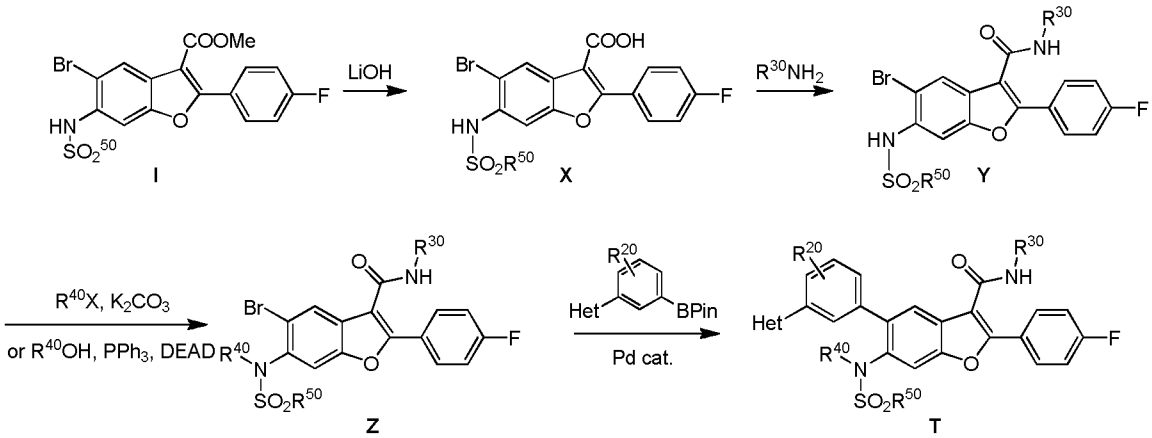


L V W

This scheme describes a method useful for making the the compounds of formula **W**, which correspond to the Compounds of Formula (I) wherein R^{10} is indole or other bicyclic pyrrole derivative; R^{60} is para-F; and R^{20}, R^{30}, R^{40} and R^{50} are defined above for the Compounds of Formula (I).

A transition metal-mediated coupling of a compound of a bromo compound of formula **L** with a heterocycle substituted phenyl boronic ester (alternatively boronic acid, alkyl tin, silicon, or other types of coupling partners may be used) provides the compounds of formula **V**. The SEM protecting group of a compound of formula **V** can subsequently be deproteted using TBAF to provide the compounds of formula **W**.

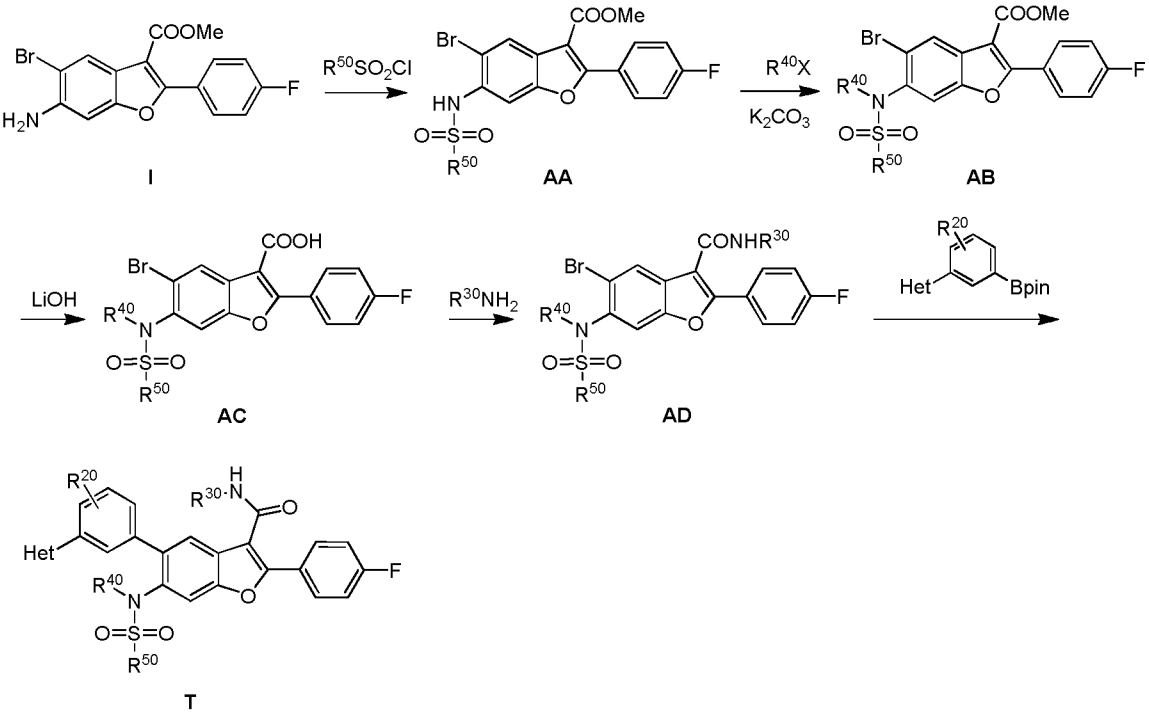
Scheme 6



This scheme describes an alternate method useful for making the compounds of formula **T**, which correspond to the Compounds of Formula (I) wherein Het is a heterocyclyl or heteroaryl group; R^{60} is para-F; and R^{20}, R^{30}, R^{40} and R^{50} are defined above for the Compounds of Formula (I).

The ester group of a compound of formula **I** can be hydrolyzed using aqueous base to provide a compound of formula **X**. The carboxylic acid moiety of **X** can then be condensed with an amine of formula $R^{30}NH_2$ using common amide forming reagents, such as EDCI and HOBT, to provide the compounds of formula **Y**. The sulfonamide group of **Y** can then be coupled with a reagent of formula $R^{40}X$ in the presence of potassium carbonate or with a regent of formula $R^{40}OH$ in the presence of PPh_3 and DEAD to provide compounds of fomrula **Z**. Transition metal mediated coupling of a compound of formula **Z** with a heterocycle-substituted phenyl boronic ester (alternatively boronic acid, alkyl tin, silicon, or other types of coupling partners may be used) provides the compounds of formula **T**.

Scheme 7



This scheme describes yet another alternate method useful for making the compounds of formula **T**, which correspond to the Compounds of Formula (I) wherein Het is a heterocyclyl or heteroaryl group; R^{60} is para-F; and R^{20}, R^{30}, R^{40} and R^{50} are defined above for the Compounds of Formula (I).

The amino group of a compound of formula **I** can be sulfonylated using a reagent of formula $R^{50}SO_2Cl$ to provide the sulfonamide compounds of formula **AA**. A compound of formula **AA** can then be coupled with a reactant of formula $R^{40}X$ in the presence of potassium carbonate to provide the compounds of formula **AB**. The ester moiety of the compounds of formula **AB** can be readily hydrolyzed using aqueous base to provide the compounds of formula **AC**. The carboxylic acid group of **AC** is then condensed with an amine of formula $R^{30}NH_2$ using common amide forming reagents, such as EDCI and HOBT, to provide the compounds of formula to **AD**. Transition metal mediated coupling of a compound of formula **AD** with a heterocycle-substituted phenyl boronic ester (alternatively boronic acid, alkyl tin, silicon, or other types of coupling partners may be used) provides the compounds of formula **T**.

List of Abbreviations

AcOH	Acetic acid
i-AmONO	*iso*-Amylnitrite
n-BuLi	*n*-butyllithium

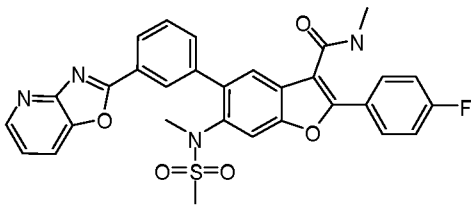
Bu_3N	Tributylamine
$CDCl_3$	Deuterated chloroform
Cs_2CO_3	Cesium carbonate
DCM	Dichloromethane
DEAD	Diethylazodicarboxylate
DMF	Dimethylformamide
DMSO	Dimethylsulfoxide
EDCI	N-(3-Dimethylaminopropyl)-N'-ethylcarbodiimide (also EDC)
Et_3N	Triethylamine
EtOAc	Ethyl acetate
EtOH	Ethanol
EtOOCCl, ClCOOEt	Ethyl chloroformate
HOBT	1-Hydroxy benzotriazole
^{1}H-NMR	Proton Nuclear Magnetic Resonance
HPLC	High Performance Liquid Chromatography
KOAc	Potassium acetate
K_3PO_4	Potassium Phosphate
LDA	Lithium diisopropylamide
LiHMDS	Lithium bis(trimethylsilyl) amide
$LiOH{\cdot}H_2O$	Lithium hydroxide monohydrate
$MeNH_2$	Methanamine
MeCN	Acetonitrile
MeOD	Deuterated methanol
MeOH	Methanol
$MeONH_2$	Methoxyamine
MS	Mass spectroscopy
Ms	Methanesulfonyl (mesyl)
MsCl	Methanesulfonyl chloride
NBS	*N*-Bromosuccinimide
NCS	*N*-Chlorosuccinimide
PE	Petroleum ether
PPh_3	Triphenylphosphine

Pd-C, Pd/C	Palladium on carbon
$Pd(dppf)Cl_2$	1,1'-bis(diphenylphosphino)ferrocene-palladium(II)dichloride
$Pd(PPh_3)_2Cl_2$	1,1'-bis(tetrakis(triphenylphosphine))palladium(II)dichloride
$Pd(PPh_3)_4$	Tetrakis(triphenylphospine)palladium(0)
Ph	Phenyl
$PhB(OH)_2$	Phenylboronic acid
$PhNO_2$	Nitrobenzene
$PhSO_2Cl$	Benzenesulfonyl chloride
i-$PrNH_2$	Diisopropylamine
Py	Pyridine
RT	Room temperature, approximately 25°C
SEM	2-(Trimethylsilyl)ethoxymethyl
TBAF	Tetrabutyl ammonium fluoride
TBATB	Tetrabutylammonium tribromide
TBS	Tert-butyldimethylsilyl
TBSCl	Tert-butyldimethylsilylchloride
Tf	Trifluoromethanesulfonate (triflate)
THF	Tetrahydrofuran
TLC	Thin layer chromatography

EXAMPLES

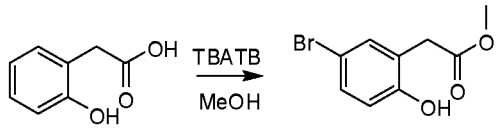
Example 1

Preparation of Compound **1**



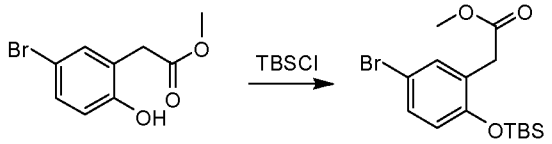
1

Step 1 - Synthesis of Methyl 2-(5-bromo-2-hydroxyphenyl)acetate



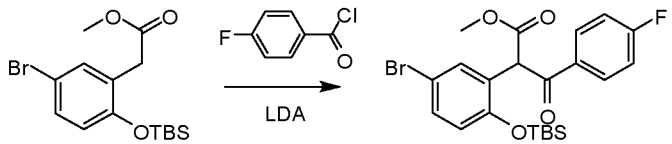
2-(2-hydroxyphenyl)acetic acid (484 g, 3.18 mol) was dissolved in methanol, and then tetrabutylammonium tribromide (1549 g, 3.18 mol) was added to the solution. The resulting mixture was allowed to stir at room temperature for 18 hours. After evaporation of solvent *in vacuo*, the residue obtained was dissolved in EtOAc. The organic layer was washed with 1 N HCl, water and brine, dried and concentrated, the residue obtained was purified using flash column chromatography on silica gel (eluted with PE / EtOAc = 10 / 1) to give pure methyl 2-(5-bromo-2-hydroxyphenyl)acetate (750 g, 94%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.48 (br s, 1H), 7.20~7.25 (m, 2H), 6.75~6.78 (m, 1H), 3.74 (s, 3H), 3.62 (s, 2H). MS $(M+H)^+$: 245.

Step 2 - Synthesis of Methyl 2-(5-bromo-2-(tert-butyldimethylsilyloxy)phenyl)acetate



To a stirring solution of methyl 2-(5-bromo-2-hydroxyphenyl)acetate (750 g, 3.06 mol) in dichloromethane (4 L) was added imidazole (416 g, 6.1 mol) and TBSCl (692 g, 4.6 mol) at 0 °C. After stirred for about 15 hours at room temperature, the reaction mixture was washed with water, brine and concentrated *in vacuo*, the residue obtained was purified using flash column chromatography on silica gel (eluted with PE / EtOAc = 30 / 1) to furnish pure product of methyl 2-(5-bromo-2-(tertbutyldimethylsilyloxy) phenyl)acetate (880 g, 80%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.23 (d, J = 2.4 Hz, 1H), 7.17 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 6.61 (d, J = 8.4 Hz, 1H), 3.61 (s, 3H), 3.50 (s, 2H), 0.91 (s, 9H), 0.15 (s, 6H). MS $(M+H)^+$: 359.

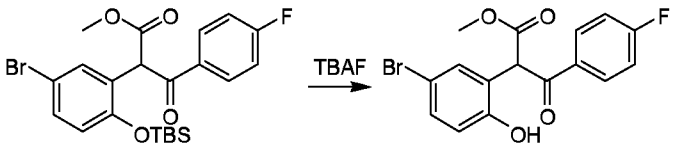
Step 3 - Synthesis of Methyl 2-(5-bromo-2-(tert-butyldimethylsilyloxy)phenyl)-3-(4-fluorophenyl)-3-oxopropanoate



A solution of methyl 2-(5-bromo-2-(tert-butyldimethylsilyloxy)phenyl)acetate (220 g, 0.62 mol) in THF (1.5 L) at -78 °C was treated dropwise with a THF solution of LDA (0.74 mol, freshly prepared from i-Pr_2NH and n-BuLi). After stirred for 1 hour, a solution of 4-

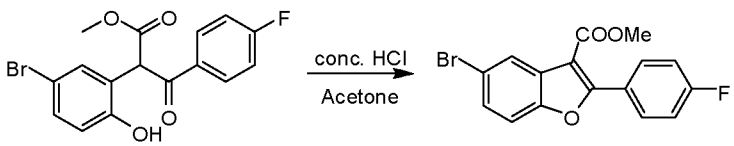
fluorobenzoyl chloride (106 g, 0.68 mol) in THF was added dropwise. The reaction mixture was allowed to stir at -78 °C for 1 hour and at 0 °C for another 1 hours. The mixture was quenched with 1 N HCl, and then THF was removed *in vacuo*, the residue obtained was extracted with EtOAc. The organic layer was concentrated and purified using flash column chromatography on silica gel (eluted with PE / EtOAc = 10 / 1) to providepure product of methyl 2-(5-bromo-2-(tert-butyldimethylsilyloxy)phenyl)-3-(4-fluorophenyl)-3-oxopropanoate (236 g, 80%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.83~7.87 (m, 2H), 7.28 (d, J = 2.4 Hz, 1H), 7.16 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 6.93~6.98 (m, 2H), 6.63 (d, J = 8.4 Hz, 1H), 5.86 (s, 1H), 3.65 (s, 3H), 0.91 (s, 9H), 0.18 (s, 3H), 0.10 (s, 3H). MS $(M+H)^+$: 481.

Step 4 - Synthesis of Methyl 2-(5-bromo-2-hydroxyphenyl)-3-(4-fluorophenyl)-3-oxopropanoate



TBAF (217.5 g, 0.83 mol) was added to a solution of methyl 2-(5-bromo-2-(tert-butyldimethylsilyloxy)phenyl)-3-(4-fluorophenyl)-3-oxopropanoate (267 g, 554.6 mol) in THF (2 L), and the mixture was allowed to stir at 0 °C for 1 hours. The reaction mixture was then concentrated *in vacuo* and the resulting residue was suspended in H_2O and extracted with ethyl acetate. The organic layer was washed with H_2O, brine and concentrated *in vacuo*. The residue obtained was purified using flash column chromatography on silica gel (eluted with PE / EtOAc from 10 / 1 to 5 / 1) to provide methyl 2-(5-bromo-2-hydroxyphenyl)-3-(4-fluorophenyl)-3-oxopropanoate (178.6 g, 88%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.99 (m, 2H), 7.33 (s, 1H), 7.18 (d, J = 8.0 Hz, 1H), 7.07 (m, 2H), 6.68 (d, J = 8.0 Hz, 1H), 5.93 (s, 1H), 3.77 (s, 3H). MS $(M+H)^+$: 367.

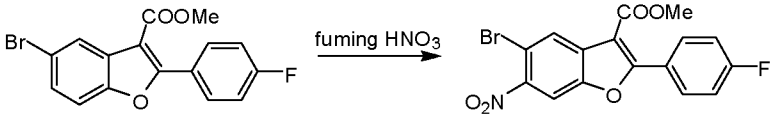
Step 5 - Synthesis of. Methyl 5-bromo-2-(4-fluorophenyl)-1-benzofuran-3-carboxylate



To a solution of methyl 2-(5-bromo-2-hydroxyphenyl)-3-(4-fluorophenyl)-3-oxopropanoate (50 g, 136.1 mmol) in acetone (200 mL) was added concentrated hydrochloric acid and the mixture was heated to reflux for 1 hour. Then the reaction mixture was

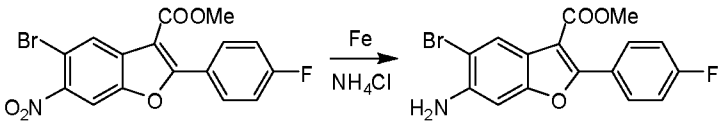
concentrated *in vacuo*, suspended in H_2O and extracted with ethyl acetate. The organic layer was washed with aq. $NaHCO_3$ and brine. Then the organic layer was concentrated to provide the crude product of methyl 5-bromo-2-(4-fluorophenyl)-1-benzofuran-3-carboxylate. It was used for the next step without further purification. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 8.05 (m, 2H), 7.43 (m, 1H), 7.37 (m, 1H), 7.16 (m, 2H), 3.94 (s, 3H). MS $(M+H)^+$: 349.

Step 6 - Synthesis of Methyl 5-bromo-2-(4-fluorophenyl)-6-nitro-1-benzofuran-3-carboxylate



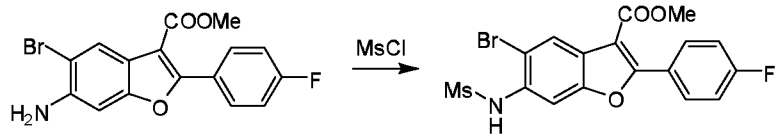
To a solution of methyl 5-bromo-2-(4-fluorophenyl)-1-benzofuran-3-carboxylate (50 g, 143.2 mmol) in $CHCl_3$ (300 mL) at room temperature, was added dropwise fuming HNO_3 (50 mL) and the reaction was allowed to stir for 4 hours. The reaction mixture was poured into ice water and extracted with ethyl acetate. The organic layer was washed with $NaHCO_3$ and brine, then concentrated *in vacuo* to provide methyl 5-bromo-2-(4-fluorophenyl)-6-nitro-1-benzofuran-3-carboxylate, which was used without further purification.

Step 7 - Synthesis of Methyl 6-amino-5-bromo-2-(4-fluorophenyl)-1-benzofuran-3-carboxylate



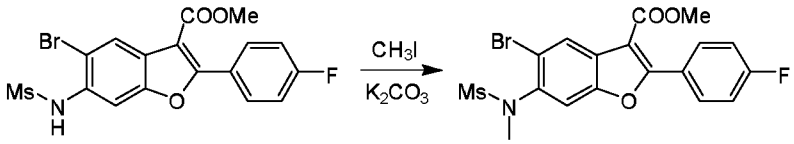
A mixture of methyl 5-bromo-2-(4-fluorophenyl)-6-nitro-1-benzofuran-3-carboxylate (100 g, crude), iron filings (100 g, 1.79 mol) and NH_4Cl (200 g, 3.74 mol) in MeOH / THF / H_2O (8 / 8 / 5, 1 L) was heated to reflux and allowed to stir at this temperature for 3 hours. The reaction mixture was then filtered and concentrated *in vacuo*, the residue obtained was purified using flash column chromatography on silica gel (eluted with PE / EtOAc = 10 / 1 and then with pure dichloromethane) to furnish pure product of methyl 6-amino-5-bromo-2-(4-fluorophenyl)-1-benzofuran-3-carboxylate (41.2 g, 44.5%, 3 steps overall). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.96 (m, 2H), 7.05~7.10 (m, 2H), 6.82 (s, 1H), 4.18 (br s, 2H), 3.86 (s, 3H). MS $(M+H)^+$: 364.

Step 8 - Synthesis of Methyl 5-bromo-2-(4-fluorophenyl)-6-(methylsulfonamido)-1-benzofuran-3-carboxylate



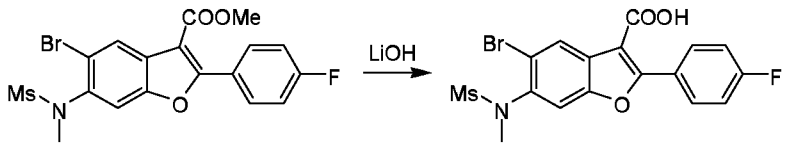
MsCl (25.2 g, 219.7 mmol) was added to a solution of methyl 6-amino-5-bromo-2-(4-fluorophenyl)-1-benzofuran-3-carboxylate (40 g, 109.8 mmol) and pyridine (26.1 g, 329.5 mmol) in dry dichloromethane (300 mL) at 0 °C. After stirred for about 15 hours at room temperature, the mixture was diluted with water, and extracted with dichloromethane. The organic layer was washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue obtained was crystalized from EtOAc to providethe product of methyl 5-bromo-2-(4-fluorophenyl)-6-(methylsulfonamido)-1-benzofuran-3-carboxylate (38.2 g, 78.6%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1H), 7.99~8.03 (m, 2H), 7.83 (s, 1H), 7.11~7.16 (m, 2H), 6.82 (br s, 1H), 3.90 (s, 3H), 2.96 (s, 3H). MS $(M+H)^+$: 442.

Step 9 - Synthesis of Methyl 5-bromo-2-(4-fluorophenyl)-6-(N-methylmethylsulfonamido)-1-benzofuran-3-carboxylate



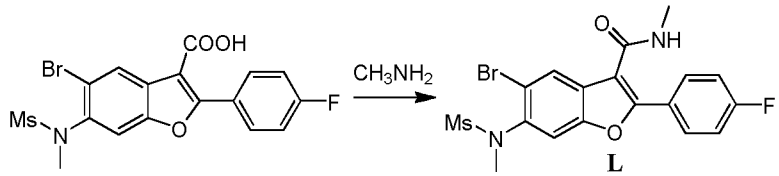
CH_3I (3.53 g, 24.9 mmol) was added to a mixture of methyl 5-bromo-2-(4-fluorophenyl)-6-(methylsulfonamido)-1-benzofuran-3-carboxylate (10 g, 22.61 mmol), K_2CO_3 (6.25 g, 45.2 mmol) and KI (1.88 g, 11.31 mmol) in DMF (100 mL) under N_2 protection. The mixture was allowed to stir at reflux for about 15 hours. After concentrated, H_2O was added and the mixture was extracted with dichloromethane. The combined organic layer was washed with H_2O, brine and concentrated *in vacuo*. The residue obtained was crystalized from EtOAc to provide methyl 5-bromo-2-(4-fluorophenyl)-6-(N-methylmethylsulfonamido)-1-benzofuran-3-carboxylate (9.6 g, 93%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1H), 8.05~8.09 (m, 2H), 7.72 (s, 1H), 7.17~7.22 (m, 2H), 3.96 (s, 3H), 3.35 (s, 3H), 3.10 (s, 3H). MS $(M+H)^+$: 456.

Step 10 – Synthesis of 5-bromo-2-(4-fluorophenyl)-6-(N-methylmethylsulfonamido)-1-benzofuran-3-carboxylic acid



To a solution of methyl 5-bromo-2-(4-fluorophenyl)-6-(N-methylmethylsulfonamido)-1-benzofuran-3-carboxylate (20 g, 43.8 mmol) in dioxane / H_2O (1 / 1, 100 mL) was added $LiOH \cdot H_2O$ (18.39 g, 0.44 mol), and the mixture was heated to reflux for 3 hours, filtered and concentrated *in vacuo*. The residue obtained was dissolved in H_2O, 1 N HCl was added until pH reached 3, and the mixture was extracted with dichloromethane. The organic layer was washed with brine, dried over Na_2SO_4 and filtered. The solvent was removed by concentration to provide the crude product of 5-bromo-2-(4-fluorophenyl)-6-(N-methylmethylsulfonamido)-1-benzofuran-3-carboxylic acid (18.2 g, 93.8%). It was used for the next step without further purification.

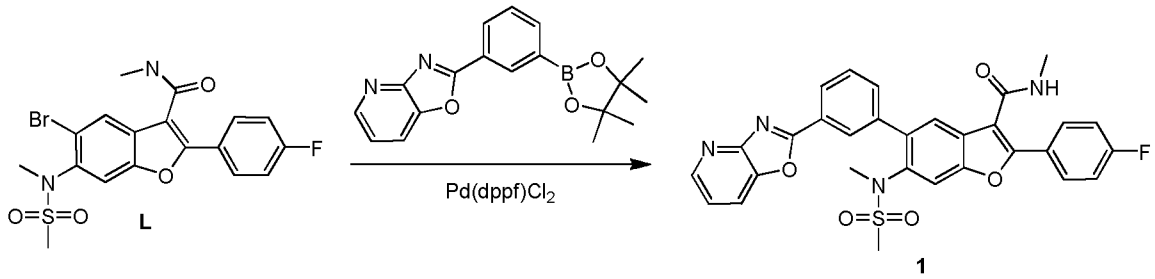
*Step 11 – Synthesis of 5-bromo-2-(4-fluorophenyl)-N-methyl-6-(N-methylmethylsulfonamido)-1-benzofuran-3-carboxamide (Compound **L**)*



L

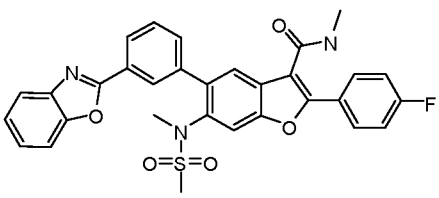
A solution of 5-bromo-2-(4-fluorophenyl)-6-(N-methylmethylsulfonamido)-1-benzofuran-3-carboxylic acid (21 g, 47.5 mmol), HOBT (7.06 g, 52.2 mmol) and EDCI (9 g, 47.5 mmol) in dry DMF (200 mL) was allowed to stir at room temperature. After 30 minutes, Et_3N (16 mL) and CH_3NH_2 (HCl salt, 6.41 g, 95 mmol) was added to the mixture, and the mixture was allowed to stir for about 15 hours. After the solvent was removed, H_2O was added and the mixture was extracted with dichloromethane. The combined organic layer was washed with H_2O, brine and concentrated *in vacuo*. The residue obtained was crystalized from EtOAc to provide compound **L** (19.5 g, 90%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.88~7.92 (m, 2H), 7.70 (s, 1H), 7.18~7.23 (m, 2H), 5.78 (br s, 1H), 3.34 (s, 3H), 3.09 (s, 3H), 3.00 (d, J = 4.8 Hz, 3H). MS $(M+H)^+$: 455.

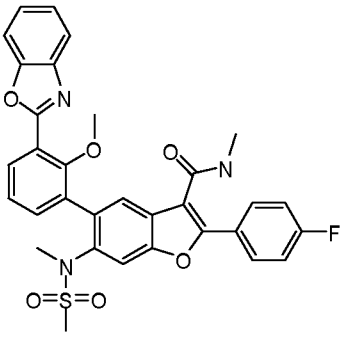
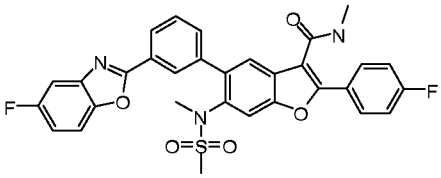
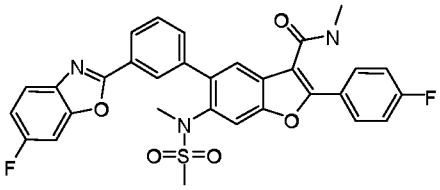
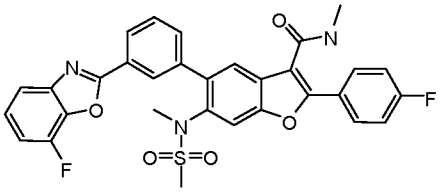
Step 12 - Synthesis of 2-(4-fluorophenyl)-N-methyl-6-(N-methylmethylsulfonamido)-5-(3-(oxazolo[4,5-b]pyridin-2-yl)phenyl)benzofuran-3-carboxamide (Compound 1)

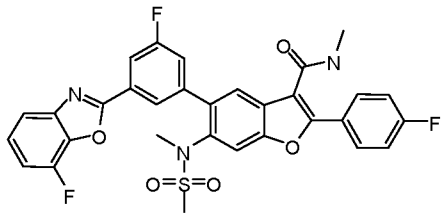
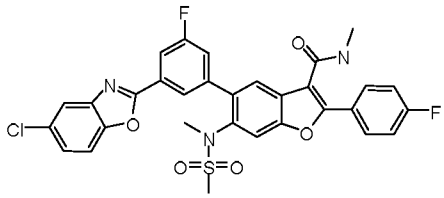
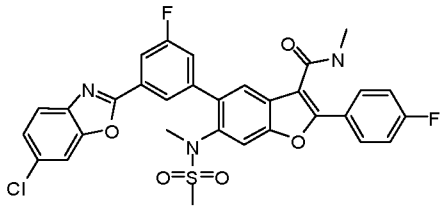
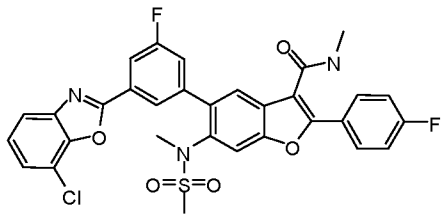


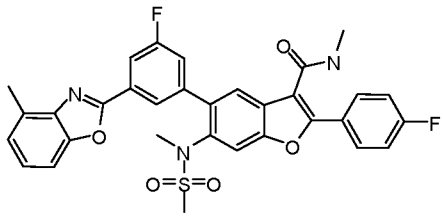
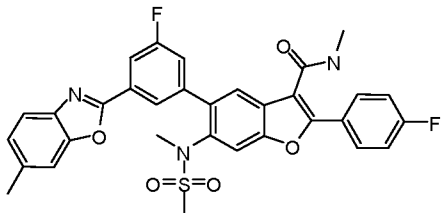
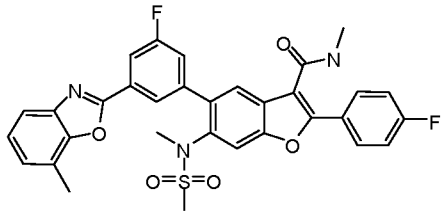
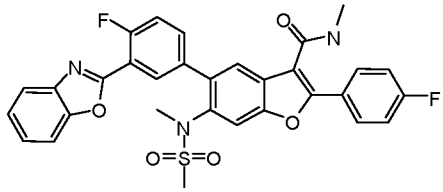
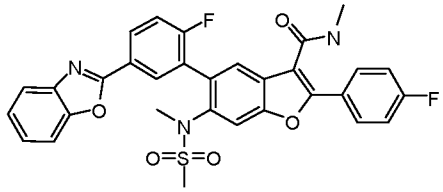
To a degassed solution of 2-[3-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-oxazolo[4,5-b]pyridine (prepared from corresponding bromide, 587 mg, 1.82 mmol) was added a solution of Compound **L** (635 mg, 1.40 mmol) and K_3PO_4 (771 mg, 3.64 mmol) in dry DMF (6 mL). To the resulting solution was added $Pd(dppf)Cl_2$ (30 mg) and the reaction mixture was placed under N_2 atmosphere, heated to 100 °C and allowed to stir at this temperature for 6 hours. After cooled to room temperature and filtered, the filtrate was washed with H_2O, brine, and dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue obtained was purified using column chromatography (PE : EtOAc = 1: 1) to provide Compound **1** (430 mg, 53.9%) as white solid. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.60~8.61 (m, 1H), 8.39 (s, 1H), 8.33 (d, J = 6.8 Hz, 1H), 7.91~7.95 (m, 3H), 7.88 (s, 1H), 7.72 (d, J = 7.6 Hz, 1H), 7.62~7.66 (m, 2H), 7.35~7.38 (m, 1H), 7.20 (d, J = 8.8 Hz, 2H), 5.93~5.94 (m, 1H), 3.18 (s, 3H), 2.99 (d, J = 4.8 Hz, 3H), 2.71 (s, 3H). MS $(M+H)^+$: 571.

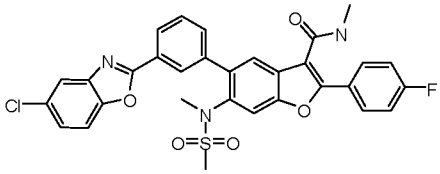
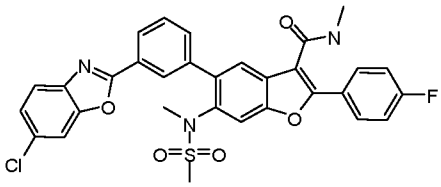
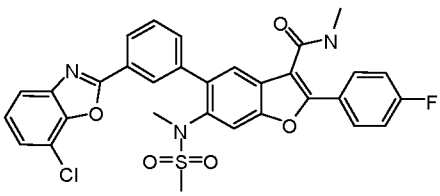
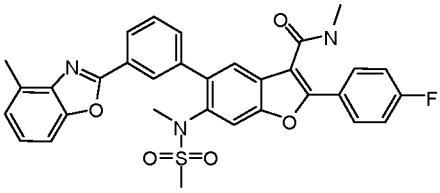
Compounds **2-29**, **31-126**, **199**, **248-250** and **252-256**, depicted in the table below, were prepared using the method described in Example 1 and substituting the appropriate reactants and/or reagents.

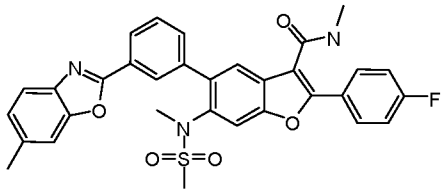
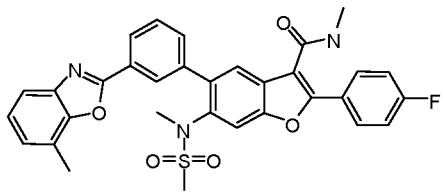
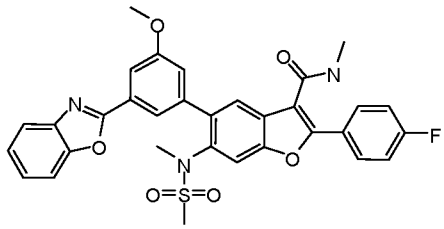
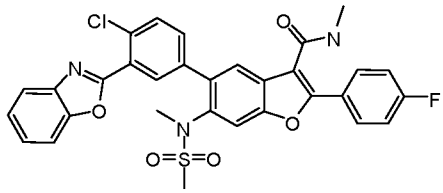
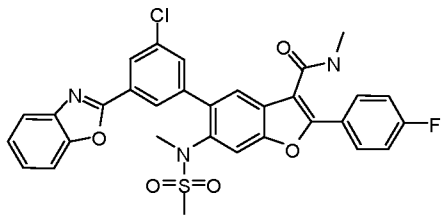
Compound	Structure	NMR	MS $(M+H)^+$
2		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.30~8.36 (m, 2H), 7.98 (s, 2H), 7.90 (s, 1H), 7.80 (s, 1H), 7.62~7.68 (m, 4H), 7.40 (s, 2H), 7.21~7.25 (m, 2H), 5.97 (s, 1H), 3.21 (s, 3H), 3.03 (s, 3H), 2.71 (s, 3H).	**570**

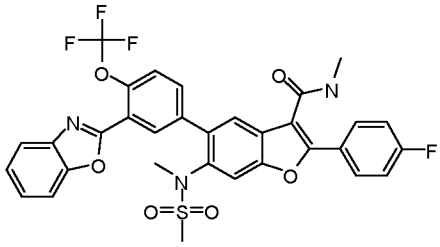
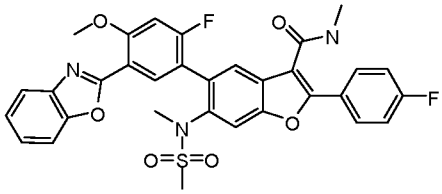
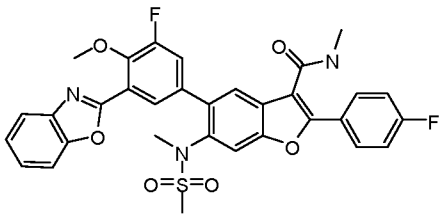
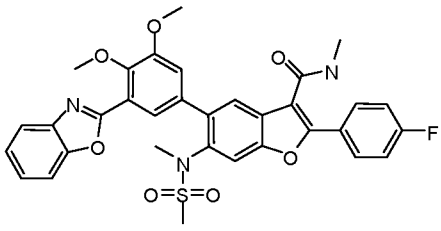
3		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.10 (d, *J* = 8.0 Hz, 1H), 7.79~7.85 (m, 4H), 7.52~7.59 (m, 3H), 7.31~7.37 (m, 3H), 7.16 (t, *J* = 8.8 Hz, 2H), 5.91 (d, *J* = 4.8 Hz, 1H), 3.45 (s, 3H), 3.19 (s, 3H), 2.94 (d, *J* = 4.8 Hz, 3H), 2.42 (s, 3H).	**600**
4		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 7.92~7.95 (m, 2H), 7.87 (s, 1H), 7.59~7.68 (m, 3H), 7.49~7.52 (m, 2H), 7.42~7.45 (m, 2H), 7.20 (t, *J* = 8.8 Hz, 2H), 7.06~7.11 (m, 1H), 5.87 (d, *J* = 4.4 Hz, 1H), 3.17 (s, 3H), 2.97 (d, *J* = 4.8 Hz, 3H), 2.68 (s, 3H).	**588**
5		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.33 (s, 1H), 8.27 (d, *J* = 5.2 Hz, 1H), 7.96~8.00 (m, 2H), 7.91 (s, 1H), 7.65~7.76 (m, 3H), 7.34~7.37 (m, 2H), 7.22~7.27 (m, 2H), 7.13~7.18 (m, 1H), 5.87 (s, 1H), 3.22 (s, 3H), 3.04 (d, *J* = 4.8 Hz, 3H), 2.72 (s, 3H).	**588**
6		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.37 (s, 1H), 8.33 (d, *J* = 7.6 Hz, 1H), 7.96~7.99 (m, 2H), 7.90 (s, 1H), 7.64~7.74 (m, 3H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.31~7.36 (m, 1H), 7.23 (t, *J* = 8.4 Hz, 2H), 7.15 (t, *J* = 9.2 Hz, 1H), 6.03 (d, *J* = 4.4 Hz, 1H), 3.22 (s, 3H), 3.02 (d, *J* = 4.8 Hz, 3H), 2.73 (s, 3H).	**588**

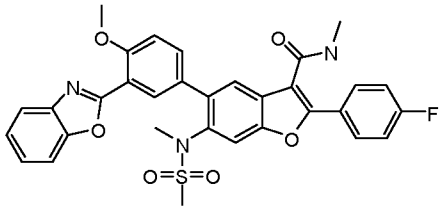
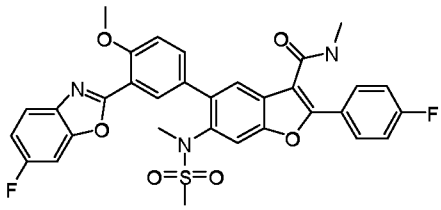
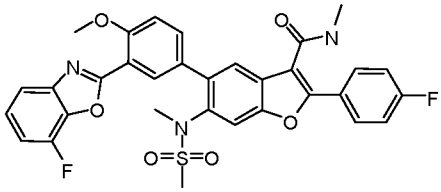
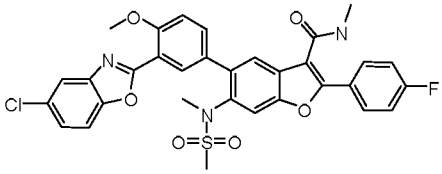
7		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.07 (s, 1H), 7.82~7.93 (m, 4H), 7.58 (s, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.35 (d, *J* = 8.8 Hz, 1H), 7.23~7.28 (m, 1H), 7.14 (t, *J* = 8.8 Hz, 2H), 7.08 (t, *J* = 8.6 Hz, 1H), 5.87 (d, *J* = 4.4 Hz, 1H), 3.14 (s, 3H), 2.93 (d, *J* = 4.8 Hz, 3H), 2.73 (s, 3H).	606
8		**^{1}H-NMR** (DMSO, 400 MHz) δ 8.54 (s, 1H), 8.10~8.11 (d, *J* = 4.0 Hz, 2H), 8.00~8.03 (m, 4H), 7.97~7.98 (d, *J* = 1.6 Hz, 1H), 7.85~7.87 (d, *J* = 8.8 Hz, 1H), 7.72 (s, 1H), 7.60~7.62 (d, *J* = 9.6 Hz, 1H), 7.52~7.53 (d, *J* = 2.0 Hz, 1H), 3.19 (s, 3H), 3.02 (s, 3H), 2.81~2.82 (d, *J* = 4.4 Hz, 3H).	622
9		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.15 (s, 1H), 7.94~7.99 (m, 4H), 7.68~7.73 (m, 2H), 7.64 (d, *J* = 1.6 Hz, 1H), 7.38~7.45 (m, 2H), 7.23~7.27 (m, 2H), 5.88 (d, *J* = 3.6 Hz, 1H), 3.23 (s, 3H), 3.03 (d, *J* = 5.2 Hz, 3H), 2.82 (s, 3H).	622
10		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 7.93 (s, 1H), 7.89~7.91 (m, 1H), 7.87~7.89 (m, 1H), 7.83 (s, 2H), 7.64~7.68 (m, 2H), 7.36~7.39 (m, 2H), 7.25~7.27 (m, 2H), 7.15~7.18 (m, 1H), 5.84~5.86 (m, 1H), 3.15 (s, 3H), 2.94 (d, *J* = 4.8 Hz, 3H), 2.70 (s, 3H).	622

