HETEROARYL COMPOUNDS FOR TREATING HUNTINGTON'S DISEASE

An aspect of the present description relates to compounds, forms, and pharmaceutical compositions thereof and methods of using such compounds, forms, or compositions thereof useful for treating or ameliorating Huntington's disease. In particular, another aspect of the present description relates to substituted benzothiazole compounds, forms and pharmaceutical compositions thereof and methods of using such compounds, forms, or compositions thereof for treating or ameliorating Huntington's disease.

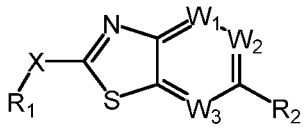
BACKGROUND

Huntington's disease (HD) is a progressive, autosomal dominant neurodegenerative disorder of the brain, having symptoms characterized by involuntary movements, cognitive impairment, and mental deterioration. Death, typically caused by pneumonia or coronary artery disease, usually occurs 13 to 15 years after the onset of symptoms. The prevalence of HD is between three and seven individuals per 100,000 in populations of western European descent. In North America, an estimated 30,000 people have HD, while an additional 200,000 people are at risk of inheriting the disease from an affected parent. The disease is caused by an expansion of uninterrupted trinucleotide CAG repeats in the "mutant" huntingtin (Htt) gene, leading to production of HTT (Htt protein) with an expanded poly-glutamine (polyQ) stretch, also known as a "CAG repeat" sequence. There are no current small molecule therapies targeting the underlying cause of the disease, leaving a high unmet need for medications that can be used for treating or ameliorating HD. Consequently, there remains a need to identify and provide small molecule compounds for treating or ameliorating HD.

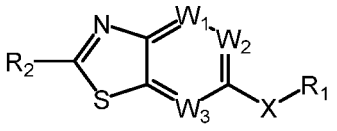
All other documents referred to herein are incorporated by reference into the present application as though fully set forth herein.

SUMMARY

An aspect of the present description includes compounds comprising, a compound of Formula (I) or Formula (II):



(I)



(II)

or a form thereof, wherein R_1, R_2, X, W_1, W_2, and W_3 are as defined herein.

An aspect of the present description includes a method for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of a compound of Formula (I) or Formula (II) or a form thereof.

An aspect of the present description includes a method for use of a compound of Formula (I) or Formula (II) or a form or composition thereof for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of the compound of Formula (I) or Formula (II) or a form or composition thereof.

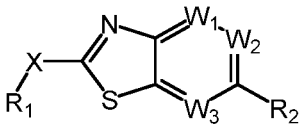
An aspect of the present description includes a use for a compound of Formula (I) or a form thereof for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of the compound of Formula (I) or a form thereof.

An aspect of the present description includes a use for a compound of Formula (I) or a form thereof in the manufacture of a medicament for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of the medicament.

An aspect of the present description includes a use for a compound of Formula (I) or a form thereof in a combination product with one or more therapeutic agents for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of the compound of Formula (I) or a form thereof in combination with an effective amount of the one or more agents.

DETAILED DESCRIPTION

An aspect of the present description relates to compounds comprising, a compound of Formula (I) or Formula (II):



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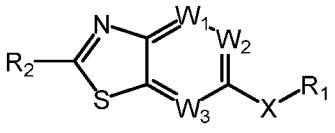


(II)

or a form thereof, wherein:

W_1, W_2 and W_3 are independently C-R_a or N;

R_a is, in each instance, independently selected from hydrogen, cyano, halogen, hydroxy, $C_{1\text{-}6}$alkyl, halo-$C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$alkyl-carbonyl, $C_{1\text{-}6}$alkoxy, halo-$C_{1\text{-}6}$alkoxy, $C_{1\text{-}6}$alkoxy-$C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$alkoxy-carbonyl, amino, $C_{1\text{-}6}$alkyl-amino, ($C_{1\text{-}6}$alkyl)$_2$-amino, amino-$C_{1\text{-}6}$alkyl, and hydroxy-$C_{1\text{-}6}$alkyl;

X is selected from N-R_b, O, or a bond;

R_b is selected from hydrogen and $C_{1\text{-}6}$alkyl;

R_1 is selected from $C_{3\text{-}10}$cycloalkyl and heterocyclyl,

wherein heterocyclyl is a saturated or partially unsaturated 3-7 membered monocyclic, 6-10 membered bicyclic or 13-16 membered polycyclic ring system having 1, 2, or 3 heteroatom ring members independently selected from N, O, or S, and

wherein, each instance of $C_{3\text{-}10}$cycloalkyl and heterocyclyl is optionally substituted with one, two three, or four R_3 substituents and optionally, with one additional R_4 substituent, or,

wherein, alternatively, each instance of $C_{3\text{-}10}$cycloalkyl and heterocyclyl is optionally substituted with one, two, three, four, or five R_3 substituents;

R_3 is, in each instance, independently selected from cyano, halogen, hydroxy, $C_{1\text{-}6}$alkyl, halo-$C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$alkyl-carbonyl, $C_{1\text{-}6}$alkoxy, halo-$C_{1\text{-}6}$alkoxy, $C_{1\text{-}6}$alkoxy-$C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$alkoxy-carbonyl, amino, $C_{1\text{-}6}$alkyl-amino, ($C_{1\text{-}6}$alkyl)$_2$-amino, amino-$C_{1\text{-}6}$alkyl, and hydroxy-$C_{1\text{-}6}$alkyl;

R_4 is selected from $C_{3\text{-}10}$cycloalkyl, phenyl, heterocyclyl, and heteroaryl;

wherein heterocyclyl is a saturated or partially unsaturated 3-7 membered monocyclic, 6-10 membered bicyclic or 13-16 membered polycyclic ring system having 1, 2, or 3 heteroatom ring members independently selected from N, O, or S,

wherein heteroaryl is a 3-7 membered monocyclic or 6-10 membered bicyclic ring system having 1, 2, 3, or 4 heteroatom ring members independently selected from N, O, or S, and

wherein, each instance of C_{3-10}cycloalkyl, phenyl, heterocyclyl, and heteroaryl is optionally substituted with one, two or three R_7 substituents;

R_2 is selected from phenyl and heteroaryl,

wherein heteroaryl is a 3-7 membered monocyclic or 6-10 membered bicyclic ring system having 1, 2, 3, or 4 heteroatom ring members independently selected from N, O, or S,

wherein, each instance of phenyl and heteroaryl is optionally substituted with one, two or three R_5 substituents and optionally, with one additional R_6 substituent, or,

wherein, alternatively, each instance of phenyl and heteroaryl is optionally substituted with one, two, three or four R_5 substituents;

R_5 is, in each instance, independently selected from cyano, halogen, hydroxy, C_{1-6}alkyl, halo-C_{1-6}alkyl, C_{1-6}alkyl-carbonyl, C_{1-6}alkoxy, halo-C_{1-6}alkoxy, C_{1-6}alkoxy-C_{1-6}alkyl, C_{1-6}alkoxy-carbonyl, C_{1-6}alkoxy-carbonyl-C_{1-6}alkyl, carboxyl, C_{1-6}alkyl-carboxyl, amino, C_{1-6}alkyl-amino, $(C_{1-6}alkyl)_2$-amino, amino-C_{1-6}alkyl, amino-carbonyl, and hydroxy-C_{1-6}alkyl;

R_6 is selected from C_{3-10}cycloalkyl, phenyl, phenyl-C_{1-6}alkoxy, phenyl-oxy, heterocyclyl, and heteroaryl;

wherein heterocyclyl is a saturated or partially unsaturated 3-7 membered monocyclic, 6-10 membered bicyclic or 13-16 membered polycyclic ring system having 1, 2, or 3 heteroatom ring members independently selected from N, O, or S,

wherein heteroaryl is a 3-7 membered monocyclic or 6-10 membered bicyclic ring system having 1, 2, 3, or 4 heteroatom ring members independently selected from N, O, or S, and

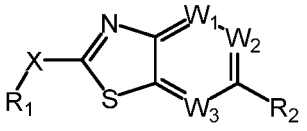
wherein, each instance of C_{3-10}cycloalkyl, phenyl, heterocyclyl, and heteroaryl is optionally substituted with one, two or three R_7 substituents; and

R_7 is, in each instance, independently selected from cyano, halogen, hydroxy, C_{1-6}alkyl, halo-C_{1-6}alkyl, C_{1-6}alkyl-carbonyl, C_{1-6}alkoxy, halo-C_{1-6}alkoxy, C_{1-6}alkoxy-C_{1-6}alkyl, C_{1-6}alkoxy-carbonyl, amino, C_{1-6}alkyl-amino, $(C_{1-6}alkyl)_2$-amino, amino-C_{1-6}alkyl, and hydroxy-C_{1-6}alkyl;

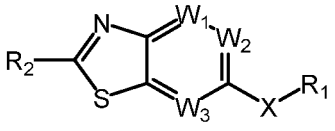
wherein a form of the compound is selected from the group consisting of a salt, hydrate, solvate, racemate, enantiomer, diastereomer, stereoisomer, and tautomer form thereof.