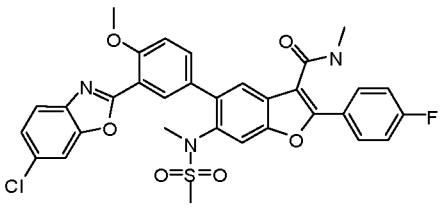
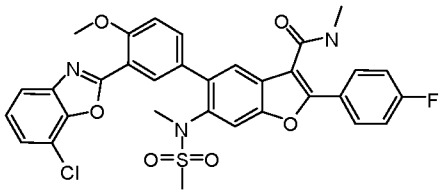
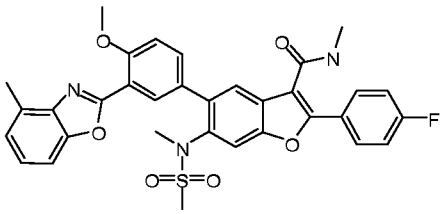
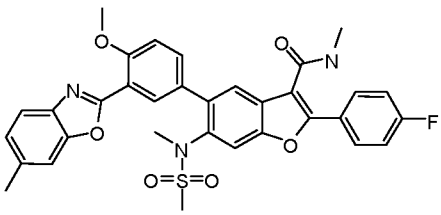
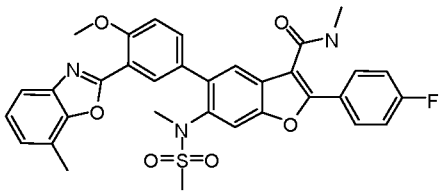
11		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.64 (d, *J* = 4.8 Hz, 1H), 8.18 (d, *J* = 3.2 Hz, 2H), 8.12~8.05 (m, 3H), 7.83 (s, 1H), 7.71 (t, *J* = 22.0 Hz, 2H), 7.53 (t, *J* = 18.0 Hz, 2H), 7.46 (t, *J* = 12.0 Hz, 1H), 3.28 (s, 3H), 3.12 (s, 3H), 2.92 (d, *J* = 4.8 Hz, 3H), 2.69 (s, 3H).	602
12		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.06 (s, 1H), 7.86~7.89 (m, 2H), 7.81 (s, 2H), 7.59~7.62 (m, 2H), 7.13~7.37 (m, 5H), 6.02~6.21 (m, 1H), 3.16 (s, 3H), 2.98 (d, *J* = 4.4 Hz, 3H), 2.76 (s, 3H), 2.49 (s, 3H).	602
13		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.08 (s, 1H), 7.84~7.93 (m, 4H), 7.59 (s, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.31 (d, *J* = 12.0 Hz, 1H), 7.20~7.22 (m, 1H), 7.10~7.17 (m, 3H), 5.81 (d, *J* = 4.0 Hz, 1H), 3.13 (s, 3H), 2.93 (d, *J* = 4.8 Hz, 3H), 2.71 (s, 3H), 2.52 (s, 3H).	602
14		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.73 (s, 1H), 8.45 (d, *J* = 4.8 Hz, 1H), 8.13~8.15 (m, *J* = 7.6 Hz, 1H), 7.19~8.13 (m, 2H), 7.92 (s, 1H), 7.69 (s, 1H), 7.60~7.67 (m, 2H), 7.30~7.47 (m, 2H), 7.21~7.26 (m, 2H), 5.31 (s, 1H), 3.22 (s, 3H), 3.03 (d, *J* = 4.8 Hz, 3H), 2.82 (s, 3H).	588
15		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.21~8.26 (m, 2H), 7.86~7.89 (m, 2H), 7.80 (s, 1H), 7.69 (t, *J* = 4.4 Hz, 1H), 7.60 (s, 1H), 7.50~7.52 (m, 1H), 7.22~7.31 (m, 3H), 7.13 (t, *J* = 8.4 Hz, 2H), 6.01 (d, *J* = 3.6 Hz, 1H), 3.22 (s, 3H), 2.92 (d, *J* = 4.4 Hz, 3H), 2.55 (s, 3H).	588

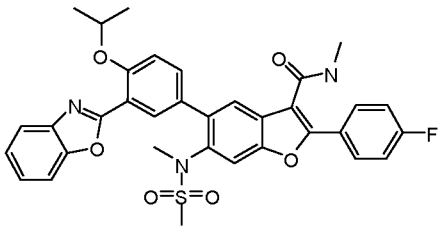
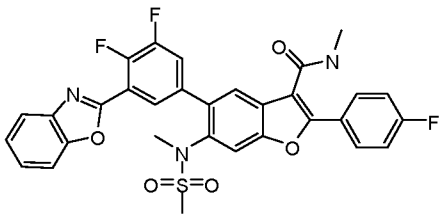
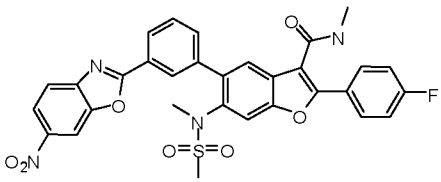
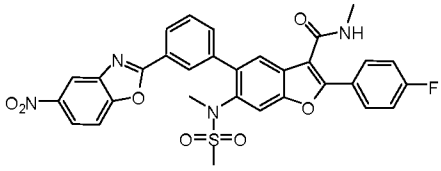
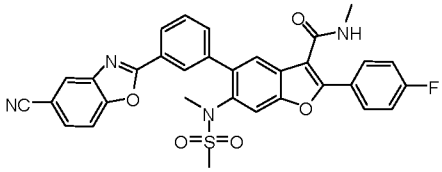
16		**^{1}H-NMR** (DMSO, 400 MHz) δ 8.54~8.55 (d, *J* = 4.4 Hz, 1H), 8.25 (s, 1H), 8.20~8.22 (d, *J* = 6.4 Hz, 1H), 8.06 (s, 1H), 7.99~8.03 (m, 1H), 7.94~7.95 (d, *J* = 1.6 Hz, 1H), 7.84~7.86 (d, *J* = 8.8 Hz, 2H), 7.75 (s, 1H), 7.67~7.73 (m, 1H), 7.49~7.50 (d, *J* = 2.0 Hz, 1H), 7.47~7.48 (d, *J* = 2.0 Hz, 1H), 7.40~7.44 (m, 1H), 3.15 (s, 3H), 2.96, (s, 3H), 2.80~2.81 (d, *J* = 4.4 Hz, 3H).	**604**
17		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.33 (s, 1H), 8.28 (d, *J* = 7.6 Hz, 1H), 7.95~7.98 (m, 2H), 7.90 (s, 1H), 7.71 (d, *J* = 8.0 Hz, 2H), 7.63~7.67 (m, 3H), 7.38 (d, *J* = 8.4 Hz, 1H), 7.21~7.26 (m, 2H), 5.98 (s, 1H), 3.21 (s, 3H), 3.02 (d, *J* = 8.8 Hz, 3H), 2.73 (s, 3H).	**604**
18		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.36~8.39 (m, 2H), 7.97~7.99 (m, 2H), 7.90 (s, 1H), 7.67~7.69 (m, 3H), 7.37~7.39 (m, 1H), 7.29~7.32 (m, 2H), 7.20~7.23 (m, 2H), 5.84 (t, *J* = 7.6 Hz, 1H), 3.15 (s, 3H), 2.94 (d, *J* = 4.8 Hz, 3H), 2.70 (s, 3H).	**604**
19		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.55 (d, *J* = 4.8 Hz, 1H), 8.24 (t, *J* = 12.0 Hz, 2H), 8.05~8.00 (m, 3H), 7.72 (t, *J* = 16.4 Hz, 3H), 7.60 (d, *J* = 8.4 Hz, 1H), 7.44 (t, *J* = 18 Hz, 1H), 7.34 (t, *J* = 16.8 Hz, 1H), 7.24 (d, *J* = 7.6 Hz, 1H), 3.15 (s, 3H), 2.96 (s, 3H), 2.82 (d, *J* = 4.8 Hz, 3H), 2.60 (s, 3H).	**584**

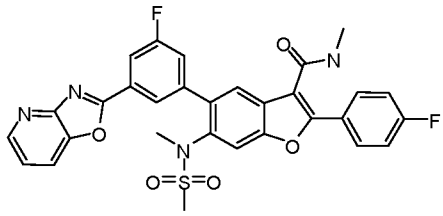
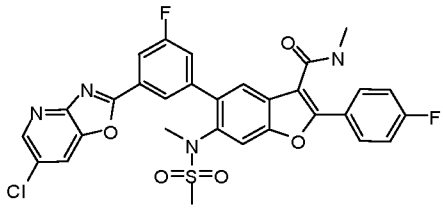
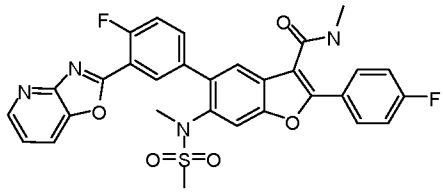
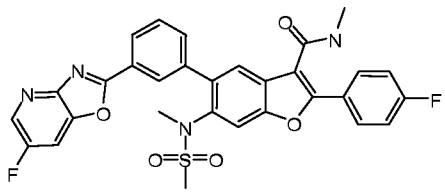
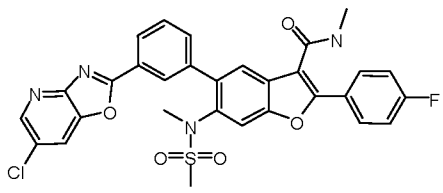
20		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.22 (s, 1H), 8.17 (d, *J* = 7.6 Hz, 1H), 7.85~7.88 (m, 2H), 7.77 (s, 1H), 7.50~7.58 (m, 4H), 7.31 (s, 1H), 7.09~7.14 (m, 3H), 5.97~5.98 (m, 1H), 3.10 (s, 3H), 2.91 (d, *J* = 4.8 Hz, 3H), 2.60 (s, 3H), 2.44 (s, 3H).	**584**
21		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.24~8.22 (m, 2H), 7.90~7.81 (m, 3H), 7.61~7.52 (m, 4H), 7.21~7.09 (m, 4H), 5.90 (d, *J* = 4.4 Hz, 1H), 3.12 (s, 3H), 2.94 (d, *J* = 5.2 Hz, 3H), 2.62 (s, 3H), 2.53 (s, 3H).	**584**
22		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 7.79~7.95 (m, 6H), 7.58~7.61 (m, 2H), 7.36~7.38 (m, 2H), 7.16~7.27 (m, 3H), 6.04~6.05 (m, 1H), 3.95 (s, 3H), 3.14 (s, 3H), 2.98 (d, *J* = 4.4 Hz, 3H), 2.77 (s, 3H).	**600**
23		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.18 (d, *J* = 2.0 Hz, 1H), 7.86~7.90 (m, 2H), 7.82 (s, 1H), 7.78 (d, *J* = 8.8 Hz, 1H), 7.54~7.61 (m, 4H), 7.32~7.35 (m, 2H), 7.15 (t, *J* = 8.4 Hz, 2H), 5.70 (br s, 1H), 3.10 (s, 3H), 2.93 (d, *J* = 5.2 Hz, 3H), 2.76 (s, 3H).	**604**
24		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.21 (s, 1H), 8.18 (s, 1H), 7.87 (t, *J* = 1.4 Hz, 2H), 7.85 (s, 1H), 7.70~7.81 (m, 1H), 7.54~7.58 (m, 2H), 7.52~7.53 (m, 1H), 7.29~7.33 (m, 2H), 7.12~7.18 (m, 2H), 5.84 (s, 1H), 3.12 (s, 3H), 2.93 (d, *J* = 4.8 Hz, 3H), 2.72 (s, 3H).	**604**

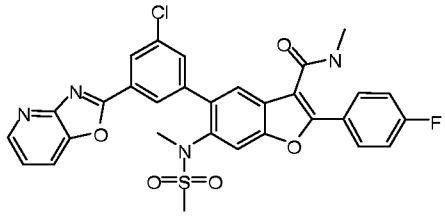
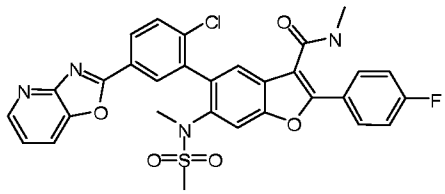
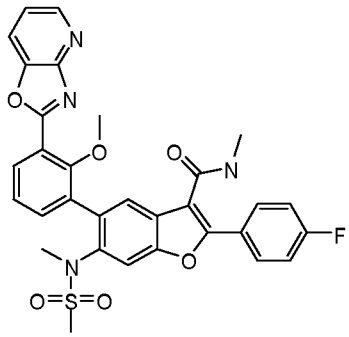
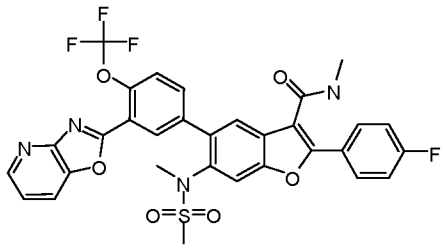
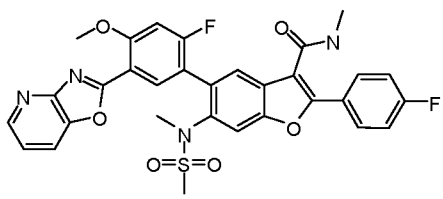
25		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.31 (s, 1H), 8.43 (s, 1H), 7.84~7.92 (m, 4H), 7.71~7.74 (m, 1H), 7.59 (s, 1H), 7.48~7.50 (m, 2H), 7.29~7.31 (m, 1H), 7.14~7.16 (m, 2H), 5.79~5.80 (m, 1H), 3.12 (s, 3H), 2.93~2.94 (m, 3H), 2.72 (s, 3H).	**654**
26		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.21 (d, *J* = 8.0 Hz, 1H), 7.94~7.97 (m, 2H), 7.86 (s, 1H), 7.81 (d, *J* = 4.0 Hz, 1H), 7.69 (s, 1H), 7.55~7.58 (m, 1H), 7.34~7.36 (m, 2H), 7.19~7.13 (m, 2H), 6.90 (d, *J* = 12.0 Hz, 1H), 5.89 (s, 1H), 4.07 (s, 3H), 3.28 (s, 3H), 3.00 (d, *J* = 8.0 Hz, 3H), 2.67 (s, 3H).	**618**
27		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 7.92 (s, 1H), 7.85~7.88 (m, 2H), 7.79 (s, 1H), 7.73~7.75 (m, 1H), 7.53~7.56 (m, 2H), 7.37~7.41 (m, 1H), 7.30~7.33 (m, 2H), 7.11~7.15 (m, 2H), 5.87 (d, *J* = 4.0 Hz, 1H), 4.09 (d, *J* = 1.6 Hz, 3H), 3.12 (s, 3H), 2.94 (d, *J* = 4.8 Hz, 3H), 2.77 (s, 3H).	**618**
28		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 7.89~7.91 (m, 2H), 7.82 (s, 1H), 7.73~7.76 (m, 1H), 7.69 (d, *J* = 2.0 Hz, 1H), 7.54~7.56 (m, 1H), 7.52 (s, 1H), 7.36 (d, *J* = 2.0 Hz, 1H), 7.30~7.33 (m, 2H), 7.12~7.18 (m, 2H), 5.77~5.82 (m, 1H), 4.01 (s, 3H), 3.92 (s, 3H), 3.02 (s, 3H), 2.94 (d, *J* = 4.4 Hz, 3H), 2.87 (s, 3H).	**630**

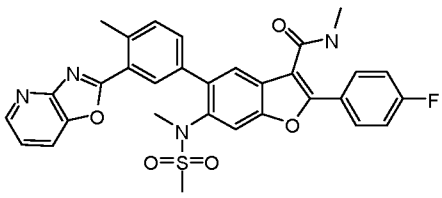
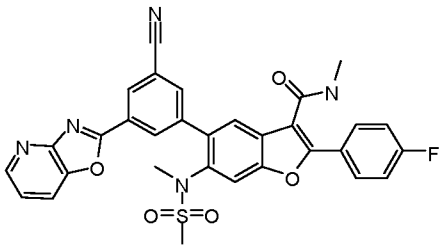
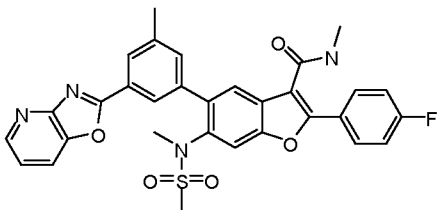
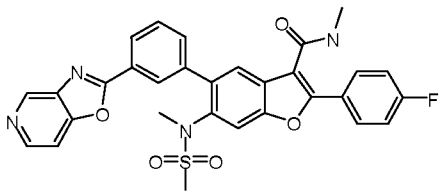
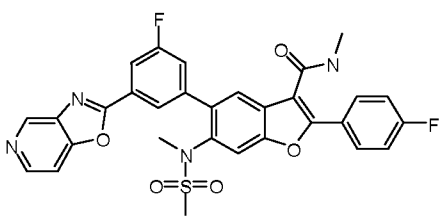
29		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.43 (d, *J* = 4.8 Hz, 1H), 8.12~8.14 (m, 1H), 7.96~8.10 (m, 2H), 7.90 (s, 1H), 7.72 (s, 1H), 7.56~7.66 (m, 2H), 7.36~7.46 (m, 2H), 7.20~7.24 (m, 3H), 5.96 (s, 1H), 3.22 (s, 3H), 3.03 (d, *J* = 4.8 Hz, 3H), 2.82 (s, 3H), 2.73 (s, 3H).	600
31		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.04 (s, 1H), 7.84~7.9 (m, 4H), 7.63~7.66 (m, 1H), 7.59 (s, 1H), 7.32~7.34 (m, 1H), 7.25~7.27 (m, 1H), 7.14~7.16 (m, 2H), 7.04~7.09 (m, 1H), 5.76 (s, 1H), 3.14 (s, 3H), 2.94 (m, 3H), 2.72 (s, 3H), 2.10 (s, 3H).	618
32		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.15 (d, *J* = 2.0 Hz, 1H), 7.87~7.89 (m, 2H), 7.80 (s, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.57 (s, 1H), 7.53 (d, *J* = 7.6 Hz, 1H), 7.19~7.22 (m, 1H), 7.14 (t, *J* = 8.8 Hz, 3H), 7.04 (t, *J* = 8.4 Hz, 1H), 5.81 (s, 1H), 4.03 (s, 3H), 3.11 (s, 3H), 2.93 (d, *J* = 4.4 Hz, 3H), 2.71 (s, 3H).	618
33		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.11 (s, 1H), 7.83~7.87 (m, 2H), 7.77 (s, 1H), 7.69 (s, 1H), 7.60 (d, *J* = 3.6 Hz, 1H), 7.52 (s, 1H), 7.42 (d, *J* = 8.4 Hz, 1H), 7.24 (d, *J* = 8.4 Hz, 1H), 7.41~7.43 (m, 3H), 5.95~5.96 (d, *J* = 4.8 Hz, 1H), 4.00 (s, 3H). 3.08 (s, 3H), 2.90~2.91 (d, *J* = 4.4 Hz, 3H), 2.70 (s, 3H).	634

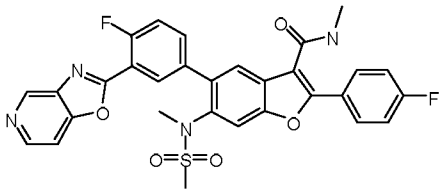
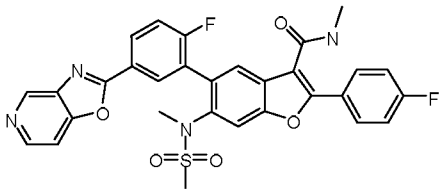
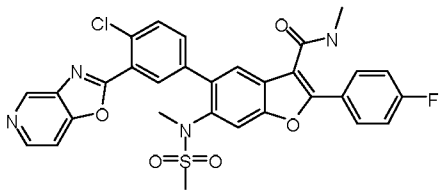
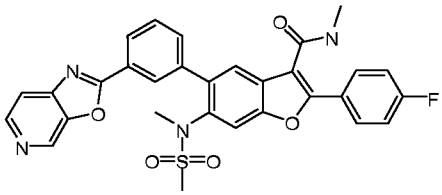
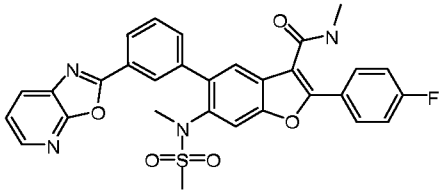
34		**^{1}H-NMR** ($CDCl_3$, 400 MHz) 8.16 (s, 1H), 7.91~7.93 (m, 2H), 7.83 (s, 1H), 7.65~7.71 (m, 2H), 7.59 (d, *J* = 5.6 Hz, 2H), 7.31 (d, *J* = 7.6 Hz, 1H), 7.15~7.20 (m, 3H), 5.88 (d, *J* = 4.0 Hz, 1H), 4.06 (s, 3H), 3.14 (s, 3H), 2.97 (d, *J* = 4.8 Hz, 3H), 2.76 (s, 3H).	634
35		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.17 (s, 1H), 7.90 (m, 2H), 7.80 (s, 1H), 7.65~7.68 (m, 2H), 7.58 (s, 1H), 7.24~7.27 (m, 2H), 7.16~7.19 (m, 3H), 5.84 (t, *J* = 4.8 Hz, 1H), 4.03 (s, 3H), 3.15 (s, 3H), 2.94 (d, *J* = 4.8 Hz, 3H), 2.70 (s, 3H).	634
36		**^{1}H-NMR** (DMSO, 400 MHz) δ 8.62 (d, *J* = 4.4 Hz, 1H), 8.15 (d, *J* = 2.4 Hz, 1H), 8.10 (t, *J* = 14.4 Hz, 3H), 7.79~7.76 (m, 1H), 7.71 (s, 1H), 7.66 (d, *J* = 8.0 Hz, 1H), 7.51~7.42 (m, 2H), 7.39 (t, *J* = 15.6 Hz, 1H), 7.30 (d, *J* = 7.6 Hz, 1H), 4.06 (s, 3H), 3.21 (s, 3H), 3.09 (s, 3H), 2.89 (d, *J* = 4.4 Hz, 3H), 2.65 (s, 3H).	614
37		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.12 (d, *J* = 2.4 Hz, 1H), 7.91~7.87 (m, 2H), 7.78 (s, 1H), 7.65~7.55 (m, 3H), 7.33 (s, 1H), 7.16~7.10 (m, 4H), 5.88 (d, *J* = 4.8 Hz, 1H), 4.00 (s, 3H), 3.09 (s, 3H), 2.94 (d, *J* = 4.8 Hz, 3H), 2.70 (s, 3H), 2.44 (s, 3H).	614
38		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.22 (s, 1H), 7.93~7.94 (m, 2H), 7.87 (s, 1H), 7.65~7.68 (m, 3H), 7.16~7.25 (m, 5H), 5.91 (d, *J* = 4.4 Hz, 1H), 4.08 (s, 3H), 3.17 (s, 3H), 3.00 (d, *J* = 8.0 Hz, 3H), 2.77 (s, 3H), 2.58 (s, 3H).	614

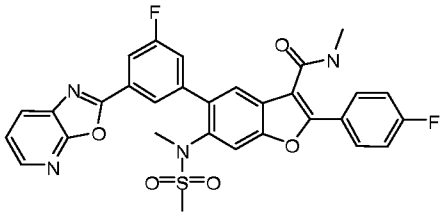
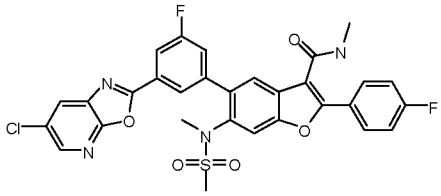
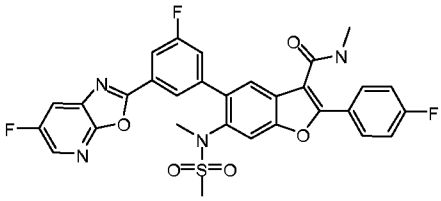
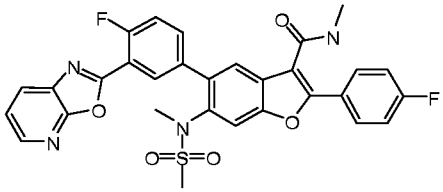
39		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.05~8.06 (m, 1H), 7.86~7.90 (m, 2H), 7.76~7.78 (m, 2H), 7.53~7.61 (m, 3H), 7.32~7.34 (m, 2H), 7.10~7.14 (m, 3H), 6.01~6.02 (m, 1H), 4.66~4.72 (m, 1H), 3.09 (s, 3H), 2.94 (d, *J* = 4.8 Hz, 3H), 2.70 (s, 3H), 1.41 (d, *J* = 6.0 Hz, 6H).	628
40		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.04 (s, 1H), 7.77~7.88 (m, 4H), 7.58~7.63 (m, 2H), 7.50 (br s, 1H), 7.39 (br s, 2H), 7.14~7.18 (m, 2H), 6.23 (br s, 1H), 3.17 (s, 3H), 3.00 (br s, 3H), 2.87 (s, 3H).	606
41		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.44 (s, 1H), 8.32 (s, 1H), 8.24~8.28 (m, 2H), 7.85~7.89 (m, 3H), 7.78~7.80 (d, *J* = 8.4 Hz, 1H), 7.68~7.70 (m, 1H), 7.58~7.62 (m, 2H), 7.13~7.18 (m, 2H), 5.77~5.78 (m, 1H), 3.03 (s, 3H), 2.92~2.93 (d, *J* = 4.0 Hz, 3H), 2.68 (s, 3H).	615
42		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.71 (s, 1H), 8.33~8.39 (m, 2H), 7.96~7.99 (m, 3H), 7.77 (d, *J* = 8.0 Hz, 1H), 7.71~7.75 (m, 2H), 7.69 (d, *J* = 4.8 Hz, 2H), 7.24~7.29 (m, 2H), 5.89 (d, *J* = 5.2 Hz, 1H), 3.23 (s, 3H), 3.03 (d, *J* = 5.2 Hz, 3H), 2.78 (s, 3H).	615
43		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.27 (s, 1H), 8.21 (d, *J* = 7.6 Hz, 1H), 8.01 (s, 1H), 7.83~7.88 (m, 2H), 7.67 (s, 1H), 7.64 (d, *J* = 5.2 Hz, 1H), 7.56~7.61 (s, 4H), 7.14 (t, *J* = 8.8 Hz, 2H), 5.87 (d, *J* = 4.4 Hz, 1H), 3.12 (s, 3H), 2.91 (d, *J* = 5.2 Hz, 3H), 2.67 (s, 3H).	595

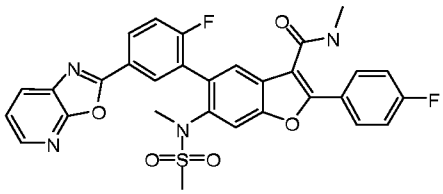
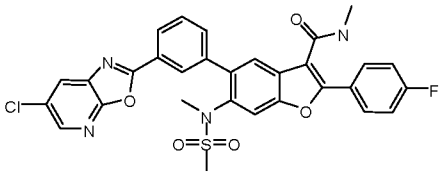
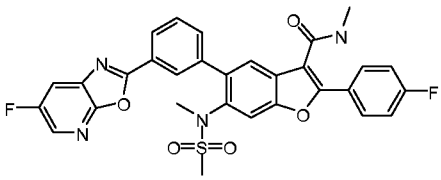
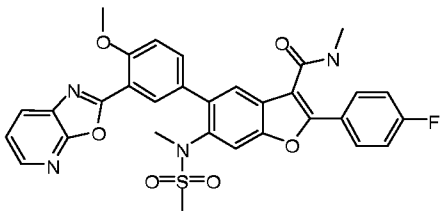
44		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.73 (s, 1H), 8.24 (s, 1H), 8.11 (d, *J* = 8.0 Hz, 1H), 8.02 (d, *J* = 8.4 Hz, 1H), 7.90~7.94 (m, 3H), 7.66 (s, 1H), 7.47~7.62 (m, 2H), 7.23 (t, *J* = 8.4 Hz, 2H), 6.29 (d, *J* = 4.0 Hz, 1H), 3.23 (s, 3H), 3.05 (d, *J* = 4.4 Hz, 3H), 2.87 (s, 3H).	**589**
45		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.44 (s, 1H), 8.23 (s, 2H), 8.17~8.19 (m, 1H), 7.80~7.83 (m, 2H), 7.64 (s, 1H), 7.59~7.61 (m, 1H), 7.41~7.43 (m, 1H), 7.15 (s, 2H), 5.67 (s, 1H), 3.10 (s, 3H), 2.84 (d, *J* = 4.8 Hz, 3H), 2.55 (s, 3H).	**623**
46		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.62~8.61 (m, 1H), 8.41~8.39 (m, 1H), 7.95~7.91 (m, 3H), 7.88 (s, 1H), 7.74~7.70 (m, 1H), 7.62 (s, 1H), 7.38~7.33 (m, 2H), 7.22~7.18 (m, 2H), 5.86~5.84 (m, 1H), 3.19 (s, 3H), 2.99 (d, *J* = 4.8 Hz, 3H), 2.81 (s, 3H).	**589**
47		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.43 (s, 1H), 8.31 (s, 1H), 8.25 (d, *J* = 7.6 Hz, 1H), 7.86~7.90 (m, 2H), 7.84 (s, 1H), 7.66~7.68 (m, 1H), 7.57~7.61 (m, 3H), 7.13~7.18 (m, 2H), 5.81 (br s, 1H), 3.14 (s, 3H), 2.94 (d, *J* = 4.8 Hz, 3H), 2.65 (s, 3H).	**589**
48		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.49 (s, 1H), 8.32 (s, 2H), 8.27~8.29 (m, 1H), 7.90~7.93 (m, 2H), 7.84 (s, 1H), 7.69~7.72 (m, 1H), 7.61~7.65 (m, 2H), 7.15 (s, 2H), 5.77 (s, 1H), 3.13 (s, 3H), 2.94 (d, *J* = 4.8 Hz, 3H), 2.65 (s, 3H).	**605**

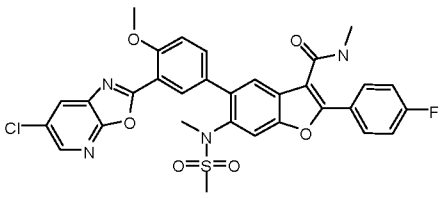
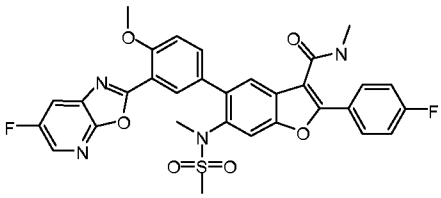
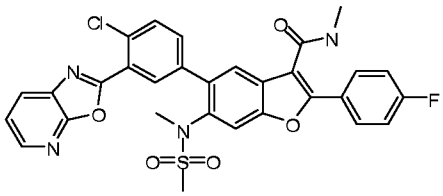
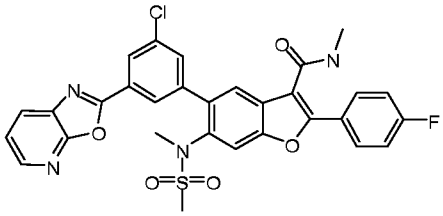
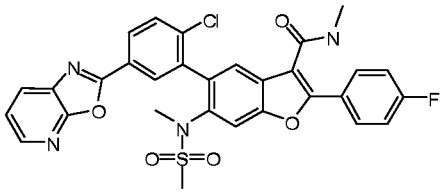
49		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.57 (d, *J* = 4.8 Hz, 1H), 8.27 (t, *J* = 5.2 Hz, 2H), 7.85~7.89 (m, 4H), 7.64 (d, *J* = 2.0 Hz, 1H), 7.60 (s, 1H), 7.30~7.33 (m, 1H), 7.15 (d, *J* = 8.8 Hz, 2H), 5.79 (d, *J* = 4.4 Hz, 1H), 3.15 (s, 3H), 2.94 (d, *J* = 4.8 Hz, 3H), 2.75 (s, 3H).	605
50		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.63~8.67 (m, 3H), 8.29~8.31 (m, 2H), 7.90~7.92 (m, 2H), 7.56~7.58 (m, 2H), 7.33~7.36 (m, 3H), 3.20 (s, 3H), 3.01 (s, 3H), 2.85 (s, 3H).	605
51		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.75 (d, *J* = 4.4 Hz, 1H), 8.33~8.35 (m, 1H), 8.17 (d, *J* = 7.2 Hz, 1H), 7.93~7.97 (m, 3H), 7.70 (d, *J* = 5.6 Hz, 2H), 7.56~7.59 (m, 1H), 7.46 (t, *J* = 7.6 Hz, 1H), 7.28 (t, *J* = 8.8 Hz, 2H), 6.07 (t, *J* = 4.4 Hz, 1H), 3.63 (s, 3H), 3.28 (s, 3H), 3.06 (d, *J* = 4.8 Hz, 3H), 2.59 (s, 3H).	570
52		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.56 (s, 1H), 8.43 (s, 1H), 7.84~7.90 (m, 4H), 7.71~7.74 (m, 1H), 7.59 (s, 1H), 7.48~7.50 (m, 1H), 7.29~7.31 (m, 1H), 7.14~7.16 (m, 2H), 5.79~5.81 (m, 1H), 3.14 (s, 3H), 2.93~2.94 (m, 3H), 2.72 (s, 3H).	655
53		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.49 (d, *J* = 4.0 Hz, 1H), 8.22 (d, *J* = 8.0 Hz, 1H), 7.87~7.90 (m, 2H), 7.78~7.81 (m, 2H), 7.59 (s, 1H), 7.39~7.46 (m, 1H), 7.12~7.16 (m, 2H), 6.83 (d, *J* = 12.0 Hz, 1H), 5.89 (s, 1H), 4.00 (s, 3H), 3.22 (s, 3H), 2.94 (d, *J* = 8.0 Hz, 3H), 2.63 (s, 3H).	619

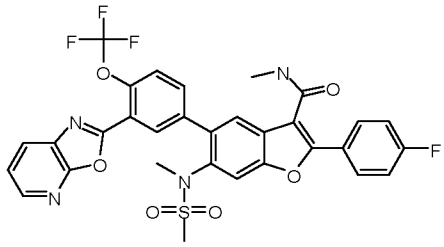
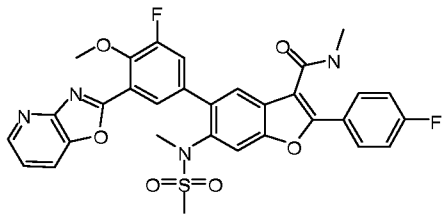
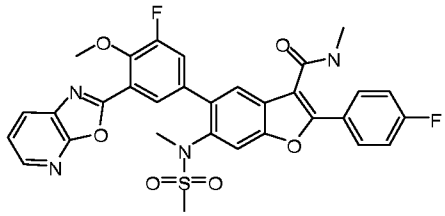
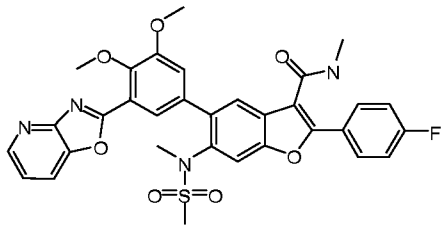
54		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.55 (d, *J* = 1.2 Hz, 1H), 8.27 (s, 1H), 7.90~7.81 (m, 4H), 7.57~7.53 (m, 2H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.31~7.28 (m, 2H), 7.16~7.12 (m, 1H), 5.82 (d, *J* = 4.4 Hz, 1H), 3.12 (s, 3H), 2.93 (d, *J* = 4.8 Hz, 3H), 2.85 (s, 3H), 2.68 (s, 3H).	585
55		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.56~8.58 (m, 2H), 8.53 (s, 1H), 7.85~7.89 (m, 5H), 7.59 (s, 1H), 7.29~7.33 (m, 1H), 7.17 (t, *J* = 8.4 Hz, 2H), 5.80 (t, *J* = 4.0 Hz, 1H), 3.20 (s, 3H), 2.94 (d, *J* = 4.8 Hz, 3H), 2.78 (s, 3H).	596
56		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.59 (d, *J* = 4.4 Hz, 1H), 8.17 (d, *J* = 10.0 Hz, 2H), 7.91~7.95 (m, 3H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.63 (s, 1H), 7.53 (s, 1H), 7.31~7.34 (m, 1H), 7.20 (t, *J* = 8.4 Hz, 2H), 5.87 (s, 1H), 3.17 (s, 3H), 2.99 (d, *J* = 4.8 Hz, 3H), 2.71 (s, 3H), 2.53 (s, 3H).	585
57		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.25 (s, 1H), 8.82 (d, *J* = 6.0 Hz, 1H), 8.36 (s, 1H), 8.27 (d, *J* = 8.0 Hz, 1H), 7.81~7.92 (m, 4H), 7.74~7.76 (d, *J* = 8.0 Hz, 1H), 7.61~7.65 (m, 1H), 7.56 (s, 1H), 7.14~7.16 (m, 2H), 5.83 (s, 1H), 3.13 (s, 3H), 2.92 (d, *J* = 4.8 Hz, 3H), 2.68 (s, 3H).	571
58		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.21 (s, 1H), 8.75 (d, *J* = 6.0 Hz, 1H), 8.17 (s, 1H), 7.95 (d, *J* = 7.6 Hz, 1H), 7.90 (s, 1H), 7.81~7.87 (m, 3H), 7.57 (s, 1H), 7.43~7.46 (m, 1H), 7.15~7.17 (m, 2H), 5.76 (br s, 1H), 3.16 (s, 3H), 2.93 (d, *J* = 4.8 Hz, 3H), 2.80 (s, 3H).	589

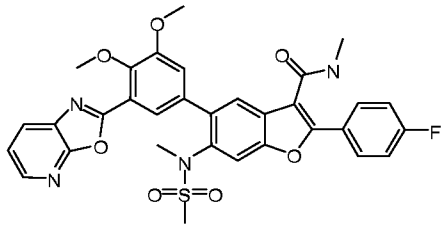
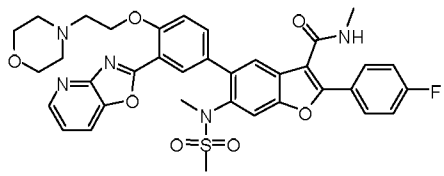
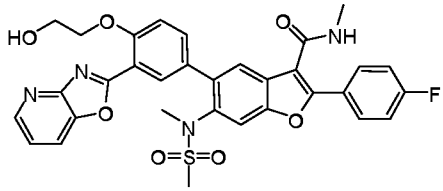
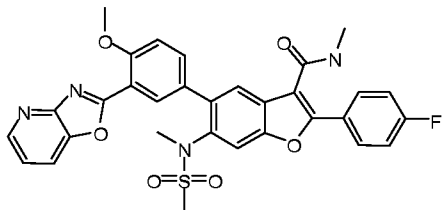
59		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.95 (s, 1H), 8.43 (d, *J* = 4.0 Hz, 1H), 8.20 (d, *J* = 5.6 Hz, 2H), 7.78~7.8 (m, 2H), 7.67 (s, 1H), 7.57~7.58 (m, 2H), 7.52 (s, 1H), 7.05~7.09 (m, 2H), 5.83 (s, 1H), 3.06 (s, 3H), 2.82 (d, *J* = 4.8 Hz, 3H), 2.75 (s, 3H).	589
60		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.53 (d, *J* = 5.2 Hz, 1H), 8.29~8.23 (m, 2H), 7.89~7.85 (m, 2H), 7.56~7.61 (m, 3H), 7.49~7.47 (m, 1H), 7.27 (t, *J* = 17.6 Hz, 2H), 7.19 (s, 1H), 5.83 (s, 1H), 3.16 (s, 3H), 2.97 (d, *J* = 4.8 Hz, 3H), 2.77 (s, 3H).	589
61		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.45 (s, 1H), 8.90~8.94 (m, 1H), 8.41 (s, 1H), 8.04 (d, *J* = 5.6 Hz, 1H), 7.99 (s, 1H), 7.91~7.95 (m, 2H), 7.76 (s, 2H), 7.65 (s, 1H), 7.25~7.27 (m, 2H), 5.96 (s, 1H), 3.22 (s, 3H), 3.02 (d, *J* = 4.8 Hz, 3H), 2.95 (s, 3H).	605
62		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.59 (s, 1H), 8.43 (d, *J* = 8.0 Hz, 1H), 8.01 (d, *J* = 7.2 Hz, 1H), 7.70~7.77 (m, 4H), 7.51~7.57 (m, 4H), 7.28~7.30 (m, 2H), 3.30 (s, 3H), 3.12 (s, 3H), 2.85 (s, 3H).	571
63		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.35~8.29 (m, 3H), 8.08~8.05 (m, 1H), 7.96~7.92 (m, 2H), 7.86 (s, 1H), 7.71 (d, *J* = 7.6 Hz, 1H), 7.65~7.61 (m, 2H), 7.37~7.34 (m, 1H), 7.19 (t, *J* = 8.8 Hz, 2H), 5.88~5.87 (m, 1H), 3.19 (s, 3H), 2.99 (d, *J* = 4.8 Hz, 3H), 2.68 (s, 3H).	571

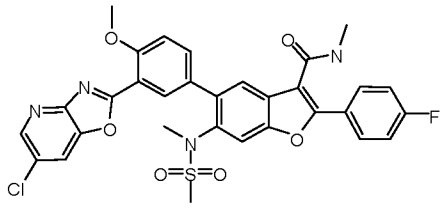
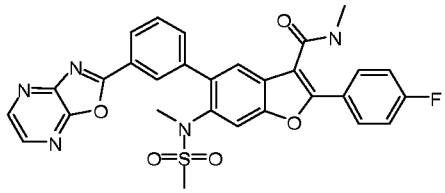
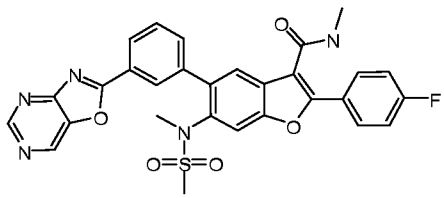
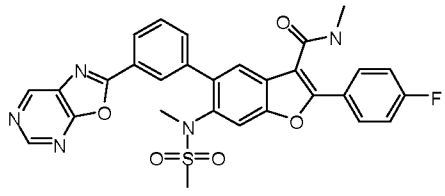
64		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.42 (d, *J* = 4.8 Hz, 1H), 8.18 (s, 1H), 8.14 (d, *J* = 8.0 Hz, 1H), 8.02 (d, *J* = 4.8 Hz, 1H), 7.97~7.93 (m, 2H), 7.91 (s, 1H), 7.67 (s, 1H), 7.45~7.42 (m, 2H), 7.26~7.21 (m, 2H), 5.93 (s, 1H), 3.25 (s, 3H), 3.04 (d, *J* = 4.8 Hz, 3H), 2.82 (s, 3H).	589
65		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.27 (s, 1H), 8.08 (s, 1H), 7.99 (s, 1H), 7.83~7.92 (m, 4H), 7.57 (s, 1H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.13~7.17 (m, 2H), 5.83 (s, 1H), 3.15 (s, 3H), 2.93 (d, *J* = 4.0 Hz, 3H), 2.73 (s, 3H).	623
66		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.38 (s, 1H), 8.34 (d, *J* = 7.6 Hz, 1H), 8.27 (s, 1H), 7.97~8.00 (m, 2H), 7.93 (s, 1H), 7.81~7.84 (m, 1H), 7.67~7.78 (m, 2H), 7.25 (t, *J* = 8.4 Hz, 2H), 5.88 (s, 1H), 3.24 (s, 3H), 3.03 (d, *J* = 4.8 Hz, 3H), 2.74 (s, 3H).	607
67		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.36~8.35 (m, 1H), 8.29~8.27 (m, 1H), 8.11~8.09 (m, 1H), 7.93~7.89 (m, 2H), 7.84 (s, 1H), 7.70~7.66 (m, 1H), 7.59 (s, 1H), 7.37~7.32 (m, 2H), 7.18 (t, *J* = 8.8 Hz, 2H), 5.81 (s, 1H), 3.16 (s, 3H), 2.97 (d, *J* = 4.8 Hz, 3H), 2.77 (s, 3H).	589

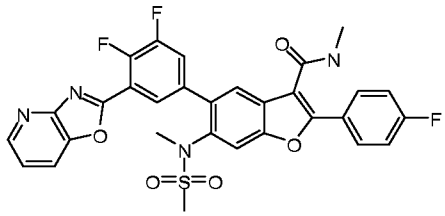
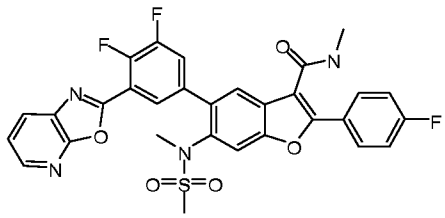
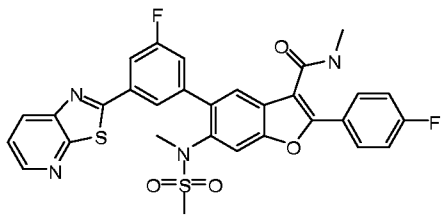
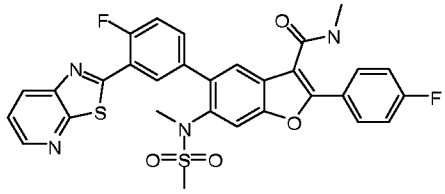
68		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.25~8.30 (m, 3H), 8.01 (t, *J* = 6.8 Hz, 1H), 7.88~7.92 (m, 2H), 7.83 (s, 1H), 7.62 (s, 1H), 7.26~7.32 (m, 2H), 7.15 (t, *J* = 8.4 Hz, 2H), 5.81 (d, *J* = 4.8 Hz, 1H), 3.23 (s, 3H), 2.95 (d, *J* = 4.8 Hz, 3H), 2.58 (s, 3H).	**589**
69		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.22~8.28 (m, 3H), 7.98~7.99 (d, *J* = 4.0 Hz, 1H), 7.86~7.90 (m, 2H), 7.82 (s, 1H), 7.66~7.68 (d, *J* = 8.0 Hz, 1H), 7.57~7.61 (m, 2H), 7.13~7.15 (m, 2H), 5.79~7.80 (m, 1H), 3.14 (s, 3H), 2.94 (d, *J* = 4.0 Hz, 3H), 2.64 (s, 3H).	**605**
70		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.38 (s, 1H), 8.34 (d, *J* = 7.6 Hz, 1H), 8.27 (s, 1H), 7.97~8.00 (m, 2H), 7.93 (s, 1H), 7.67~7.84 (m, 4H), 7.25 (t, *J* = 8.4 Hz, 2H), 5.88 (br, s, 1H), 3.24 (s, 3H), 3.03 (d, *J* = 4.8 Hz, 3H), 2.74 (s, 3H).	**589**
71		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.37 (d, *J* = 4.0 Hz, 1H), 8.25 (d, *J* = 4.0 Hz, 1H), 8.15 (d, *J* = 8.0 Hz, 1H), 7.94~7.98 (m, 2H), 7.86 (s, 1H), 7.72~7.74 (m, 1H), 7.63 (s, 1H), 7.36~7.39 (m, 1H), 7.19~7.23 (m, 3H), 4.17 (s, 3H), 3.21 (s, 3H), 3.01 (d, *J* = 4.0 Hz, 3H), 2.78 (s, 3H).	**601**

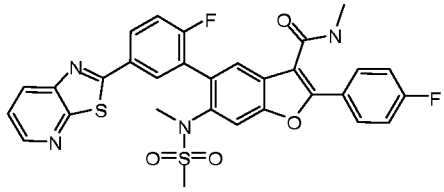
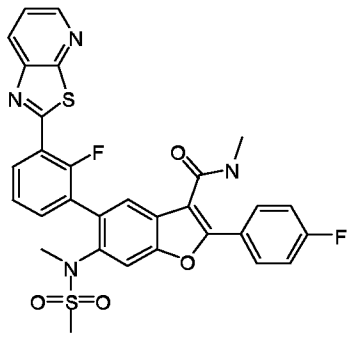
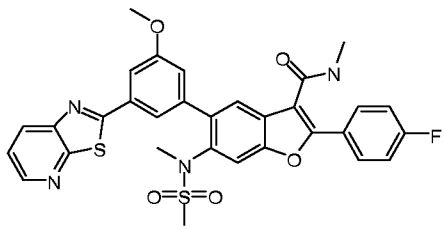
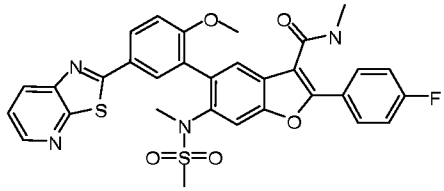
72		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.23 (s, 1H), 8.16 (d, *J* = 4.0 Hz, 1H), 8.01 (d, *J* = 4.0 Hz, 1H), 7.87~7.89 (m, 2H), 7.86 (s, 1H), 7.65~7.79 (m, 1H), 7.55 (s, 1H), 7.12~7.16 (m, 3H), 5.81 (s, 1H), 4.03 (s, 3H), 3.12 (s, 3H), 2.93 (d, *J* = 4.0 Hz, 3H), 2.72 (s, 3H).	635
73		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.17 (d, *J* = 8.4 Hz, 2H), 7.77~7.86 (m, 4H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.56 (s, 1H), 7.13~7.17 (m, 3H), 5.82 (s, 1H), 4.03 (s, 3H), 3.13 (s, 3H), 2.93 (d, *J* = 4.8 Hz, 3H), 2.72 (s, 3H).	619
74		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.43 (d, *J* = 3.2 Hz, 1H), 8.35 (t, *J* = 1.2 Hz, 1H), 8.21 (d, *J* = 2.0 Hz, 1H), 8.06 (s, 1H), 8.00~7.96 (m, 1H), 7.79 (d, *J* = 8.4 Hz, 2H), 7.72~7.67 (m, 2H), 7.55~7.52 (m, 1H), 7.39 (t, *J* =17.6 Hz, 2H), 3.16 (s, 3H), 2.98 (s, 3H), 2.78 (d, *J* = 4.4 Hz, 3H).	605
75		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.42 (d, *J* = 3.6 Hz, 1H), 8.34 (s, 1H), 8.29 (s, 2H), 8.13 (d, *J* = 7.6 Hz, 1H), 7.96~7.99 (m, 1H), 7.93 (s, 1H), 7.70 (d, *J* = 10.0 Hz, 2H), 7.41~7.44 (m, 1H), 7.25 (t, *J* = 8.4 Hz, 2H), 5.90 (s, 1H), 3.25 (s, 3H), 3.04 (d, *J* = 4.8 Hz, 3H), 2.83 (s, 3H).	605
76		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.30 (s, 2H), 8.17~8.20 (m, 1H), 8.00 (d, *J* = 7.6 Hz, 1H), 7.89~7.93 (m, 2H), 7.75 (s, 1H), 7.61 (d, *J* = 6.4 Hz, 2H), 7.29~7.32 (m, 1H), 7.15 (t, *J* = 8.8 Hz, 2H), 5.81 (s, 1H), 3.22 (s, 3H), 2.93 (d, *J* = 4.8 Hz, 3H), 2.57 (s, 3H).	605

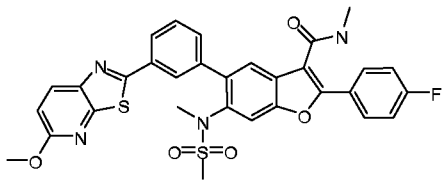
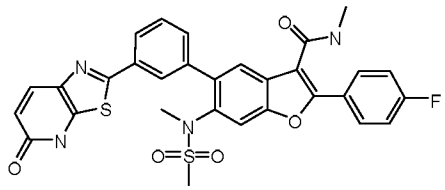
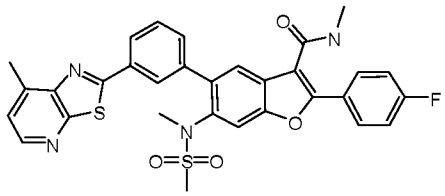
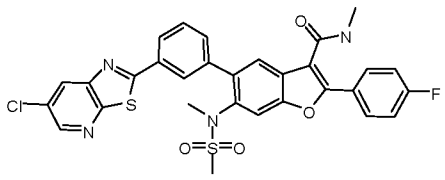
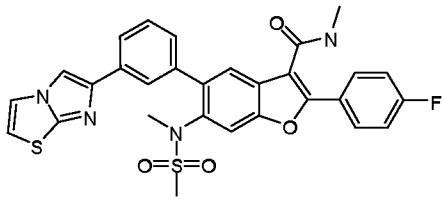
77		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.56 (s, 1H), 8.43 (s, 1H), 7.84~7.90 (m, 4H), 7.71~7.74 (m, 1H), 7.59 (s, 1H), 7.48~7.50 (m, 1H), 7.29~7.31 (m, 1H), 7.14~7.16 (m, 2H), 5.79~5.80 (m, 1H), 3.14 (s, 3H), 2.93~2.94 (m, 3H), 2.72 (s, 3H).	655
78		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.61 (d, *J* = 4.4 Hz, 1H), 8.06 (s, 1H), 7.90~7.96 (m, 3H), 7.85 (s, 1H), 7.61 (s, 1H), 7.50 (d, *J* = 3.6 Hz, 1H), 7.35~7.38 (m, 1H), 7.17~7.21 (m, 2H), 5.93 (s, 1H), 4.12 (d, *J* = 1.2 Hz, 3H), 3.19 (s, 3H), 2.99 (d, *J* = 4.4 Hz, 3H), 2.85 (s, 3H).	619
79		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.34 (d, *J* = 4.0 Hz, 1H), 8.05~8.32 (m, 1H), 7.93 (s, 1H), 7.86~7.89 (m, 2H), 7.80 (s, 1H), 7.57 (s, 1H), 7.42~7.45 (m, 1H), 7.30~7.33 (m, 1H), 7.12~7.16 (m, 2H), 5.89 (s, 1H), 4.14 (s, 3H), 3.15 (s, 3H), 2.94 (d, *J* = 4.0 Hz, 3H), 2.78 (s, 3H).	619
80		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.58~8.61 (m, 1H), 7.89~7.98 (m, 4H), 7.84 (d, *J* = 2.0 Hz, 1H), 7.59 (s, 1H), 7.46 (d, *J* = 2.0 Hz, 1H), 7.31~7.35 (m, 1H), 7.19~7.23 (m, 2H), 5.94~5.95 (m, 1H), 4.11 (s, 3H), 4.00 (s, 3H), 3.11 (s, 3H), 3.02 (d, *J* = 4.8 Hz, 3H), 2.94 (s, 3H).	631

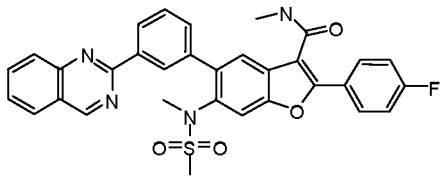
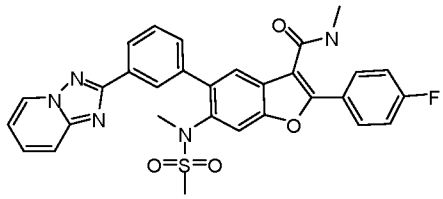
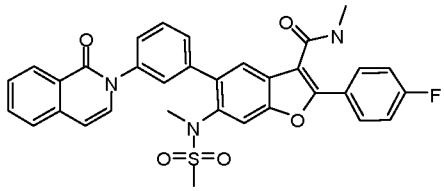
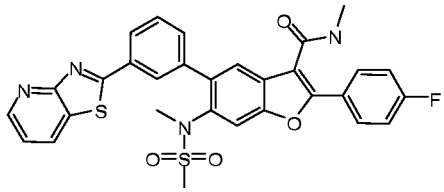
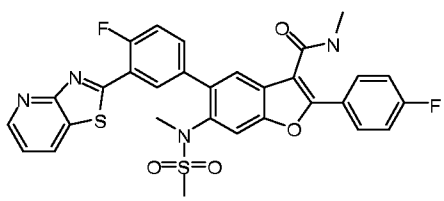
81		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.30~8.32 (m, 1H), 8.03~8.06 (m, 1H), 7.89~7.92 (m, 2H), 7.81 (s, 1H), 7.71 (d, *J* = 2.0 Hz, 1H), 7.52 (s, 1H), 7.39 (d, *J* = 2.0 Hz, 1H), 7.29~7.32 (m, 1H), 7.12~7.16 (m, 2H), 5.79~5.81 (m, 1H), 4.06 (s, 3H), 3.93 (s, 3H), 3.04 (s, 3H), 2.94 (d, *J* = 4.8 Hz, 3H), 2.87 (s, 3H).	631
82		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.54 (d, *J* = 4.4 Hz, 1H), 8.27 (s, 1H), 7.83~7.93 (m, 4H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.59 (s, 1H), 7.28~7.31 (m, 1H), 7.14~7.19 (m, 3H), 6.25 (br s, 1H), 4.46 (br s, 2H), 3.82 (br s, 4H), 3.15 (br s, 5H), 2.99 (d, *J* = 4.8 Hz, 3H), 2.93 (br s, 4H), 2.81 (s, 3H).	700
83		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.55 (br s, 1H), 8.22 (s, 1H), 7.83~7.95 (m, 4H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.60 (s, 1H), 7.27~7.29 (m, 1H), 7.17~7.22 (m, 3H), 6.14 (br s, 1H), 4.36 (br s, 2H), 4.04 (br s, 2H), 3.14 (s, 3H), 3.00 (d, *J* = 4.8 Hz, 3H), 2.81 (s, 3H).	631
84		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.53 (s, 1H), 8.25 (s, 1H), 7.84~7.91 (m, 3H), 7.80 (s, 1H), 7.66 (d, *J* = 8.0 Hz, 1H), 7.56 (s, 1H), 7.25 (t, *J* = 5.2 Hz, 1H), 7.14 (t, *J* = 8.8 Hz, 3H), 5.83 (s, 1H), 4.02 (s, 3H), 3.12 (s, 3H), 2.94 (d, *J* = 4.8 Hz, 3H), 2.73 (s, 3H).	601

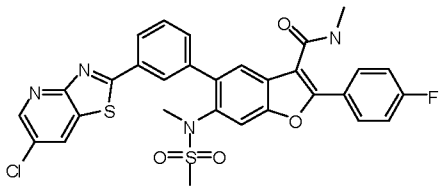
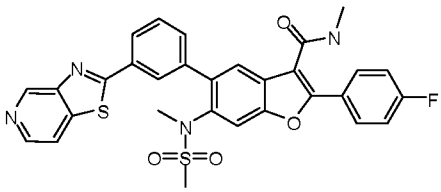
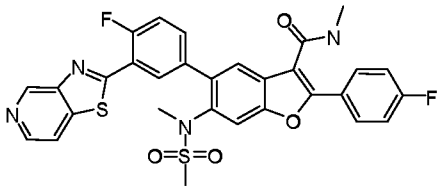
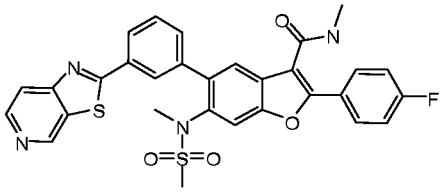
85		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.85 (s, 1H), 8.54~8.57 (m, 2H), 8.13 (s, 1H), 8.02~8.04 (m, 3H), 7.75~7.78 (m, 1H), 7.62 (s, 1H), 7.42~7.45 (m, 2H), 5.80 (br s, 1H), 4.00 (s3H), 3.15 (s, 3H), 2.99 (s, 3H), 2.80 (d, *J* = 4.8 Hz, 3H).	635
86		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.52 (d, *J* = 2.8 Hz, 1H), 8.38 (s, 1H), 8.33 (d, *J* = 7.6 Hz, 1H), 8.26 (d, *J* = 2.4 Hz, 1H), 7.87~7.91 (m, 2H), 7.84 (s, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.59~7.64 (m, 2H), 7.15 (t, *J* = 8.4 Hz, 2H), 5.78 (br, s, 1H), 3.16 (s, 3H), 2.93 (d, *J* = 5.2 Hz, 3H), 2.66 (s, 3H).	572
87		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.14 (s, 1H), 8.97 (s, 1H), 8.40 (s, 1H), 8.30~8.34 (m, 1H), 7.84~7.89 (m, 3H), 7.87 (d, *J* = 7.6 Hz, 1H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.58 (s, 1H), 7.16 (t, *J* = 8.0 Hz, 2H), 5.80 (br, s, 1H), 3.14 (s, 3H), 2.93 (d, *J* = 4.8 Hz, 3H), 2.69 (s, 3H).	572
88		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.09 (s, 1H), 8.98 (s, 1H), 8.31 (s, 2H), 8.27~8.29 (m, 1H), 7.88~7.89 (m, 2H), 7.84 (s, 1H), 7.72~7.74 (m, 1H), 7.63~7.65 (m, 1H), 7.58 (s, 1H), 7.16~7.19 (m, 1H), 5.77 (s, 1H), 3.15 (s, 3H), 2.94 (d, *J* = 4.8 Hz, 3H), 2.67 (s, 3H).	572

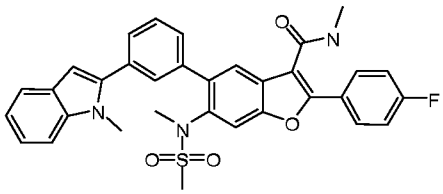
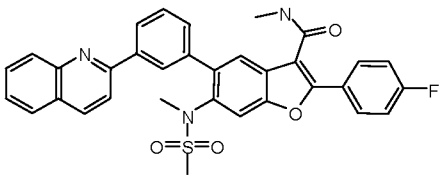
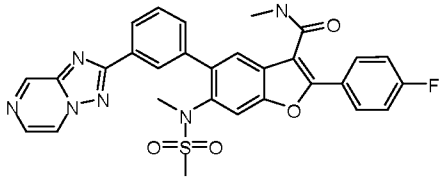
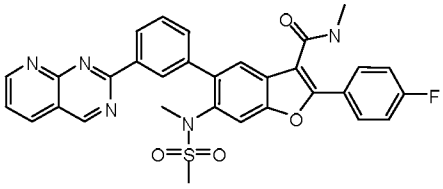
89		**^{1}H-NMR** (DMSO, 400 MHz) δ 8.62 (s, 1H), 8.56 (d, *J* = 4.8 Hz, 1H), 8.32~8.36 (m, 1H), 8.12 (s, 2H), 8.00~8.04 (m, 2H), 7.85~7.90 (m, 1H), 7.75 (s, 1H), 7.53~7.57 (m, 1H), 7.40~7.43 (m, 2H), 3.22 (s, 3H), 3.05 (s, 3H), 2.83 (d, *J* = 4.4 Hz, 3H).	607
90		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.42 (s, 1H), 8.17 (d, *J* = 8.0 Hz, 1H), 8.10 (d, *J* = 4.8 Hz, 1H), 7.92~7.96 (m, 2H), 7.90 (s, 1H), 7.64 (s, 1H), 7.56~7.61 (m, 1H), 7.40~7.44 (m, 1H), 7.20~7.23 (m, 2H), 5.86 (br s, 1H), 3.22 (s, 3H), 3.01 (d, *J* = 4.8 Hz, 3H), 2.88 (s, 3H).	607
91		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.54~8.55 (m, 1H), 8.24~8.26 (m, 1H), 7.80~7.91 (m, 5H), 7.58 (s, 1H), 7.41~7.44 (m, 1H), 7.30 (d, *J* = 8.4 Hz, 1H), 7.13~7.17 (m, 2H), 5.83~5.84 (m, 1H), 3.13 (s, 3H), 2.94 (d, *J* = 4.8 Hz, 3H), 2.74 (s, 3H).	605
92		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.51 (s, 1H), 8.75 (s, 1H), 8.57 (dd, *J* = 2.0 Hz, *J* = 2.0 Hz, 1H), 8.36 (d, *J* = 5.6 Hz, 1H), 7.93 (s, 1H), 7.87~7.90 (m, 2H), 7.76~7.80 (m, 1H), 7.60 (s, 1H), 7.37 (m, 1H), 7.22~7.18 (m, 2H), 5.96 (s, 1H), 3.21 (s, 3H), 2.98 (d, *J* = 4.8 Hz, 3H), 2.88 (s, 3H).	605

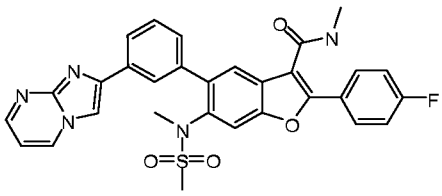
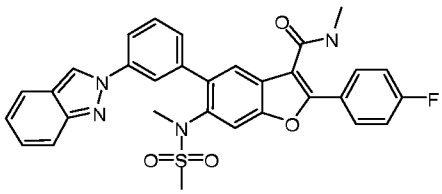
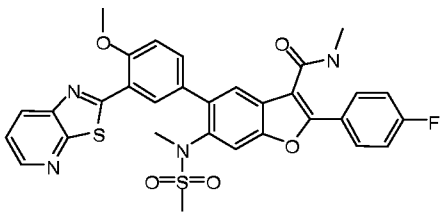
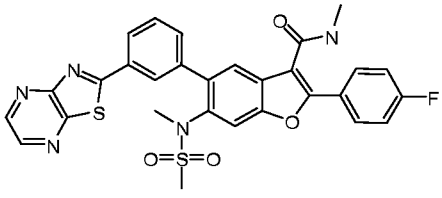
93		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.55~8.62 (m, 1H), 8.29~8.32 (m, 1H), 8.15~8.20 (m, 2H), 7.94~7.98 (m, 2H), 7.91 (s, 1H), 7.68 (s, 1H), 7.46~7.50 (m, 1H), 7.29~7.34 (m, 1H), 7.20~7.27 (m, 2H), 5.93 (br s, 1H), 3.29 (s, 3H), 3.00 (d, *J* = 4.8 Hz, 3H), 2.67 (s, 3H).	605
94		**^{1}H NMR**: ($CDCl_3$, 400 MHz) δ 9.78 (s, 1H), 7.84~7.88 (m, 2H), 7.81 (s, 1H), 7.56 (s, 1H), 7.48~7.50 (m, 2H), 7.17~7.31 (m, 3H), 7.15 (t, *J* = 8.8 Hz, 2H), 5.70 (s, 1H), 3.28 (s, 3H), 2.93 (d, *J* = 4.8 Hz, 3H), 2.69 (s, 3H).	605
95		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.63~8.64 (m, 1H), 8.36 (d, *J* = 8.4 Hz, 1H), 7.98~7.80 (m, 2H), 7.96 (s, 1H), 7.91 (s, 1H), 7.72 (s, 1H), 7.66 (s, 1H), 7.51~7.55 (m, 1H), 7.22~7.29 (m, 3H), 5.96~5.97 (m, 1H), 4.00 (s, 3H), 3.19 (s, 3H), 3.02 (d, *J* = 4.8 Hz, 3H), 2.84 (s, 3H).	617
96		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.66 (s, 1H), 9.36 (d, *J* = 8.4 Hz, 1H), 9.28~9.26 (m, 1H), 9.18 (d, *J* = 2.0 Hz, 1H), 9.11~9.08 (m, 2H), 8.93 (s, 1H), 8.77 (s, 1H), 8.57~8.54 (m, 1H), 8.33 (t, *J* = 8.8 Hz, 1H), 8.23 (d, *J* = 8.8 Hz, 1H), 7.01 (d, *J* = 3.6 Hz, 1H), 4.99 (s, 3H), 4.32 (s, 3H), 4.12 (d, *J* = 4.8 Hz, 3H), 3.73 (s, 3H).	617

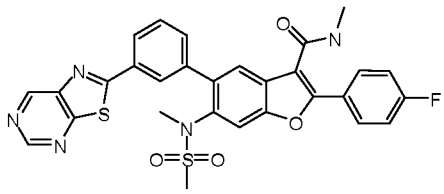
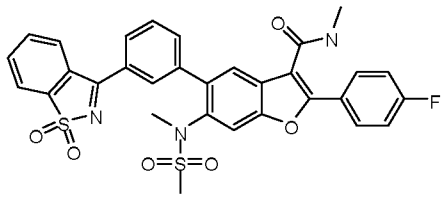
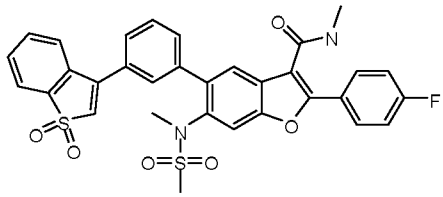
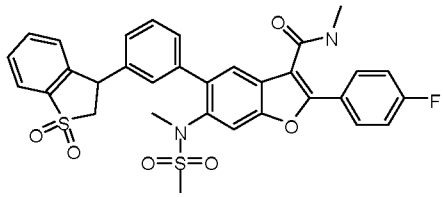
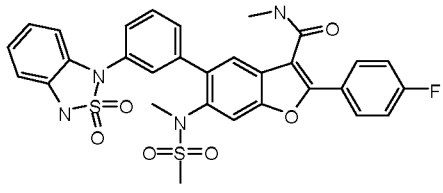
97		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.18 (d, *J* = 8.0 Hz, 2H), 8.06 (d, *J* = 8.0 Hz, 1H), 7.95~7.99 (m, 2H), 7.90 (s, 1H), 7.52~7.65 (m, 3H), 7.19~7.24 (m, 2H), 6.89 (d, *J* = 8.0 Hz, 1H), 5.96 (s, 1H), 4.04 (s, 3H), 3.19 (s, 3H), 3.01 (d, *J* = 4.0 Hz, 3H), 2.72 (s, 3H).	617
98		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.42 (d, *J* = 4.0 Hz, 1H), 8.09 (s, 1H), 7.91~7.96 (m, 4H), 7.64 (s, 2H), 7.39 (s, 1H), 7.34~7.36 (m, 2H), 6.80 (s, 1H), 4.80 (d, *J* = 4.0 Hz, 1H), 3.24 (s, 3H), 2.76 (d, *J* = 4.0 Hz, 3H), 2.40 (s, 3H).	603
99		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.45 (d, *J* = 4.8 Hz, 1H), 8.13~8.15 (m, *J* = 7.6 Hz, 1H), 7.99~8.13 (m, 2H), 7.92 (s, 1H), 7.69 (s, 1H), 7.60~7.67 (m, 2H), 7.40~7.57 (m, 1H), 7.21~7.26 (m, 3H), 5.31 (s, 1H), 3.22 (s, 3H), 3.03 (d, *J* = 4.8 Hz, 3H), 2.82 (s, 3H), 2.73 (s, 3H).	601
100		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.53 (s, 1H), 8.24 (s, 1H), 8.17 (s, 1H), 8.08 (d, *J* = 8.0 Hz, 1H), 7.93 (dd, *J* = 8.0 Hz, 2H), 7.88 (s, 1H), 7.62~7.67 (m, 3H), 7.21 (t, *J* = 4.0 Hz, 2H), 5.86 (d, *J* = 4.0 Hz, 1H), 3.16 (s, 3H), 2.97 (d, *J* = 4.0 Hz, 3H), 2.72 (s, 3H).	621
101		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 7.90~7.93 (m, 2H), 7.88 (s, 1H), 7.82 (d, *J* = 7.6 Hz, 1H), 7.77 (s, 2H), 7.55 (s, 1H), 7.39~7.44 (m, 2H), 7.30 (d, *J* = 7.2 Hz, 1H), 7.13 (t *J* = 8.4 Hz, 2H), 6.79 (d, *J* = 4.4 Hz, 1H), 5.86 (s, 1H), 3.07 (s, 3H), 2.94 (d, *J* = 4.8 Hz, 3H), 2.61 (s, 3H).	575

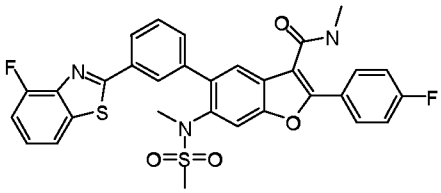
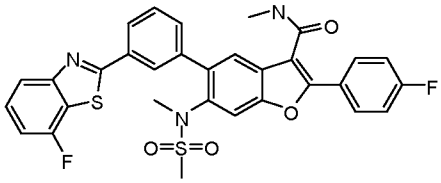
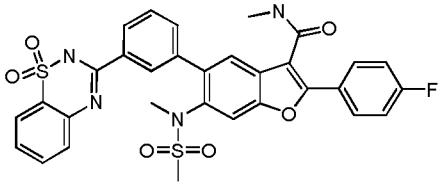
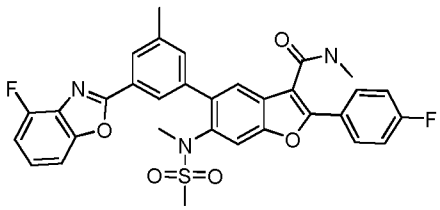
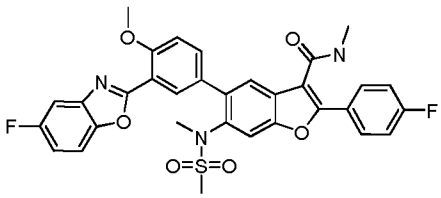
102		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.53 (s, 1H), 8.69 (s, 1H), 8.63~8.65 (m, 1H), 8.09~8.12 (m, 1H), 7.93~7.97 (m, 4H), 7.88 (s, 1H), 7.60~7.68 (m, 4H), 7.12~7.20 (m, 2H), 5.91 (br s, 1H), 3.20 (s, 3H), 3.02 (s, 3H), 2.62 (s, 3H).	502
103		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.60 (d, *J* = 6.8 Hz, 1H), 8.28 (s, 1H), 8.22 (d, *J* = 7.2 Hz, 1H), 7.99 (d, *J* = 9.2 Hz, 1H), 7.91~7.94 (m, 2H), 7.80 (s, 1H), 7.68 (d, *J* = 7.6 Hz, 1H), 7.57~7.64 (m, 3H), 7.14 (t, *J* = 8.4 Hz, 3H), 6.18 (s, 1H), 3.13 (s, 3H), 2.94 (d, *J* = 4.4 Hz, 3H), 2.60 (s, 3H).	570
104		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.38 (d, *J* = 8.0 Hz, 1H), 7.87~7.90 (m, 2H), 7.77 (s, 1H), 7.61 *J* = 8.0 Hz, 1H), 7.39~7.54 (m, 8H), 7.14 (t, *J* = 8.0 Hz, 2H), 6.54 (d, *J* = 8.0 Hz, 1H), 5.81 (s, 1H), 3.15 (s, 3H), 2.93 (d, *J* = 4.0 Hz, 3H), 2.67 (s, 3H).	596
105		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.71 (d, *J* = 4.0 Hz, 1H), 8.28 (s, 2H), 8.16 (d, *J* = 8.0 Hz, 1H), 7.88~7.92 (m, 2H), 7.82 (s, 1H), 7.63~7.54 (m, 3H), 7.30~7.34 (m, 1H), 7.13~7.17 (m, 2H), 5.84~5.85 (s, 1H), 3.12 (s, 3H), 2.94 (d, *J* = 4.0 Hz, 3H), 2.68 (s, 3H).	587
106		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.83~8.84 (m, 1H), 8.67~8.70 (m, 1H), 8.43~8.45 (m, 1H), 7.95~7.99 (m, 2H), 7.89 (s, 1H), 7.73~7.76 (m, 2H), 7.35~7.47 (m, 2H), 7.19~7.24 (m, 2H), 5.96~5.97 (m, 1H), 3.24 (s, 3H), 3.02 (d, *J* = 4.4 Hz, 3H), 2.84 (s, 3H).	605

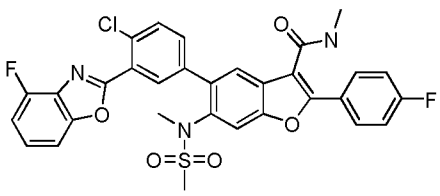
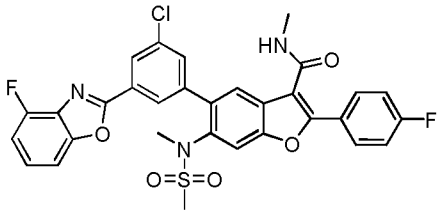
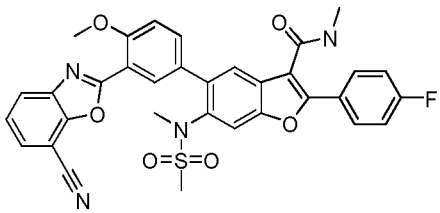
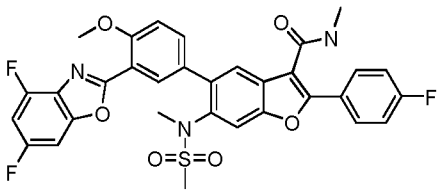
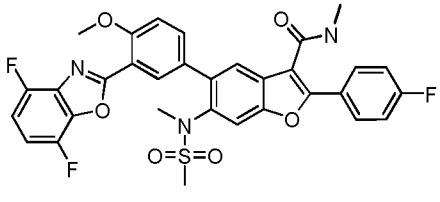
107		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.60 (d, *J* = 4.0 Hz, 1H), 8.21 (s, 1H), 8.18 (s, 1H), 8.13 (d, *J* = 8.0 Hz, 1H), 7.90 (dd, *J* = 4.0 Hz, 2H), 7.81 (s, 1H), 7.53~7.62 (m, 3H), 7.15 (t, *J* = 8.0 Hz, 2H), 5.85 (s, 1H), 3.10 (s, 3H), 2.93 (d, *J* = 4.0 Hz, 3H), 2.69 (s, 3H).	621
108		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.50 (s, 1H), 8.75 (d, *J* = 8.0 Hz, 1H), 8.36 (s, 1H), 8.31 (d, *J* = 4.0 Hz, 1H), 8.24 (d, *J* = 8.0 Hz, 1H), 7.93~7.97 (m, 3H), 7.78 (s, 1H), 7.70~7.76 (m, 1H), 7.68 (s, 1H), 7.26~7.30 (m, 2H), 6.00 (d, *J* = 4.0 Hz, 1H), 3.17 (s, 3H), 3.02 (d, *J* = 4.0 Hz, 3H), 2.92 (s, 3H).	587
109		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.45 (s, 1H), 8.55~8.59 (m, 2H), 7.94~7.99 (m, 4H), 7.71~7.75 (m, 2H), 7.67 (s, 1H), 7.23~7.27 (m, 2H), 5.89 (s, 1H), 3.21 (s, 3H), 3.03 (d, *J* = 4.8 Hz, 3H), 2.89 (s, 3H).	605
110		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.47 (d, *J* = 5.6 Hz, 1H), 8.68 (d, *J* = 5.2 Hz, 1H), 8.32 (s, 1H), 8.18~8.21 (m, 2H), 7.89 (s, 1H), 7.84~7.89 (m, 2H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.60~7.64 (m, 1H), 7.60 (s, 1H), 7.15~7.17 (m, 2H), 5.77 (br s, 1H), 3.09 (s, 3H), 2.92 (d, *J* = 4.0 Hz, 3H), 2.81 (s, 3H).	587

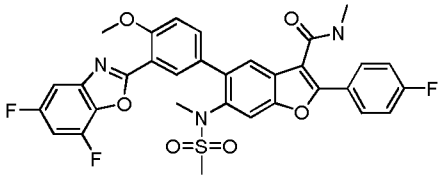
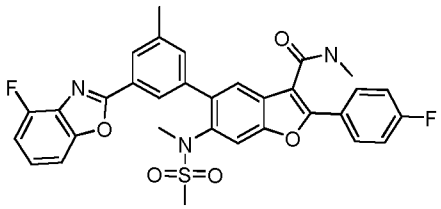
111		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 7.96~7.99 (m, 2H), 7.88 (s, 1H), 7.62~7.68 (m, 3H), 7.57 (s, 2H), 7.50 (s, 1H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.16~7.26 (m, 4H), 6.65 (s, 1H), 5.88 (s, 1H), 3.83 (s, 3H), 3.25 (s, 3H), 3.01 (d, *J* = 4.8 Hz, 3H), 2.67 (s, 3H).	582
112		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.79 (d, *J* = 8.0 Hz, 1H), 8.63 (d, *J* = 8.0 Hz, 1H), 8.35 (s, 1H), 8.24 (d, *J* = 8.4 Hz, 1H), 8.03~8.14 (m, 5H), 7.92 (s, 1H), 7.83~7.88 (m, 2H), 7.75 (t, *J* = 7.6 Hz, 1H), 7.62 (s, 1H), 7.23 (t, *J* = 8.4 Hz, 2H), 6.77 (s, 1H), 3.13 (s, 3H), 3.06 (d, *J* = 7.2 Hz, 3H), 2.93 (s, 3H).	580
113		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.24 (s, 1H), 8.50~8.51 (m, 1H), 8.33 (s, 1H), 8.27~8.29 (m, 1H), 8.14~8.15 (m, 1H), 7.88~7.92 (m, 2H), 7.82 (s, 1H), 7.55~7.60 (m, 3H), 7.56 (t, *J* = 8.4 Hz, 2H), 5.79~5.80 (m, 1H), 3.14 (s, 3H), 2.93 (d, *J* = 5.2 Hz, 3H), 2.58 (s, 3H).	571
114		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.56 (s, 1H), 9.28 (d, *J* = 2.4 Hz, 1H), 8.74~8.80 (m, 2H), 8.36~8.39 (m, 1H), 7.95~7.99 (m, 2H), 7.87 (s, 1H), 7.60~7.65 (m, 4H), 7.16~7.21 (m, 2H), 6.16 (br s, 1H), 3.21 (s, 3H), 3.00 (d, *J* = 4.8 Hz, 3H), 2.63 (s, 3H).	582

115		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.68 (d, *J* = 3.2 Hz, 1H), 8.62 (d, *J* = 3.2 Hz, 1H), 8.03 (d, *J* = 9.6 Hz, 2H), 7.90~7.93 (m, 2H), 7.73~7.74 (d, *J* = 6.0 Hz, 1H), 7.35~7.46 (m, 3H), 7.09~7.13 (m, 3H), 6.79 (d, *J* = 4.4 Hz, 1H), 3.06 (s, 3H), 2.94 (d, *J* = 4.8 Hz, 3H), 2.80 (s, 3H).	570
116		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.55 (s, 1H), 8.08 (s, 1H), 7.94~7.98 (m, 3H), 7.90 (s, 1H), 7.70~7.80 (m, 2H), 7.61~7.68 (m, 2H), 7.49~7.51 (m, 1H), 7.32~7.38 (m, 1H), 7.20~7.26 (m, 2H), 7.08~7.14 (m, 1H), 5.85 (s, 1H), 3.24 (s, 3H), 2.30 (d, 3H), 2.80 (s, 3H).	569
117		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.66 (s, 2H), 8.37 (d, *J* = 7.6 Hz, 1H), 7.98~8.01 (m, 2H), 7.92 (s, 1H), 7.76 (t, *J* = 8.8 Hz, 1H), 7.67 (s, 1H), 7.54 (d, *J* = 5.6 Hz, 1H), 7.24 (t, *J* = 8.8 Hz, 3H), 5.99 (s, 1H), 4.19 (s, 3H), 3.19 (s, 3H), 3.03 (d, *J* = 5.2 Hz, 3H), 2.86 (s, 3H).	617
118		**^{1}H-NMR** (DMSO, 400 MHz) δ 8.82 (d, *J* = 2.4 Hz, 1H), 8.69 (d, *J* = 2.4 Hz, 1H), 8.56 (d, *J* = 4.4 Hz, 1H), 8.27 (s, 1H), 8.22~8.24 (m, 1H), 8.08 (s, 1H), 8.01~8.05 (m, 2H), 7.71~7.78 (m, 3H), 7.40~7.45 (m, 2H), 3.17 (s, 3H), 3.02 (s, 3H), 2.83 (d, *J* = 4.4 Hz, 3H).	588