ASPECTS OF THE DESCRIPTION

Another aspect of the present description includes a compound of Formula (I) or Formula (II):



(I)



(II)

or a form thereof, wherein:

W_1, W_2 and W_3 are independently C-R_a or N;

R_a is, in each instance, independently selected from hydrogen, cyano, halogen, hydroxy, $C_{1\text{-}6}$alkyl, halo-$C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$alkyl-carbonyl, $C_{1\text{-}6}$alkoxy, halo-$C_{1\text{-}6}$alkoxy, $C_{1\text{-}6}$alkoxy-$C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$alkoxy-carbonyl, amino, $C_{1\text{-}6}$alkyl-amino, ($C_{1\text{-}6}$alkyl)$_2$-amino, amino-$C_{1\text{-}6}$alkyl, and hydroxy-$C_{1\text{-}6}$alkyl;

X is selected from N-R_b, O, or a bond;

R_b is selected from hydrogen and $C_{1\text{-}6}$alkyl;

R_1 is selected from $C_{3\text{-}10}$cycloalkyl and heterocyclyl,

wherein heterocyclyl is a saturated or partially unsaturated 3-7 membered monocyclic, 6-10 membered bicyclic or 13-16 membered polycyclic ring system having 1, 2, or 3 heteroatom ring members independently selected from N, O, or S, and

wherein, each instance of $C_{3\text{-}10}$cycloalkyl and heterocyclyl is optionally substituted with one, two three, or four R_3 substituents and optionally, with one additional R_4 substituent, or,

wherein, alternatively, each instance of $C_{3\text{-}10}$cycloalkyl and heterocyclyl is optionally substituted with one, two, three, four, or five R_3 substituents;

R_3 is, in each instance, independently selected from cyano, halogen, hydroxy, $C_{1\text{-}6}$alkyl, halo-$C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$alkyl-carbonyl, $C_{1\text{-}6}$alkoxy, halo-$C_{1\text{-}6}$alkoxy, $C_{1\text{-}6}$alkoxy-$C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$alkoxy-carbonyl, amino, $C_{1\text{-}6}$alkyl-amino, ($C_{1\text{-}6}$alkyl)$_2$-amino, amino-$C_{1\text{-}6}$alkyl, and hydroxy-$C_{1\text{-}6}$alkyl;

R_4 is selected from $C_{3\text{-}10}$cycloalkyl, phenyl, heterocyclyl, and heteroaryl;

wherein heterocyclyl is a saturated or partially unsaturated 3-7 membered monocyclic, 6-10 membered bicyclic or 13-16 membered polycyclic ring system having 1, 2, or 3 heteroatom ring members independently selected from N, O, or S,

wherein heteroaryl is a 3-7 membered monocyclic or 6-10 membered bicyclic ring system having 1, 2, 3, or 4 heteroatom ring members independently selected from N, O, or S, and

wherein, each instance of C_{3-10}cycloalkyl, phenyl, heterocyclyl, and heteroaryl is optionally substituted with one, two or three R_7 substituents;

R_2 is selected from phenyl and heteroaryl,

wherein heteroaryl is a 3-7 membered monocyclic or 6-10 membered bicyclic ring system having 1, 2, 3, or 4 heteroatom ring members independently selected from N, O, or S,

wherein, each instance of phenyl and heteroaryl is optionally substituted with one, two or three R_5 substituents and optionally, with one additional R_6 substituent, or,

wherein, alternatively, each instance of phenyl and heteroaryl is optionally substituted with one, two, three or four R_5 substituents;

R_5 is, in each instance, independently selected from cyano, halogen, hydroxy, C_{1-6}alkyl, halo-C_{1-6}alkyl, C_{1-6}alkyl-carbonyl, C_{1-6}alkoxy, halo-C_{1-6}alkoxy, C_{1-6}alkoxy-C_{1-6}alkyl, C_{1-6}alkoxy-carbonyl, C_{1-6}alkoxy-carbonyl-C_{1-6}alkyl, carboxyl, C_{1-6}alkyl-carboxyl, amino, C_{1-6}alkyl-amino, $(C_{1-6}alkyl)_2$-amino, amino-C_{1-6}alkyl, amino-carbonyl, and hydroxy-C_{1-6}alkyl;

R_6 is selected from C_{3-10}cycloalkyl, phenyl, phenyl-C_{1-6}alkoxy, phenyl-oxy, heterocyclyl, and heteroaryl;

wherein heterocyclyl is a saturated or partially unsaturated 3-7 membered monocyclic, 6-10 membered bicyclic or 13-16 membered polycyclic ring system having 1, 2, or 3 heteroatom ring members independently selected from N, O, or S,

wherein heteroaryl is a 3-7 membered monocyclic or 6-10 membered bicyclic ring system having 1, 2, 3, or 4 heteroatom ring members independently selected from N, O, or S, and

wherein, each instance of C_{3-10}cycloalkyl, phenyl, heterocyclyl, and heteroaryl is optionally substituted with one, two or three R_7 substituents; and

R_7 is, in each instance, independently selected from cyano, halogen, hydroxy, C_{1-6}alkyl, halo-C_{1-6}alkyl, C_{1-6}alkyl-carbonyl, C_{1-6}alkoxy, halo-C_{1-6}alkoxy, C_{1-6}alkoxy-C_{1-6}alkyl,

C_{1-6}alkoxy-carbonyl, amino, C_{1-6}alkyl-amino, $(C_{1-6}alkyl)_2$-amino, amino-C_{1-6}alkyl, and hydroxy-C_{1-6}alkyl.

One aspect includes a compound of Formula (I) or Formula (II), wherein W_1, W_2 and W_3 are C-R_a.

One aspect includes a compound of Formula (I) or Formula (II), wherein W_1 is N.

Another aspect includes a compound of Formula (I) or Formula (II), wherein W_1 is N, and W_2 and W_3 are C-R_a.

One aspect includes a compound of Formula (I) or Formula (II), wherein W_2 is N.

Another aspect includes a compound of Formula (I) or Formula (II), wherein W_2 is N, and W_1 and W_3 are C-R_a.

One aspect includes a compound of Formula (I) or Formula (II), wherein W_3 is N.

Another aspect includes a compound of Formula (I) or Formula (II), wherein W_3 is N, and W_1 and W_2 are C-R_a.

One aspect includes a compound of Formula (I) or Formula (II), wherein W_1 and W_2 are N.

Another aspect includes a compound of Formula (I) or Formula (II), wherein W_1 and W_2 are N and W_3 is C-R_a.

One aspect includes a compound of Formula (I) or Formula (II), wherein W_1 and W_3 are N.

Another aspect includes a compound of Formula (I) or Formula (II), wherein W_1 and W_3 are N and W_2 is C-R_a.

One aspect includes a compound of Formula (I) or Formula (II), wherein W_2 and W_3 are N.

Another aspect includes a compound of Formula (I) or Formula (II), wherein W_2 and W_3 are N and W_2 is C-R_a.

One aspect includes a compound of Formula (I) or Formula (II), wherein W_1, W_2 and W_3 are N.

One aspect includes a compound of Formula (I) or Formula (II), wherein R_a is, in each instance, independently selected from hydrogen, cyano, halogen, hydroxy, C_{1-6}alkyl, halo-C_{1-6}alkyl, C_{1-6}alkyl-carbonyl, C_{1-6}alkoxy, halo-C_{1-6}alkoxy, C_{1-6}alkoxy-C_{1-6}alkyl,

C_{1-6}alkoxy-carbonyl, amino, C_{1-6}alkyl-amino, $(C_{1-6}alkyl)_2$-amino, amino-C_{1-6}alkyl, and hydroxy-C_{1-6}alkyl.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_a is, in each instance, independently selected from hydrogen, cyano, halogen, hydroxy, and C_{1-6}alkoxy.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_a is, in each instance, hydrogen.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_a is, in each instance, cyano.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_a is, in each instance, halogen selected from bromo, chloro, fluoro, and iodo.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_a is, in each instance, halogen selected from chloro and fluoro.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_a is, in each instance, hydroxy.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_a is, in each instance, C_{1-6}alkoxy selected from methoxy, ethoxy, propoxy, isopropoxy, and tert-butoxy.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_a is, in each instance, methoxy.