119		**^{1}H-NMR** (DMSO, 400 MHz) δ 9.27 (s, 1H), 9.05 (s, 1H), 8.17 (s, 1H), 8.08~8.09 (m, 1H), 7.85~7.89 (m, 3H), 7.63~7.65 (m, 1H), 7.57~7.59 (m, 2H), 7.14~7.18 (m, 2H), 5.78~5.79 (m, 1H), 3.11 (s, 3H), 2.93 (d, *J* = 8.0 Hz, 3H), 2.70 (s, 3H).	588
120		**^{1}H-NMR** (MeOD, 400 MHz) δ 7.94~7.98 (m, 4H), 7.86~7.89 (m, 2H), 7.79 (s, 1H), 7.67~7.72 (m, 2H), 7.63 (t, *J* = 8.0 Hz, 2H), 7.57 (s, 1H), 7.15 (t, *J* = 8.8 Hz, 2H), 5.79 (s, 1H), 3.16 (s, 3H), 2.92 (d, *J* = 4.8 Hz, 3H), 2.71 (s, 3H).	618
121		**^{1}H NMR**: ($CDCl_3$, 400 MHz) δ 7.85~7.87 (m, 2H), 7.78 (s, 1H), 7.72~7.74 (m, 1H), 7.46~7.57 (m, 8H), 7.12~7.16 (m, 2H), 6.70 (s, 1H), 5.77 (s, 1H), 3.12 (s, 3H), 2.92 (d, *J* = 4.8 Hz, 3H), 2.71 (s, 3H).	617
122		**^{1}H NMR**: ($CDCl_3$, 400 MHz) δ 7.84~7.88 (m, 2H), 7.71~7.74 (m, 2H), 7.28~7.53 (m, 6H), 7.22 (s, 1H), 7.12~7.16 (m, 3H), 5.76 (s, 1H), 4.80 (t, *J* = 8.0 Hz, 1H), 3.88~3.93 (m, 1H), 3.49~3.54 (m, 1H), 2.99 (s, 3H), 2.92 (d, *J* = 4.8 Hz, 3H), 2.60 (s, 3H).	619
123		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 7.87~7.90 (m, 2H), 7.77 (s, 1H), 7.54~7.59 (m, 5H), 7.12~7.17 (m, 2H), 6.93~6.97 (m, 4H), 6.64~6.66 (br s, 1H), 5.80~5.82 (m, 1H), 3.13 (s, 3H), 2.95 (d, *J* = 4.8 Hz, 3H), 2.58 (s, 3H).	621

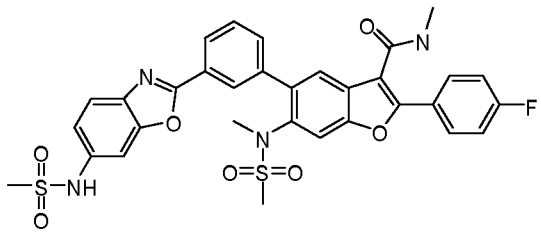
124		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.21 (s, 1H), 8.12 (d, *J* = 7.2 Hz, 1H), 7.92~7.96 (m, 2H), 7.85 (s, 1H), 7.55~7.67 (m, 4H), 7.31~7.36 (m, 1H), 7.18 (t, *J* = 8.4 Hz, 3H), 5.92 (s, 1H), 3.14 (s, 3H), 2.98 (d, *J* = 4.8 Hz, 3H), 2.73 (s, 3H).	604
125		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.18 (s, 1H), 8.08~8.11 (m, 1H), 7.90~7.94 (m, 2H), 7.84~7.85 (m, 2H), 7.55~7.64 (m, 3H), 7.42~7.48 (m, 1H), 7.09~7.20 (m, 3H), 6.06 (br s, 1H), 3.16 (s, 3H), 2.97 (d, *J* = 4.8 Hz, 3H), 2.62 (s, 3H).	604
126		**^{1}H-NMR** (CDCl3, 400 MHz) δ10.00 (s, 1H), 8.08 (d, *J* = 8.0 Hz, 2H), 7.85~8.05 (m, 4H), 7.49~7.59 (m, 3H), 7.33~7.42 (m, 1H), 7.16~7.19 (m, 2H), 7.12~7.14 (m, 2H), 5.93 (d, *J* = 4.0 Hz, 1H), 3.22 (s, 3H), 2.93 (d, *J* = 4.0 Hz, 3H), 2.70 (s, 3H).	633
199		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.18 (s, 2H), 7.97~8.18 (m, 2H), 7.90 (s, 1H), 7.68 (s, 1H), 7.54 (s, 1H), 7.44 (d, *J* = 7.6 Hz, 1H), 7.34~7.37 (m, 1H), 7.22~7.27 (m, 2H), 7.10~7.15 (m, 1H), 5.93~5.95 (br s, 1H), 3.21 (s, 3H). 3.04 (d, *J* = 4.8 Hz, 3H), 2.74 (s, 3H), 2.56 (s, 3H).	602
248		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.13 (s, 1H), 7.85~7.88 (m, 2H), 7.79 (s, 1H), 7.62~7.66 (m, 1H), 7.55 (s, 1H), 7.45~7.48 (m, 2H), 7.05~7.15 (m, 3H), 7.02~7.05 (m, 1H), 5.85 (s, 1H), 4.00 (s, 3H), 3.09 (s, 3H), 2.94 (d, *J* = 4.8 Hz, 3H), 2.73 (s, 3H).	618

249		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.26 (d, *J* = 1.2 Hz, 1H), 7.91~7.94 (m, 2H), 7.86 (s, 1H), 7.62~7.63 (m, 3H), 7.42~7.44 (m, 1H), 7.32~7.37 (m, 1H), 7.17~7.22 (m, 2H), 7.08~7.12 (m, 1H), 5.86 (s, 1H), 3.15 (s, 3H), 2.98 (d, *J* = 4.8 Hz, 3H), 2.83 (s, 3H).	622
250		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.15 (s, 1H), 8.10 (s, 1H), 7.86~7.89 (m, 2H), 7.82 (s, 1H), 7.60 (t, *J* = 2.8 Hz, 2H), 7.34~7.36 (m, 1H), 7.25~7.31 (m, 1H), 7.13~7.17 (m, 2H), 7.04 (t, *J* = 8.8 Hz, 1H), 5.86 (d, *J* = 4.4 Hz, 1H), 3.13 (s, 3H), 2.94 (d, *J* = 4.8 Hz, 3H), 2.74 (s, 3H).	622
252		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.18 (m, 1H), 8.16 (d, *J* = 4.8 Hz, 1H), 8.10 (s, 1H), 7.96~8.00 (m, 3H), 7.89~7.91 (m, 1H), 7.71~7.74 (m, 1H), 7.61 (s, 1H), 7.53~7.57 (m, 1H), 7.36~7.41 (m, 2H), 3.99 (s, 3H), 3.13 (s, 3H), 2.97 (s, 3H), 2.78 (d, *J* = 8.0 Hz, 3H).	625
253		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.17 (d, *J* = 2.0 Hz, 1H), 7.89~7.93 (m, 2H), 7.83 (s, 1H), 7.65~7.68 (m, 1H), 7.59 (s, 1H), 7.13~7.19 (m, 4H), 6.86~6.91 (m, 1H), 6.34 (d, *J* = 4.8 Hz, 1H), 4.06 (s, 3H). 3.15 (s, 3H), 3.01 (d, *J* = 4.8 Hz, 3H), 2.82 (s, 3H).	636
254		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.26 (s, 1H), 7.95~7.98 (m, 2H), 7.88 (s, 1H), 7.74 (d, *J* = 8.4 Hz, 1H), 7.65 (s, 1H), 7.20~7.23 (m, 3H), 7.02~7.11 (m, 2H), 6.07 (s, 1H), 4.11 (s, 3H), 3.20 (s, 3H), 3.05 (d, *J* = 4.8 Hz, 3H), 2.57 (s, 3H).	636

255		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.19 (d, *J* = 2.0 Hz, 1H), 7.91~7.93 (m, 2H), 7.90 (s, 1H), 7.70~7.72 (m, 1H), 7.62 (s, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.18~7.22 (m, 3H), 6.89~6.94 (m, 1H), 6.01 (d, *J* = 4.0 Hz, 1H), 4.07 (s, 3H), 3.17 (s, 3H), 2.99 (d, *J* = 4.0 Hz, 3H), 2.80 (s, 3H).	636
256		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.18 (s, 2H), 7.97~8.18 (m, 2H), 7.90 (s, 1H), 7.68 (s, 1H), 7.54 (s, 1H), 7.44 (d, *J* = 7.6 Hz, 1H), 7.34~7.37 (m, 1H), 7.22~7.27 (m, 2H), 7.10~7.15 (m, 1H), 5.93~5.95 (br s, 1H), 3.21 (s, 3H). 3.04 (d, *J* = 4.8 Hz, 3H), 2.74 (s, 3H), 2.56 (s, 3H).	602

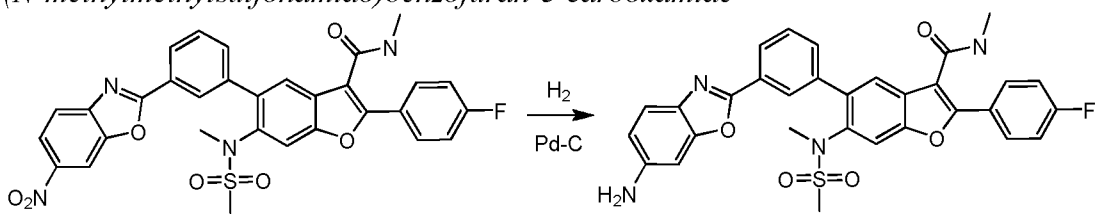
Example 2

Preparation of Compound **127**



127

Step 1 - Synthesis of 5-(3-(6-aminobenzo[d]oxazol-2-yl)phenyl)-2-(4-fluorophenyl)-N-methyl-6-(N-methylmethylsulfonamido)benzofuran-3-carboxamide

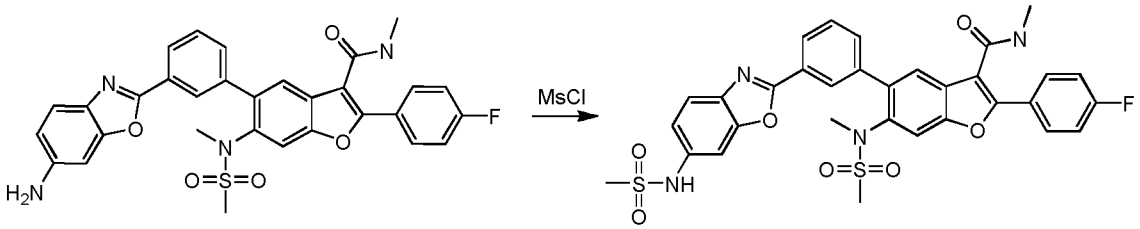


41

To a solution of Compound **41** (prepared according to the method described in Example 1, 530 mg, 0.13 mmol) in MeOH (10 mL), Pd/C (10 mg) was added, and the resulting reaction mixture was allowed to stir under 40 psi of H_2 atmosphere for 24 hours at 25 °C. The

reaction mixture was filtered, concentrated *in vacuo* and the residue obtained was purified using flash column chromatography (PE : EtOAc = 2 : 1) to provide 5-(3-(6-aminobenzo[d]oxazol-2-yl)phenyl)-2-(4-fluorophenyl)-N-methyl-6-(N-methylmethylsulfonamido)benzofuran-3-carboxamide (420 mg, 85%). ^{1}H-NMR (DMSO, 400 MHz) δ 8.55 (s, 1H), 8.00~8.11 (m, 5H), 7.59~7.63 (m, 3H), 7.38~7.40 (m, 3H), 6.80 (s, 1H), 6.62~6.64 (d, J = 8.4 Hz, 1H), 5.47 (s, 2H), 3.12 (s, 3H), 2.93 (s, 3H), 2.79~2.80 (d, J = 4.0 Hz, 3H). MS $(M+H)^+$: 585.

Step 2 - Synthesis of 2-(4-fluorophenyl)-N-methyl-6-(N-methylmethylsulfonamido)-5-(3-(6-(methylsulfonamido)benzo[d]oxazol-2-yl)phenyl)benzofuran-3-carboxamide (Compound 127)

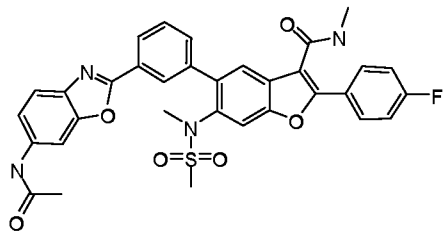
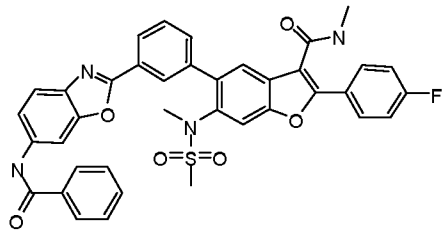
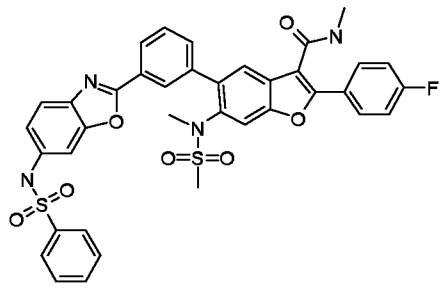
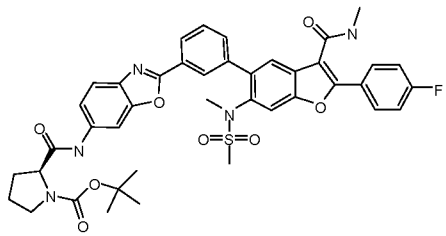


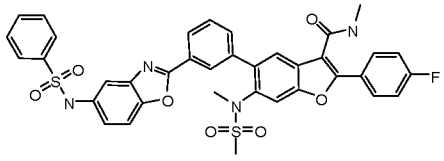
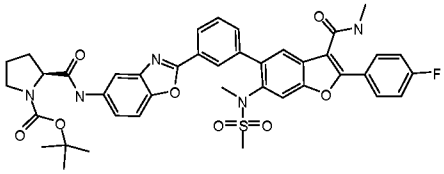
127

To a solution of 5-(3-(6-aminobenzo[d]oxazol-2-yl)phenyl)-2-(4-fluorophenyl)-N-methyl-6-(N-methylmethylsulfonamido)benzofuran-3-carboxamide (50 mg, 0.13 mmol) and pyridine (0.2 mL) in 1 mL of dry dichloromethane, MsCl (50 mg, 0.44 mmol) was added dropwise at 0 °C. After stirred at room temperature for 4 hours, the mixture was quenched with 20% aq. NH_4Cl, then extracted with dichloromethane and washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue obtained was purified using preparative HPLC to provide 2-(4-fluorophenyl)-N-methyl-6-(N-methylmethylsulfonamido)-5-(3-(6-(methylsulfonamido)benzo[d]oxazol-2-yl)phenyl)benzofuran-3-carboxamide (Compound **127**, 43 mg, 90.1%). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.17~8.23 (m, 3H), 7.88~7.92 (m, 2H), 7.80 (s, 1H), 7.55~7.60 (m, 4H), 7.25 (s, 1H), 7.12~7.14 (m, 2H), 7.06~7.08 (m, 1H), 5.79 (s, 1H), 3.13 (s, 3H), 2.93~2.94 (d, J = 4.8 Hz, 3H), 2.60 (s, 3H), 2.56 (s, 3H). MS $(M+H)^+$: 663.

Compounds **128-133**, depicted in the table below, were prepared using the method described in Example 2 and substituting the appropriate reactants and/or reagents.

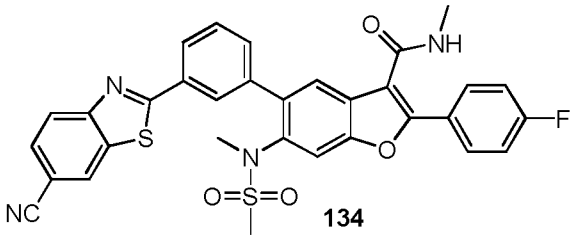
Compound	Structure	NMR	MS $(M+H)^+$

128		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.17~8.23 (m, 3H), 7.88~7.92 (m, 2H), 7.80 (s, 1H), 7.55~7.60 (m, 4H), 7.25 (s, 1H), 7.12~7.14 (m, 2H), 7.06~7.08 (m, 1H), 5.79 (s, 1H), 3.13 (s, 3H), 2.94 (d, *J* = 4.8 Hz, 3H), 2.60 (s, 3H), 2.16 (s, 3H).	628
129		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 10.61 (s, 1H), 8.60~8.61 (m, 1H), 8.48 (s, 1H), 8.33 (s, 1H), 8.27~8.29 (m, 1H), 8.04~8.12 (m, 5H), 7.46~7.89 (m, 10H), 3.23 (s, 3H), 3.04 (s, 3H), 2.89 (d, *J* = 4.4 Hz, 3H).	690
130		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.15 (m, 2H), 7.86~7.90 (m, 2H), 7.81 (s, 1H), 7.67~7.70 (m, 2H), 7.58~7.61 (m, 2H), 7.49~7.56 (m, 2H), 7.42~7.47 (m, 2H), 7.35~7.39 (m, 2H), 7.13~7.15 (m, 2H), 6.81~6.86 (m, 1H), 6.54 (s, 1H), 5.81 (d, *J* = 4.8 Hz, 1H) 3.13 (s, 3H), 2.94 (d, *J* = 4.8 Hz, 3H), 2.62 (s, 3H).	726
131		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.87 (br s, 1H), 8.17~8.24 (m, 3H), 7.92~7.96 (m, 2H), 7.83 (s, 1H), 7.57~7.63 (m, 4H), 7.14~7.21 (m, 3H), 6.08 (br s, 1H), 4.52 (br s, 1H), 3.37~3.47 (m, 2H), 3.18 (s, 3H), 2.98 (d, *J* = 4.8 Hz, 3H), 2.65 (s, 3H), 2.53 (br s, 1H), 1.95 (br s, 3H), 1.52 (s, 9H).	783

132		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.25 (s, 1H), 8.15 (d, *J* = 8.0 Hz, 1H), 7.87~7.90 (m, 2H), 7.82 (s, 1H), 7.62~7.68 (m, 2H), 7.52~7.60 (m, 3H), 7.45~7.48 (m, 1H), 7.34~7.40 (m, 4H), 7.15 (t, *J* = 8.8 Hz, 2H), 7.04~7.07 (m, 1H), 6.44 (s, 1H), 5.77 (d, *J* = 3.6 Hz, 1H), 3.12 (s, 3H), 2.92 (d, *J* = 4.8 Hz, 3H), 2.63 (s, 3H).	726
133		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.25 (s, 1H), 8.20 (d, *J* = 8.0 Hz, 1H), 7.91 (t, *J* = 8.0 Hz, 3H), 7.81 (s, 1H), 7.59 (t, *J* = 9.6 Hz, 2H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.45 (s, 2H), 7.15 (t, *J* = 8.4 Hz, 2H), 5.79 (d, *J* = 4.4 Hz, 1H), 4.44~4.48 (m, 1H), 3.27~3.41 (m, 2H), 3.12 (s, 3H), 2.94 (d, *J* = 5.2 Hz, 3H), 2.62 (s, 3H), 2.50~2.57 (m, 1H), 1.86~1.90 (m, 3H), 1.45 (s, 9H).	783

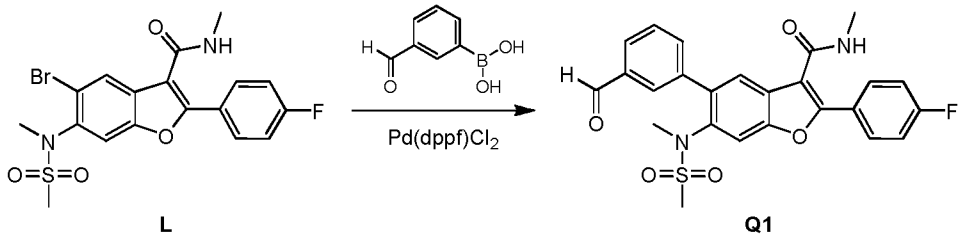
Example 3

Preparation of Compound **134**



134

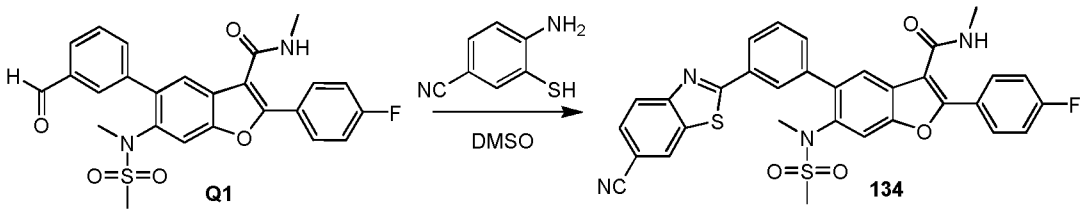
Step 1 - Synthesis of 2-(4-fluorophenyl)-5-(3-formylphenyl)-N-methyl-6-(N-methylmethylsulfonamido)benzofuran-3-carboxamide (Q1)



L **Q1**

To a degassed solution of 3-formylphenylboronic acid (440 mg, 2.64 mmol) in dry DMF (20 mL) was added Compound **L** (1.0 g, 2.20 mmol), K_3PO_4 (1.2 g, 4.40 mmol) and $Pd(dppf)Cl_2$ (20 mg). Then the reaction mixture was placed under N_2 atmosphere and stirred at 100 °C for 6 hours. After cooled to room temperature and filtered, the filtrate was washed with H_2O, brine, and dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue obtained was purified using column chromatography (PE : EtOAc = 3: 1) to provide aryl aldehyde **Q1** (760 mg, 72.1%) as white solid. **^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 10.05 (s, 1H), 7.98~7.88 (m, 4H), 7.82 (s, 1H), 7.75 (s, 1H), 7.62~7.59 (m, 2H), 7.59~7.16 (m, 2H), 5.96 (s, 1H), 3.10 (s, 3H), 2.96 (s, 3H), 2.69 (s, 3H). MS $(M+H)^+$: 481.5.

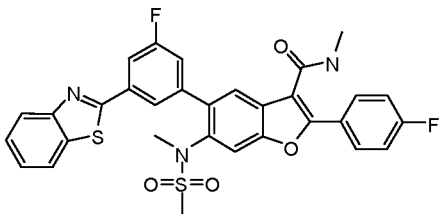
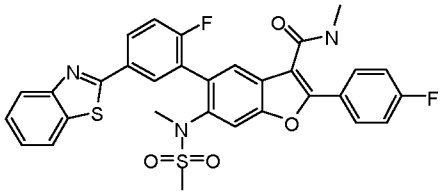
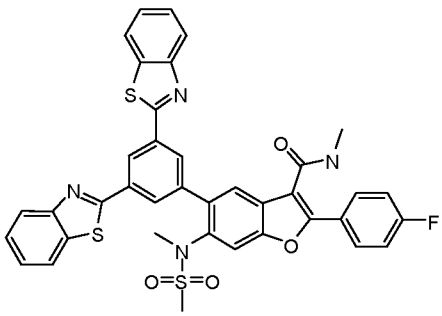
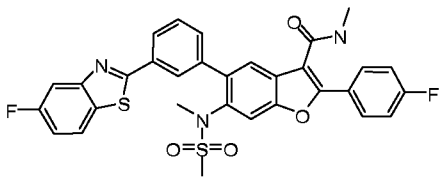
Step 2 - Synthesis of 5-(3-(6-cyanobenzo[d]thiazol-2-yl)phenyl)-2-(4-fluorophenyl)-N-methyl-6-(N-methylmethylsulfonamido)benzofuran-3-carboxamide (Compound 134)

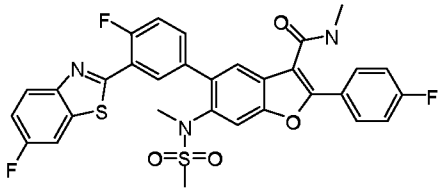
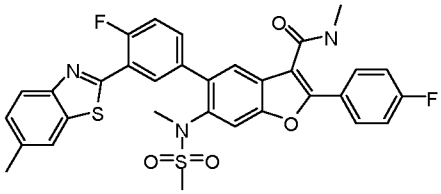
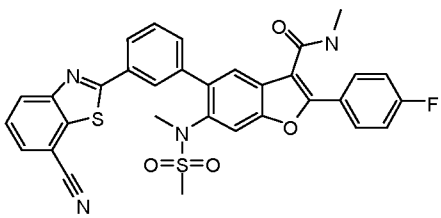
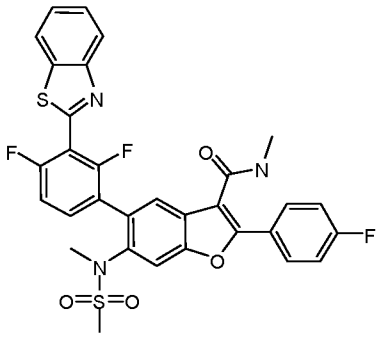


A mixture of the aryl aldehyhyde **Q1** (150 mg, 0.31 mmol) and 4-amino-3-mercaptobenzonitrile (56 mg, 0.37 mmol) in DMSO (3 mL) was allowed to stir at 200 °C for 2 hours. After cooled, the mixture was diluted with water and extracted with EtOAc. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified using preparative HPLC to provide Compound **134** (150 mg, 79%). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.27~8.28 (m, 2H), 8.14~8.19 (m, 2H), 7.94~7.99 (m, 3H), 7.76~7.84 (m, 1H), 7.63~7.72 (m, 3H), 7.23~7.25 (m, 2H), 5.91~5.92 (m, 1H), 3.19 (s, 3H), 3.20 (d, J = 4.4 Hz, 3H), 2.81 (s, 3H). MS $(M+H)^+$: 611.

Compounds **135-142**, depicted in the table below, were prepared using the method described in Example 3 and substituting the appropriate reactants and/or reagents.

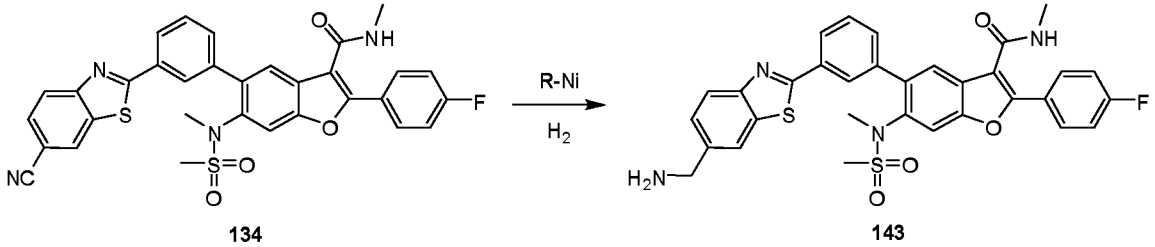
Compound	Structure	NMR	MS $(M+H)^+$

135		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.01~8.10 (m, 1H), 7.89~7.98 (m, 6H), 7.68 (s, 1H), 7.53~7.57 (m, 1H), 7.43~7.48 (m, 1H), 7.34~7.37 (m, 1H), 7.24 (t, *J* = 8.8 Hz, 2H), 5.97 (br s, 1H), 3.21 (s, 3H), 3.04 (d, *J* = 4.8 Hz, 3H), 2.84 (s, 3H).	604
136		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.13~8.16 (m, 2H), 8.02~8.05 (m, 1H), 7.90~7.96 (m, 2H), 7.88 (d, *J* = 4.0 Hz, 2H), 7.67 (s, 1H), 7.47~7.51 (m, 1H), 7.37~7.41 (m, 1H), 7.26~7.31 (m, 1H), 7.17~7.12 (m, 2H), 6.00 (br s, 1H), 3.25 (s, 3H), 2.99 (d, *J* = 4.8 Hz, 3H), 2.64 (s, 3H).	604
137		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.78 (s, 2H), 8.29 (s, 2H), 8.05 (d, *J* = 8.0 Hz, 2H), 7.90~7.95 (m, 4H), 7.86 (s, 1H), 7.65 (s, 1H), 7.47~7.51 (m, 2H), 7.38~7.41 (m, 2H), 7.13~7.18 (m, 2H), 3.17 (s, 3H), 2.94 (s, 3H), 2.82 (s, 3H).	719
138		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.15 (s, 1H), 8.04~8.06 (m, 1H), 7.87~7.91 (m, 2H), 7.82 (s, 1H), 7.76~7.79 (m, 1H), 7.66~7.69 (m, 1H), 7.57 (d, *J* = 9.2 Hz, 1H), 7.51~7.56 (m, 2H), 7.09~7.17 (m, 3H), 5.80 (d, *J* = 3.6 Hz, 1H), 3.11 (s, 3H), 2.92 (d, *J* = 5.2 Hz, 3H), 2.66 (s, 3H).	604

139		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.39~8.41 (m, 1H), 7.94~7.97 (m, 1H), 7.87~7.90 (m, 2H), 7.82 (s, 1H), 7.56~7.58 (m, 3H), 7.25~7.30 (m, 1H), 7.13~7.17 (m, 3H), 5.78 (s, 1H), 3.09 (s, 3H), 2.93 (d, *J* = 4.8 Hz, 3H), 2.77 (s, 3H).	622
140		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.41 (d, *J* = 5.6 Hz, 1H), 7.88~7.92 (m, 3H), 7.81 (s, 1H), 7.68 (s, 1H), 7.55~7.58 (m, 2H), 7.25~7.29 (m, 2H), 7.12~7.15 (m, 2H), 5.81 (br s, 1H), 3.08 (s, 3H), 2.94 (d, *J* = 4.8 Hz, 3H), 2.76 (s, 3H), 2.46 (s, 3H).	618
141		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.22~8.24 (m, 1H), 8.12 (s, 1H), 8.03~8.05 (m, 1H), 7.81~7.85 (m, 2H), 7.78 (s, 1H), 7.68~7.70 (m, 1H), 7.52~7.62 (m, 4H), 7.13~7.18 (m, 2H), 6.12~6.13 (m, 1H), 3.12 (s, 3H), 2.96 (d, *J* = 5.2 Hz, 3H), 2.68 (s, 3H).	611
142		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.18 (d, *J* = 4.0 Hz, 1H), 7.91~7.99 (m, 3H), 7.85 (s, 1H), 7.64 (s, 1H), 7.53~7.58 (m, 2H), 7.45~7.50 (m, 1H), 7.17~7.23 (m, 3H), 5.93 (br s, 1H), 3.23 (s, 3H), 3.00 (d, *J* = 4.8 Hz, 3H), 2.75 (s, 3H).	622

Example 4

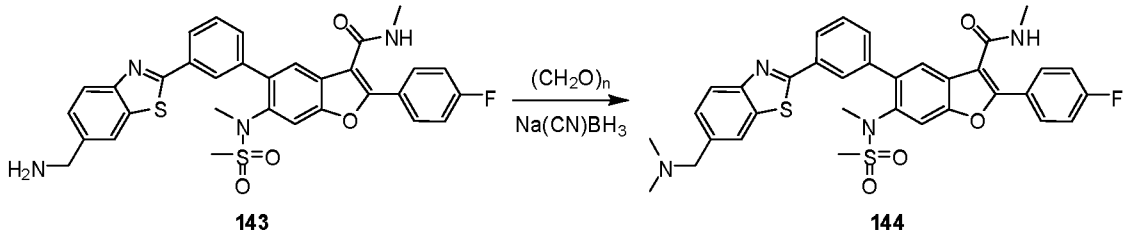
Preparation of Compound **143**



To a solution of Compound **134** (120 mg, 0.20 mmol) and NH_4OH (0.5 mL) in MeOH (10 mL), was added Raney-Ni (100 mg). The resulting solution was degassed and then was shaken under hydrogen gas atmosphere (30 psi) for about 15 hours. The reaction mixture was filtered and the collected solid was washed with MeOH. The filtrate and washing were combined and concentrated *in vacuo* to provide Compound **143** (80 mg, 66%). **^{1}H-NMR** (MeOD, 400 MHz) δ 8.23 (s, 1H), 8.12~8.14 (m, 1H), 8.06~8.09 (m, 2H), 7.94~7.97 (m, 2H), 7.82 (s, 1H), 7.74 (s, 1H), 7.69 (s, 1H), 7.57~7.67 (m, 2H), 7.22~7.26 (m, 2H), 4.24 (s, 2H), 3.18 (s, 3H), 2.92 (s, 3H), 2.89 (s, 3H). MS $(M+H)^+$: 615.

Example 5

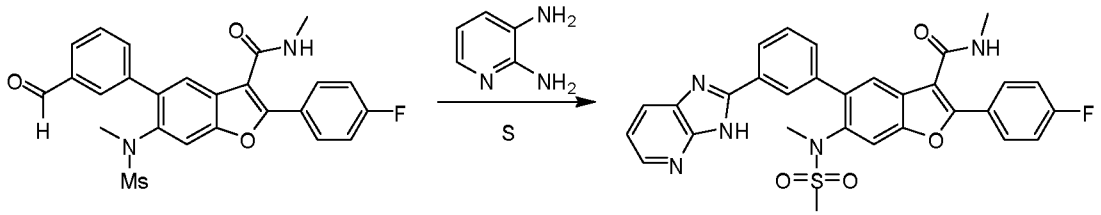
Preparation of Compound **144**



CF_3COOH (0.1 mL) was added to a solution of Compound **143** (50 mg, 0.08 mmol) and paraformaldehyde (5 mg, 0.16 mmol) in MeOH (2 mL). The resulting reaction was allowed to stir at room temperature for 3 hours, then $Na(CN)BH_3$ (10 mg, 0.16 mmol) was added. The reaction mixture was allowed to stir at room temperature for about 15 hours, then was quenched with saturated NH_4Cl solution and extracted with EtOAc. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue obtained was purified using preparative HPLC to provide Compound **144** (20 mg, 38%). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.14 (s, 1H), 8.03~8.08 (m, 2H), 7.99 (s, 1H), 7.87~7.91 (m, 2H), 7.83 (s, 1H), 7.53~7.60 (m, 3H), 7.44~7.46 (m, 1H), 7.13~7.17 (m, 2H), 5.82~5.83 (m, 1H), 4.25 (s, 2H), 3.11 (s, 3H), 2.92 (d, J = 8.0 Hz, 3H), 2.75 (s, 6H), 2.67 (s, 3H). MS $(M+H)^+$: 643.

Example 6

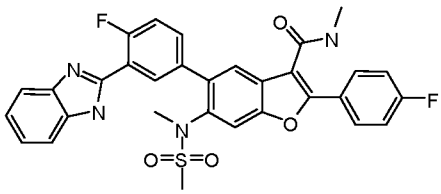
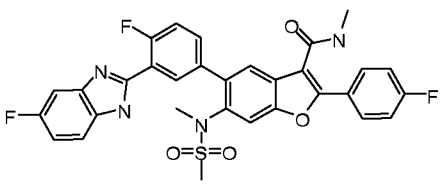
Preparation of Compound **145**

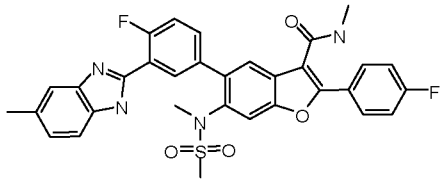
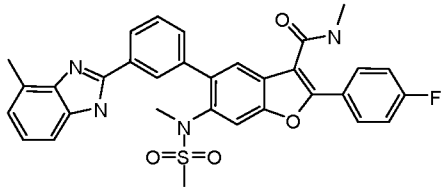
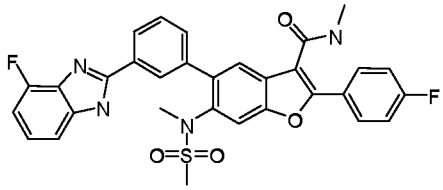
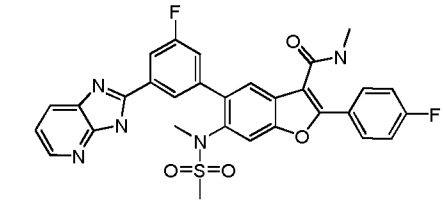
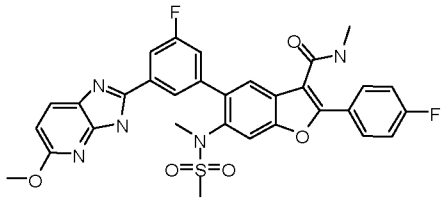


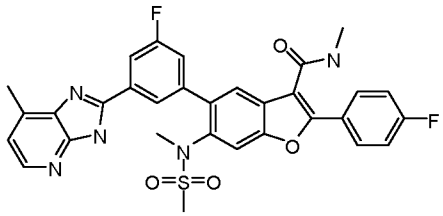
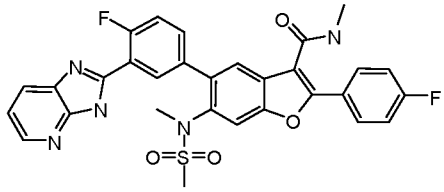
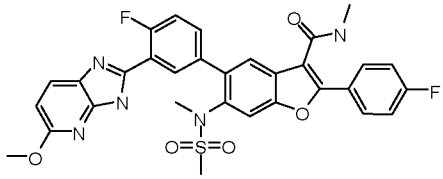
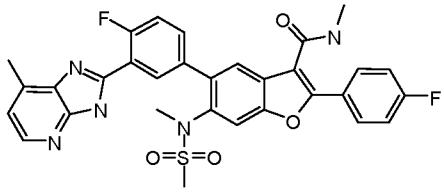
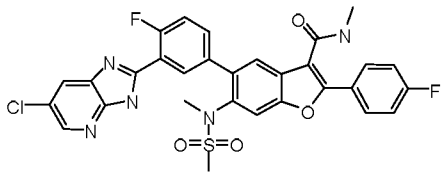
145

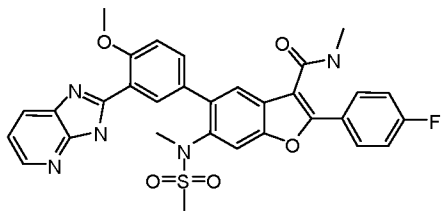
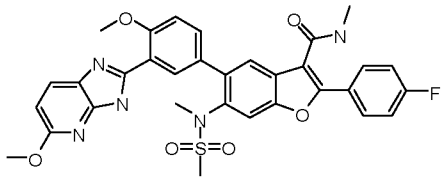
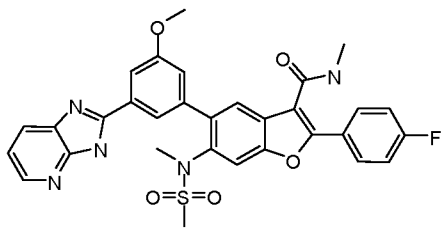
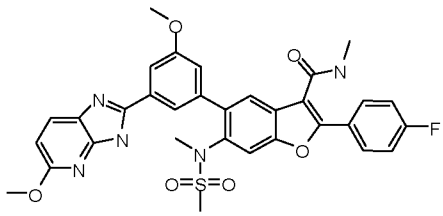
A solution of aryl aldehyde **Q1** (100 mg, 0.385 mmol) in pyridine-2,3-diamine (58 mg, 0.42 mmol) was heated to 160 °C and allowed to stir at this temperature for 2 hours. The reaction mixture was cooled to room temperature, quenched with water, and extracted with EtOAc. The organic layer was concentrated *in vacuo* and the resulting residue was purified using prep-TLC (DCM : MeOH = 20 : 1) to provide Compound **145** (50 mg, 53.7%). **^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.26~8.29 (m, 2H), 8.07 (s, 1H), 7.74~7.82 (m, 4H), 7.41~7.52 (m, 3H), 7.25~7.27 (m, 1H), 7.05~7.15 (m, 3H), 3.14 (s, 3H), 2.94 (s, 3H), 2.82 (d, J = 4.8 Hz, 3H). MS $(M+H)^+$: 570.

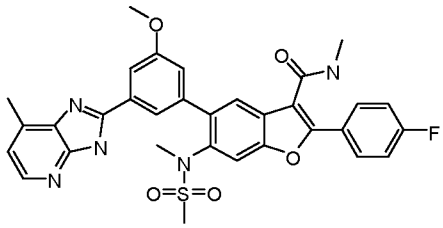
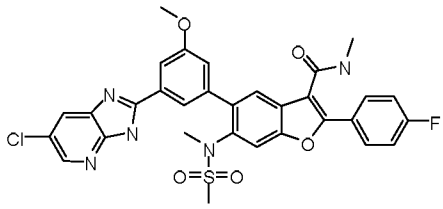
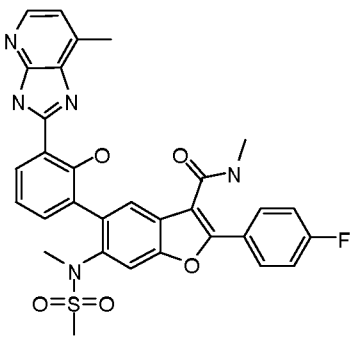
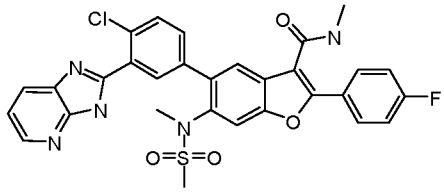
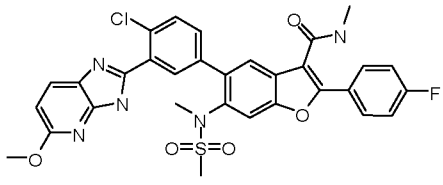
Compounds **146-196**, depicted in the table below, were prepared using the method described in Example 6 and substituting the appropriate reactants and/or reagents.

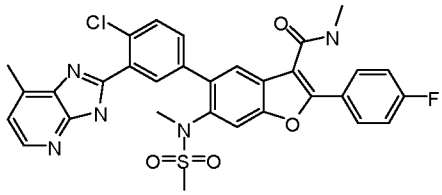
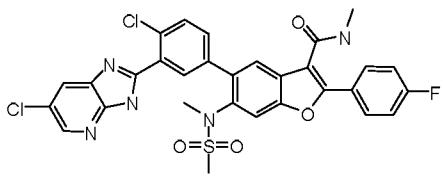
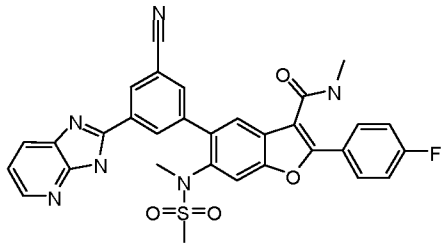
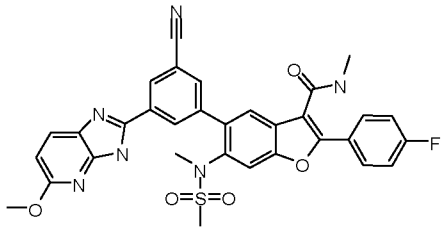
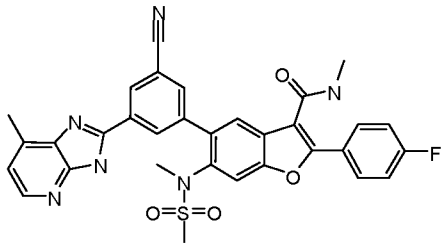
Compound	Structure	NMR	MS $(M+H)^+$
146		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.53~8.56 (m, 1H), 7.98~8.01 (m, 2H), 7.88 (s, 1H), 7.63~7.70 (m, 3H), 7.61 (s, 1H), 7.32~7.34 (m, 4H), 7.20~7.25 (m, 2H), 6.14 (s, 1H), 3.15 (s, 3H), 3.04 (d, J = 4.8 Hz, 3H), 2.92 (s, 3H).	**587**
147		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.15~8.17 (m, 1H), 7.76~7.79 (m, 2H), 7.70 (s, 1H), 7.64 (m, 3H), 7.43 (s, 1H), 7.33~7.36 (m, 1H), 7.14~7.17 (m, 1H), 7.03~7.07 (m, 2H), 6.95~7.00 (m, 1H), 3.00~3.01 (m, 6H), 2.92 (s, 3H).	**605**

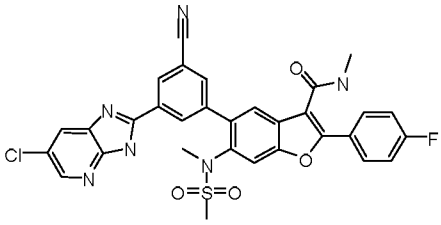
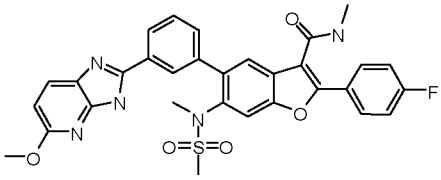
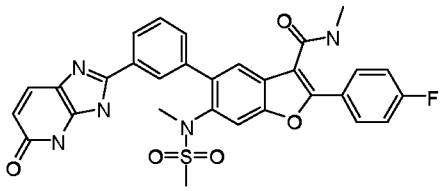
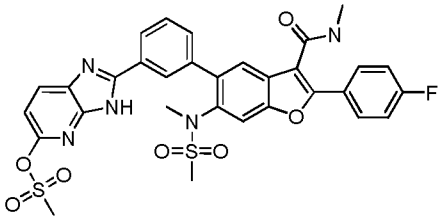
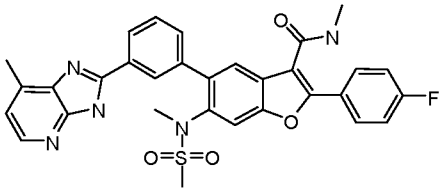
148		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.24~8.26 (m, 1H), 7.81~7.87 (m, 3H), 7.73 (s, 1H), 7.63~7.64 (m, 1H), 7.49~7.51 (m, 1H), 7.39~7.41 (m, 2H), 7.16 (s, 1H), 7.03~7.07 (m, 2H), 6.88~6.93 (m, 1H), 3.02 (s, 3H), 2.99 (d, *J* = 4.0 Hz, 3H), 2.91 (s, 3H), 2.37 (s, 3H).	601
149		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.33 (s, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 7.88~7.92 (m, 2H), 7.78 (s, 1H), 7.51~7.55 (m, 3H), 7.44 (d, *J* = 7.6 Hz, 1H), 7.17~7.27 (m, 2H), 7.10~7.13 (m, 3H), 3.03 (s, 3H), 2.94 (s, 6H), 2.57 (s, 3H).	583
150		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.19 (d, *J* = 7.2 Hz, 1H), 8.13 (s, 1H), 7.92~7.96 (m, 2H), 7.82 (s, 1H), 7.54~7.61 (m, 3H), 7.36 (s, 1H), 7.14~7.19 (m, 3H), 6.95 (t, *J* = 8.0 Hz, 1H), 3.36 (s, 3H), 2.97 (s, 3H), 2.78 (s, 3H).	587
151		**^{1}H-NMR** (MeOD, 400 MHz) δ 8.48~8.51 (d, *J* = 4.4 Hz, 1H), 8.30~8.32 (m, 1H), 8.15 (s, 1H), 7.95~7.99 (m, 3H), 7.91 (s, 1H), 7.78 (s, 1H), 7.52~7.56 (m, 2H), 7.25~7.30 (t, *J* = 8.8 Hz, 2H), 3.24 (s, 3H), 2.93~2.95 (m, 6H).	588
152		**^{1}H-NMR** (MeOD, 400 MHz) δ 8.52 (d, *J* = 4.8 Hz, 1H), 8.04~8.06 (m, 1H), 7.97~8.00 (m, 3H), 7.68 (s, 1H), 7.38~7.42 (m, 3H), 7.19 (s, 1H), 7.07 (s, 1H), 3.89 (s, 3H), 3.17 (s, 3H), 2.97 (s, 3H), 2.79~2.80 (m, 3H).	618

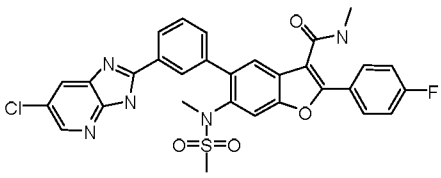
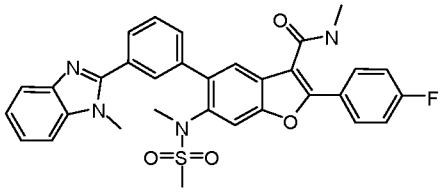
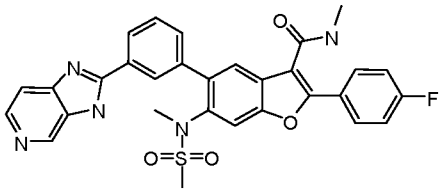
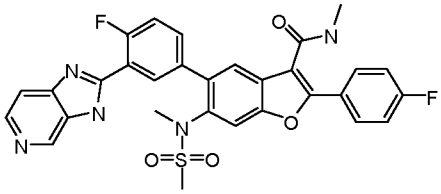
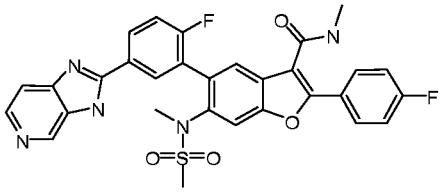
153		**^{1}H-NMR** (MeOD, 400 MHz) δ 8.39 (d, *J* = 4.8 Hz, 1H), 8.23 (s, 1H), 8.04~8.07 (m, 1H), 7.95~7.98 (m, 2H), 7.92 (s, 1H), 7.79 (s, 1H), 7.54~7.56 (m, 1H), 7.47~7.48 (m, 1H), 7.25~7.30 (t, *J* = 8.8 Hz, 2H), 3.24 (s, 3H), 2.98 (s. 3H), 2.92 (s, 3H), 2.3 (m, 3H).	602
154		**^{1}H-NMR**: ($CDCl_3$, 400 MHz) δ 8.54 (s, 1H), 8.41 (s, 1H), 8.08~9.00 (m, 1H), 7.89~7.92 (m, 2H), 7.86 (s, 1H), 7.64~7.65 (m, 1H), 7.24~7.30 (m, 3H), 7.14 (t, *J* = 8.4 Hz, 3H), 6.17 (s, 1H), 3.08 (s, 3H), 2.98 (d, *J* = 4.8 Hz, 3H), 2.84 (s, 3H).	588
155		**^{1}H-NMR** (MeOD, 400 MHz) δ 8.12 (s, 1H), 8.06 (d, *J* = 9.2 Hz, 1H), 7.91~7.97 (m, 3H), 7.82~7.86 (m, 1H), 7.76 (s, 1H), 7.50~7.55 (m, 1H), 7.27 (t, *J* = 8.8 Hz, 2H), 7.00 (d, *J* = 9.2 Hz, 1H), 4.03 (s, 3H), 3.23 (s, 3H), 2.97 (s, 3H), 2.93 (s, 3H).	618
156		**^{1}H-NMR** (MeOD, 400 MHz) δ 8.34 (d, *J* = 2.4 Hz, 1H), 8.32 (d, *J* = 2.4 Hz, 1H), 7.95~7.98 (m, 2H), 7.90 (s, 1H), 7.79~7.83 (m, 1H), 7.76 (s, 1H), 7.47~7.56 (m, 2H), 7.27 (t, *J* = 8.8 Hz, 2H), 3.21 (s, 3H), 2.97 (s, 3H), 2.93 (s, 3H), 2.88 (s, 3H).	602
157		**^{1}H-NMR** (DMSO, 400 MHz) δ 9.32 (s, 1H), 9.05 (s, 1H), 8.20~8.21 (m, 1H), 7.70-7.78 (m, 4H), 7.46~7.48 (m, 2H), 7.29~7.31 (m, 3H), 3.10 (s, 3H), 3.01 (s, 3H), 2.85 (s, 3H).	622

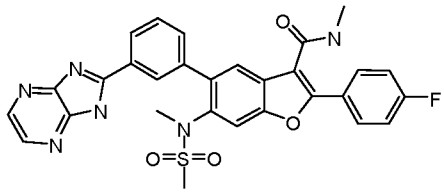
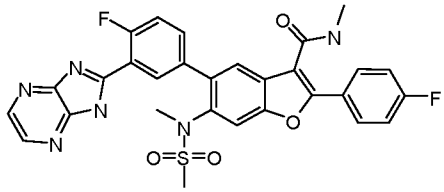
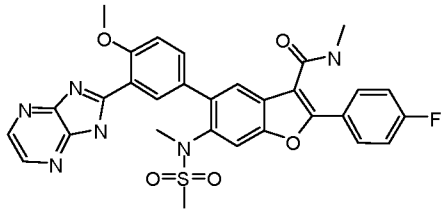
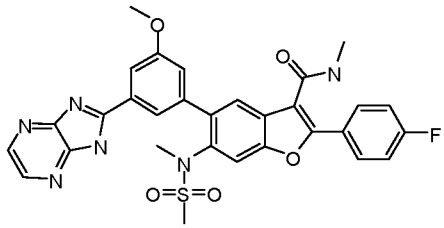
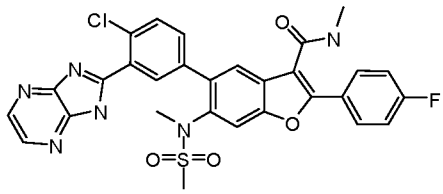
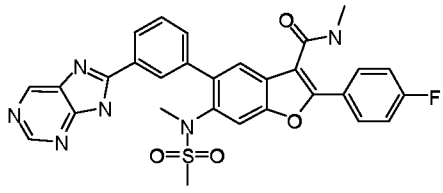
158		**^{1}H-NMR**: ($CDCl_3$, 400 MHz) δ 8.48 (s, 1H), 8.30~8.35 (m, 2H), 7.90~7.94 (m, 2H), 7.82 (s, 1H), 7.69~7.71 (m, 1H), 7.50 (s, 1H), 7.43~7.45 (m, 1H), 7.08~7.14 (m, 3H), 6.62 (br s, 1H), 4.12 (s, 3H), 3.08 (s, 3H), 2.94 (d, *J* = 4.8 Hz, 3H), 2.80 (s, 3H).	600
159		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.52~9.61 (m, 1H), 8.36 (s, 1H), 7.96~8.00 (m, 1H), 7.88~7.92 (m, 2H), 7.78~7.81 (m, 3H), 7.44 (s, 1H), 7.05~7.10 (m, 3H), 6.82~6.83 (m, 1H), 4.07 (s, 3H), 3.92 (s, 3H), 3.01 (s, 3H), 2.96 (d, *J* = 4.8 Hz, 3H), 2.86 (s, 3H).	630
160		**^{1}H-NMR** (MeOD, 400 MHz) δ 8.54 (d, *J* = 4.4 Hz, 1H), 8.43 (d, *J* = 4.0 Hz, 1H), 7.95~7.98 (m, 2H), 7.93 (s, 1H), 7.89 (s, 1H), 7.83 (s, 1H), 7.76 (s, 1H), 7.64~7.67 (m, 1H), 7.30 (s, 1H), 7.28 (t, *J* = 8.8 Hz, 2H), 3.97 (s, 3H), 3.18 (s, 3H), 2.98 (s, 3H), 2.92 (s, 3H).	600
161		**^{1}H-NMR** (MeOD, 400 MHz) δ 7.85~7.91 (m, 2H), 7.77 (s, 1H), 7.65 (s, 1H), 7.64 (s, 1H), 7.59 (s, 1H), 7.58 (s, 1H), 7.32 (s, 1H), 7.17 (t, *J* = 8.8 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 1H), 3.94 (s, 3H), 3.89 (s, 3H), 3.11 (s, 3H), 2.91 (s, 3H), 2.86 (s, 3H).	630

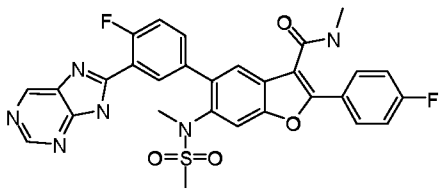
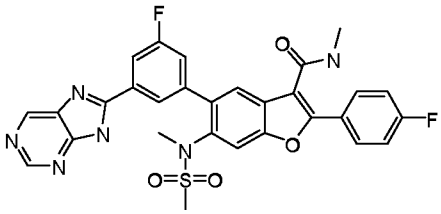
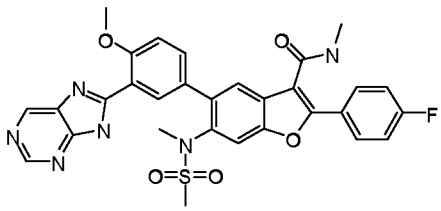
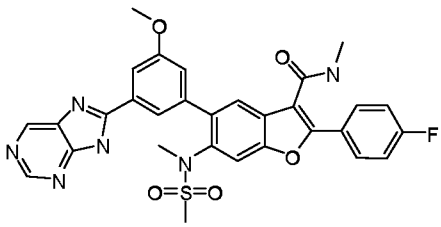
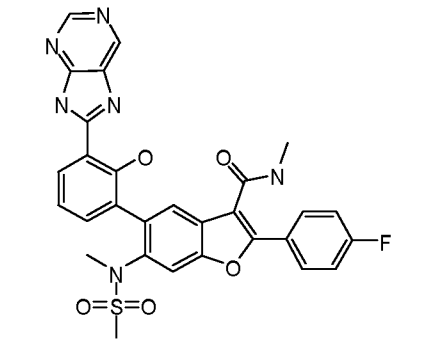
162		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.32 (d, *J* = 8.0 Hz, 1H), 7.86~7.92 (m, 3H), 7.80~7.82 (m, 2H), 7.69 (s, 1H), 7.43 (d, *J* = 4.0 Hz, 1H), 7.351~7.35 (m, 1H), 7.17~7.22 (m, 2H), 3.89 (s, 3H), 3.08 (s, 3H), 2.91(s, 3H), 2.84 (s, 3H), 2.78 (s, 3H).	614
163		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.22 (s, 1H), 7.84~7.89 (m, 3H), 7.73 (s, 1H), 7.66~7.67 (m, 1H), 7.52 (s, 1H), 7.09~7.14 (m, 4H), 3.87 (s, 3H), 3.04 (s, 3H), 2.87 (s, 3H), 2.77 (s, 3H).	634
164		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.18~8.19 (m, 1H), 7.97~8.01 (m, 3H), 7.77 (s, 1H), 7.66 (s, 1H), 7.45~7.47 (m, 1H), 7.11~7.21 (m, 4H), 3.39 (s, 3H), 3.26 (s, 3H), 2.96 (s, 3H), 2.66 (s, 3H).	600
165		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.51 (d, *J* = 4.0 Hz, 1H), δ 8.26 (d, *J* = 8.0 Hz, 1H), 8.05 (s, 1H), 7.98~8.00 (m, 2H), 7.97 (s, 1H), 7.90 (s, 1H), 7.74~7.78 (m, 2H), 7.49~7.52 (m, 2H), 7.26~7.30 (m, 2H), 3.22 (s, 3H), 2.99 (s, 3H), 2.96 (s, 3H).	604
166		**^{1}H-NMR** (400 MHz, MeOH) δ 7.96~8.02 (m, 4H), 7.90 (s, 1H), 7.74~7.77 (m, 3H), 7.25~7.30 (m, 2H), 6.90 (d, *J* = 8.0 Hz, 1H), 4.02 (s, 3H), 3.22 (s, 3H), 2.98 (s, 3H), 2.96 (s, 3H).	634

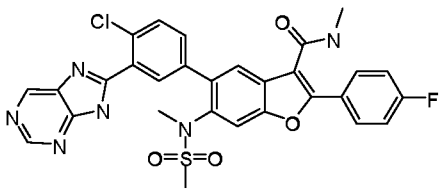
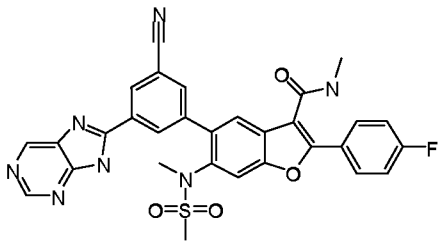
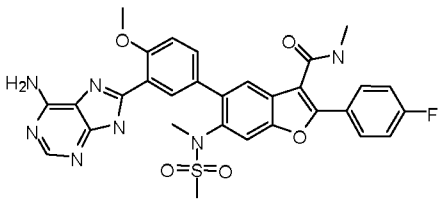
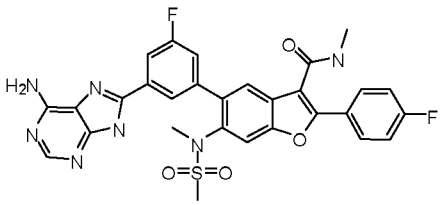
167		**^{1}H-NMR** (MeOD, 400 MHz) δ 8.45 (d, *J* = 8.0 Hz, 1H), 7.96~7.99 (m, 3H), 7.91 (s, 1H), 7.76~7.87 (d, *J* = 8.0 Hz, 3H), 7.50~751 (d, *J* = 4.0 Hz, 1H), 7.36~7.31 (m, 2H), 3.21 (s, 3H), 3.00 (s, 3H), 2.95 (s, 3H), 2.84 (s, 3H).	618
168		**^{1}H-NMR** (MeOD, 400 MHz) δ 8.42~8.43 (d, *J* = 4.0 Hz, 1H), 8.11~8.12 (d, *J* = 4.0 Hz, 1H), 7.97~8.01 (m, 3H), 7.89 (s, 1H), 7.79 (s, 1H), 7.24 (s, 2H), 7.26~7.30 (m, 2H), 3.22 (s, 3H), 2.97 (s, 3H), 2.96 (s, 3H)	638
169		**^{1}H-NMR** (MeOD, 400 MHz) δ 8.50 (s, 1H), 8.42~8.45 (m, 2H), 8.23~8.25 (m, 1H), 7.98 (s, 1H), 7.79~7.91 (m, 3H), 7.73 (s, 1H), 7.45~7.48 (m, 1H), 7.17~7.21 (m, 2H), 3.21 (s, 3H), 2.86~2.89 (m, 6H).	595
170		**^{1}H-NMR** (MeOD, 400 MHz) δ 8.42~8.44 (m, 2H), 8.06 (s, 1H), 7.98~8.02 (m, 4H), 7.83 (s, 1H), 7.28~7.32 (m, 2H), 6.87~6.89 (m, 1H), 4.02 (s, 3H), 3.31 (s, 3H), 2.97~2.99 (m, 6H).	625
171		**^{1}H-NMR** (MeOD, 400 MHz) δ 8.72 (s, 1H), 8.68 (s, 1H), 8.49~8.51 (m, 1H), 8.15 (s, 1H), 8.98~9.00 (m, 3H), 7.85 (s, 1H), 7.61~.63 (m, 1H), 7.29~7.34 (m, 2H), 3.31 (s, 3H), 3.01 (s, 3H), 2.92~2.95 (m, 6H).	609

172		**^{1}H-NMR** (MeOD, 400 MHz) δ 8.51 (s, 1H), 8.47 (s, 1H), 8.38 (s, 1H), 8.07 (s, 1H), 8.03 (s, 1H), 7.94~7.97 (m, 3H), 7.99 (s, 1H), 7.24~7.28 (m, 2H), 3.29 (s, 3H), 2.94~2.95 (m, 6H).	629
173		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.13 (s, 1H), 7.80~7.94 (m, 4H), 7.65 (s, 1H), 7.48 (d, *J* = 7.6 Hz, 1H), 7.07~7.35 (m, 4H), 6.77 (d, *J* = 8.0 Hz, 1H), 3.86 (s, 3H), 2.96 (s, 3H), 2.92 (d, *J* = 4.4 Hz, 3H), 2.88 (s, 3H).	600
174		**^{1}H NMR** ($CDCl_3$, 400 MHz) δ 8.03~8.07 (m, 2H), 7.78~7.81 (m, 2H), 7.38~7.45 (m, 3H), 7.04~7.15 (m, 3H), 6.79 (s, 1H), 6.27 (d, *J* = 2.0 Hz, 1H), 3.42 (s, 3H), 2.91 (d, *J* = 4.4 Hz, 3H), 2.83 (s, 3H).	586
175		**^{1}H NMR** ($CDCl_3$, 400 MHz) δ 8.19 (s, 1H), 8.15 (d, *J* = 3.6 Hz, 1H), 8.09 (d, *J* = 7.6 Hz, 1H), 7.86~7.89 (m, 3H), 7.57 (s, 2H), 7.43 (s, 1H), 7.06~7.18 (m, 3H), 6.05 (s, 1H), 3.49 (s, 3H), 3.12 (s, 3H), 2.94 (d, *J* = 4.8 Hz, 3H), 2.83 (s, 3H).	664
176		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 7.96~8.00 (m, 2H), 7.84 (s, 1H), 7.81 (s, 1H), 7.76 (d, *J* = 7.6 Hz, 1H), 7.67~7.71 (m, 1H), 7.54~7.61 (m, 4H), 7.13~7.18 (m, 2H), 6.72 (d, *J* = 4 Hz, 1H), 4.08 (s, 3H), 3.14 (s, 3H), 2.96 (d, *J* = 4.4 Hz, 3H), 2.88 (s, 3H).	584

177		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.54 (d, *J* = 4.0 Hz, 1H), 8.35 (s, 1H), 8.27 (s, 1H), 8.23 (s, 1H), 8.17(s, 1H), 8.04 (s, 1H), 7.97~8.01 (m, 2H), 7.63~7.66 (m, 2H), 7.38~7.43 (m, 2H), 3.14 (s, 3H), 2.92 (s, 3H), 2.80 (d, *J* = 4.0 Hz, 3H).	604
178		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 7.96~8.00 (m, 4H), 7.84 (s, 1H), 7.81 (s, 1H), 7.76 (d, *J* = 7.6 Hz, 1H), 7.67~7.71 (m, 1H), 7.54~7.61 (m, 4H), 7.13~7.18 (m, 2H), 6.72 (d, *J* = 4 Hz, 1H), 4.08 (s, 3H), 3.14 (s, 3H), 2.96 (d, *J* = 4.4 Hz, 3H), 2.88 (s, 3H).	583
179		**^{1}H-NMR** (MeOD, 400 MHz) δ 9.23 (s, 1H), 8.53 (d, *J* = 6.4 Hz, 1H), 8.39 (s, 1H), 8.28 (d, *J* = 8 Hz, 1H), 8.09 (d, *J* = 6.4 Hz, 1H), 7.79~8.01 (m, 2H), 7.92 (s, 1H), 7.71~7.83 (m, 3H), 7.27~7.33 (m, 2H), 3.24 (s, 3H), 2.95 (s, 3H), 2.92 (s, 3H).	570
180		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.78 (s, 1H), 8.67~8.70 (m, 1H), 8.61~8.63 (m, 1H), 8.39~8.41 (m, 1H), 8.24~8.30 (m, 1H), 8.16 (s, 1H), 7.85~7.88 (m, 2H), 7.75 (s, 1H), 7.50 (t, *J* = 8.8 Hz, 2H), 5.70 (s, 1H), 3.28 (s, 3H), 3.09 (s, 3H), 2.88 (d, *J* = 4.8 Hz, 3H).	588
181		**^{1}H-NMR** ($CDCl_3$, 400 MHz) 9.08 (s, 1H), 8.27~8.32 (m, 2H), 8.12 (s, 1H), 7.86~7.89 (m, 2H), 7.77 (s, 2H), 7.51 (s, 1H), 7.27 (t, *J* = 8.8 Hz, 1H), 7.11 (t, *J* = 8.0 Hz, 2H), 6.53 (s, 1H), 3.23 (s, 3H), 2.90 (d, *J* = 4.0 Hz, 3H), 2.70 (s, 3H).	588

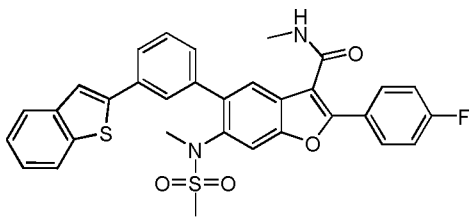
182		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.30~8.57 (m, 4H), 7.99~8.06 (m, 3H), 7.69~7.70 (m, 3H), 7.40~7.44 (m, 2H), 3.18 (s, 3H), 2.94 (s, 3H), 2.81 (s, 3H).	571
183		**^{1}H-NMR** (MeOD, 400 MHz,) δ 8.43 (s, 2H), 8.34 (d, *J* = 7.2 Hz, 1H), 7.96~8.00 (m, 2H), 7.88 (s, 1H), 7.76~7.79 (m, 2H), 7.43~7.47 (m, 1H), 7.24~7.28 (m, 2H), 3.22 (s, 3H), 2.94 (s, 3H), 2.93 (s, 3H).	589
184		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 10.78 (br s, 1H), 8.54 (s, 1H), 8.40 (s, 2H), 7.84~7.88 (m, 2H), 7.72~7.74 (m, 2H), 7.50 (s, 1H), 7.08~7.13 (m, 3H), 6.68 (s, 1H), 4.14 (s, 3H), 3.07 (s, 1H), 3.13 (s, 3H), 2.96 (d, *J* = 4.8 Hz, 3H), 2.82 (s, 3H).	601
185		**^{1}H-NMR** (MeOD, 400 MHz) δ 8.29 (s, 2H), 7.87~7.90 (m, 2H), 7.79 (s, 1H), 7.75 (s, 1H), 7.72 (s, 1H), 7.67 (s, 1H), 7.28 (s, 1H), 7.15~7.20 (m, 2H), 3.87 (s, 3H), 3.09 (s, 3H), 2.86 (d, *J* = 4.8 Hz, 6H).	601
186		**^{1}H-NMR** (MeOD, 400 MHz) δ 8.49 (s, 2H), 7.97~8.01 (m, 3H), 7.90 (s, 1H), 7.74~7.78 (m, 3H), 7.26~7.30 (m, 2H), 3.22 (s, 3H), 2.98 (s, 3H), 2.96 (s, 3H).	605
187		**^{1}H-NMR** (DMSO, 400 MHz) δ 9.32 (s, 1H), 9.05 (s, 1H), 8.20~8.21 (m, 1H), 7.70~7.77 (m, 4H), 7.46~7.48 (m, 2H), 7.29~7.31 (m, 3H), 3.10 (s, 3H), 3.01 (s, 3H), 2.85 (s, 3H).	571

188		**^{1}H-NMR** (MeOD, 400 MHz) δ 9.04 (s, 1H), 8.89 (s, 1H), 8.28~8.31 (m, 1H), 7.87~7.91 (m, 2H), 7.81 (s, 1H), 7.67~7.73 (m, 2H), 7.36~7.41 (m, 2H), 7.36~7.41 (m, 1H), 7.19 (t, *J* = 8.8 Hz, 2H), 3.15 (s, 3H), 2.86 (s, 6H).	589
189		**^{1}H-NMR** (DMSO, 400 MHz) δ 9.10 (s, 1H), 8.95 (s, 1H), 8.52~8.53 (m, 1H), 8.15 (s, 1H), 7.97~8.08 (m, 4H), 7.70 (s, 1H), 7.50~7.52 (m, 1H), 7.38~7.42 (m, 2H), 3.18 (s, 3H), 2.98 (s. 3H), 2.79~2.80 (m, 3H).	589
190		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.02 (s, 1H), 8.91 (s, 1H), 8.51 (s, 1H), 7.90~7.94 (m, 2H), 7.77 (s, 1H), 7.68~7.70 (m, 1H), 7.55 (s, 1H), 7.12~7.18 (m, 3H), 4.17 (s, 3H), 3.33 (s, 1H), 3.13 (s, 3H), 2.93 (s, 3H), 2.80 (s, 3H).	601
191		**^{1}H-NMR** (MeOD, 400 MHz) δ 9.10 (s, 1H), 8.98 (s, 1H), 7.95~7.98 (m, 2H), 7.85~7.89 (m, 2H), 7.81 (s, 1H), 7.74 (s, 1H), 7.39 (s, 1H), 7.24~7.28 (m, 2H), 3.97 (s, 3H), 317 (s, 3H), 2.95 (s, 3H), 2.92 (s, 3H).	601
192		**^{1}H-NMR** (DMSO, 400 MHz) δ 9.14 (s, 1H), 8.95 (s, 1H), 8.48~8.49 (m, 1H), 8.16~8.18 (m, 1H), 7.95~7.99 (m, 3H), 7.52 (s, 1H), 7.37~7.41 (m, 3H), 7.11~7.15 (m, 1H), 3.16 (s, 3H), 2.79 (s, 3H), 2.77 (s, 3H).	587

193		**^{1}H-NMR** (DMSO, 400 MHz) δ 9.29 (s, 1H), 9.06 (s, 1H), 8.59 (d, *J* = 4.0 Hz, 1H), 8.04~8.08 (m, 3H), 8.01 (d, *J* = 4.0 Hz, 1H), 7.83~7.85 (m, 2H), 7.76~7.78 (m, 2H), 3.21 (s, 3H), 3.10 (s, 3H), 2.88 (d, *J* = 8.0 Hz, 3H).	**605**
194		**^{1}H-NMR** (MeOD, 400 MHz) δ 9.21 (s, 1H), 9.05 (s, 1H), 8.61 (s, 1H), 8.56 (s, 1H), 8.10 (s, 1H), 7.97~7.99 (m, 3H), 7.78 (s, 1H), 7.27~7.31 (m, 2H), 3.31 (s, 3H), 2.97~3.00 (m, 6H).	**596**
195		**^{1}H-NMR** (DMSO, 400 MHz) δ 8.55~8.56 (m, 1H), 8.30~8.31 (m, 1H), 8.04 (s, 1H), 8.04~7.97 (m, 2H), 7.68~7.70 (m, 1H), 7.59 (s, 1H), 7.40~7.45 (m, 3H), 4.11 (br s, 2H), 3.15 (d, *J* = 4.0 Hz, 6H), 3.00 (s, 3H), 2.80 (d, *J* = 4.8 Hz, 3H).	**616**
196		**^{1}H-NMR** (DMSO, 400 MHz) δ 8.07~8.26 (m, 5H), 7.78~7.81 (m, 1H), 7.42~7.50 (m, 3H), 7.33 (s, 1H), 4.20 (br s, 2H), 3.05 (s, 3H), 2.97 (s, 3H), 2.88 (s, 3H).	**604**

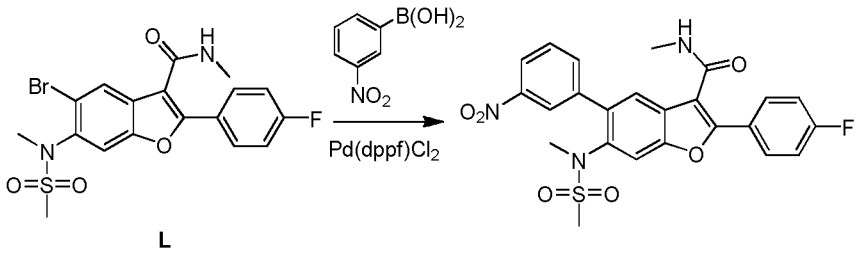
Example 7

Preparation of Compound **197**



197

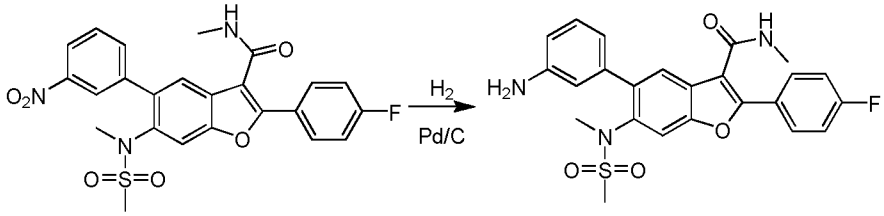
Step 1 - Synthesis of 2-(4-fluorophenyl)-N-methyl-6-(N-methylmethylsulfonamido)-5-(3-nitrophenyl)benzofuran-3-carboxamide



L

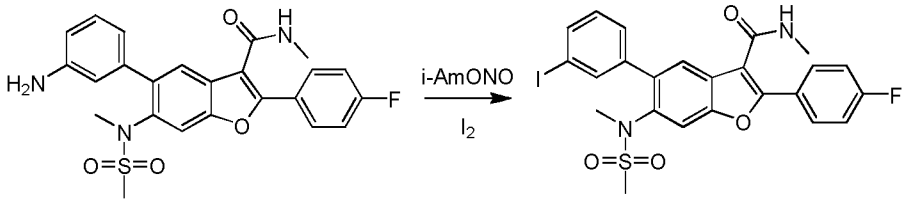
To a degassed solution of Compound **L** (prepared as described in Example 1, Step 11, 2.0 g, 4.39 mmol) and 3-nitrophenylboronic acid (880 mg, 5.27 mmol) in dry DMF (1.5 mL) were added $Pd(dppf)Cl_2$ (20 mg) and K_3PO_4 (1.86 g, 8.79 mmol) under N_2. The mixture was allowed to stir at 90 °C for about 15 hours. After the mixture was cooled to room temperature, diluted with EtOAc and filtered, the filtrate was washed with H_2O, brine, and dried over Na_2SO_4. After concentrated, the crude was purified using column chromatography (PE : EtOAc = 3 : 1) to provide 2-(4-fluorophenyl)-N-methyl-6-(N-methylmethylsulfonamido)-5-(3-nitrophenyl)benzofuran-3-carboxamide (1.78 g, 84%). **^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.24 (s, 1H), 8.18 (d, J = 8.4 Hz, 1H), 7.83~7.87 (m, 2H), 7.79 (d, J = 5.6 Hz, 1H), 7.77 (s, 1H), 7.58 (s, 1H), 7.55 (t, J = 4.0 Hz, 1H), 7.15 (t, J = 8.8 Hz, 2H), 5.83 (d, J = 3.2 Hz, 1H), 3.09 (s, 3H), 2.92 (d, J = 4.8 Hz, 3H), 2.73 (s, 3H).

Step 2 - Synthesis of 5-(3-aminophenyl)-2-(4-fluorophenyl)-N-methyl-6-(N-methylmethylsulfonamido)benzofuran-3-carboxamide



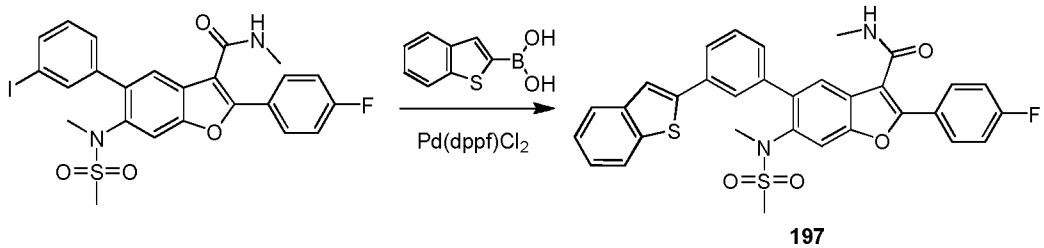
To a solution of 2-(4-fluorophenyl)-N-methyl-6-(N-methylmethylsulfonamido)-5-(3-nitrophenyl)benzofuran-3-carboxamide (1.0 g, 2.01 mmol) in MeOH (30 mL), Pd/C (200 mg) was added and the resulting reaction mixture was allowed to stir under 40 psi of H_2 atmosphere for 24 hours at 25 °C. Then the reaction mixture was filtered, and the filtrate was concentrated *in vacuo* to provide 5-(3-aminophenyl)-2-(4-fluorophenyl)-N-methyl-6-(N-methylmethylsulfonamido)benzofuran-3-carboxamide (846 mg, 89%). **^{1}H-NMR** (DMSO, 400 MHz) δ 8.49 (d, J = 4.8 Hz, 1H), 7.94~7.97 (m, 2H), 7.84 (s, 1H), 7.43 (s, 1H), 7.38 (t, J = 9.2 Hz, 2H), 7.03 (t, J = 8.0 Hz, 1H), 6.53~6.58 (m, 3H), 5.09 (s, 2H), 3.13 (d, J = 5.6 Hz, 3H), 3.04 (s, 3H), 2.81 (s, 3H). MS $(M+H)^+$: 468.

Step 3 - Synthesis of 2-(4-fluorophenyl)-5-(3-iodophenyl)-N-methyl-6-(N-methylmethylsulfonamido)benzofuran-3-carboxamide



To a stirred solution of 5-(3-aminophenyl)-2-(4-fluorophenyl)-N-methyl-6-(N-methylmethylsulfonamido)benzofuran-3-carboxamide (1.5 g, 3.21 mmol) in MeCN (20 mL) was added I_2 (488.6 mg, 1.93 mmol) and CuI (6 mg) at 0 °C, then i-AmONO (394.6 mg, 3.37 mmol) was added dropwise. After the solution was allowed to stir at 25 °C for 6 hours, the mixture was heated to 90 °C for 1 hour. The mixture was diluted with $Na_2S_2O_3$ and concentrated to remove the organic solvent, and then the residue obtained was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue obtained was purified using flash column chromatography (PE : EtOAc = 10 : 1) to provide 2-(4-fluorophenyl)-5-(3-iodophenyl)-N-methyl-6-(N-methylmethylsulfonamido)benzofuran-3-carboxamide (1.17 g, 65%). **^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 7.85~7.88 (m, 2H), 7.72 (d, J = 7.6 Hz, 2H), 7.66 (d, J = 8.0 Hz, 1H), 7.53 (s, 1H), 7.38 (d, J = 7.6 Hz, 1H), 7.14 (t, J = 6.0 Hz, 2H), 5.77 (d, J = 4.0 Hz, 1H), 3.06 (s, 3H), 2.92 (d, J = 4.8 Hz, 3H), 2.61 (s, 3H). MS $(M+H)^+$: 579.