One aspect includes a compound of Formula (I) or Formula (II), wherein X is selected from N-R_b, O, or a bond.

Another aspect includes a compound of Formula (I) or Formula (II), wherein X is N-R_b.

Another aspect includes a compound of Formula (I) or Formula (II), wherein X is O.

Another aspect includes a compound of Formula (I) or Formula (II), wherein X is a bond.

One aspect includes a compound of Formula (I) or Formula (II), wherein R_b is selected from hydrogen and C_{1-6}alkyl.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_b is hydrogen.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_b is C_{1-6}alkyl selected from methyl, ethyl, propyl, isopropyl, and tert-butyl.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_b is C_{1-6}alkyl selected from methyl and ethyl.

One aspect includes a compound of Formula (I) or Formula (II), wherein R_1 is selected from C_{3-10}cycloalkyl and heterocyclyl,

wherein heterocyclyl is a saturated or partially unsaturated 3-7 membered monocyclic, 6-10 membered bicyclic or 13-16 membered polycyclic ring system having 1, 2, or 3 heteroatom ring members independently selected from N, O, or S, and

wherein, each instance of C_{3-10}cycloalkyl and heterocyclyl is optionally substituted with one, two three, or four R_3 substituents and optionally, with one additional R_4 substituent, or,

wherein, alternatively, each instance of C_{3-10}cycloalkyl and heterocyclyl is optionally substituted with one, two, three, four, or five R_3 substituents.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_1 is C_{3-10}cycloalkyl selected from cyclopropyl, cylcobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, bicyclo[2.2.1]hexanyl, and adamantyl, optionally substituted with one, two three, or four R_3 substituents and optionally, with one additional R_4 substituent, or, alternatively, optionally substituted with one, two, three, four, or five R_3 substituents.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_1 is C_{3-10}cycloalkyl selected from cylcobutyl and cyclohexyl, optionally substituted with one, two three, or four R_3 substituents and optionally, with one additional R_4 substituent, or, alternatively, optionally substituted with one, two, three, four, or five R_3 substituents.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_1 is heterocyclyl selected from azetidinyl, tetrahydrofuranyl, pyrrolidinyl, piperidinyl, piperazinyl, 1*H*-azepinyl, 2,3,6,7-tetrahydro-1*H*-azepinyl, azepanyl, 1,4-diazepanyl, 1,2,5,6-tetrahydropyridinyl, 1,2,3,6-tetrahydropyridinyl, octahydroindolizinyl, octahydro-1*H*-pyrrolo[3,2-*c*]pyridinyl, (3a*S*,7a*R*)-octahydro-1*H*-pyrrolo[3,2-*c*]pyridinyl, 1-azabicyclo[2.2.2]octyl, 3-azabicyclo[3.1.0]hexyl, (1*R*,5*S*)-3-azabicyclo[3.1.0]hexyl, 3-azabicyclo[3.2.1]octyl, 8-azabicyclo[3.2.1]octyl, (1*R*,5*S*)-8-azabicyclo[3.2.1]octyl, 8-azabicyclo[3.2.1]oct-2-en-yl, (1*R*,5*S*)-8-azabicyclo[3.2.1]oct-2-en-yl, 9-azabicyclo[3.3.1]nonyl, (1*R*,5*S*)-9-azabicyclo[3.3.1]nonyl, 2,5-diazabicyclo[2.2.1]heptyl, (1*S*,4*S*)-2,5-diazabicyclo[2.2.1]heptyl, 1,4-diazabicyclo[3.1.1]heptyl, 3,6-diazabicyclo[3.2.0]heptyl, 2,5-diazabicyclo[2.2.2]octyl, 1,4-diazabicyclo[3.2.1]octyl, 3,8-diazabicyclo[3.2.1]octyl, (1*R*,5*S*)-3,8-diazabicyclo[3.2.1]octyl, 1,4-diazabicyclo[3.2.2]nonyl, 3,8-diazabicyclo[4.2.0]octyl, (1*S*,6*R*)-3,8-diazabicyclo[4.2.0]octyl, (1*R*,6*S*)-3,8-

diazabicyclo[4.2.0]octyl, 2-azaspiro[3.3]heptyl, 4,7-diazaspiro[2.5]octyl, 2,6-diazaspiro[3.3]heptyl, 2,6-diazaspiro[3.4]octyl, 1,6-diazaspiro[3.5]nonyl, 1,7-diazaspiro[3.5]nonyl, 2,6-diazaspiro[3.5]nonyl, 2,7-diazaspiro[3.5]nonyl, 5,8-diazaspiro[3.5]nonyl, 1,7-diazaspiro[4.4]nonyl, 2,7-diazaspiro[4.4]nonyl, 2,7-diazaspiro[4.5]decyl, and 6,9-diazaspiro[4.5]decyl, optionally substituted with one, two three, or four R_3 substituents and optionally, with one additional R_4 substituent, or, alternatively, optionally substituted with one, two, three, four, or five R_3 substituents.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_1 is heterocyclyl selected from azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, 2,3,6,7-tetrahydro-1*H*-azepinyl, azepanyl, 1,4-diazepanyl, 1,2,3,6-tetrahydropyridinyl, octahydroindolizinyl, octahydro-1*H*-pyrrolo[3,2-*c*]pyridinyl, (3a*S*,7a*R*)-octahydro-1*H*-pyrrolo[3,2-*c*]pyridinyl, 1-azabicyclo[2.2.2]octyl, 8-azabicyclo[3.2.1]octyl, (1*R*,5*S*)-8-azabicyclo[3.2.1]octyl, 9-azabicyclo[3.3.1]nonyl, 3,8-diazabicyclo[4.2.0]octyl, (1*S*,6*R*)-3,8-diazabicyclo[4.2.0]octyl, (1*R*,6*S*)-3,8-diazabicyclo[4.2.0]octyl, 2-azaspiro[3.3]heptyl, 2,6-diazaspiro[3.3]heptyl, 1,6-diazaspiro[3.5]nonyl, 1,7-diazaspiro[3.5]nonyl, 2,6-diazaspiro[3.5]nonyl, 2,7-diazaspiro[3.5]nonyl, and 2,7-diazaspiro[4.4]nonyl, optionally substituted with one, two three, or four R_3 substituents and optionally, with one additional R_4 substituent, or, alternatively, optionally substituted with one, two, three, four, or five R_3 substituents.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_1 is heterocyclyl selected from azetidin-2-yl, azetidin-3-yl, tetrahydrofuran-3-yl, pyrrolidin-2-yl, pyrrolidin-3-yl, piperidin-1-yl, piperidin-2-yl, piperidin-3-yl, piperidin-4-yl, piperazin-1-yl, piperazin-2-yl, 1*H*-azepin-2-yl, 1*H*-azepin-3-yl, 1*H*-azepin-4-yl, 2,3,6,7-tetrahydro-1*H*-azepin-4-yl, azepan-2-yl, azepan-3-yl, azepan-4-yl, 1,4-diazepan-1-yl, 1,4-diazepan-2-yl, 1,4-diazepan-3-yl, 1,2,5,6-tetrahydropyridin-5-yl, 1,2,3,6-tetrahydropyridin-4-yl, octahydroindolizin-7-yl, octahydro-1*H*-pyrrolo[3,2-*c*]pyridin-1-yl, (3a*S*,7a*R*)-octahydro-1*H*-pyrrolo[3,2-*c*]pyridin-1-yl, 1-azabicyclo[2.2.2]oct-4-yl, 3-azabicyclo[3.1.0]hexan-3-yl, 3-azabicyclo[3.2.1]octan-8-yl, 8-azabicyclo[3.2.1]oct-3-yl, (1*R*,5*S*)-8-azabicyclo[3.2.1]octan-3-yl, 8-azabicyclo[3.2.1]oct-2-en-3-yl, (1*R*,5*S*)-8-azabicyclo[3.2.1]oct-2-en-3-yl, 9-azabicyclo[3.3.1]non-3-yl, (1*R*,5*S*)-9-azabicyclo[3.3.1]nonan-3-yl, 2,5-diazabicyclo[2.2.1]heptan-2-yl, (1*S*,4*S*)-2,5-diazabicyclo[2.2.1]heptan-2-yl, 1,4-diazabicyclo[3.1.1]heptan-4-yl,