Step 4 – Synthesis of 5-(3-(benzo[b]thiophen-2-yl)phenyl)-2-(4-fluorophenyl)-N-methyl-6-(N-methylmethylsulfonamido)benzofuran-3-carboxamide (Compound 197)

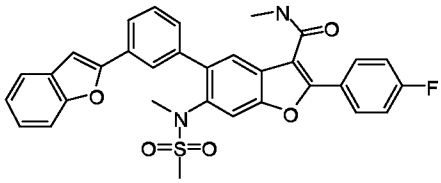
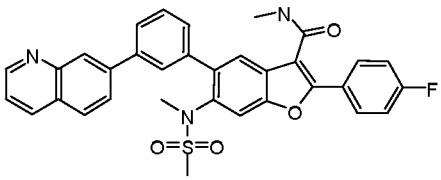
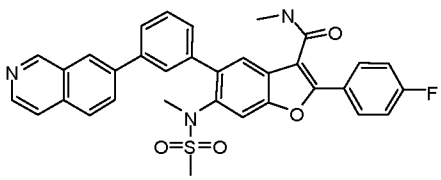


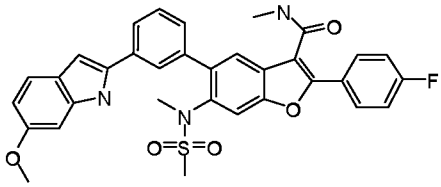
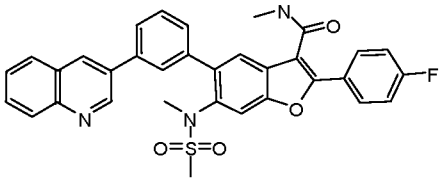
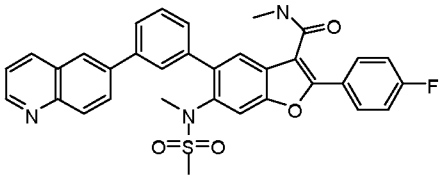
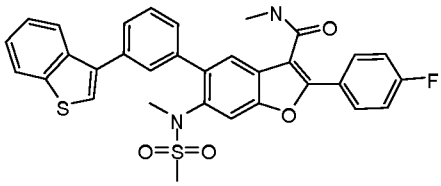
197

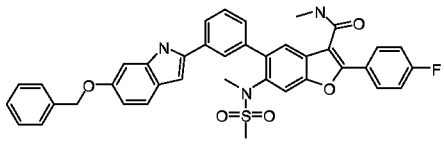
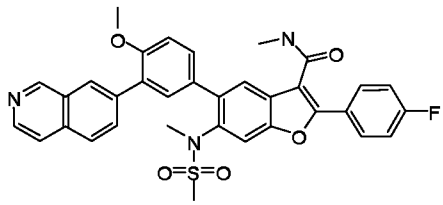
To a degassed solution of 5-(3-aminophenyl)-2-(4-fluorophenyl)-N-methyl-6-(N-methylmethylsulfonamido)benzofuran-3-carboxamide (70 mg, 121.0 umol) and benzo[b]thiophen-2-ylboronic acid (26.1 mg, 145.1 umol) in dry DMF (1.5 mL) were added $Pd(dppf)Cl_2$ (5 mg) and K_3PO_4 (51.4 mg, 171.2 umol) under N_2. The mixture was heated to 90 °C for about 15 hours. After the reaction mixture was cooled to room temperature, diluted with EtOAc and filtered, the filtrate was washed with H_2O, brine, dried over Na_2SO_4. After

concentrated, the crude was purified using prep-TLC (PE : EtOAc = 3 : 1) to provide 5-(3-(benzo[b]thiophen-2-yl)phenyl)-2-(4-fluorophenyl)-N-methyl-6-(N-methylmethylsulfonamido)benzofuran-3-carboxamide (Compound **197**, 38 mg, 60%). **^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 7.95~7.98 (m, 2H), 7.85 (d, *J* = 7.2 Hz, 3H), 7.80 (d, *J* = 7.6 Hz, 1H), 7.76 (d, *J* = 6.8 Hz, 1H), 7.64 (t, *J* = 3.2 Hz, 2H), 7.52 (d, *J* = 7.6 Hz, 1H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.37 (t, *J* = 8.8 Hz, 2H), 7.22 (t, *J* = 8.8 Hz, 2H), 6.04 (d, *J* = 4.4 Hz, 1H), 3.20 (s, 3H), 2.99 (d, *J* = 4.8 Hz, 3H), 2.67 (s, 3H). MS $(M+H)^+$: 585.

Compounds **198-207**, depicted in the table below, were prepared using the method described in Example 7 and substituting the appropriate reactants and/or reagents.

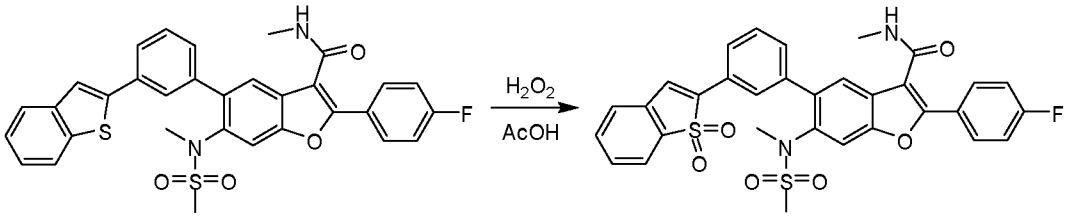
Compound	Structure	NMR	MS $(M+H)^+$
198		**^{1}H-NMR** (DMSO, 400 MHz) δ 8.53 (d, *J* = 4.8 Hz, 1H), 8.02 (d, *J* = 6.8 Hz, 1H), 8.00 (d, *J* = 5.6 Hz, 2H), 7.93 (d, *J* = 7.6 Hz, 1H), 7.62~7.67 (m, 3H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.48 (t, *J* = 6.0 Hz, 2H), 7.39~7.45 (m, 2H), 7.24~7.33 (m, 2H), 3.11 (s, 3H), 2.96 (s, 3H), 2.80 (d, *J* = 4.4 Hz, 3H).	**569**
200		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.19 (s, 1H), 8.71 (d, *J* = 7.2 Hz, 2H), 8.09~8.20 (m, 2H), 7.88~7.91 (m, 3H), 7.77~7.82 (m, 3H), 7.53~7.60 (m, 3H), 7.11~7.16 (m, 2H), 6.04 (s, 1H), 3.12 (s, 3H), 2.93 (d, *J* = 4.4 Hz, 3H), 2.72 (s, 3H).	**580**
201		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.67 (s, 1H), 8.60 (s, 2H), 8.43 (d, *J* = 8.8 Hz, 1H), 8.15 (m, 2H), 7.95~8.03 (m, 4H), 7.78 (d, *J* = 7.2 Hz, 1H), 7.58~7.68 (m, 3H), 7.22~7.27 (m, 2H), 5.91 (s, 1H) 3.12 (s, 3H), 3.01 (d, *J* = 4.8 Hz, 3H), 2.96 (s, 3H).	**580**

202		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.94 (s, 1H), 7.89~7.86 (m, 2H), 7.82 (s, 1H), 7.79 (s, 1H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.46 (s, 1H), 7.43~7.40 (m, 2H), 7.26 (d, *J* = 7.6 Hz, 1H), 7.13 (t, *J* = 8.4 Hz, 2H), 6.83 (s, 1H), 6.70 (d, *J* = 8.4 Hz, 2H), 5.83 (d, *J* = 4.0 Hz, 1H), 3.78 (s, 3H), 2.91 (d, *J* = 6.8 Hz, 9H).	598
203		**^{1}H NMR** ($CDCl_3$, 400 MHz) δ 9.18 (s, 1H), 8.35 (s, 1H), 8.06 (d, *J* = 8.8 Hz, 1H), 7.67~7.86 (m, 3H), 7.66 (s, 1H), 7.64 (d, *J* = 1.2 Hz, 1H), 7.52~7.56 (m, 2H), 7.46~7.52 (m, 3H), 7.44 (d, *J* = 1.6 Hz, 1H), 7.13 (t, *J* = 8.8 Hz, 2H), 5.94 (d, *J* = 4.8 Hz, 1H), 3.09 (s, 3H), 2.91 (d, *J* = 4.8 Hz, 3H), 2.66 (s, 3H).	580
204		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.85~8.88 (m, 1H), 8.05~8.20 (m, 2H), 7.99 (d, *J* = 1.6 Hz, 1H), 7.97 (d, *J* = 1.6 Hz, 1H), 7.87~7.91 (m, 2H), 7.80 (d, *J* = 9.2 Hz, 2H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.56 (s, 1H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.37~7.43 (m, 2H), 7.14 (t, *J* = 8.8 Hz, 2H), 5.80 (d, *J* = 4.4 Hz, 1H), 3.10 (s, 3H), 2.92 (d, *J* = 4.8 Hz, 3H), 2.64 (s, 3H).	580
205		**^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.92~7.95 (m, 4H), 7.83 (s, 1H), 7.67 (s, 1H), 7.60~7.62 (m, 2H), 7.53~7.57 (m, 1H), 7.45~7.49 (m, 2H), 7.36~7.39 (m, 2H), 7.16~7.20 (m, 2H), 5.84 (s, 1H), 3.19 (s, 3H), 2.97 (d, *J* = 4.8 Hz, 3H), 2.62 (s, 3H).	585

206		**^{1}H NMR** ($CDCl_3$, 400 MHz) δ 8.92 (s, 1H), 7.92~7.96 (m, 2H), 7.87 (s, 2H), 7.66~7.68 (m, 1H), 7.53 (s, 1H), 7.45~7.49 (m, 3H), 7.30~7.39 (m, 3H), 7.17~7.21 (m, 2H), 6.97 (s, 1H), 6.83~6.85 (m, 1H), 6.76 (s, 1H), 5.84 (s, 1H), 5.10 (s, 2H), 2.93~2.98 (m, 9H).	674
207		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.25 (s, 1H), 8.46 (d, J = 5.6 Hz, 1H), 8.16 (s, 1H), 7.94 (d, J = 8.4 Hz, 1H), 7.86~7.90 (m, 2H), 7.81 (d, J = 10.8 Hz, 2H), 7.64 (d, J = 4.8 Hz, 1H), 7.51 (t, J = 2.0 Hz, 2H), 7.42~7.45 (m, 1H), 7.14 (t, J = 8.8 Hz, 2H), 7.05 (d, J = 8.4 Hz, 1H), 5.76 (d, J = 3.6 Hz, 1H), 3.85 (s, 3H), 3.09 (s, 3H), 2.92 (d, J = 4.8 Hz, 3H), 2.75 (s, 3H).	610

Example 8

Preparation of Compound **208**

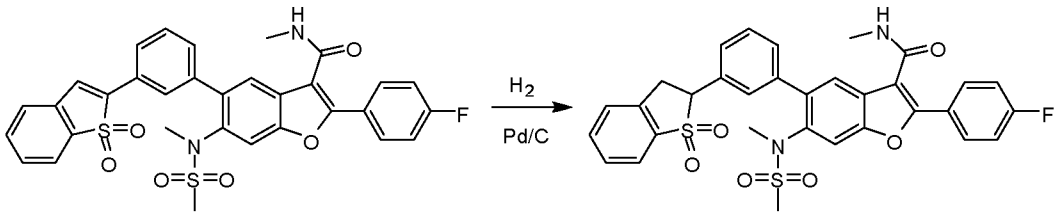


197 208

To a solution of Compound **197** (100 mg, 0.38 mmol) in 10 mL of acetic acid was added H_2O_2 (2 mL) and the resulting reaction mixture was heated to 65 °C and allowed to stir at this temperature for 3 hours. The reaction was then was quenched with aq. Na_2SO_3 and extracted with EtOAc. The organic phase was washed with H_2O and brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue obtained was purified using preparative HPLC to provide Compound **208** (45 mg, 28%). ^{1}H NMR: ($CDCl_3$, 400 MHz) δ 7.92 (s, 1H), 7.86~7.90 (m, 2H), 7.74~7.76 (s, 2H), 7.69~7.70 (m, 1H), 7.43~7.56 (m, 5H), 7.34~7.38 (m, 2H), 7.14 (t, J = 8.8 Hz, 2H), 5.84 (s, 1H), 3.18 (s, 3H), 2.93 (d, J = 4.8 Hz, 3H), 2.54 (s, 3H). MS $(M+H)^+$: 617.

Example 9

Preparation of Compound **209**

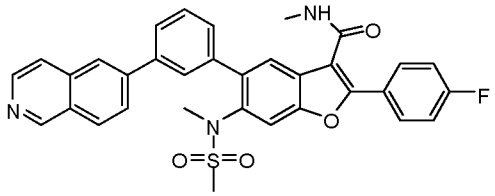


208 209

To a solution of Compound **208** (30 mg, 0.13 mmol) in 10 mL of MeOH, was added Pd/C (10 mg), and the resulting reaction was placed under H_2 atmosphere (40 Psi) and allowed to stir at room temperature for 24 hours. The reaction mixture was then filtered and concentrated *in vacuo*, and the residue obtained was purified using preparative HPLC to provide Compound **209** (20 mg, 85%). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.86~7.90 (m, 2H), 7.72~7.73 (m, 2H), 7.54~7.58 (m, 2H), 7.39~7.46 (m, 6H), 7.11~7.16 (m, 2H), 5.77~5.78 (m, 1H), 4.68 (t, J = 8.2 Hz, 1H), 3.64 (d, J = 8.2 Hz, 2H), 3.09 (s, 3H), 2.93 (d, J = 4.8 Hz, 3H), 2.46 (s, 3H). MS $(M+H)^+$: 619.

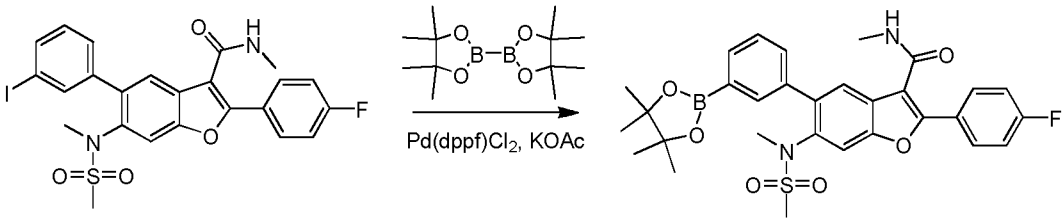
Example 10

Preparation of Compound **210**



210

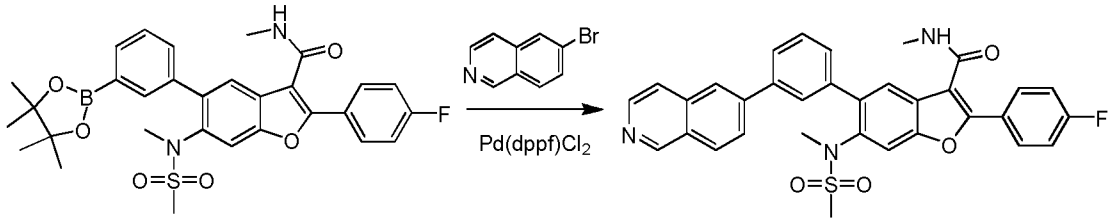
Step 1 - Synthesis of 2-(4-fluorophenyl)-N-methyl-6-(N-methylmethylsulfonamido)-5-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)benzofuran-3-carboxamide



To a degassed solution of 2-(4-fluorophenyl)-5-(3-iodophenyl)-N-methyl-6-(N-methylmethylsulfonamido)benzofuran-3-carboxamide (Prepared as described in Example 7, Step 3, 200 mg, 0.346 mmol) and pinacol diborane (132 mg, 0.519 mmol) in dry DMF (1.5 mL) was

added $Pd(dppf)Cl_2$ (10 mg) and KOAc (102 mg, 1.04 mmol). The mixture was placed under N_2 atmosphere, then heated to 90 °C and allowed to stir at this temperature for about 15 hours. The reaction mixture was cooled to room temperature, filtered, and the filtrate was washed with H_2O, brine, dried over Na_2SO_4, filtered and concentrated *in vacuo* to provide 2-(4-fluorophenyl)-N-methyl-6-(N-methylmethylsulfonamido)-5-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)benzofuran-3-carboxamide (200 mg, 100%), which was used without further purification. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.88~7.92 (m, 2H), 7.75~7.78 (m, 2H), 7.72 (s, 1H), 7.56 (s, 1H), 7.49~7.52 (m, 1H), 7.37~7.41 (m, 1H), 7.11~7.15 (m, 2H), 5.81~5.82 (m, 1H), 3.05 (s, 3H), 2.93 (d, J = 4.8 Hz, 3H), 2.51 (s, 3H), 1.29 (s, 12H). MS $(M+H)^+$: 579.

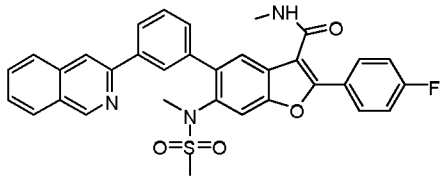
Step 2 - Synthesis of 2-(4-fluorophenyl)-5-(3-(isoquinolin-6-yl)phenyl)-N-methyl-6-(N-methylmethylsulfonamido)benzofuran-3-carboxamide (Compound 210)



210

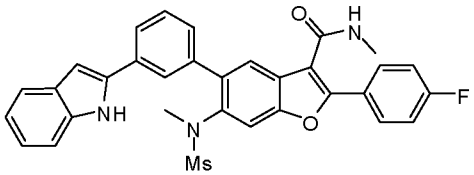
To a degassed solution of 2-(4-fluorophenyl)-N-methyl-6-(N-methylmethylsulfonamido)-5-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)benzofuran-3-carboxamide (90 mg, 0.189 mmol) and 6-bromo-isoquinoline (51 mg, 0.246 mmol) in dry DMF (1.5 mL) was added $Pd(dppf)Cl_2$ (20 mg) and K_3PO_4 (81 mg, 0.381 mmol) under N_2. The mixture was heated to 100 °C for about 15 hours. The reaction mixture was cooled to room temperature and filtered. The filtrate was washed with H_2O, brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue obtained was purified using prep-TLC (PE : EtOAc = 2 : 1) to provide 2-(4-fluorophenyl)-5-(3-(isoquinolin-6-yl)phenyl)-N-methyl-6-(N-methylmethylsulfonamido)benzofuran-3-carboxamide (Compound **210**, 85 mg, 93%). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 9.62 (s, 1H), 8.46 (d, J = 6.0 Hz, 1H), 8.38 (s, 1H), 8.31~8.33 (m, 1H), 8.21~8.23 (m, 1H), 8.15 (d, J = 6.0 Hz, 1H), 7.98 (s, 1H), 7.81~7.85 (m, 3H), 7.71~7.72 (m, 1H), 7.51~7.60 (m, 3H), 7.12~7.19 (m, 2H), 6.02~6.03 (m, 1H), 3.02 (s, 3H), 2.89~2.92 (m, 6H). MS $(M+H)^+$: 580.

Compound **211**, depicted in the table below, was prepared using the method described in Example 10 and substituting the appropriate reactants and/or reagents.

Compound	Structure	NMR	MS $(M+H)^+$
211		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.79 (s, 1H), 8.50 (s, 1H), 8.31 (d, *J* = 8.0 Hz, 1H), 8.04~8.12 (m, 3H), 7.85~7.92 (m, 4H), 7.80 (s, 1H), 7.64~7.65 (m, 2H), 7.52 (s, 1H), 7.11~7.15 (m, 2H), 6.43~6.44 (m, 1H), 3.02 (s, 3H), 2.94 (d, *J* = 4.8 Hz, 3H), 2.87 (s, 3H).	580

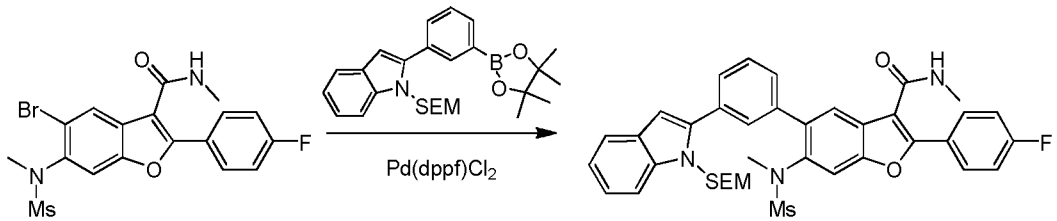
Example 11

Preparation of Compound **212**



212

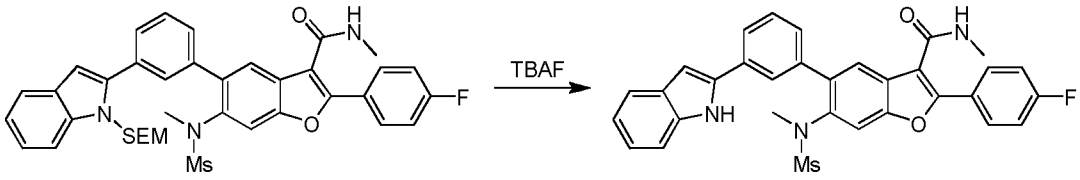
Step 1 - Synthesis of 2-(4-fluorophenyl)-N-methyl-6-(N-methylmethylsulfonamido)-5-(3-(1-((2-(trimethylsilyl)ethoxy)methyl)-1H-indol-2-yl)phenyl)benzofuran-3-carboxamide



5-bromo-2-(4-fluorophenyl)-N-methyl-6-(N-methylmethylsulfonamido)-1-benzofuran-3-carboxamide (prepared as described in Example 1, Step 11) was converted to 2-(4-fluorophenyl)-N-methyl-6-(N-methylmethylsulfonamido)-5-(3-(1-((2-(trimethylsilyl)ethoxy)methyl)-1H-indol-2-yl)phenyl)benzofuran-3-carboxamide (120 mg, 53.4%) using the method described in Example 1, Step 1. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.07~8.03 (m, 2H), 7.93 (s, 1H), 7.82~7.80 (m, 2H), 7.74~7.72 (m, 2H), 7.65~7.60 (m, 2H), 7.37~7.35 (m, 2H), 7.32~7.27 (m, 3H), 6.77 (s, 1H), 6.05 (d, *J* = 4.4 Hz, 1H), 5.61 (s, 2H), 3.62

(t, J = 8.4 Hz, 2H), 3.31 (s, 3H), 3.08 (d, J = 4.8 Hz, 3H), 2.72 (s, 3H), 0.95 (t, J = 8.4 Hz, 2H), 0.00 (s, 9H). MS $(M+H)^+$: 698.

Step 2 - Synthesis of 5-(3-(1H-indol-2-yl)phenyl)-2-(4-fluorophenyl)-N-methyl-6-(N-methylmethylsulfonamido)benzofuran-3-carboxamide (Compound 212)

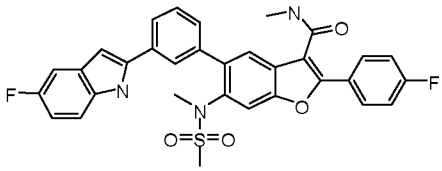
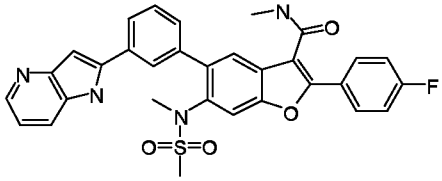
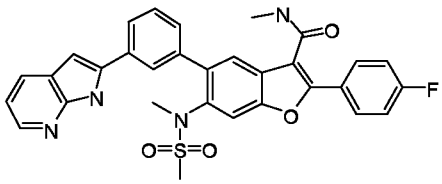
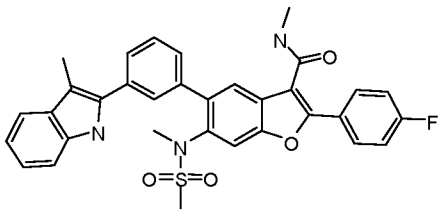


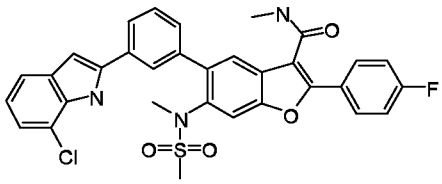
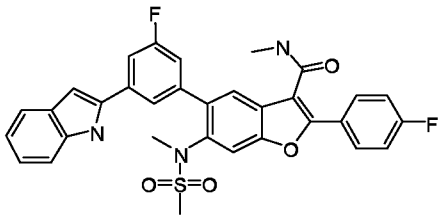
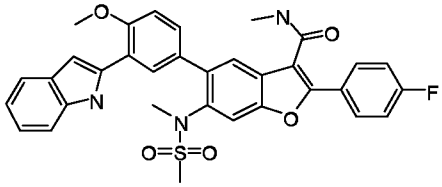
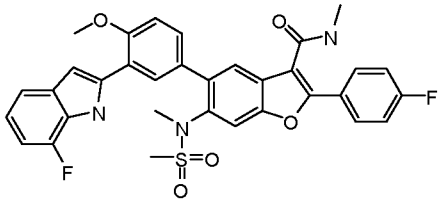
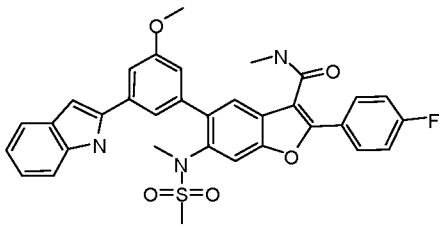
212

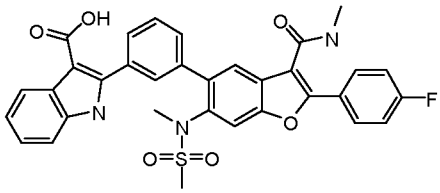
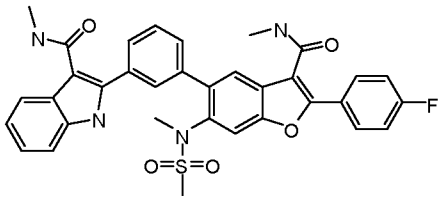
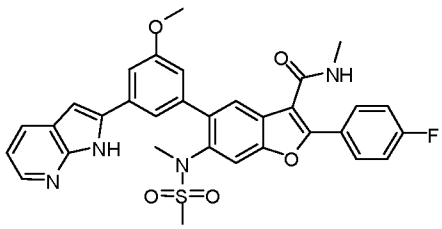
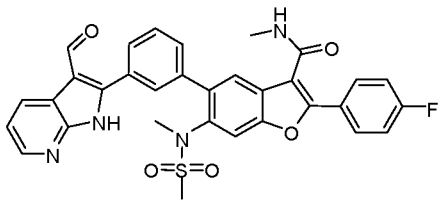
2-(4-fluorophenyl)-N-methyl-6-(N-methylmethylsulfonamido)-5-(3-(1-((2-(trimethylsilyl)ethoxy)methyl)-1H-indol-2-yl)phenyl)benzofuran-3-carboxamide (60 mg, 0.86 mmol) and TBAF (67.44 mg, 2.57 mmol) in DMF (2 mL) was added to a flask, ethylene diamine (25.83 mg, 0.95 mmol) was added. The mixture was purged with nitrogen and heated at 80 °C for about 15 hours. The mixture was diluted with EtOAc and washed with 0.1 M HCl. The phases were separated, and the organic phase was washed with water and brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The resulting redisue was purified using preparative TLC to provde 5-(3-(1H-indol-2-yl)phenyl)-2-(4-fluorophenyl)-N-methyl-6-(N-methylmethylsulfonamido)benzofuran-3-carboxamide (Compound **212**, 20 mg, 41.4%). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 9.30 (s, 1H), 7.94 (d, J = 8.8 Hz, 3H), 7.83 (s, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.65 (t, J = 7.2 Hz, 1H), 7.52~7.47 (m, 2H), 7.43 (d, J = 8.0 Hz, 1H), 7.35 (d, J = 6.8 Hz, 1H), 7.22~7.17 (m, 3H), 7.14~7.10 (m, 1H), 6.85 (s, 1H), 6.09 (d, J = 4.4 Hz, 1H), 2.99 (s, 3H), 2.97 (d, J = 4.0 Hz, 3H), 2.92 (s, 3H). MS $(M+H)^+$: 568.

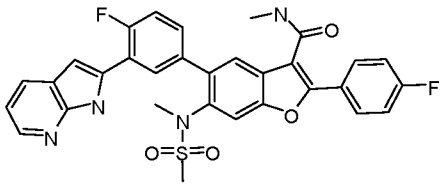
Compounds **213-226**, depicted in the table below, were prepared using the method described in Example 11 and substituting the appropriate reactants and/or reagents.

Compound	Structure	NMR	MS $(M+H)^+$

213		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.10 (s, 1H), 7.89~7.84 (m, 4H), 7.66 (d, *J* = 8.0 Hz, 1H), 7.45 (t, *J* = 5.6 Hz, 2H), 7.33 (d, *J* = 7.2 Hz, 1H), 7.28~7.25 (m, 1H), 7.17~7.12 (m, 3H), 6.88~6.83 (m, 1H), 6.73 (d, *J* = 1.2 Hz, 1H), 5.84 (d, *J* = 4.4 Hz, 1H), 2.96 (s, 3H), 2.93 (d, *J* = 4.8 Hz, 3H), 2.88 (s, 3H).	586
214		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.26 (d, *J* = 6.0 Hz, 1H), 8.17 (d, *J* = 8.0 Hz, 2H), 7.95~7.99 (m, 3H), 7.87 (s, 1H), 7.70 (d, *J* = 6.4 Hz, 1H), 7.57 (d, *J* = 16 Hz, 2H), 7.50 (d, *J* = 7.2 Hz, 2H), 7.19~7.24 (m, 2H), 6.98 (s, 1H), 6.52 (s, 1H), 2.99~3.99 (m, 9H).	569
215		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 14.50 (s, 1H), 8.30 (d, *J* = 4.4 Hz, 1H), 8.03~8.05 (m, 1H), 7.84~7.95 (m, 4H), 7.81 (s, 1H), 7.55~7.86 (m, 2H), 7.48~7.50 (m, 1H), 7.30~7.32 (m, 1H), 7.12~7.16 (m, 2H), 7.01 (s, 1H), 5.94 (d, *J* = 4.8 Hz, 1H), 3.16 (s, 3H), 2.93 (d, *J* = 4.8 Hz, 3H), 2.66 (s, 3H).	569
216		**^{1}H-NMR** (DMSO, 400 MHz) δ 11.18 (s, 1H), 8.55 (d, *J* = 4.8 Hz, 1H), 8.01~8.04 (m, 3H), 7.74 (s, 1H), 7.61~7.70 (m, 2H), 7.53~7.61 (m, 2H), 7.36~7.46 (m, 4H), 7.09~7.13 (m, 1H), 7.00~7.04 (m, 1H), 3.16 (s, 3H), 2.95 (s, 3H), 2.82 (d, *J* = 4.4 Hz, 3H), 2.45 (s, 3H).	582

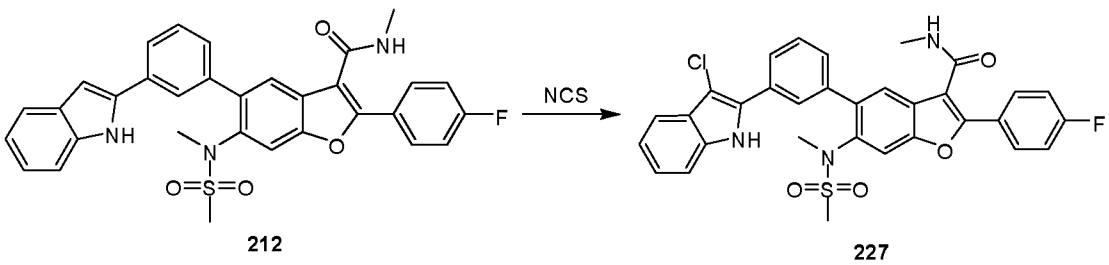
217		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.15 (s, 1H), 7.96~8.01 (m, 3H), 7.93 (s, 1H), 7.78 (d, *J* = 7.6 Hz, 1H), 7.59 (s, 1H), 7.54~7.57 (m, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.20~7.26 (m, 3H), 7.07 (d, *J* = 8.0 Hz, 1H), 6.91 (s, 1H), 5.89 (d, *J* = 3.6 Hz, 1H), 3.02~3.03 (m, 9H).	602
218		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.13 (s, 1H), 7.86~7.90 (m, 3H), 7.71 (s, 1H), 7.56~7.58 (m, 1H), 7.48 (s, 1H), 7.36~7.38 (m, 2H), 7.12~7.17 (m, 3H), 7.03~7.06 (m, 2H), 6.78 (s, 1H), 5.86 (s, 1H), 2.94~2.99 (m, 9H).	586
219		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.74 (s, 1H), 7.98~8.01 (m, 2H), 7.87 (s, 1H), 7.64 (d, *J* = 10.8 Hz, 2H), 7.41~7.47 (m, 3H), 7.19~7.26 (m, 3H), 7.11~7.16 (m, 2H), 6.98 (s, 1H), 5.88 (d, *J* = 4.8 Hz, 1H), 4.11 (s, 3H), 3.15 (s, 3H), 3.02 (d, *J* = 4.8 Hz, 3H), 2.82 (s, 3H).	598
220		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.79 (s, 1H), 7.88~7.90 (m, 3H), 7.87 (s, 1H), 7.77 (s, 1H), 7.34~7.36 (m, 2H), 7.14 (s, 2H), 6.91~6.94 (m, 1H), 6.82~6.90 (m, 2H), 6.79~6.81 (m, 1H), 5.80 (s, 1H), 4.02 (s, 3H), 3.39 (s, 3H), 3.20 (d, *J* = 4.8 Hz, 3H), 2.91 (s, 3H).	616
221		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.00 (s, 1H), 7.85~7.88 (m, 2H), 7.81 (s, 1H), 7.56 (d, *J* = 6.8 Hz, 1H), 7.46~7.49 (m, 2H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.26 (s, 1H), 7.10~7.14 (m, 3H), 7.02~7.05 (m, 1H), 6.90 (s, 1H), 6.77 (s, 1H), 5.88 (s, 1H), 3.86 (s, 3H), 2.91~2.95 (m, 9H).	598

222		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.03~8.06 (m, 1H), 7.88 (br, 2H), 7.70 (br, 2H), 7.63 (br, 2H), 7.46~7.48 (m, 2H), 7.32~7.34 (m, 1H), 7.10~7.13 (m, 4H), 3.06 (s, 3H), 2.84 (s, 3H), 2.72 (s, 3H).	612
223		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.57 (s, 1H), 8.07 (d, *J* = 7.6 Hz, 1H), 7.92~7.98 (m, 4H), 7.81~7.83 (m, 1H), 7.52~7.58 (m, 2H), 7.43~7.48 (m, 2H), 7.21~7.27 (m, 4H), 6.05~6.06 (m, 1H), 5.76~5.78 (m, 1H), 3.15 (s, 3H), 3.01 (d, *J* = 4.8 Hz, 3H), 2.96~2.97 (m, 6H).	625
224		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.32 (d, *J* = 7.6 Hz, 1H), 8.01 (d, *J* = 5.6 Hz, 1H), 7.89~7.93 (m, 2H), 7.81 (s, 1H), 7.55 (s, 2H), 7.41 (s, 1H), 7.32 (m, 1H), 7.12~7.16 (m, 2H), 7.15 (s, 1H), 7.09 (s, 1H), 6.99 (s, 1H), 5.96 (s, 1H), 3.91 (s, 3H), 3.12 (s, 3H), 2.95 (d, *J* = 4.8 Hz, 3H), 2.75 (s, 3H).	599
225		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.98 (s, 1H), 8.54~8.57 (m, 1H), 8.23~8.15 (m, 1H), 7.81~7.84 (m, 2H), 7.70~7.75 (m, 2H), 7.61~7.66 (m, 1H), 7.52~7.56 (m, 3H), 7.17~7.20 (m, 1H), 7.07~7.12 (m, 2H), 3.05 (s, 3H), 2.85 (s, 3H), 2.79 (s, 3H).	597

226		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 9.75 (s, 1H), 8.29~8.31 (m, 1H), 8.01~8.04 (m, 1H), 7.91~7.95 (m, 3H), 7.88 (s, 1H), 7.55 (s, 1H), 7.37~7.41 (m, 1H), 7.27~7.30 (m, 1H), 7.20 (t, *J* = 8.8 Hz, 2H), 7.04~7.07 (m, 1H), 6.95 (s, 1H), 5.84 (d, *J* = 4.4 Hz, 1H), 3.02 (s, 3H), 2.98 (d, *J* = 4.8 Hz, 3H), 2.97 (s, 3H).	587

Example 12

Preparation of Compound **227**

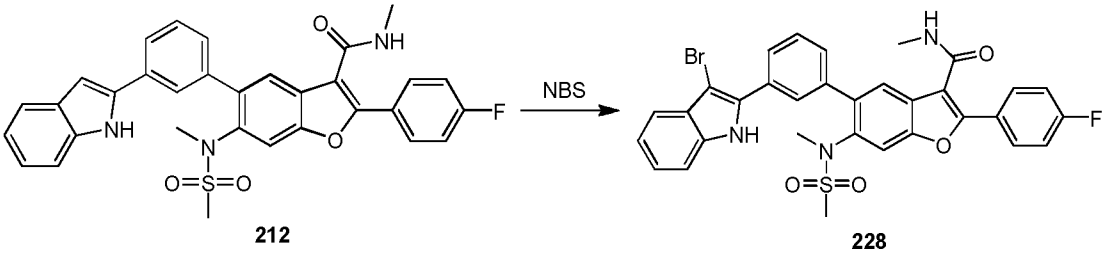


212 **227**

To a solution of Compound **212** (50 mg, 0.088 mmol) in 2 mL of DMF, was added NCS (15 mg, 0.088 mmol), and the resulting reaction was allowed to stir under N_2 atmosphere for 4 hours at 25 °C. The reaction mixture was concentrated *in vacuo* and the resulting residue was diluted EtOAc. The resulting solution was washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The resulting residue was purified using prep-TLC (PE : EtOAc = 2 : 1) to provide Compound **227** (20 mg, 50%) as a white solid. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 9.29 (s, 1H), 7.97 (d, *J* = 7.6 Hz, 1H), 7.83~7.86 (m, 2H), 7.78 (s, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 1H), 7.41 (s, 1H), 7.33 (t, *J* = 5.6 Hz, 2H), 7.17 (d, *J* = 7.6 Hz, 1H), 7.09~7.15 (m, 3H), 5.92 (d, *J* = 4.4 Hz, 1H), 2.97 (s, 3H), 2.87 (d, *J* = 4.8 Hz, 3H), 2.85 (s, 3H). MS $(M+H)^+$: 602.

Example 13

Preparation of Compound **228**

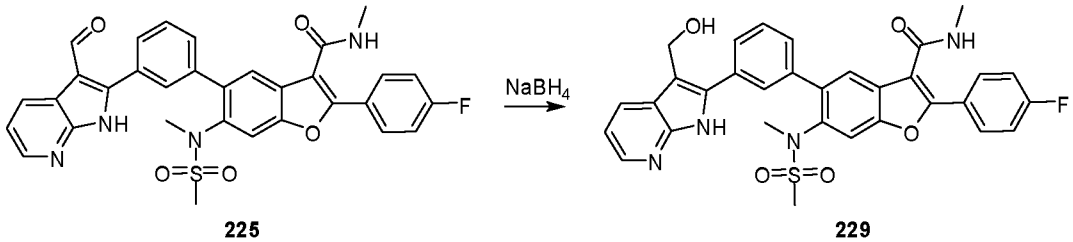


212 228

To a solution of Compound **212** (50 mg, 0.088 mmol) in 3 mL of DMF, was added NBS (16 mg, 0.088 mmol) and the resulting reaction was heated to 75 °C and allowed to stir at this temperature for 4 hours. The reaction mixture was cooled to room temperature and concentrated *in vacuo*. The resulting residue was diluted with EtOAc and the resulting solution was washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue obtained was purified using prep-TLC (PE : EtOAc = 2 : 1) to provide Compound **228** (40 mg, 89%) as a white solid. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 9.38 (s, 1H), 8.02 (d, J = 8.0 Hz, 1H), 7.94 (s, 1H), 7.88~7.94 (m, 2H), 7.84 (s, 1H), 7.53 (t, J = 7.6 Hz, 2H), 7.46 (d, J = 4.8 Hz, 1H), 7.35~7.40 (m, 2H), 7.11~7.15 (m, 4H), 5.80 (s, 1H), 3.04 (s, 3H), 2.94 (d, J = 5.2 Hz, 3H), 2.87 (s, 3H). MS $(M+H)^+$: 646.

Example 14

Preparation of Compound **229**

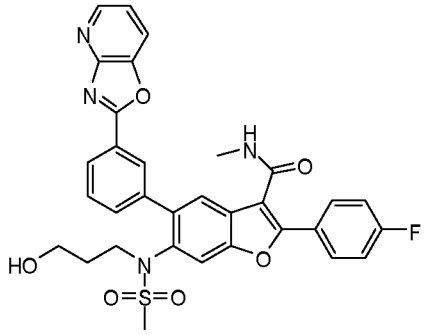


225 229

To a solution of Compound **225** (50 mg, 0.084 mmol) in MeOH (5 mL) was added $NaBH_4$ (17 mg, 0.5 mmol) and the resulting reacton was allowed to stir at room temperature for 2 hours. The reaction mixture was diluted with water and extracted with dichloromethane and the organic extract was dried over Na_2SO_4, filtered and concentrated *in vacuo* to provide Compound **229** (20 mg, 40%). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 10.15~10.25 (m, 1H), 8.22 (d, J = 3.6 Hz, 1H), 8.02~8.04 (m, 1H), 7.88~7.91 (m, 3H), 7.82 (s, 1H), 7.70~7.72 (m, 1H), 7.50~7.54 (m, 1H), 7.48 (s, 1H), 7.40~7.42 (m, 1H), 7.12~7.16 (m, 2H), 7.05~7.08 (m, 1H), 5.93~5.98 (m, 1H), 4.92 (s, 2H), 2.96 (s, 3H), 2.91~2.93 (m, 6H).

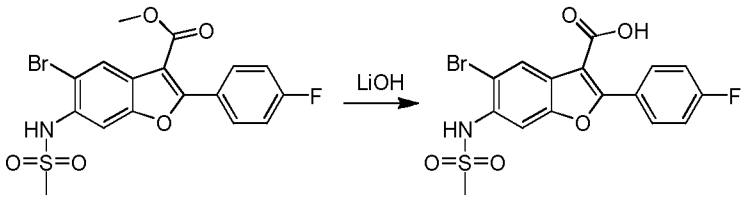
Example 15

Preparation of Compound **230**



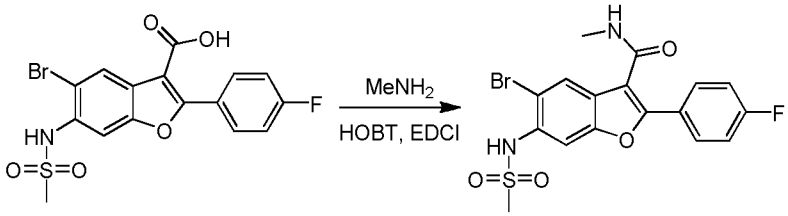
230

Step 1 - Synthesis of 5-bromo-2-(4-fluorophenyl)-6-(methylsulfonamido)benzofuran-3-carboxylic acid



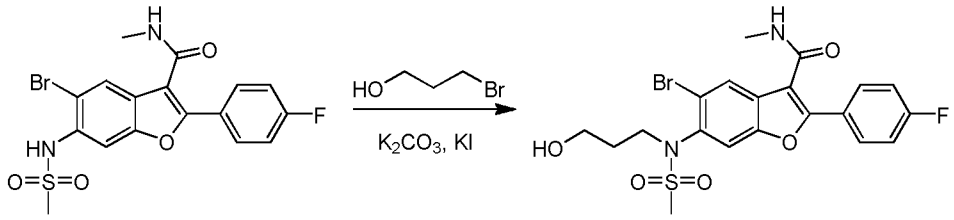
To a solution of methyl 5-bromo-2-(4-fluorophenyl)-6-(methylsulfonamido)benzofuran-3-carboxylate (prepared as described in Example 1, Step 8, 0.5 g, 1.13 mmol) in dioxane (3 mL) and water (1 mL) was $LiOH \cdot H_2O$ (0.24 g, 5.65 mmol). The resulting reaction was heated to 80 °C and allowed to stir at this temperature for 2 hours. The reaction mixture was cooled to room temperature and adjusted to pH = 6~7 using conc. HCl. The resulting solution was extracted with EtOAc, and the organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo* to provide 5-bromo-2-(4-fluorophenyl)-6-(methylsulfonamido) benzofuran-3-carboxylic acid (0.4 g. 87 %) as a white solid. ^{1}H-NMR (DMSO, 400 MHz) δ 13.49 (s, 1H), 9.67 (s, 1H), 8.30 (s, 1H), 8.12~8.17 (m, 2H), 7.87 (s, 1H), 7.45~7.50 (m, 2H), 3.16 (s, 3H). MS $(M+H)^+$: 428.

Step 2 - Synthesis of 5-bromo-2-(4-fluorophenyl)-N-methyl-6-(methylsulfonamido) benzofuran-3-carboxamide



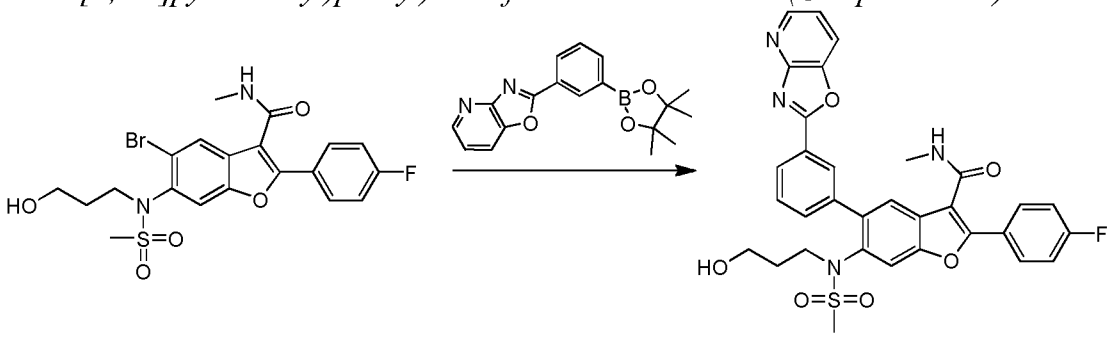
To a solution of 5-bromo-2-(4-fluorophenyl)-6-(methylsulfonamido) benzofuran-3-carboxylic acid (420 mg, 0.77 mmol) in DMF (10 mL) was added EDCI (295 mg, 1.57 mmol) and HOBT (104 mg, 0.77mmol), and the resulting reaction was allowed to stir at room temperature for 3 hours. $CH_3NH_2 \cdot HCl$ (102 mg, 1.54 mmol) and Et_3N (3 mL) were then added to the reaction mixture and the resulting reaction was allowed to stir at room temperature for an additional 8 hours. The reaction mixture was then concentrated *in vacuo* and the residue obtained was diluted with EtOAc. The resulting solution was washed with HCl (1 N) and NaOH (1 N), dried over Na_2SO_4, filtered and concentrated *in vacuo* to provide 5-bromo-2-(4-fluorophenyl)-N-methyl-6-(methylsulfonamido)benzofuran-3-carboxamide (400 mg. 87 %). ^{1}H-NMR (DMSO, 400 MHz) δ 9.55 (br s, 1H), 8.46~8.48 (m, 1H), 8.12~8.17 (m, 2H), 7.96 (s, 1H), 7.87 (s, 1H), 7.45~7.50 (m, 2H), 3.16 (s, 3H), 2.93 (d, J = 8.4 Hz, 3H). MS $(M+H)^+$: 441.

Step 3 - Synthesis of 5-bromo-2-(4-fluorophenyl)-6-(N-(3-hydroxypropyl)methylsulfonamido)-N-methylbenzofuran-3-carboxamide



To a solution of 5-bromo-2-(4-fluorophenyl)-N-methyl-6-(methylsulfonamido)benzofuran-3-carboxamide (300 mg, 0.68 mmol) in DMF (10 mL) was added 3-bromopropan-1-ol (190 mg, 1.36 mmol), K_2CO_3 (188 mg, 1.36 mmol) and KI (11 mg, 0.068 mmol). The resulting reaction was heated to 100 °C and allowed to stir at this temperature for 10 hours. The reaction mixture was cooled to room temperature and concentrated *in vacuo*. The resulting residue was taken up in EtOAc and the resulting solution was washed with H_2O, brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue obtained was purified by flash column chromatography (PE : EtOAc = 2 : 1) to provide 5-bromo-2-(4-fluorophenyl)-6-(N-(3-hydroxypropyl)methylsulfonamido)-N-methylbenzofuran-3-carboxamide (320 mg., 78.6 %). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.12 (s, 1H), 7.76 (d, J = 8.0 Hz, 2H), 7.65 (s, 1H), 7.14 (d, J = 8.4 Hz, 2H), 5.78 (br s, 1H), 3.64~3.67 (m, 2H), 3.55~3.60 (m, 2H), 3.08 (s, 3H), 2.97 (d, J = 4.4 Hz, 3H), 1.72~1.76 (m, 2H). MS $(M+H)^+$: 499.

Step 4 - Synthesis of 2-(4-fluorophenyl)-6-(N-(3-hydroxypropyl)methylsulfonamido)-N-methyl-5-(3-(oxazolo[4,5-b]pyridin-2-yl)phenyl)benzofuran-3-carboxamide (Compound 230)

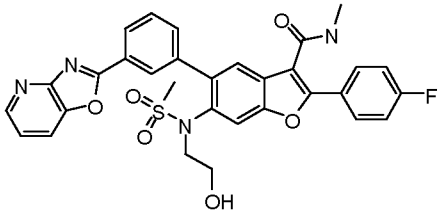
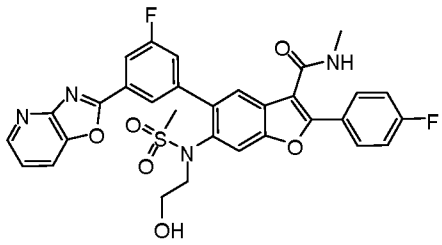
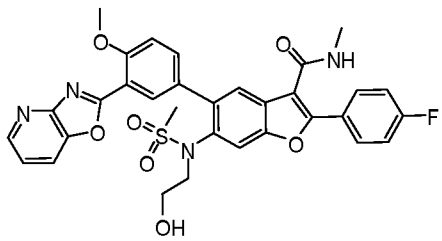
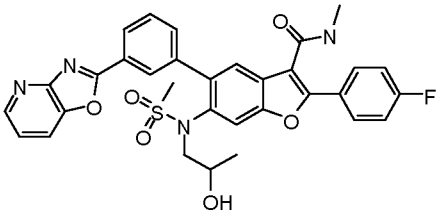


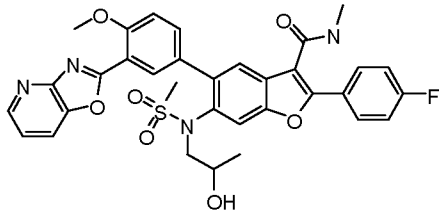
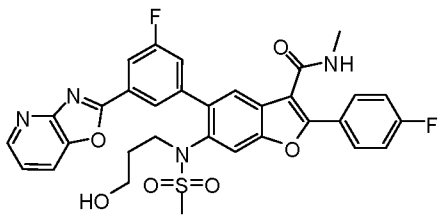
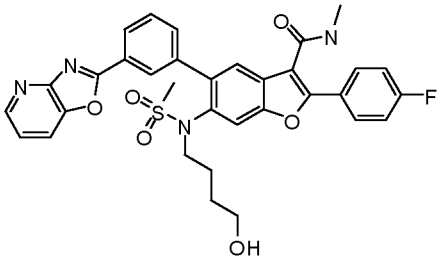
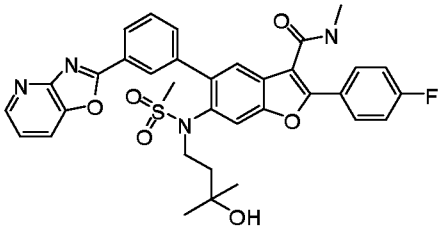
230

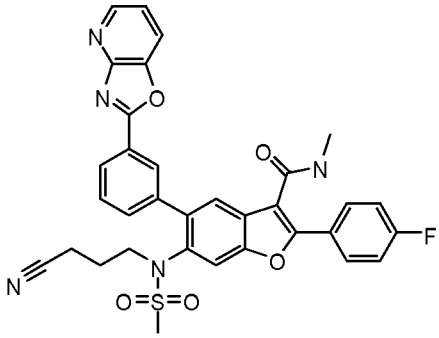
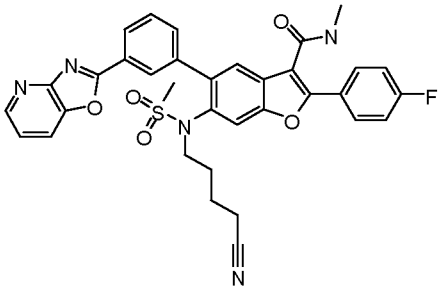
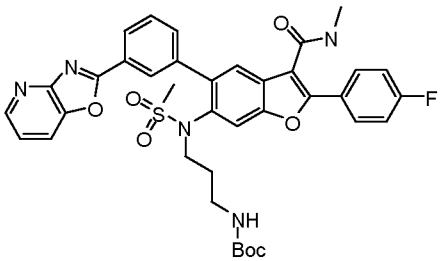
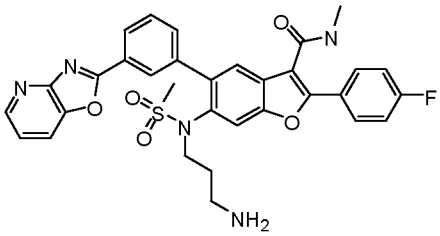
To a degassed solution of 5-bromo-2-(4-fluorophenyl)-6-(N-(3-hydroxypropyl)methylsulfonamido)-N-methylbenzofuran-3-carboxamide (100 mg, 0.20 mmol) and 2-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)oxazolo[4,5-b]pyridine (77 mg, 0.24 mmol) in dioxane / CH_3CN / H_2O (10 / 1 / 1, 5 mL) was added $Pd(PPh_3)_4$ (2 mg) and K_3CO_3 (100 mg, 0.40 mmol). The reaction was put under N_2 atmosphere and heated to 100 °C in microwave for 30 minutes. The reaction mixture was filtered, and the filtrate was diluted with EtOAc, and the resulting solution washed with H_2O, brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The resulting residue was purified using flash column chromatography (PE : EtOAc = 1 : 1) 2-(4-fluorophenyl)-6-(N-(3-hydroxypropyl)methylsulfonamido)-N-methyl-5-(3-(oxazolo[4,5-b]pyridin-2-yl)phenyl)benzofuran-3-carboxamide (Compound **230**, 38 mg, 30.9%). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.50 (J = 4.4 Hz, 1H), 8.38~8.41 (m, 1H), 8.23 (d, J = 8.0 Hz, 1H), 7.81~7.87 (m, 2H), 7.56~7.58 (m, 3H), 7.25~7.26 (m, 2H), 7.18~7.20 (m, 1H), 7.11~7.15 (m, 2H), 6.07 (br s, 1H), 3.64~3.67 (m, 2H), 3.41~3.52 (m, 2H), 2.92~2.93 (m, 3H), 2.81 (s, 3H), 1.72~1.76 (m, 2H). MS $(M+H)^+$: 615.

Compounds **231-242**, depicted in the table below, were prepared using the method described in Example 230 and substituting the appropriate reactants and/or reagents.

Compound	Structure	NMR	MS $(M+H)^+$

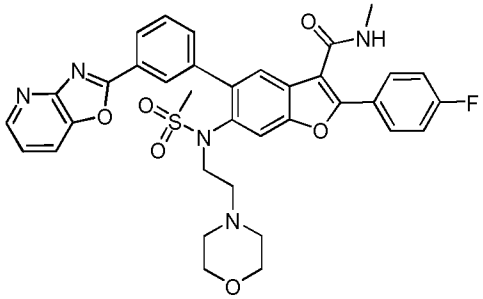
231		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.57 (d, *J* = 4.8 Hz, 1H), 8.46 (s, 1H), 8.23 (d, *J* = 8.0 Hz, 1H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.81~7.88 (m, 4H), 7.58~7.62 (m, 2H), 7.36~7.41 (m, 1H), 7.12~7.17 (m, 2H), 5.98 (br s, 1H), 3.60~3.70 (m., 3H), 3.38~3.44 (m, 1H), 2.93 (d, *J* = 4.4 Hz, 3H), 2.89 (s, 3H).	**601**
232		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.64 (s, 1H), 8.36 (s, 1H), 7.92~8.03 (m, 5H), 7.73 (d, *J* = 4.0 Hz, 1H), 7.64 (d, *J* = 8.8 Hz, 1H), 7.38~7.42 (m, 1H), 7.23~7.25 (m, 2H), 5.96 (br s, 1H), 3.74~3.87 (m, 3H), 3.47~3.51 (m, 1H), 3.04 (d, *J* = 4.8 Hz, 3H), 3.03 (s, 3H).	**619**
233		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.53 (d, *J* = 4.0 Hz, 1H), 8.38 (d, *J* = 4.0 Hz, 1H), 8.13~8.15 (m, 1H), 7.98~8.00 (m, 2H), 7.94 (d, *J* = 4.0 Hz, 1H), 7.86 (s, 1H), 7.73 (s, 1H), 7.37~7.49 (m, 1H), 7.30~7.35 (m, 1H), 7.26~7.30 (m, 2H), 4.08 (s, 3H), 3.71~3.74 (m, 1H), 3.46~3.49 (m, 2H), 3.23 (m, 3H), 3.09~3.14 (m, 1H), 2.95 (s, 3H).	**631**
234		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.49~8.50 (m, 1H), 8.38~8.41 (m, 1H), 8.23~8.24 (m, 1H), 7.81~7.87 (m, 2H), 7.56~7.58 (m, 3H), 7.25~7.26 (m, 2H), 7.18~7.20 (m, 1H), 7.11~7.15 (m, 2H), 5.98 (s, 1H), 3.84~3.85 (m, 1H), 3.53~3.60 (m, 2H), 2.94~3.19 (m, 6H), 1.07~1.12 (m, 3H).	**615**

235		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.58 (d, *J* = 4.4 Hz, 1H), 8.36 (d, *J* = 2.0 Hz, 1H), 7.94~7.97 (t, *J* = 8.0 Hz, 1H), 7.79~7.86 (m, 4H), 7.62 (s, 1H), 7.33~7.35 (m, 2H), 7.12~7.15 (m, 2H), 5.91 (br s, 1H), 4.02 (s, 3H), 3.71~3.76 (m, 1H), 3.43~3.50 (m, 2H), 2.88~2.94 (m, 6H), 0.97~1.07 (m, 3H).	**645**
236		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.55 (d, *J* = 4.0 Hz, 1H), 8.53 (s, 1H), 8.18~8.20 (m, 1H), 8.08 (d, *J* = 8.0 Hz, 1H), 8.00~8.03 (m, 2H), 7.93 (s, 1H), 7.78 (s, 1H), 7.71 (d, *J* = 12.0 Hz, 1H), 7.50~7.53 (m, 1H), 7.27~7.32 (m, 2H), 3.55~3.59 (m, 2H), 3.15 (s, 3H), 2.95 (s, 3H), 1.30~1.60 (m, 4H).	**633**
237		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.50 (d, *J* = 4.0 Hz, 1H), 8.35 (s, 1H), 8.30 (d, *J* = 8.0 Hz, 1H), 7.86~7.90 (m, 5H), 7.70~7.72 (t, *J* = 8.0 Hz, 2H), 7.23~7.26 (t, *J* = 7.6 Hz, 1H), 7.11~7.15 (m, 2H), 6.03 (br s, 1H), 3.32~3.51 (m, 4H), 2.92 (d, *J* = 4.8 Hz, 3H), 2.75 (s, 3H), 1.30~1.56 (m, 4H).	**629**
238		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.50 (d, *J* = 4.4 Hz, 1H), 8.38~8.41 (m, 1H), 8.23 (d, *J* = 8.0 Hz, 1H), 7.81~7.87 (m, 2H), 7.56~7.58 (m, 3H), 7.25~7.26 (m, 2H), 7.18~7.20 (m, 1H), 7.11~7.15 (m, 2H), 5.87 (br s, 1H), 3.52~3.62 (m, 2H), 2.93 (d, *J* = 4.8 Hz, 3H), 2.74 (s, 3H) 1.65~1.67 (m, 2H), 1.07~1.12 (m, 6H).	**643**

239		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.74~8.75 (m, 1H), 8.52 (s, 1H), 8.41~8.42 (m, 1H), 8.18~8.20 (m, 1H), 7.95~7.98 (m, 4H), 7.73~7.77 (m, 1H), 7.69 (s, 1H), 7.56~7.59 (m, 1H), 7.24~7.28 (m, 2H), 3.57 (s, 2H), 3.05~3.08 (m, 6H), 2.06~2.10 (m, 2H), 1.75~1.80 (m, 2H).	624
240		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.72~8.73 (m, 1H), 8.51 (s, 1H), 8.36~8.38 (m, 1H), 8.20~8.22 (m, 1H), 7.90~7.95 (m, 4H), 7.69~7.73 (m, 1H), 7.67 (s, 1H), 7.56~7.58 (m, 1H), 7.22~7.30 (m, 2H), 3.41~3.49 (m, 2H), 3.02~3.05 (m, 6H), 2.22~2.25 (m, 2H), 1.39~1.58 (m, 4H).	638
241		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.67 (d, *J* = 4.4 Hz, 1H), 8.47 (s, 1H), 8.38 (d, *J* = 8.0 Hz, 1H), 8.03 (d, *J* = 8.0 Hz, 1H), 7.96~8.00 (m, 2H), 7.92 (s, 1H), 7.89 (d, *J* = 7.6 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.66 (s, 1H), 7.42~7.46 (m, 1H), 7.23~7.31 (m, 2H), 6.10 (br s, 1H), 4.75 (br s, 1H), 3.43~3.49 (m, 2H), 3.04 (d, *J* = 4.8 Hz, 3H), 3.02 (s, 3H), 2.84~2.96 (m, 2H), 1.57~1.64 (m, 2H), 1.38 (s, 9H).	714
242		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.39~8.42 (m, 2H), 8.09~8.16 (m, 2H), 7.95~8.01 (m, 2H), 7.82~7.85 (m, 2H), 7.62 (t, *J* = 8.0 Hz, 1H), 7.57 (s, 1H), 7.38~7.40 (m, 1H), 7.20~7.25 (m, 2H), 6.44 (br s, 1H), 3.50~3.70 (m, 2H), 3.01 (d, *J* = 4.8 Hz, 3H), 2.97 (s, 3H), 2.80~2.90 (m, 2H), 1.85~1.95 (m, 2H).	614

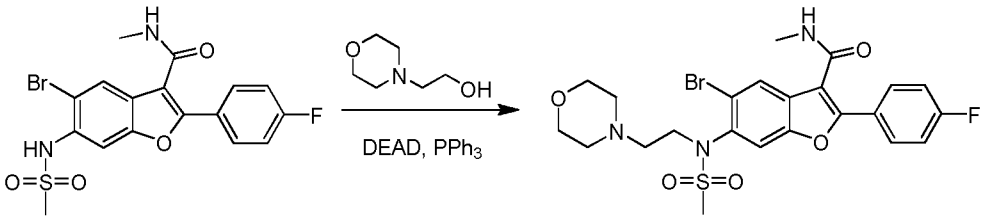
Example 16

Preparation of Compound **243**



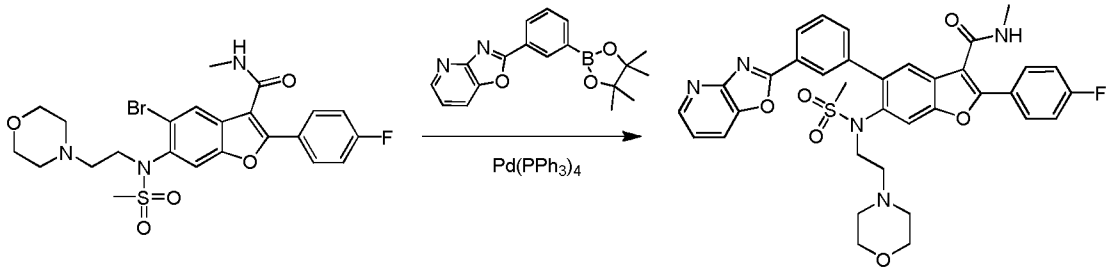
243

Step 1 - Synthesis of 5-bromo-2-(4-fluorophenyl)-N-methyl-6-(N-(2-morpholinoethyl) methylsulfonamido)benzofuran-3-carboxamide



Triphenylphosphine (180 mg, 0.69 mmol) and 5-bromo-2-(4-fluorophenyl)-N-methyl-6-(methylsulfonamido)benzofuran-3-carboxamide (200 mg, 0.45 mmol, prepared by taking the product of Example 1, Step 8 and subjecting it to the methods described in Example 1, Steps 10 and 11) were taken up in anhydrous THF (10 mL) and to the resulting suspension was added DEAD (120 mg, 0.69 mmol). The resulting reaction was allowed to stir at room temperature in the dark for 1 hour, then a solution of 2-morpholinoethanol (90 mg, 0.69 mmol) in anhydrous THF was added, and the resulting reaction was allowed to stir in the dark at room temperature for about 15 hours. The reaction mixture was concentrated *in vacuo* and the resulting residue was purified using flash chromatography (PE : EtOAc = 1 : 1)to provide 5-bromo-2-(4-fluorophenyl)-N-methyl-6-(N-(2-morpholinoethyl)methylsulfonamido) benzofuran-3-carboxamide (200 mg, 79%). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.15 (s, 1H), 7.87~7.91 (m, 2H), 7.73 (s, 1H), 7.18~7.23 (m, 2H), 5.93 (br s, 1H), 4.04~4.12 (m, 1H), 3.59~3.66 (m, 5H), 3.11 (s, 3H), 2.99 (d, J = 4.4 Hz, 3H), 2.48~2.55 (m, 4H), 2.33~2.37 (m,2H). MS $(M+H)^+$: 554.

Step 2 - Synthesis of 2-(4-fluorophenyl-N-methyl-6-(N-(2-morpholinoethyl)methylsulfonamido)-5-(3-(oxazolo[4,5-b]pyridine-2-yl)phenyl)benzofuran-3-carboxamide (Compound 243)

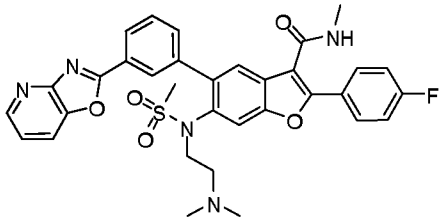
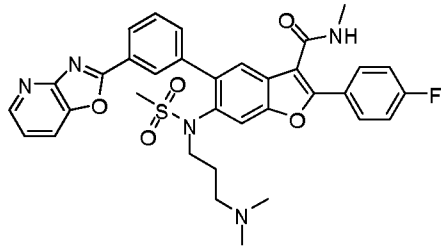


243

5-bromo-2-(4-fluorophenyl)-N-methyl-6-(N-(2-morpholinoethyl)methylsulfonamido) benzofuran-3-carboxamide (20 mg, 0.04 mmol), 2-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)oxazolo[4,5-b]pyridine (12 mg, 0.04 mmol) and K_2CO_3 (10 mg, 0.07 mmol) were taken up in a mixture of dioxane/CH_3CN/H_2O (10/1/1, 1 mL total solution volume). To the resulting solution was added $Pd(PPh_3)_4$ (2 mg) and the resulting reaction was put under N_2 atmosphere and heated to 100 °C using microwave radiation. The reaction was allowed to remain at this temperature under microwave radiation for 20 minutes, then was cooled to room temperature and concentrated *in vacuo*. The residue obtained was purified using preparative HPLC to provide 2-(4-fluorophenyl)-N-methyl-6-(N-(2-morpholinoethyl)methylsulfonamido)-5-(3-(oxazolo[4,5-b]pyridin-2-yl)phenyl)benzofuran-3-carboxamide (Compound **243**, 15 mg, 62%). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.56 (br s, 1H), 8.30 (s, 1H), 8.20~8.22 (m ,1H), 7.97 (d, J = 8.0 Hz, 1H), 7.81~7.87 (m, 3H), 7.71 (br s, 1H), 7.58~7.63 (m, 2H), 7.36~7.40 (m, 1H), 7.14~7.19 (m, 2H), 6.37 (br s, 1H), 3.80~4.05 (m, 6H), 3.42 (br s, 2H), 3.21 (br s, 2H), 2.80~3.10 (m, 8H). MS $(M+H)^+$: 670.

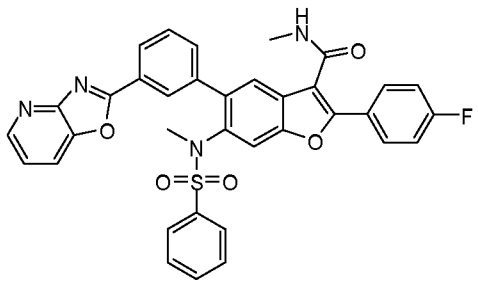
Compounds **244-245**, depicted in the table below, were prepared using the method described in Example 16 and substituting the appropriate reactants and/or reagents.

Compound	Structure	NMR	MS $(M+H)^+$

244		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.48~8.53 (m, 2H), 8.35 (d, *J* = 8.0 Hz, 1H), 8.15 (d, *J* = 8.0 Hz, 1H), 7.92~7.99 (m, 4H), 7.75~7.87 (m, 2H), 7.46~7.49 (m, 1H), 7.26~7.30 (m, 2H), 3.89~3.94 (m, 2H), 3.36~3.40 (m, 1H), 3.20~3.22 (m, 1H), 3.06 (s, 3H), 2.93 (d, *J* = 4.0 Hz, 3H), 2.81 (s, 6H).	628
245		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.64 (d, *J* = 4.8 Hz, 1H), 8.42 (s, 1H), 8.31 (d, *J* = 8.0 Hz, 1H), 8.13 (d, *J* = 8.4 Hz, 1H), 7.88~7.95 (m, 4H), 7.65 (t, *J* = 8.0 Hz, 1H), 7.63 (s, 1H), 7.50~7.54 (m, 1H), 7.23 (t, *J* = 8.8 Hz, 2H), 6.12 (d, *J* = 4.8 Hz, 1H), 3.60~3.75 (m, 2H), 2.95~3.04 (m, 7H), 2.78~2.87 (m, 7H), 1.98~2.05 (m, 2H).	642

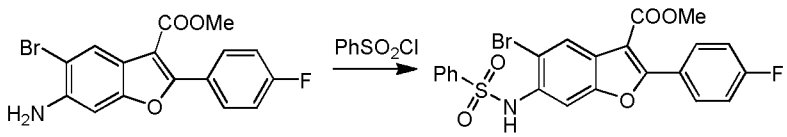
Example 17

Preparation of Compound **246**



246

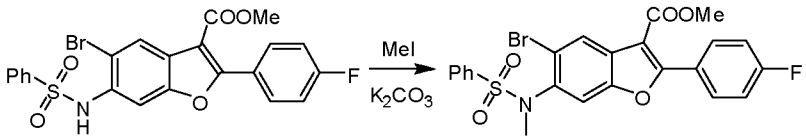
Step 1 - Synthesis of methyl 6-amino-5-bromo-2-(4-fluorophenyl)benzofuran-3-carboxylate



To a 0 °C solution of methyl 6-amino-5-bromo-2-(4-fluorophenyl)benzofuran-3-carboxylate (prepared as described in Example 1, Step 7, 500 mg, 1.4 mmol) and pyridine (5 mL)

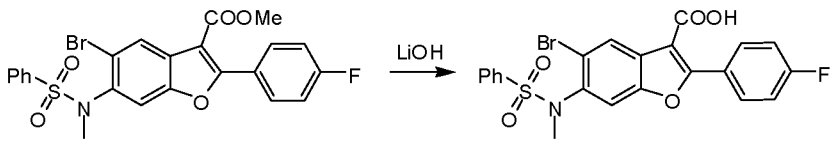
in dry dichloromethane (10 mL) was added benzenesulfonyl chloride (1.5 g, 8.5 mmol). The cold bath was removed and the resulting reaction was allowed to stir for about 15 hours at room temperature. The reaction mixture was diluted with water, extracted with dichloromethane and the organic extract was washed with brine, dried (Na_2SO_4), filtered and concentrated *in vacuo*. The residue obtained was purified using flash column chromatography (PE : EtOAc = 5 : 1) to provide methyl 5-bromo-2-(4-fluorophenyl)-6-(phenylsulfonamido) benzofuran-3-carboxylate (600 mg, 87%). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.01~8.03 (m, 2H), 7.93~7.95 (d, 2H), 7.68~7.69 (d, 1H), 7.62~7.63 (m, 1H), 7.50~7.52 (m, 2H), 7.33~7.37 (m, 1H) 7.10~7.16 (m, 2H) 5.23 (s, 1H). 3.85~3.89 (d, J = 16.8 Hz, 3H). MS $(M+H)^+$: 504.

Step 2 - Synthesis of methyl 5-bromo-2-(4-fluorophenyl)-6-(N-methylphenylsulfonamido) benzofuran-3-carboxylate



A solution of methyl 5-bromo-2-(4-fluorophenyl)-6-(phenylsulfonamido)benzofuran-3-carboxylate (0.6 g, 1.18 mmol) and K_2CO_3 (1.1 g, 8.0 mmol) in DMF (15 mL) was put under N_2 atmosphere. CH_3I (1.0 mL, 16.0 mmol) was added and the resulting reaction was heated to 40 °C and allowed to stir at this temperature for about 15 hours. The reaction mixture was then filtered and the filtrate was concentrated *in vacuo* to provide methyl 5-bromo-2-(4-fluorophenyl)-6-(N-methylphenylsulfonamido)benzofuran-3-carboxylate (500 mg, 81%) which was used without further purification.

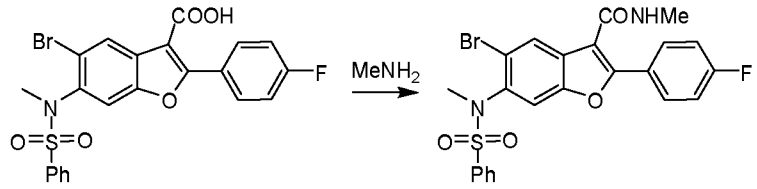
Step 3 - Synthesis of 5-bromo-2-(4-fluorophenyl)-6-(N-methylphenylsulfonamido) benzofuran-3-carboxylic acid



To a solution of methyl 5-bromo-2-(4-fluorophenyl)-6-(N-methylphenylsulfonamido)benzofuran-3-carboxylate (500 mg, 0.96 mmol) in a mixture of dioxane/H_2O (1/1, 10 mL total volume) was added $LiOH{\cdot}H_2O$ (90 mg, 2.14 mmol), and the

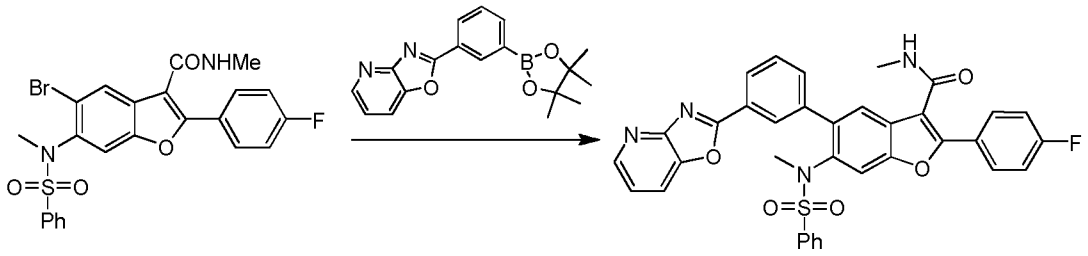
resulting reaction was heated to 100 °C and allowed to stir at this temperature for 2 hours. The reaction mixture was cooled to room temperature, then concentrated *in vacuo*. The residue obtained was dissolved in H_2O and the resulting solution was adjusted to pH 3 using HCl (1 N). The acidific solution was then extracted with EtOAc and the organic extract was washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo* to provide 5-bromo-2-(4-fluorophenyl)-6-(N-methylphenylsulfonamido)benzofuran-3-carboxylic acid (300 mg, 62%), which was used without further purification.

Step 4 - Synthesis of 5-bromo-2-(4-fluorophenyl)-N-methyl-6-(N-methylphenylsulfonamido)benzofuran-3-carboxamide



To a solution of 5-bromo-2-(4-fluorophenyl)-6-(N-methylphenylsulfonamido)benzofuran-3-carboxylic acid (300 mg, 0.59 mmol) in dry DMF (10 mL) was added HOBT (100 mg, 0.74 mmol) and EDCI (100 mg, 0.64 mmol) and the resulting reaction was allowed to stir at room temperature for 1 hour. Et_3N (2.0 mL) and CH_3NH_2 (HCl salt, 100 mg, 1.48 mmol) were then added to the reaction mixture and the resulting reaction was allowed to stir for about 15 hours at room temperature. The reaction mixture was concentrated *in vacuo*, the resulting residue was diluted with H_2O, and the resulting aqueous solution was extracted with ethyl acetate. The organic extract was washed with H_2O and brine, then concentrated *in vacuo*. The residue obtained was purified by flash column chromatography (PE : EtOAc = 2 : 1) to provide 5-bromo-2-(4-fluorophenyl)-N-methyl-6-(N-methylphenylsulfonamido)benzofuran-3-carboxamide (130 mg, 42%). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.02 (s, 1H), 7.83~7.86 (m, 2H), 7.75~7.77 (d, 2H), 7.54~7.56 (m, 1H), 7.44~7.48 (m, 2H), 7.36 (s, 1H), 7.11~7.19 (m, 2H), 5.71 (br s, 1H), 3.20 (s, 3H), 2.94 (d, J = 4.8 Hz, 3H). MS $(M+H)^+$: 517.

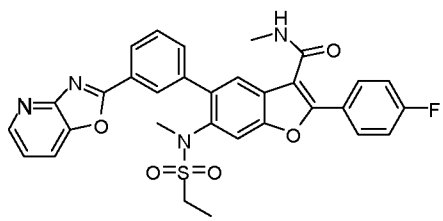
Step 5 - Synthesis of 2-(4-fluorophenyl)-N-methyl-6-(N-methylphenylsulfonamido)-5-(3-(oxazolo[4,5-b]pyridin-2-yl)phenyl)benzofuran-3-carboxamide (Compound 246)



246

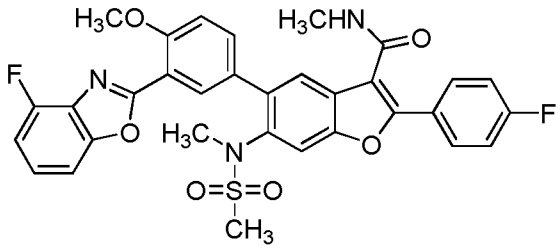
5-bromo-2-(4-fluorophenyl)-N-methyl-6-(N-methylphenylsulfonamido)benzofuran-3-carboxamide (30 mg, 0.06 mmol), 2-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)oxazolo[4,5-b]pyridine (22.5 mg, 0.07 mmol) and K_2CO_3 (16 mg, 0.12 mmol) were taken up in a mixture of dioxane-acetonitrile-water (10:1:1, 2 mL total volume). To the resulting solution was added $Pd(PPh_3)_4$ (5 mg) and the resulting reaction was put under N_2 atmosphere and heated to 100 °C using microwave radiation. The reaction was allowed to remain at this temperature under microwave radiation for 20 minutes, then was cooled to room temperature and concentrated *in vacuo*. The residue obtained was purified using preparative HPLC to provide 2-(4-fluorophenyl)-N-methyl-6-(N-methylphenylsulfonamido)-5-(3-(oxazolo[4,5-b]pyridin-2-yl)phenyl)benzofuran-3-carboxamide (Compound **246**, 4 mg, 11%). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.57 (d, 1H), 8.30 (m, 2H), 7.86~7.90 (m, 3H), 7.82 (s, 1H), 7.68 (d, 1H), 7.53~7.58 (m, 3H), 7.47~7.49 (m, 1H), 7.36~7.40 (m, 2H), 7.30~7.33 (m, 1H), 7.12~7.15 (m, 3H), 5.83 (br s, 1H), 3.06 (s, 3H), (d, J = 4.8 Hz, 3H). MS $(M+H)^+$: 633.

Compound **247**, depicted in the table below, was prepared using the method described in Example 17 and substituting the appropriate reactants and/or reagents.

Compound	Structure	NMR	MS $(M+H)^+$
247		**^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.57~8.58 (d, J = 4.0 Hz, 1H), 8.36 (s, 1H), 8.29~8.31 (d, J = 8.2 Hz, 1H), 7.82~7.98 (m, 4H), 7.57~7.60 (m, 3H), 7.27~7.29 (m, 1H), 7.13~7.17 (m, 2H), 5.82~5.83 (d, J = 8.1 Hz, 1H), 3.15 (s, 3H), 2.93~2.94 (d, J = 5.2 Hz, 3H), 2.76~2.78 (m, 2H), 1.09~1.13 (m, 3H).	**585**

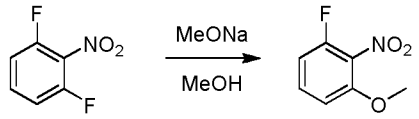
Example 18

Preparation of Compound **30**



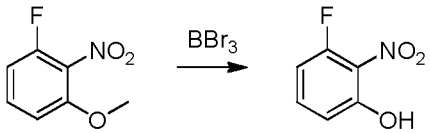
30

Step 1 - Synthesis of 1-fluoro-3-methoxy-2-nitrobenzene



To a 0 °C solution of 1,3-difluoro-2-nitrobenzene (100 g, 0.63 mol) in MeOH (1.3 L) was slowly added a solution of MeONa (0.69 mol, in MeOH, freshly prepared from 15.9 g of sodium metal and 200 mL of MeOH). The resulting reaction was allowed to stir for about 15 hours at room temperature, then the reaction mixture was concentrated and diluted with EtOAc. The organic phase was washed sequentially with water and brine, dried over Na_2SO_4, then filtered and concentrated *in vacuo* to provide 1-fluoro-3-methoxy-2-nitrobenzene (98 g, yield: 91.4%), which was used without further purification. **^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 7.38~7.44 (m, 1H), 6.72~6.88 (m, 2H), 3.95 (s, 3H).

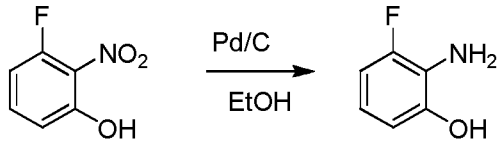
Step 2 - Synthesis of 3-fluoro-2-nitrophenol



To a -40 °C solution of 1-fluoro-3-methoxy-2-nitrobenzene (98 g, 0.57 mol) in dichloromethane (500 mL) was added dropwise a solution of BBr_3 (1 L, 1 M in dichloromethane The resulting reaction was allowed to stir for about 15 hours at room temperature, then the reaction mixture was slowly poured into ice water (500 mL). The resulting solution was extracted with EtOAc (300 mL x 3), and the combined organic layers were washed with sequentially with 5% aqueous $NaHCO_3$ and brine, then dried over Na_2SO_4, filtered and concentrated *in vacuo* to provide 3-fluoro-2-nitrophenol (85 g, yield: 95%), which was used

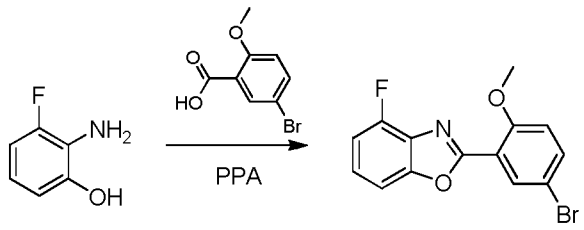
without further purification. **^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 7.43~7.49 (m, 1H), 6.88 (d, *J* = 8.0 Hz, 1H), 6.73~6.78 (m, 1H).

Step 3 - Synthesis of 5-(3-(4-fluorobenzo[d]oxazol-2-yl)-4-methoxyphenyl)-2-(4-fluorophenyl)-N-methyl-6-(N-methylsulfonamido)benzofuran-3-carboxamide (Compound 251)



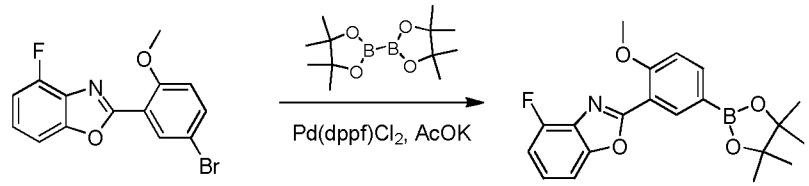
3-fluoro-2-nitrophenol (38 g, 0.24 mol) was dissolved in EtOH and then palladium on carbon (5 g, 10% Pd) was added. The reaction flask was evacuated and the reaction mixture was put under H_2 atmosphere (1 atm) and allowed to stir for 3 hours at room temperature. The reaction mixture was then filtered through a short pad of celite and the celite was washed with EtOH. The combined filtrate and washing was concentrated *in vacuo* to provide 2-amino-3-fluorophenol (26 g, yield: 85.7%), which was used without further purification. **^{1}H-NMR** (DMSO, 400 MHz) δ 9.43 (s, 1H), 6.42~6.53 (m, 2H), 6.32~6.42 (m, 1H), 4.34 (s, 2H).