3,6-diazabicyclo[3.2.0]heptan-3-yl, 3,6-diazabicyclo[3.2.0]heptan-6-yl, 2,5-diazabicyclo[2.2.2]octan-2-yl, 1,4-diazabicyclo[3.2.1]octan-4-yl, 3,8-diazabicyclo[3.2.1]octan-3-yl, (1*R*,5*S*)-3,8-diazabicyclo[3.2.1]octan-3-yl, 1,4-diazabicyclo[3.2.2]nonan-4-yl, 3,8-diazabicyclo[4.2.0]oct-8-yl, (1*S*,6*R*)-3,8-diazabicyclo[4.2.0]oct-8-yl, (1*R*,6*S*)-3,8-diazabicyclo[4.2.0]oct-8-yl, 2-azaspiro[3.3]hept-2-yl, 2-azaspiro[3.3]hept-6-yl, 4,7-diazaspiro[2.5]oct-4-yl, 4,7-diazaspiro[2.5]oct-7-yl, 2,6-diazaspiro[3.3]hept-2-yl, 2,6-diazaspiro[3.4]oct-2-yl, 2,6-diazaspiro[3.4]oct-6-yl, 1,6-diazaspiro[3.5]non-1-yl, 1,7-diazaspiro[3.5]non-1-yl, 1,7,-diazaspiro[4.4]non-1-yl, 1,7-diazaspiro[4.4]non-7-yl, 2,6-diazaspiro[3.5]non-2-yl, 2,6-diazaspiro[3.5]non-6-yl, 2,7-diazaspiro[3.5]non-7-yl, 5,8-diazaspiro[3.5]non-8-yl, 2,7-diazaspiro[4.4]non-2-yl, 2,7-diazaspiro[4.5]deca-2-yl, 2,7-diazaspiro[4.5]dec-7-yl, and 6,9-diazaspiro[4.5]dec-9-yl, optionally substituted with one, two three, or four R_3 substituents and optionally, with one additional R_4 substituent, or, alternatively, optionally substituted with one, two, three, four, or five R_3 substituents.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_1 is heterocyclyl selected from azetidin-3-yl, pyrrolidin-3-yl, piperidin-1-yl, piperidin-3-yl, piperidin-4-yl, piperazin-1-yl, 2,3,6,7-tetrahydro-1*H*-azepin-4-yl, azepan-4-yl, 1,4-diazepan-1-yl, 1,2,3,6-tetrahydropyridin-4-yl, octahydroindolizin-7-yl, octahydro-1*H*-pyrrolo[3,2-*c*]pyridin-1-yl, (3a*S*,7a*R*)-octahydro-1*H*-pyrrolo[3,2-*c*]pyridin-1-yl, 1-azabicyclo[2.2.2]oct-4-yl, 3-azabicyclo[3.2.1]octan-8-yl, 8-azabicyclo[3.2.1]oct-3-yl, 9-azabicyclo[3.3.1]non-3-yl, 3,8-diazabicyclo[4.2.0]oct-8-yl, (1*S*,6*R*)-3,8-diazabicyclo[4.2.0]oct-8-yl, (1*R*,6*S*)-3,8-diazabicyclo[4.2.0]oct-8-yl, 2-azaspiro[3.3]hept-6-yl, 2,6-diazaspiro[3.3]hept-2-yl, 1,6-diazaspiro[3.5]non-1-yl, 1,7-diazaspiro[3.5]non-1-yl, 2,6-diazaspiro[3.5]non-2-yl, 2,7-diazaspiro[3.5]non-7-yl, and 2,7-diazaspiro[4.4]non-2-yl, optionally substituted with one, two three, or four R_3 substituents and optionally, with one additional R_4 substituent, or, alternatively, each instance of heterocyclyl l is optionally substituted with one, two, three, four, or five R_3 substituents.

One aspect includes a compound of Formula (I) or Formula (II), wherein R_3 is, in each instance, independently selected from cyano, halogen, hydroxy, $C_{1\text{-}6}$alkyl, halo-$C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$alkyl-carbonyl, $C_{1\text{-}6}$alkoxy, halo-$C_{1\text{-}6}$alkoxy, $C_{1\text{-}6}$alkoxy-$C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$alkoxy-carbonyl, amino, $C_{1\text{-}6}$alkyl-amino, $(C_{1\text{-}6}\text{alkyl})_2$-amino, amino-$C_{1\text{-}6}$alkyl, and hydroxy-$C_{1\text{-}6}$alkyl.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_3 is, in each instance, independently selected from halogen, hydroxy, $C_{1\text{-}6}$alkyl, halo-$C_{1\text{-}6}$alkyl, amino, $C_{1\text{-}6}$alkyl-amino, $(C_{1\text{-}6}alkyl)_2$-amino, and hydroxy-$C_{1\text{-}6}$alkyl.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_3 is, in each instance, halogen selected from bromo, chloro, fluoro, and iodo.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_3 is, in each instance, fluoro.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_3 is, in each instance, hydroxy.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_3 is, in each instance, $C_{1\text{-}6}$alkyl selected from methyl, ethyl, propyl, isopropyl, and tert-butyl.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_3 is, in each instance, $C_{1\text{-}6}$alkyl selected from methyl and ethyl.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_3 is, in each instance, halo-$C_{1\text{-}6}$alkyl, wherein $C_{1\text{-}6}$alkyl is selected from methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, and tert-butyl partially or completely substituted with one or more halogens selected from bromo, chloro, fluoro, and iodo where allowed by available valences.

Another aspect includes a compound of Formula (I), wherein R_3 is, in each instance, halo-$C_{1\text{-}6}$alkyl selected from fluoroethyl.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_3 is, in each instance, amino.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_3 is, in each instance, $C_{1\text{-}6}$alkyl-amino wherein $C_{1\text{-}6}$alkyl is selected from methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, and tert-butyl.

Another aspect includes a compound of Formula (I), wherein R_3 is, in each instance, methylamino.

Another aspect includes a compound of Formula (I), wherein R_3 is, in each instance, $(C_{1\text{-}6}alkyl)_2$-amino wherein $C_{1\text{-}6}$alkyl is independently selected from methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, and tert-butyl.

Another aspect includes a compound of Formula (I), wherein R_3 is, in each instance, dimethylamino.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_3 is, in each instance, hydroxy-C_{1-6}alkyl, wherein C_{1-6}alkyl is selected from methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, and tert-butyl partially or completely substituted with one or more hydroxy groups where allowed by available valences.

Another aspect includes a compound of Formula (I), wherein R_3 is, in each instance, hydroxy-C_{1-6}alkyl selected from hydroxymethyl and hydroxyethyl.

One aspect includes a compound of Formula (I) or Formula (II), wherein R_4 is selected from C_{3-10}cycloalkyl, phenyl, heterocyclyl, and heteroaryl;

wherein heterocyclyl is a saturated or partially unsaturated 3-7 membered monocyclic, 6-10 membered bicyclic or 13-16 membered polycyclic ring system having 1, 2, or 3 heteroatom ring members independently selected from N, O, or S,

wherein heteroaryl is a 3-7 membered monocyclic or 6-10 membered bicyclic ring system having 1, 2, 3, or 4 heteroatom ring members independently selected from N, O, or S, and

wherein, each instance of C_{3-10}cycloalkyl, phenyl, heterocyclyl, and heteroaryl is optionally substituted with one, two or three R_7 substituents.

One aspect includes a compound of Formula (I) or Formula (II), wherein R_4 is C_{3-10}cycloalkyl selected from cyclopropyl, cylcobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, bicyclo[2.2.1]hexanyl, and adamantyl, optionally substituted with one, two or three R_7 substituents.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_4 is cyclopropyl, optionally substituted with one, two or three R_7 substituents.

One aspect includes a compound of Formula (I) or Formula (II), wherein R_2 is selected from phenyl and heteroaryl,

wherein heteroaryl is a 3-7 membered monocyclic or 6-10 membered bicyclic ring system having 1, 2, 3, or 4 heteroatom ring members independently selected from N, O, or S,

wherein, each instance of phenyl and heteroaryl is optionally substituted with one, two or three R_5 substituents and optionally, with one additional R_6 substituent, or,

wherein, alternatively, each instance of phenyl and heteroaryl is optionally substituted with one, two, three or four R_5 substituents.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_2 is phenyl,

optionally substituted with one, two or three R_5 substituents and optionally, with one additional R_6 substituent, or, alternatively, optionally substituted with one, two, three or four R_5 substituents.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_2 is heteroaryl selected from furanyl, 1*H*-pyrazolyl, 1*H*-imidazolyl, 1*H*-1,2,3-triazolyl, 4*H*-1,2,4-triazolyl, 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, 1*H*-indolyl, 2*H*-indolyl, 1*H*-indazolyl, 2*H*-indazolyl, indolizinyl, benzofuranyl, 1*H*-benzimidazolyl, 1,3-benzoxazolyl, furo[2,3-*b*]pyridinyl, furo[2,3-*c*]pyridinyl, furo[3,2-*b*]pyridinyl, furo[3,2-*c*]pyridinyl, 1*H*-pyrrolo[2,3-*b*]pyridinyl, 1*H*-pyrrolo[2,3-*c*]pyridinyl, pyrrolo[1,2-*a*]pyrimidinyl, pyrrolo[1,2-*a*]pyrazinyl, pyrrolo[1,2-*b*]pyridazinyl, pyrazolo[1,5-*a*]pyridinyl, 1*H*-pyrazolo[4,3-b]pyridinyl, 2*H*-pyrazolo[4,3-*b*]pyridinyl, 2*H*-pyrazolo[4,3-*c*]pyridinyl, pyrazolo[1,5-*a*]pyrazinyl, pyrazolo[1,5-a]pyrimidinyl, imidazo[1,2-*a*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*a*]pyrazinyl, imidazo[1,2-*b*]pyridazinyl, imidazo[1,2-*c*]pyrimidinyl, imidazo[1,5-*a*]pyridinyl, imidazo[2,1-*b*][1,3]thiazolyl, imidazo[2,1-*b*][1,3,4]thiadiazolyl, [1,3]oxazolo[4,5-*b*]pyridinyl, [1,2,4]triazolo[1,5-a]pyridnyl, [1,2,4]triazolo[1,5-b]pyridazinyl, and quinolinyl, optionally substituted with one, two or three R_5 substituents and optionally, with one additional R_6 substituent, or, alternatively, optionally substituted with one, two, three or four R_5 substituents.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_2 is heteroaryl selected from 1*H*-indazolyl, 2*H*-indazolyl, 1*H*-benzimidazolyl, 1,3-benzoxazolyl, furo[3,2-*b*]pyridinyl, pyrrolo[1,2-*a*]pyrazinyl, 1*H*-pyrazolo[4,3-b]pyridinyl, 2*H*-pyrazolo[4,3-*b*]pyridinyl, pyrazolo[1,5-a]pyrimidinyl, imidazo[1,2-*a*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*a*]pyrazinyl, imidazo[1,2-*b*]pyridazinyl, imidazo[2,1-*b*][1,3]thiazolyl, imidazo[2,1-*b*][1,3,4]thiadiazolyl, [1,2,4]triazolo[1,5-a]pyridnyl, and [1,2,4]triazolo[1,5-b]pyridazinyl, optionally substituted with one, two or three R_5 substituents and optionally, with one additional R_6 substituent, or, alternatively, optionally substituted with one, two, three or four R_5 substituents.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_2 is heteroaryl selected from furan-2-yl, furan-3-yl, 1*H*-pyrazol-3-yl, 1*H*-pyrazol-4-yl, 1*H*-pyrazol-5-yl, 1*H*-imidazol-1-yl, 1*H*-imidazol-4-yl, 1*H*-1,2,3-triazol-1-yl, 4*H*-1,2,4-triazol-4-yl, 1,2,4-oxadiazol-3-yl, 1,3,4-oxadiazol-2-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyridazin-3-yl, pyridazin-4-yl, pyridazin-5-yl, pyrimidin-4-yl, pyrazin-1-yl, 1*H*-indol-3-yl, 1*H*-indol-4-yl,

1*H*-indol-5-yl, 1*H*-indol-6-yl, 1*H*-indazol-5-yl, 1*H*-indazol-6-yl, 2*H*-indazol-5-yl, 2*H*-indazol-6-yl, indolizin-2-yl, benzofuran-2-yl, benzofuran-5-yl, 1*H*-benzimidazol-2-yl, 1*H*-benzimidazol-5-yl, 1*H*-benzimidazol-6-yl, 1,3-benzoxazol-2-yl, 1,3-benzoxazol-5-yl, 1,3-benzoxazol-6-yl, furo[2,3-*b*]pyridine-6-yl, furo[2,3-*c*]pyridin-2-yl, furo[3,2-*b*]pyridin-2-yl, furo[3,2-*c*]pyridin-2-yl, 1*H*-pyrrolo[2,3-*b*]pyridin-5-yl, 1*H*-pyrrolo[2,3-*c*]pyridin-4-yl, pyrrolo[1,2-*a*]pyrimidin-7-yl, pyrrolo[1,2-*a*]pyrazin-7-yl, pyrrolo[1,2-*b*]pyridazin-2-yl, pyrazolo[1,5-*a*]pyridin-2-yl, pyrazolo[1,5-*a*]pyridin-5-yl, 1*H*-pyrazolo[4,3-b]pyridin-5-yl, 2*H*-pyrazolo[4,3-*b*]pyridin-5-yl, 2*H*-pyrazolo[4,3-*c*]pyridin-5-yl, pyrazolo[1,5-*a*]pyrazin-2-yl, pyrazolo[1,5-a]pyrimidin-5-yl, imidazo[1,2-*a*]pyridin-2-yl, imidazo[1,2-*a*]pyridin-6-yl, imidazo[1,2-*a*]pyrimidin-2-yl, imidazo[1,2-*a*]pyrimidin-6-yl, imidazo[1,2-*a*]pyrazin-2-yl, imidazo[1,2-*a*]pyrazin-3-yl, imidazo[1,2-*a*]pyrazin-6-yl, imidazo[1,2-*b*]pyridazin-2-yl, imidazo[1,2-*b*]pyridazin-6-yl, imidazo[1,2-*c*]pyrimidin-2-yl, imidazo[1,5-*a*]pyridin-6-yl, imidazo[1,5-*a*]pyridin-7-yl, imidazo[2,1-*b*][1,3]thiazol-6-yl, imidazo[2,1-*b*][1,3,4]thiadiazol-6-yl, [1,3]oxazolo[4,5-*b*]pyridin-2-yl, [1,2,4]triazolo[1,5-a]pyridin-5-yl, [1,2,4]triazolo[1,5-a]pyridin-6-yl, [1,2,4]triazolo[1,5-b]pyridn-6-yl, [1,2,4]triazolo[1,5-b]pyridazin-5-yl, [1,2,4]triazolo[1,5-b]pyridazin-6-yl, quinolin-6-yl, quinolin-7-yl, and quinolin-8-yl, optionally substituted with one, two or three R_5 substituents and optionally, with one additional R_6 substituent, or, alternatively, optionally substituted with one, two, three or four R_5 substituents.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_2 is heteroaryl selected from 1*H*-indazol-5-yl, 2*H*-indazol-5-yl, 1*H*-benzimidazol-6-yl, 1,3-benzoxazol-6-yl, furo[2,3-*b*]pyridine-6-yl, pyrrolo[1,2-*a*]pyrazin-7-yl, 1*H*-pyrazolo[4,3-b]pyridin-5-yl, 2*H*-pyrazolo[4,3-*b*]pyridin-5-yl, pyrazolo[1,5-a]pyrimidin-5-yl, imidazo[1,2-*a*]pyridin-6-yl, imidazo[1,2-*a*]pyrimidin-6-yl, imidazo[1,2-*a*]pyrazin-2-yl, imidazo[1,2-*a*]pyrazin-6-yl, imidazo[1,2-*b*]pyridazin-6-yl, imidazo[2,1-*b*][1,3]thiazol-6-yl, imidazo[2,1-*b*][1,3,4]thiadiazol-6-yl, [1,2,4]triazolo[1,5-a]pyridin-6-yl, and [1,2,4]triazolo[1,5-b]pyridazin-6-yl, optionally substituted with one, two or three R_5 substituents and optionally, with one additional R_6 substituent, or, alternatively, optionally substituted with one, two, three or four R_5 substituents.