Step 4 - Synthesis of 2-(5-bromo-2-methoxyphenyl)-4-fluorobenzo[d]oxazole



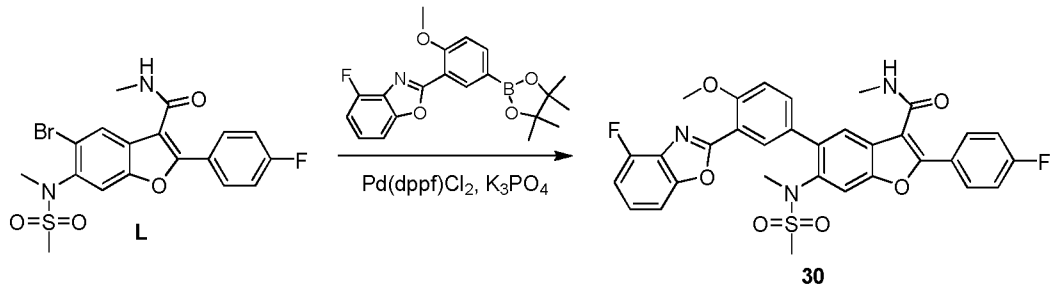
To a solution of 2-amino-3-fluorophenol (9 g 70.8 mmol) in 10 mL of PPA was added 5-bromo-2-methoxybenzoic acid (16.3 g, 70.8 mmol), and the resulting reaction was heated to 140 °C and allowed to stir at this temperature for 4 hours. The reaction mixture was then poured into ice water (50 mL), and extracted with EtOAc. The organic extract was concentrated in vacuo and the residue obtained was purified using flash column chromatography on silica gel (petroleum ether/ethyl acetate = 10 / 1), to provide 2-(5-bromo-2-methoxyphenyl)-4-fluorobenzo[d]oxazole (16 g, yield: 82%) as a solid. **^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.29 (d, *J* = 2.4 Hz, 1H), 7.57~7.54 (m, 1H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.27~7.33 (m, 1H), 7.07 (m, 1H), 6.96 (d, *J* = 9.2 Hz, 1H), 3.99 (s, 3H).

Step 5 - Synthesis of 4-fluoro-2-(2-methoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)benzo[d]oxazole



A solution of 2-(5-bromo-2-methoxyphenyl)-4-fluorobenzo[d]oxazole (18.4 g, 57.1 mmol) and bis(pinacolato)diboron (17.4 g, 68.5 mmol) in DMF (10 mL) was placed under N_2 atmosphere and to the resulting solution was added $Pd(dppf)Cl_2$ (500 mg) and AcOK (10 g, 114 mmol). The reaction was heated to 80 °C and allowed to stir at this temperature for 3 hours. The reaction mixture was then concentrated *in vacuo*, the residue obtained was dissolved in dichloromethane, and the resulting solution was filtered through a pad of celite. The organic solution was washed sequentiall wiith H_2O and brine, then dried over Na_2SO_4, filtered and concentrated *in vacuo*. The resulting residue was purified using flash column chromatography on silica gel (PE / EA = 10 / 1) to provide 4-fluoro-2-(2-methoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)benzo[d]oxazole (10 g, yield: 54%) as a solid. **^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.53 (d, J = 1.6 Hz, 1H), 7.85~7.92 (m, 1H), 7.44 (d, J = 8.0 Hz, 1H), 7.20~7.28 (m, 1H), 6.96~7.05 (m, 2H), 3.97 (s, 3H), 1.29 (s, 12H).

Step 6- Synthesis of 5-(3-(4-fluorobenzo[d]oxazol-2-yl)-4-methoxyphenyl)-2-(4-fluorophenyl)-N-methyl-6-(N-methylsulfonamido)benzofuran-3-carboxamide (Compound 30)

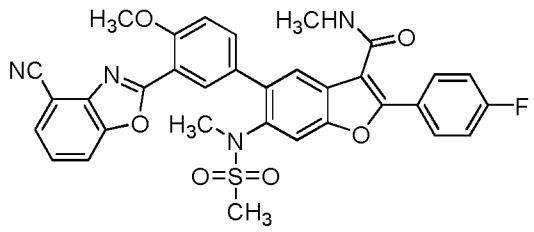


To a solution of Compound **L** (5 g, 11.0 mmol) and 4-fluoro-2-(2-methoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)benzo[d]oxazole (5.27 g, 14.3 mmol) in DMF (150 mL) under N_2 atmosphere was added $Pd(dppf)Cl_2$ (200 mg) and K_3PO_4 (4.66 g, 22.0 mmol). The resulting reaction was heated to 100 °C and allowed to stir at this temperature for 10 hours, then the reaction mixture was concentrated *in vacuo*. The residue obtained was dissolved in dichloromethane and filtrated through a short pad of celite. The filtrate was washed

sequentially with water and brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The resulting residue was purified using flash column chromatography on silica gel (petroleum ether/ethyl acetate = 4 / 1 to 2 / 1) and the product obtained was then recrystallized from dichlormethane/ethyl acetate = 5 /1 to provide Compound **30** (3.8 g, yield: 56%) as white solid. **^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.21 (d, J = 2.0 Hz, 1H), 7.91~7.95 (m, 2H), 7.83 (s, 1H), 7.68 (d, J = 2.0 Hz, 1H), 7.66 (s, 1H), 7.39 (d, J = 8.0 Hz, 1H), 7.14~7.27 (m, 4H), 7.06 (t, J = 8.4 Hz, 1H), 5.95 (br s, 1H), 4.06 (s, 3H), 3.14 (s, 3H), 2.99 (d, J = 4.8 Hz, 3H), 2.77 (s, 3H); MS $(M+H)^+$ 618.

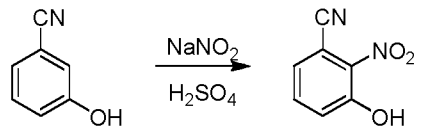
Example 19

Preparation of Compound **251**



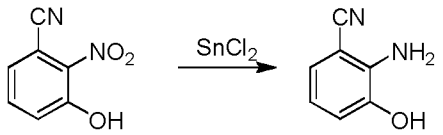
251

Step 1 - Synthesis of 3-hydroxy-2-nitrobenzonitrile



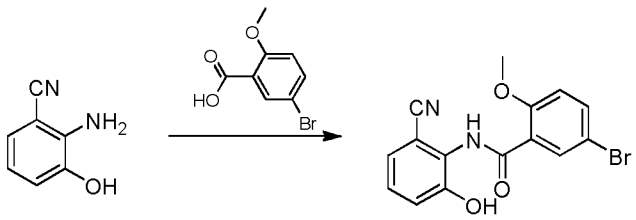
To a 0 °C solution of $NaNO_3$ (4 g, 47 mmol) and H_2SO_4 (aqueous, 3 M, 45 mL) was added a solution of 3-hydroxybenzonitrile (5 g, 42 mmol) in CH_2Cl_2 (80 mL). To the resulting solution was added $NaNO_2$ (289 mg, 4.2 mmol) and the resulting reaction was allowed to stir for 16 hours. The reaction mixture was then diluted with CH_2Cl_2 and the resulting solution was washed sequentially with H_2O and brine, filtered and concentrated *in vacuo*. The residue obtained was purified using flash column chromatography on silica gel (petroleum ether/ethyl acetate = 40 / 1) to provide 3-hydroxy-2-nitrobenzonitrile (1.7 g, yield: 25%). **^{1}H-NMR** (DMSO, 400 MHz) δ 11.73 (s, 1H), 8.25 (d, J = 8.4 Hz, 1H), 7.35 (d, J = 4.4 Hz, 1H), 7.19 (t, J = 8.4 Hz, 1H)

Step 2 - Synthesis of 2-amino-3-hydroxybenzonitrile



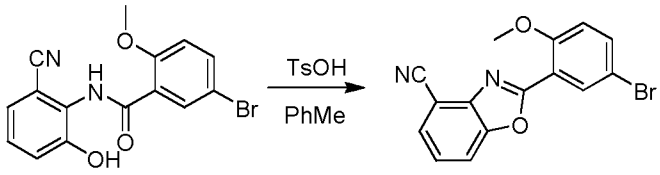
To a solution of 3-hydroxy-2-nitrobenzonitrile (1.7 g, 0.01 mol) in MeOH (30 mL) was added $SnCl_2$ (7.9 g, 4.1 mol). The resulting reaction was heated to 50 °C and allowed to stir at this temperature for 6 hours. The reaction mixture was then concentrated in vacuo and the resulting residue was taken up in EtOAc. To the resulting solution was added saturated aqueous $NaHCO_3$ solution, which caused a white solid to precipitate out of solution. The resulting suspension was filtered through celite and extracted with EtOAc. The organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to provide 2-amino-3-hydroxybenzonitrile (1.1 g, yield: 79.7%), which was used without further purification. **^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 6.94 (d, J = 8.4 Hz, 1H), 6.79 (d, J = 8.0 Hz, 1H), 6.53 (t, J = 8.0 Hz, 1H), 5.17 (s, 1H), 4.43 (s, 2H).

Step 3 - Synthesis of 5-bromo-N-(2-cyano-6-hydroxyphenyl)-2-methoxybenzamide



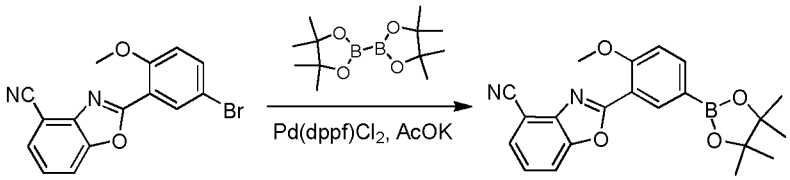
A solution of 5-bromo-2-methoxybenzoic acid (11.7 g, 50.8 mmol) in $SOCl_2$ (50 mL) was heated to 100 °C and allowed to stir at this temperature for 2 hours. The reaction mixture was then concentrated *in vacuo* and the resulting residue was dissolved in dry dichloromethane (30 mL). The resulting solution was then added dropwise to a solution of 2-amino-3-hydroxybenzonitrile (6.2 g, 46.22 mmol) in dichloromethane (30mL) and triethylamine (15 mL) at 0 °C under N_2. The resulting reaction was allowed to stir for 5 hours at room temperature, then the reaction mixture was poured into ice water (50 mL) and extracted with dichloromethane. The organic phase was washed sequentially with H_2O and brine, dried over Na_2SO_4, filtered and concentrated *in vacuo* to provide 5-bromo-*N*-(2-cyano-6-hydroxyphenyl)-2-methoxybenzamide (4.0 g), which was used without further purification.

Step 4 - Synthesis of 2-(5-bromo-2-methoxyphenyl)benzo[d]oxazole-4-carbonitrile



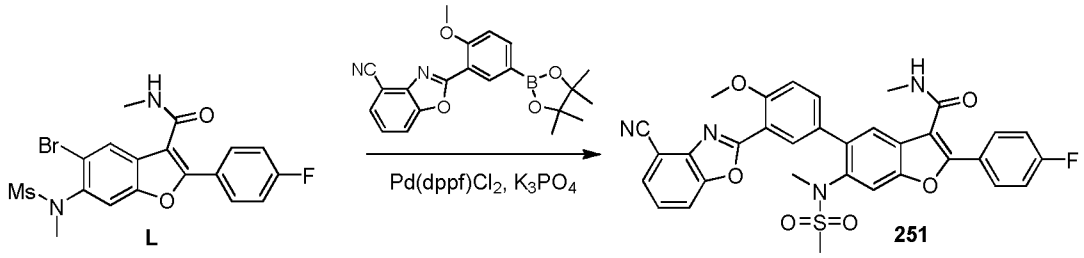
A solution of 5-bromo-*N*-(2-cyano-6-hydroxyphenyl)-2-heated to reflux and allowed to stir at this temperature for 3 hours using a reflux condenser fitted with a Dean-Stark trap. After the was removed, the residue obtained was dissolved in EtOAc (40 mL). The organic phase was washed sequentially with H_2O and brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue obtained was purified using flash column chromatography on silica gel (PE / EA = 10 / 1) to provide 2-(5-bromo-2-methoxyphenyl)benzo[d]oxazole-4-carbonitrile (2.1 g, yield: 26 % two steps) as solid. **^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.70 (s, 1H), 8.21~8.24 (m, 1H), 7.81~7.83 (m, 1H), 7.70~7.72 (m, 1H), 7.46~7.48 (m, 1H), 7.15~7.17 (m, 1H), 4.14 (s, 3H).

Step 5 - Synthesis of 2-(2-methoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)benzo[d]oxazole-4-carbonitrile



To a solution of 2-(5-bromo-2-methoxyphenyl)benzo[d]oxazole-4-carbonitrile (2.0 g, 6.08 mmol) and bis(pinacolato)diboron (2.01 g, 7.90 mmol) in toluene (25 mL) under N_2 atmosphere, was added $Pd(dppf)Cl_2$ (300 mg) and AcOK (1.19 g, 12.15 mmol). The resulting reaction was heated to 80 °C and allowed to stir at this temperature for 3 hours. The reaction mixture was then concentrated *in vacuo* and the resulting residue was dissolved in dichloromethane and filtrated through a short pad of celite. The organic phase was washed sequentially with H_2O and brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue obtained was purified using flash column chromatography on silica gel (petroleum ether/ethyl acetate = 10 / 1) to provide 2-(2-methoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)benzo[d]oxazole-4-carbonitrile (1.8 g, yield: 78.6%) as solid, which was used without further purification. **^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.65 (s, 1H), 8.00~8.02 (m, 1H), 7.84~7.86 (m, 1H), 7.68~7.70 (m, 1H), 7.42~7.46 (m, 1H), 7.10~7.12 (m, 1H), 4.08 (s, 3H), 1.41 (s, 12H).

Step 6 - Synthesis of 5-(3-(4-cyanobenzo[d]oxazol-2-yl)-4-methoxyphenyl)-2-(4-fluorophenyl)-N-methyl-6-(N-methylsulfonamido)benzofuran-3-carboxamide (Compound 251)



To a solution of Compound **L** (1.21 g, 2.66 mmol) and 2-(2-methoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)benzo[d]oxazole-4-carbonitrile (1.20 g, 3.19 mmol) in DMF (12 mL) under N_2 atmosphere, was added $Pd(dppf)Cl_2$ (400 mg) and K_3PO_4 (1.42 g, 5.32 mmol). The resulting reactionwas heated to 100 °C and allowed to stir at this temperature for 10 hours, then the reaction mixture was cooled to room temperature and concentrated *in vacuo*. The residue obtained was dissolved in dichloromethane and filtered through a short pad of celite. The filtrate was washed sequentially with water and brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The resulting residue was purified using preparative HPLC to provide Compound **251** (0.81 g, yield: 50%) as white solid. **^{1}H-NMR** ($CDCl_3$, 400 MHz) δ 8.25 (s, 1H), 7.86~7.89 (m, 2H), 7.76~7.80 (m, 2H), 7.59~7.67 (m, 3H), 7.34~7.38 (m, 1H), 7.11~7.16 (m, 3H), 5.85 (s, 1H), 4.02 (s, 3H), 3.10 (s, 3H), 2.93 (d, J = 4.8 Hz, 3H), 2.78 (s, 3H); MS $(M+H)^+$ 625.

Example 20

Measuring Compound Inhibitory Potency

Measurement of inhibition by compounds was performed using the HCV replicon system. Several different replicons encoding different HCV genotypes or mutations were used. In addition, potency measurements were made using different formats of the replicon assay, including different ways of measurements and different plating formats. *See* Jan M. Vrolijk *et al.*, *A replicons-based bioassay for the measurement of interferons in patients with chronic hepatitis C*, 110 J. VIROLOGICAL METHODS 201 (2003); Steven S. Carroll *et al.*, *Inhibition of Hepatitis C Virus RNA Replication by 2'-Modified Nucleoside Analogs*, 278(14) J. BIOLOGICAL CHEMISTRY 11979 (2003). However, the underlying principles are common to all of these determinations, and are outlined below.

Stable neomycin phosphotransferase encoding replicons-harboring cell lines were used, so all cell lines were maintained under G418 selection prior to the assay. Potency was deteremined using a cell ELISA assay with an antibody to the replicons encoded NS3/4a protease. *See* Caterina Trozzi *et al.*, *In Vitro Selection and Characterization of Hepatitis C Virus Serine Protease Variants Resistant to an Active-Site Peptide Inhibitor*, 77(6) J. Virol. 3669 (2003). To initiate an assay, replicon cells were plated in the presence of a dilution series of test compound in the absence of G418. Typically, the assays were performed in a 96-well plate formate for manual operation, or a 384-well plate format for automated assay. Replicon cells and compound were incubated for 96 hours. At the end of the assay, cells were washed free of media and compound, and the cells were then lysed. RNA was quantified indirectly through detection of replicon-encoded NS3/4A protein levels, through an ELISA-based assay with an antibody specific for NS3/4A. IC_{50} determinations were calculated as a percentage of a DMSO control by fitting the data to a four-parameter fit function and the data obtained is provided in the table below.

Compound	Replicon 1b IC_{50}(nM)	Compound	Replicon 1b IC_{50} (nM)	Compound	Replicon 1b IC_{50} (nM)
1	1.1	**73**	2.2	**168**	19.5
2	6.9	**74**	3.2	**169**	2.4
3	22.7	**75**	3.7	**170**	3.5
4	4.8	**76**	8.3	**171**	3.2
5	1.8	**77**	6.6	**173**	3.8
6	7.0	**78**	2.4	**174**	13.5
7	3.7	**79**	2.9	**175**	4.9
8	8.2	**80**	2.7	**176**	2.7
9	8.5	**81**	4.0	**177**	1.8
10	16.5	**83**	2.6	**178**	9.6
11	4.7	**84**	2.9	**179**	6.0
12	4.4	**85**	2.6	**180**	3.3
13	10.4	**86**	1.9	**181**	26.4
14	3.9	**87**	9.5	**182**	2.7
15	6.4	**88**	4.8	**183**	7.8
16	5.2	**89**	1.3	**184**	1.5
17	6.8	**90**	1.3	**185**	4.0
18	27.0	**91**	2.0	**186**	15.8
19	5.6	**92**	3.6	**187**	14.6
20	10.4	**95**	2.2	**188**	5.1
21	13.8	**96**	5.1	**189**	3.2
22	3.9	**97**	4.0	**190**	2.2
23	7.4	**98**	78.2	**191**	2.1
24	7.0	**106**	3.7	**192**	165.2

25	7.2	**107**	2.0	**193**	8.1
26	5.0	**108**	5.0	**194**	72.7
27	5.7	**110**	2.9	**195**	5.7
28	2.3	**117**	1.5	**196**	0.7
29	1.5	**118**	3.0	**199**	4.2
30	0.9	**119**	2.2	**202**	5.9
31	2.2	**124**	3.2	**206**	30.5
32	2.0	**125**	3.2	**212**	4.2
33	2.6	**127**	3.3	**213**	3.9
34	5.1	**128**	2.3	**214**	1.6
35	1.9	**129**	17.2	**215**	2.7
36	2.2	**130**	5.3	**216**	8.8
37	4.1	**131**	10.2	**217**	5.8
38	1.9	**132**	5.8	**218**	13.0
39	11.6	**135**	5.4	**219**	3.9
40	4.2	**136**	6.9	**220**	52.4
44	1.4	**138**	5.9	**221**	2.7
45	2.9	**139**	8.6	**223**	1.2
46	1.6	**140**	10.0	**224**	1.8
47	1.7	**141**	4.1	**226**	1.2
48	1.0	**142**	64.1	**227**	5.1
49	2.4	**143**	20.5	**228**	8.9
50	4.5	**144**	6.0	**229**	2.5
51	11.9	**145**	3.3	**230**	0.9
52	2.1	**146**	1.5	**232**	1.3
53	2.4	**147**	1.9	**233**	2.3
54	1.8	**148**	3.1	**237**	2.4
55	5.5	**149**	1.8	**239**	1.2
56	1.9	**150**	1.3	**240**	1.4
57	3.3	**151**	1.1	**241**	8.2
58	2.6	**152**	28.8	**242**	18.2
59	2.5	**153**	2.4	**243**	3.6
60	6.3	**154**	2.5	**244**	2.4
61	2.1	**155**	3.7	**245**	2.8
62	8.2	**156**	1.8	**246**	303.4
63	2.1	**157**	1.7	**247**	1.8
64	1.8	**158**	1.1	**248**	2.6
65	3.0	**160**	1.5	**249**	4.7
66	1.5	**161**	4.5	**250**	15.1
67	1.7	**162**	2.8	**251**	3.8
68	3.5	**163**	2.9	**252**	2.8
69	10.0	**164**	18.7	**253**	3.8
70	2.3	**165**	13.6	**254**	2.1
71	3.6	**166**	13.1	**255**	0.5
72	4.0	**167**	6.6		

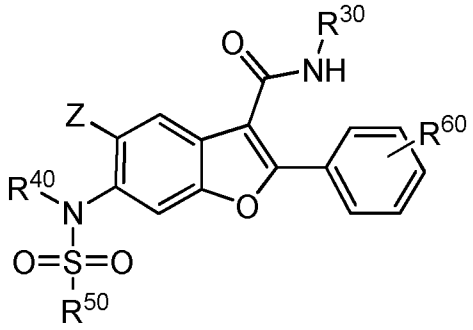
It will be appreciated that various of the above-discussed and other features and functions, or alternatives thereof, may be desirably combined into many other different systems

or applications. Also that various presently unforeseen or unanticipated alternatives, modifications, variations or improvements therein may be subsequently made by those skilled in the art which are also intended to be encompassed by the following claims.

5

CLAIMS

1. A compound having the formula:



(I)

or a pharmaceutically acceptable salt thereof,

wherein:

Z is a phenyl group which is substituted with one R^{10} group and optionally further substituted with up to four R^{20} groups;

R^{10} is an 8- to 10-membered bicyclic heteroaryl group, wherein said 8- to 10-membered bicyclic heteroaryl group is optionally substituted with up to 4 groups, which can be the same or different, and are selected from halo, C_1-C_6 alkyl, -C(O)H, -$(CH_2)_t$-$N(R^{70})_2$, -$(CH_2)_t$-OH, -$(CH_2)_t$-O-(C_1-C_6 alkyl), -CF_3, -NHC(O)-heterocyclyl, -NHC(O)-(C_1-C_6 alkyl), -C(O)NH-(C_1-C_6 alkyl), -C(O)OH, -C(O)O-(C_1-C_6 alkyl), -NHC(O)-aryl, -$NHSO_2$-aryl, -$NHSO_2$-alkyl, -O-SO_2-alkyl, -O-(C_1-C_6 alkyl) and –CN, wherein the heterocyclyl moiety of said -NHC(O)-heterocyclyl group can be optionally substituted on a ring carbon or ring nitrogen atom with a –C(O)O-(C_1-C_6 alkyl) group;

R^{20} represents up to 4 optional substituents, which can be the same or different, and are selected from halo, 8- to 10-membered heteroaryl, C_1-C_6 alkyl, -O-(C_1-C_6 alkyl), -O-$(CH_2)_t$-OH, -O-$(CH_2)_t$-heterocyclyl, -O-(C_1-C_6 haloalkyl), -O-SO_2-(C_1-C_6 alkyl) and –CN;

R^{30} is H or C_1-C_6 alkyl;

R^{40} is selected from C_1-C_6 alkyl, C_1-C_6 haloalkyl, -$(CH_2)_t$-OH, -$(CH_2)_t$-heterocyclyl,-$(CH_2)_t$-$N(R^{70})_2$, -$(CH_2)_t$-CN, -$(CH_2)_t$-$NHC(O)OR^{30}$ and -$(CH_2)_t$-$NHC(O)R^{30}$;

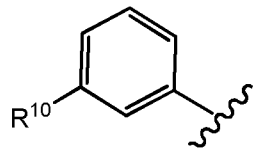
R^{50} is C_1-C_6 alkyl, C_6-C_{10} aryl or C_3-C_7 cycloalkyl;

R^{60} represents up to 4 optional ring substituents, which can be the same or different, and are selected from halo, C_1-C_6 alkyl, -O-(C_1-C_6 alkyl), -O-(C_1-C_6 haloalkyl) and –CN;

each occurrence of R^{70} is independently H or C_1-C_6 alkyl; and

each occurrence of t is independently an integer ranging from 0 to 6.

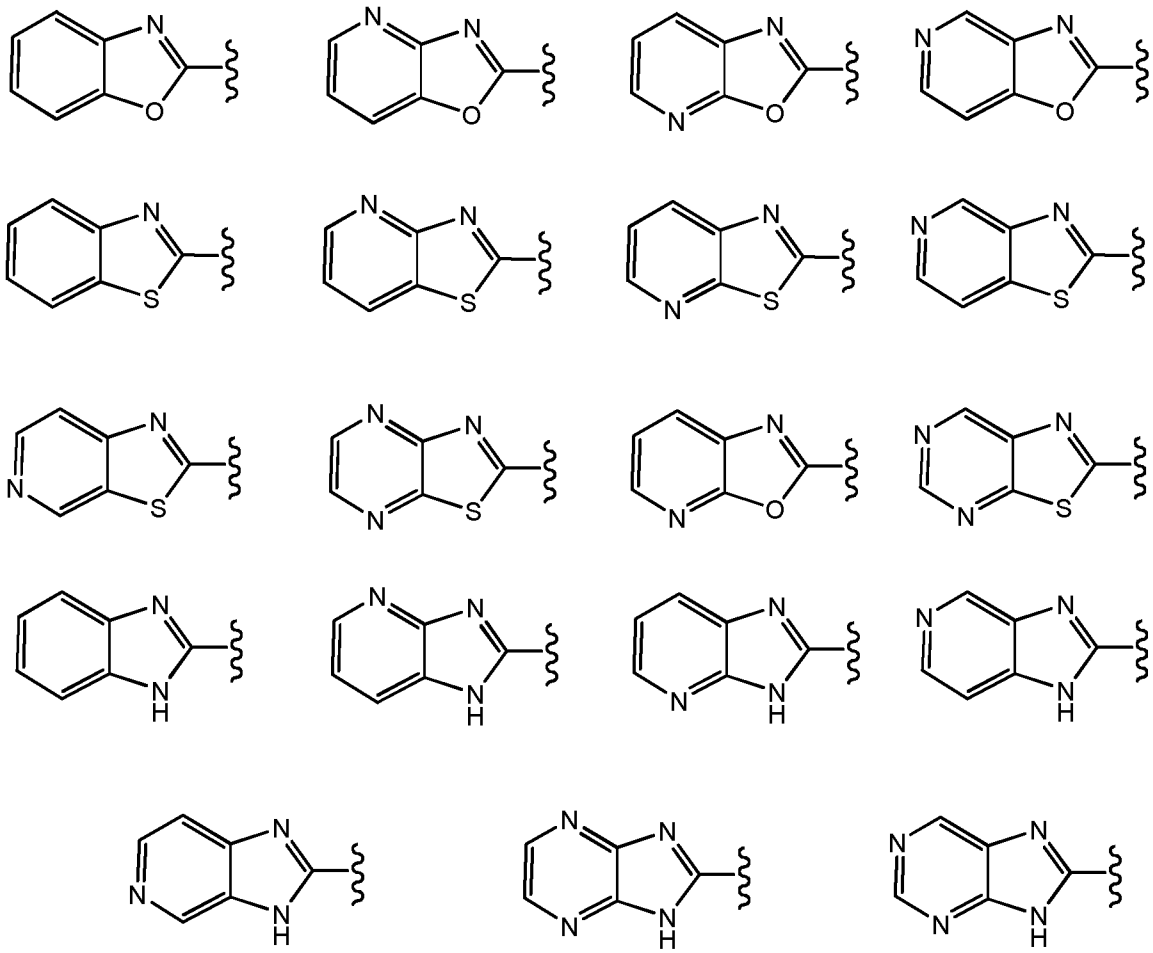
2. The compound of claim 1, wherein Z is:

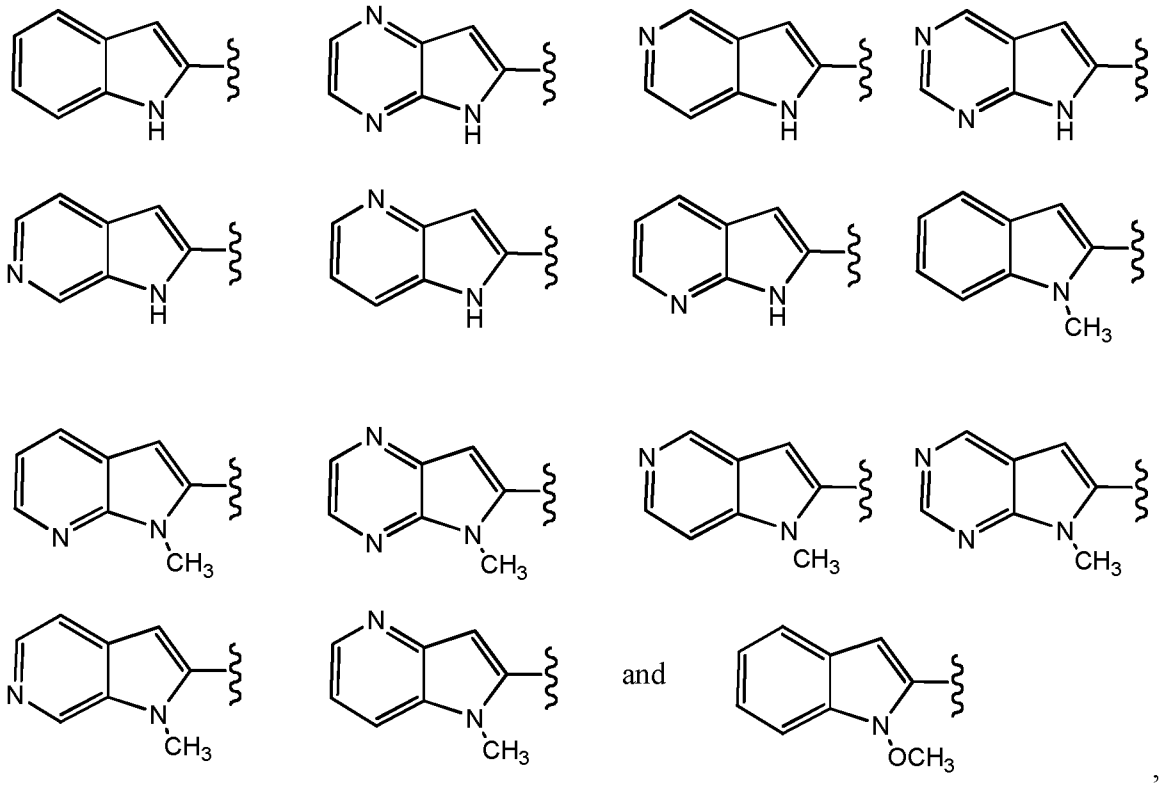


,

which can be optionally substituted on the depicted phenyl ring with one or two R^{20} groups, which can be the same or different.

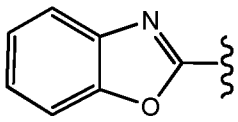
3. The compound of any of claims 1 and 2, wherein R^{10} is selected from:





wherein R^{10} can be optionally substituted as set forth in claim 1.

4. The compound of any of claims 1-3, wherein R^{10} is:



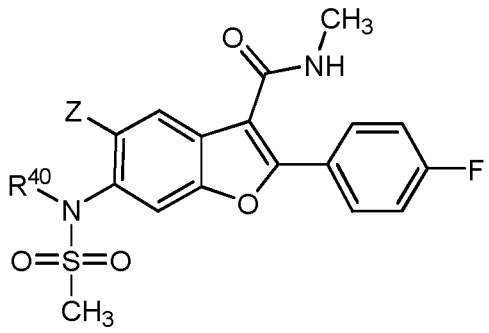
which can be optionally substituted as set forth in claim 1.

5. The compound of any of claims 1-4, wherein R^{30} and R^{50} are each methyl.

6. The compound of any of claims 1-5, wherein R^{60} represents a single F group at the para position of the phenyl ring to which it is attached.

7. The compound of any of claims 1-6, wherein R^{40} is C_1-C_6 alkyl, C_1-C_6 haloalkyl $-(CH_2)_t$-OH or $-(CH_2)_t$-CN.

8. The compound of claim 1 having the formula:

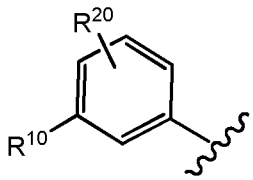


(Ia)

or a pharmaceutically acceptable salt thereof,

wherein:

Z is:



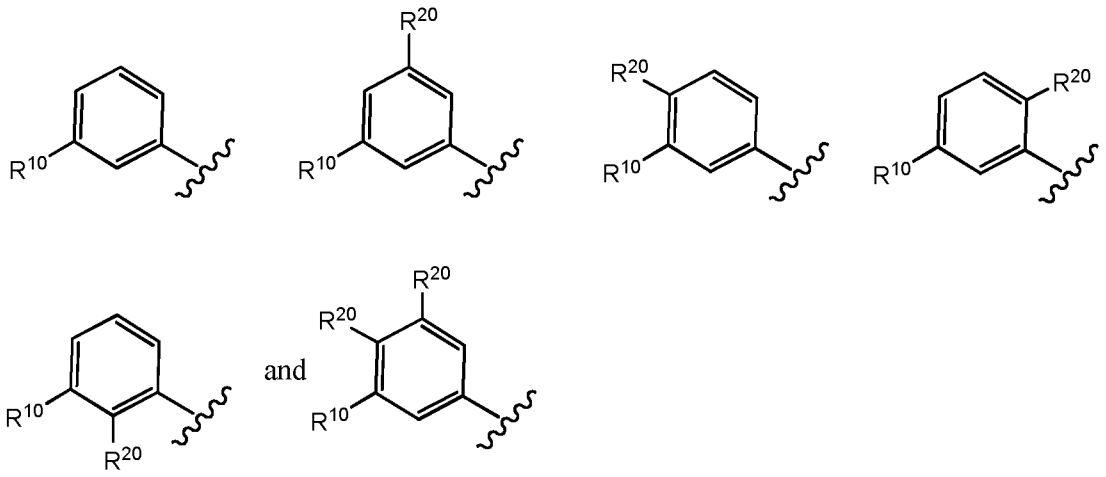
R^{10} is a 9-membered bicyclic heteroaryl group, wherein said 9-membered bicyclic heteroaryl group is optionally substituted with up to 2 groups, which can be the same or different, and are selected from halo, C_1-C_6 alkyl, -$(CH_2)_t$-$N(R^{70})_2$, -$(CH_2)_t$-OH, -$(CH_2)_t$-O-(C_1-C_6 alkyl), -CF_3, -NHC(O)-heterocyclyl, -NHC(O)-(C_1-C_6 alkyl), -C(O)NH-(C_1-C_6 alkyl), -C(O)OH, -C(O)O-(C_1-C_6 alkyl), -NHC(O)-aryl, -$NHSO_2$-aryl, -$NHSO_2$-alkyl, -O-SO_2-alkyl,-O-(C_1-C_6 alkyl) and –CN, wherein the heterocyclyl moiety of said -NHC(O)-heterocyclyl group can be optionally substituted on a ring carbon or ring nitrogen atom with a –C(O)O-(C_1-C_6 alkyl) group

R^{20} represents up to 2 optional substituents, which can be the same or different, and are selected from halo, C_1-C_6 alkyl, -O-(C_1-C_6 alkyl), -O-$(CH_2)_t$-OH, -O-$(CH_2)_t$-heterocyclyl, -O-(C_1-C_6 haloalkyl), -O-SO_2-(C_1-C_6 alkyl) and –CN;

R^{40} is C_1-C_6 alkyl, C_1-C_6 haloalkyl, -$(CH_2)_t$-OH or -$(CH_2)_t$-CN; and

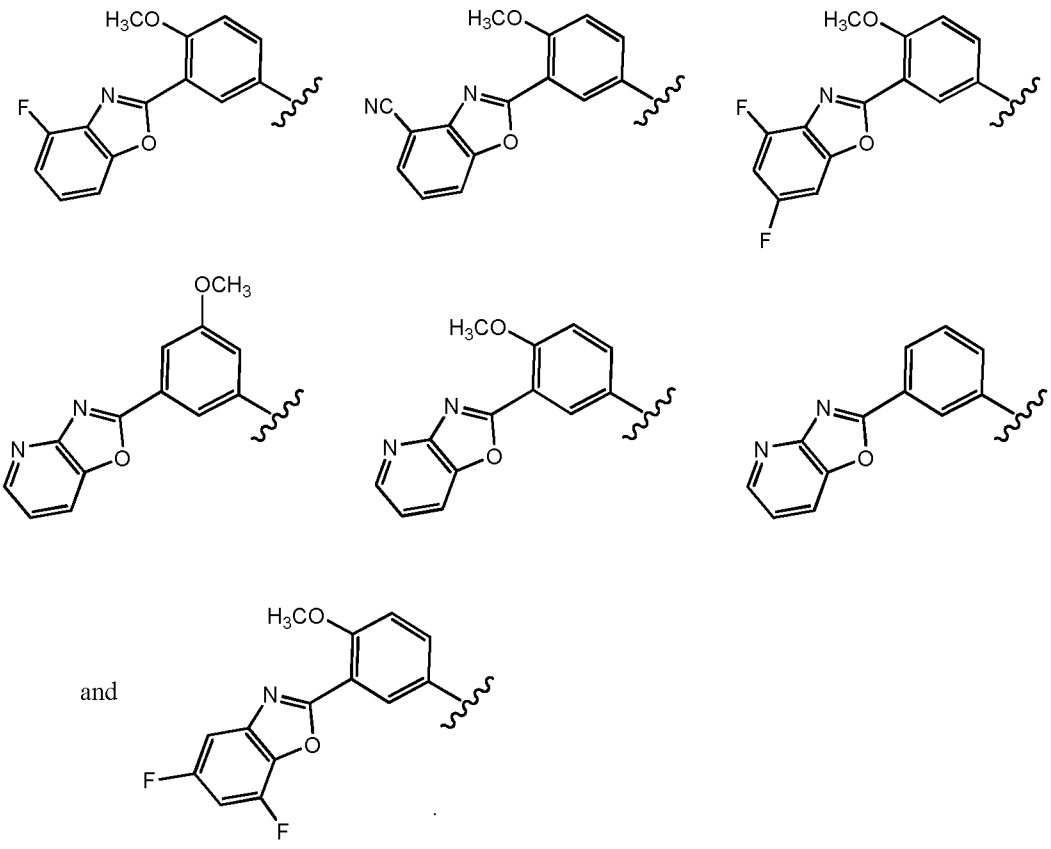
each occurrence of t is independently an integer ranging from 0 to 6.

9. The compound of any of claims 1-8, wherein Z is selected from:



wherein each occurrence of R^{20} is independently Cl, F, CN, $-OCF_3$ or $-OCH_3$.

10. The compound of any of claims 1-9, wherein Z is selected from:



11. The compound of any of claims 1-10, wherein R^{40} is $-CH_3$, $-(CH_2)_3$-CN, $-CH_2CH_2F$ or $-CH_2CH_2C(CH_3)_2$-OH.

12. A compound being any of the compounds numbered from 1-256 in the above specification, or a pharmaceutically acceptable salt thereof.

13. A pharmaceutical composition comprising an effective amount of the compound according to any of claims 1-12, and a pharmaceutically acceptable carrier.

14. The pharmaceutical composition according to claim 13, further comprising a second therapeutic agent selected from the group consisting of HCV antiviral agents, immunomodulators, and anti-infective agents.

15. The pharmaceutical composition according to claim 14, further comprising a second therapeutic agent selected from the group consisting of HCV protease inhibitors, HCV NS5A inhibitors and HCV NS5B polymerase inhibitors.

16. A use of the compound according to any of claims 1-12 in the preparation of a medicament for inhibiting HCV NS5B activity or for preventing and/or treating infection by HCV in a subject in need thereof.

17. A method of treating a patient infected with HCV comprising the step of administering an amount of the compound according to any of claims 1-12 effective to prevent and/or treat infection by HCV in a subject in need thereof.

18. A method according to claim 17, further comprising the step of administering pegylated-interferon alpha and ribovirin.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CN2010/080332

A. CLASSIFICATION OF SUBJECT MATTER

See extra sheet

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC: C07D, A61K, A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CPRS;CNKI;WPI;EPODOC;STN: hepatitis, HCV, benzofuran, carboxamide,

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CN1731993A(VIROPHARMA INC. et al), 8 Feb. 2006 (08.02.2006), See pages 15-23 and example 450 of description, claims 1-27	1-18

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim (S) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
03 Mar. 2011(03.03.2011)	**07 Apr. 2011 (07.04.2011)**
Name and mailing address of the ISA/CN The State Intellectual Property Office, the P.R.China 6 Xitucheng Rd., Jimen Bridge, Haidian District, Beijing, China 100088 Facsimile No. 86-10-62019451	Authorized officer HE, Xiangqiong Telephone No. (86-10)62084366

Form PCT/ISA /210 (second sheet) (July 2009)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CN2010/080332

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 17-18
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 17-18 are directed to a method of treatment of the human/animal body (Rule 39.1(iv) PCT). Nonetheless, the search has been carried out based on the use of the compounds in the manufacture of medicaments.

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/CN2010/080332

Patent Documents referred in the Report	Publication Date	Patent Family	Publication Date
CN1731993A	08.02.2006	WO2004041201A2	21.05.2004
		US2004162318A1	19.08.2004
		AU2003290584A1	07.06.2004
		NO20052071A	23.05.2005
		BR0315937A	13.09.2005
		EP1581207A2	05.10.2005
		TW200418452A	01.10.2004
		MXPA05004608A	01.09.2005
		JP2006510736T	30.03.2006
		KR20050065661A	29.06.2005
		ZA200503501A	25.10.2006
		INDELNP200502291E	19.01.2007
		US7265152B2	04.09.2007
		US2007231318A1	04.10.2007
		AU2003290584B2	16.07.2009
		IN219490B	27.06.2008
		MX265539B	01.04.2009
		US2009281336A1	12.11.2009
		IL168282A	18.11.2009
		US7666863B2	23.02.2010

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CN2010/080332

CLSSIFICATION OF SUBJECT MATTER

C07D405/10 (2006.01) i
C07D307/82 (2006.01) i
A61K31/343 (2006.01) i
A61P31/12 (2006.01) i