One aspect includes a compound of Formula (I) or Formula (II), wherein R_5 is, in each instance, independently selected from cyano, halogen, hydroxy, $C_{1\text{-}6}$alkyl, halo-$C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$alkyl-carbonyl, $C_{1\text{-}6}$alkoxy, halo-$C_{1\text{-}6}$alkoxy, $C_{1\text{-}6}$alkoxy-$C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$alkoxy-carbonyl,

C_{1-6}alkoxy-carbonyl-C_{1-6}alkyl, carboxyl, C_{1-6}alkyl-carboxyl, amino, C_{1-6}alkyl-amino, $(C_{1-6}alkyl)_2$-amino, amino-C_{1-6}alkyl, amino-carbonyl, and hydroxy-C_{1-6}alkyl.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_5 is, in each instance, independently selected from cyano, halogen, hydroxy, C_{1-6}alkyl, halo-C_{1-6}alkyl, C_{1-6}alkoxyC_{1-6}alkoxy-carbonyl-C_{1-6}alkyl, carboxyl, C_{1-6}alkyl-carboxyl, amino, C_{1-6}alkyl-amino, $(C_{1-6}alkyl)_2$-amino, amino-C_{1-6}alkyl, and amino-carbonyl.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_5 is, in each instance, cyano.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_5 is, in each instance, halogen selected from bromo, chloro, fluoro, and iodo.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_5 is, in each instance, fluoro.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_5 is, in each instance, hydroxy.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_5 is, in each instance, C_{1-6}alkyl selected from methyl, ethyl, propyl, isopropyl, and tert-butyl.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_5 is, in each instance, C_{1-6}alkyl selected from methyl and ethyl.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_5 is, in each instance, halo-C_{1-6}alkyl, wherein C_{1-6}alkyl is selected from methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, and tert-butyl partially or completely substituted with one or more halogens selected from bromo, chloro, fluoro, and iodo where allowed by available valences.

Another aspect includes a compound of Formula (I), wherein R_5 is, in each instance, halo-C_{1-6}alkyl selected from trifluoromethyl.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_5 is, in each instance, C_{1-6}alkoxy selected from methoxy, ethoxy, propoxy, isopropoxy, and tert-butoxy.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_a is, in each instance, methoxy.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_5 is, in each instance, C_{1-6}alkoxy-carbonyl-C_{1-6}alkyl, wherein C_{1-6}alkoxy is selected from methoxy, ethoxy,

propoxy, isopropoxy, and tert-butoxy, and wherein C_{1-6}alkyl is selected from methyl, ethyl, propyl, isopropyl, and tert-butyl.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_5 is, in each instance, $-CH_2CO_2CH_3$.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_5 is, in each instance, carboxyl.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_5 is, in each instance, C_{1-6}alkyl-carboxyl, wherein C_{1-6}alkyl is selected from methyl, ethyl, propyl, isopropyl, and tert-butyl.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_5 is, in each instance, $-CH_2CO_2H$.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_5 is, in each instance, amino.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_5 is, in each instance, C_{1-6}alkyl-amino wherein C_{1-6}alkyl is selected from methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, and tert-butyl.

Another aspect includes a compound of Formula (I), wherein R_5 is, in each instance, methylamino.

Another aspect includes a compound of Formula (I), wherein R_5 is, in each instance, $(C_{1-6}alkyl)_2$-amino wherein C_{1-6}alkyl is independently selected from methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, and tert-butyl.

Another aspect includes a compound of Formula (I), wherein R_5 is, in each instance, dimethylamino.

Another aspect includes a compound of Formula (I), wherein R_5 is, in each instance, amino-C_{1-6}alkyl wherein C_{1-6}alkyl is independently selected from methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, and tert-butyl.

Another aspect includes a compound of Formula (I), wherein R_5 is, in each instance, methanamine.

Another aspect includes a compound of Formula (I), wherein R_5 is, in each instance, amino-carbonyl.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_6 is selected from C_{3-10}cycloalkyl, phenyl, phenyl-C_{1-6}alkoxy, phenyl-oxy, heterocyclyl, and heteroaryl;

wherein heterocyclyl is a saturated or partially unsaturated 3-7 membered monocyclic, 6-10 membered bicyclic or 13-16 membered polycyclic ring system having 1, 2, or 3 heteroatom ring members independently selected from N, O, or S,

wherein heteroaryl is a 3-7 membered monocyclic or 6-10 membered bicyclic ring system having 1, 2, 3, or 4 heteroatom ring members independently selected from N, O, or S, and

wherein, each instance of C_{3-10}cycloalkyl, phenyl, heterocyclyl, and heteroaryl is optionally substituted with one, two or three R_7 substituents.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_6 is C_{3-10}cycloalkyl selected from cyclopropyl, cylcobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, bicyclo[2.2.1]hexanyl, and adamantyl, optionally substituted with one, two or three R_7 substituents.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_6 is cyclopropyl, optionally substituted with one, two or three R_7 substituents.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_6 is phenyl-C_{1-6}alkoxy, wherein C_{1-6}alkoxy is selected from methoxy, ethoxy, propoxy, isopropoxy, and tert-butoxy, and wherein C_{1-6}alkyl is selected from methyl, ethyl, propyl, isopropyl, and tert-butyl, and wherein, phenyl is optionally substituted with one, two or three R_7 substituents.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_6 is benzyloxy.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_6 is phenyl-oxy, wherein, phenyl is optionally substituted with one, two or three R_7 substituents.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_6 is benzyloxy.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_6 is heteroaryl selected from furanyl, 1*H*-pyrazolyl, 1*H*-imidazolyl, 1*H*-1,2,3-triazolyl, 4*H*-1,2,4-triazolyl, 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, and pyrazinyl, optionally substituted with one, two or three R_7 substituents.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_6 is heteroaryl selected from 1*H*-pyrazolyl and 1*H*-imidazolyl, optionally substituted with one, two or three R_7 substituents.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_6 is heteroaryl selected from furan-2-yl, furan-3-yl, 1*H*-pyrazol-3-yl, 1*H*-pyrazol-4-yl, 1*H*-pyrazol-5-yl, 1*H*-imidazol-1-yl, 1*H*-imidazol-4-yl, 1*H*-1,2,3-triazol-1-yl, 4*H*-1,2,4-triazol-4-yl, 1,2,4-oxadiazol-3-yl, 1,3,4-oxadiazol-2-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyridazin-3-yl, pyridazin-4-yl, pyridazin-5-yl, pyrimidin-4-yl, pyrazin-1-yl, optionally substituted with one, two or three R_7 substituents.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_6 is heteroaryl selected from 1*H*-pyrazol-4-yl and 1*H*-imidazol-1-yl, optionally substituted with one, two or three R_7 substituents.

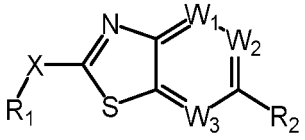
One aspect includes a compound of Formula (I) or Formula (II), wherein R_7 is, in each instance, independently selected from cyano, halogen, hydroxy, $C_{1\text{-}6}$alkyl, halo-$C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$alkyl-carbonyl, $C_{1\text{-}6}$alkoxy, halo-$C_{1\text{-}6}$alkoxy, $C_{1\text{-}6}$alkoxy-$C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$alkoxy-carbonyl, amino, $C_{1\text{-}6}$alkyl-amino, ($C_{1\text{-}6}$alkyl)$_2$-amino, amino-$C_{1\text{-}6}$alkyl, and hydroxy-$C_{1\text{-}6}$alkyl.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_7 is, in each instance, halogen, hydroxy, $C_{1\text{-}6}$alkyl, halo-$C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$alkyl-carbonyl, $C_{1\text{-}6}$alkoxy, halo-$C_{1\text{-}6}$alkoxy, $C_{1\text{-}6}$alkoxy-$C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$alkoxy-carbonyl, amino, $C_{1\text{-}6}$alkyl-amino, ($C_{1\text{-}6}$alkyl)$_2$-amino, amino-$C_{1\text{-}6}$alkyl, and hydroxy-$C_{1\text{-}6}$alkyl.

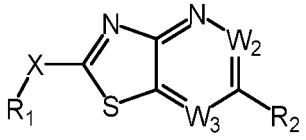
Another aspect includes a compound of Formula (I) or Formula (II), wherein R_7 is, in each instance, halogen selected from bromo, chloro, fluoro, and iodo.

Another aspect includes a compound of Formula (I) or Formula (II), wherein R_7 is, in each instance, fluoro.

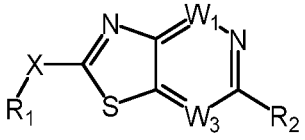
One aspect of the compound of Formula (I) includes a compound selected from Formula (Ia), Formula (Ib), Formula (Ic), Formula (Id), Formula (Ie), Formula (If), Formula (Ig), or Formula (Ih):



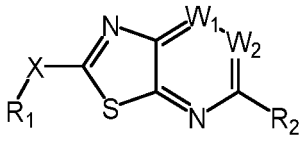
(Ia)



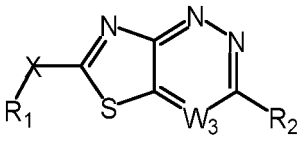
(Ib)



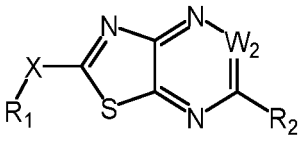
(Ic)



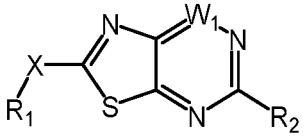
(Id)



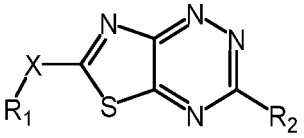
(Ie)



(If)



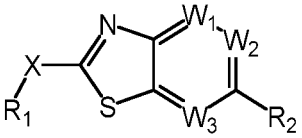
(Ig) and



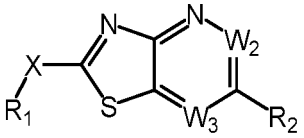
(Ih),

or a form thereof.

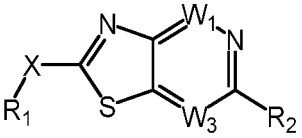
Another aspect of the compound of Formula (I) includes a compound selected from Formula (Ia), Formula (Ib), Formula (Ic), Formula (Id), Formula (Ie), Formula (If), or Formula (Ig):



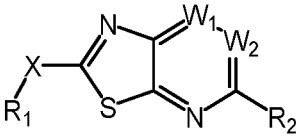
(Ia)



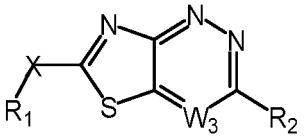
(Ib)



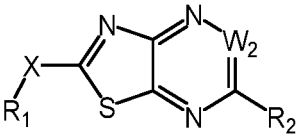
(Ic)



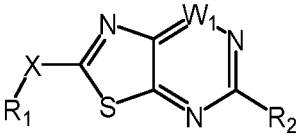
(Id)



(Ie)



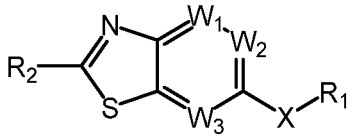
(If) and



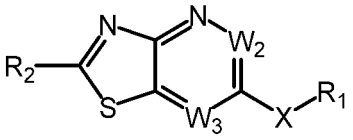
(Ig),

or a form thereof.

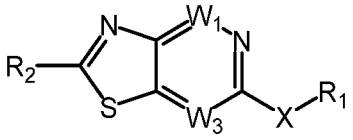
One aspect of the compound of Formula (II) includes a compound selected from Formula (IIa), Formula (IIb), Formula (IIc), Formula (IId), Formula (IIe), Formula (IIf), Formula (IIg) or Formula (IIh):



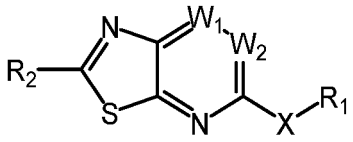
(IIa)



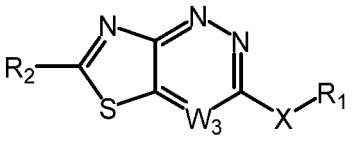
(IIb)



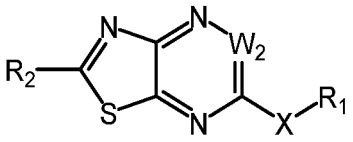
(IIc)



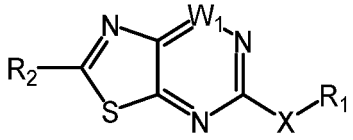
(IId)



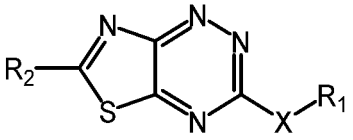
(IIe)



(IIf)



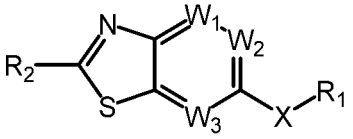
(IIg) and



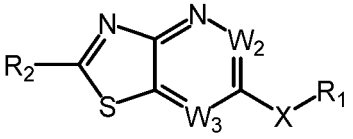
(IIh),

or a form thereof.

Another aspect of the compound of Formula (II) includes a compound selected from Formula (IIa) or Formula (IIb):



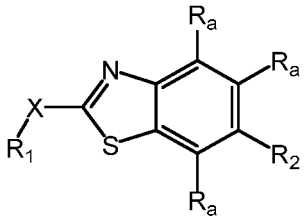
(IIa)



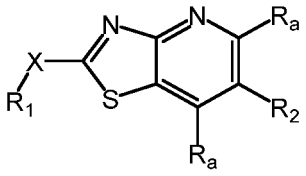
(IIb)

or a form thereof.

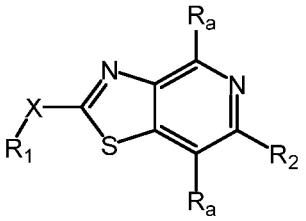
One aspect of the compound of Formula (Ia), Formula (Ib), Formula (Ic), Formula (Id), Formula (Ie), Formula (If), Formula (Ig) or Formula (Ih) includes a compound selected from Formula (Ia1), Formula (Ib1), Formula (Ic1), Formula (Id1), Formula (Ie1), Formula (If1), Formula (Ig1), or Formula (Ih1):



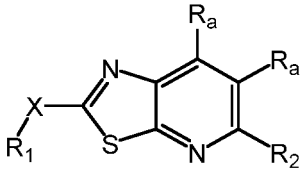
(Ia1)



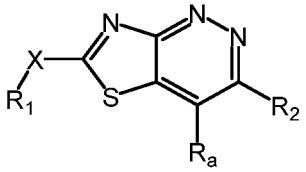
(Ib1)



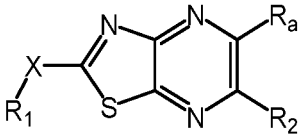
(Ic1)



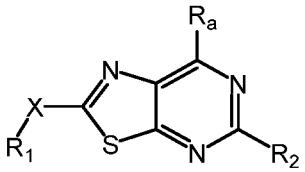
(Id1)



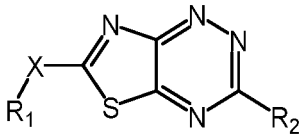
(Ie1)



(If1)



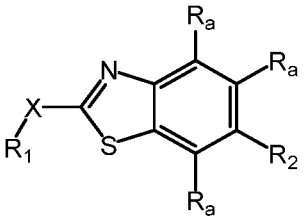
(Ig1) and



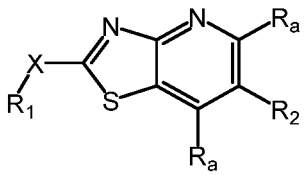
(Ih1),

or a form thereof.

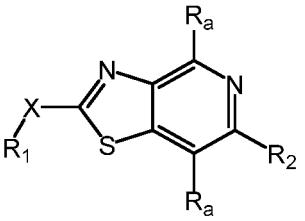
Another aspect of the compound of Formula (Ia), Formula (Ib), Formula (Ic), Formula (Id), Formula (Ie), Formula (If) or Formula (Ig) includes a compound selected from Formula (Ia1), Formula (Ib1), Formula (Ic1), Formula (Id1), Formula (Ie1), Formula (If1), or Formula (Ig1):



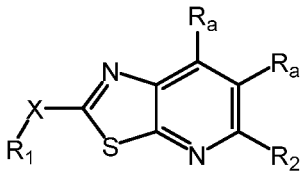
(Ia1)



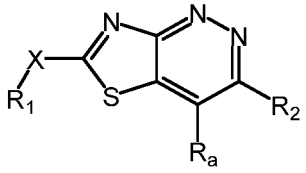
(Ib1)



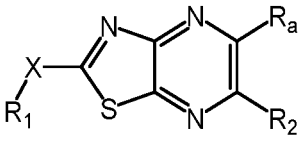
(Ic1)



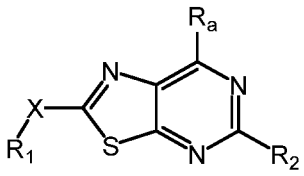
(Id1)



(Ie1)



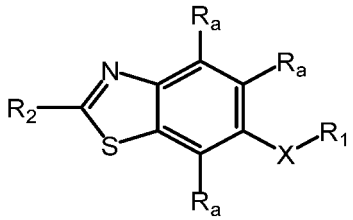
(If1) and



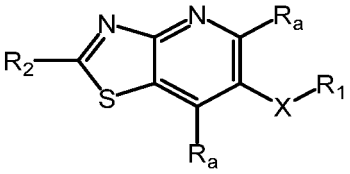
(Ig1),

or a form thereof.

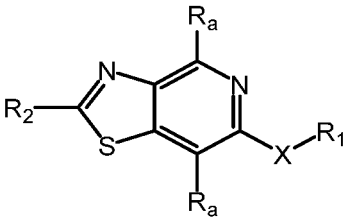
One aspect of the compound of Formula (IIa), Formula (IIb), Formula (IIc), Formula (IId), Formula (IIe), Formula (IIf), Formula (IIg) or Formula (IIh) includes a compound selected from Formula (IIa1), Formula (IIb1), Formula (Ic1), Formula (IId1), Formula (IIe1), Formula (IIf1), Formula (IIg1) or Formula (IIh1):



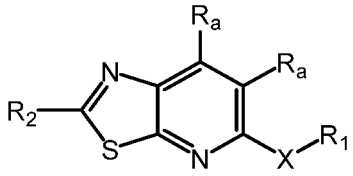
(IIa1)



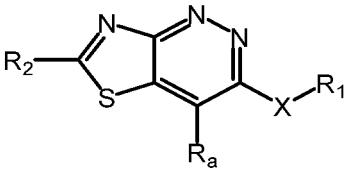
(IIb1)



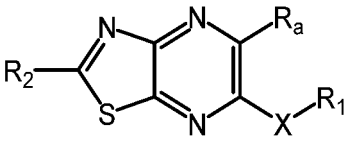
(IIc1)



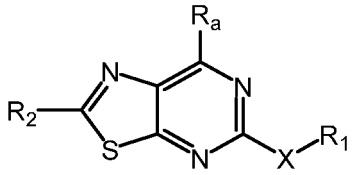
(IId1)



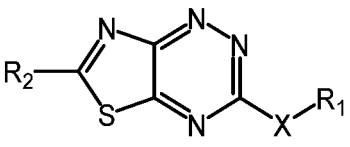
(IIe1)



(IIf1)



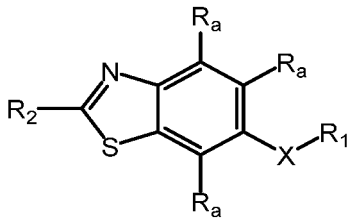
(IIg1) and



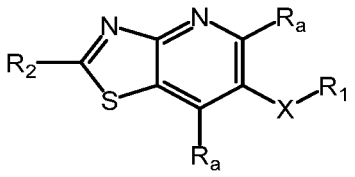
(IIh1),

or a form thereof.

Another aspect of the compound of Formula (IIa) or Formula (IIb) includes a compound selected from Formula (IIa1) or Formula (IIb1):



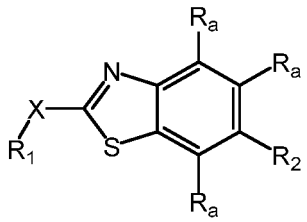
(IIa1)



(IIb1)

or a form thereof.

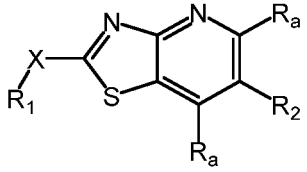
Another aspect of the compound of Formula (I) includes the compound of Formula (Ia1):



(Ia1)

or a form thereof.

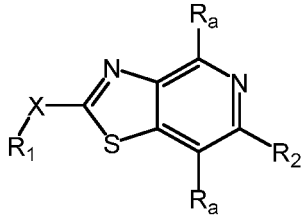
Another aspect of the compound of Formula (I) includes the compound of Formula (Ib1):



(Ib1)

or a form thereof.

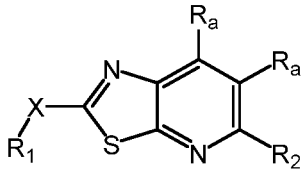
Another aspect of the compound of Formula (I) includes the compound of Formula (Ic1):



(Ic1)

or a form thereof.

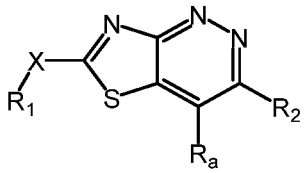
Another aspect of the compound of Formula (I) includes the compound of Formula (Id1):



(Id1)

or a form thereof.

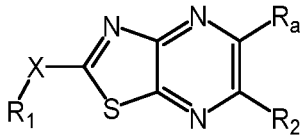
Another aspect of the compound of Formula (I) includes the compound of Formula (Ie1):



(Ie1)

or a form thereof.

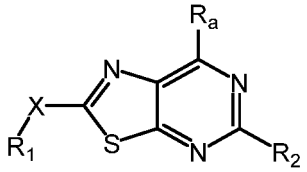
Another aspect of the compound of Formula (I) includes the compound of Formula (If1):



(If1)

or a form thereof.

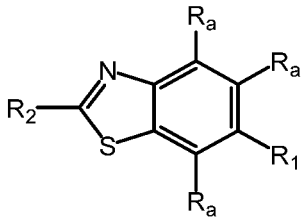
Another aspect of the compound of Formula (I) includes the compound of Formula (Ig1):



(Ig1)

or a form thereof.

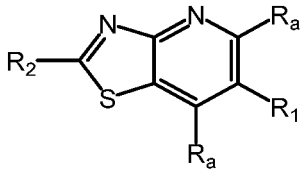
Another aspect of the compound of Formula (II) includes the compound of Formula (IIa1):



(IIa1)

or a form thereof.

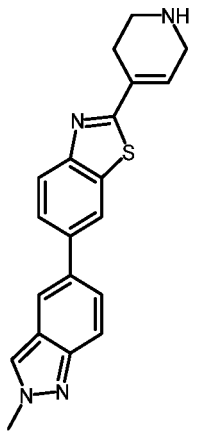
Another aspect of the compound of Formula (II) includes the compound of Formula (IIb1):



(IIb1)

or a form thereof.

An aspect of the compound of Formula (I) or Formula (II) or a form thereof includes a compound selected from the group consisting of:



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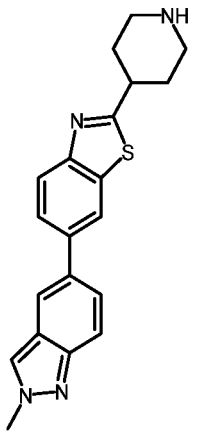

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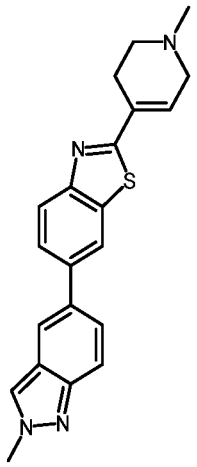

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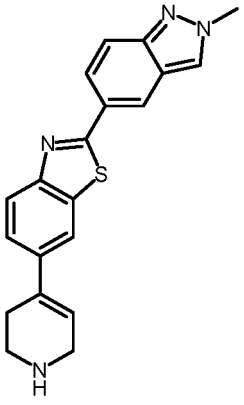

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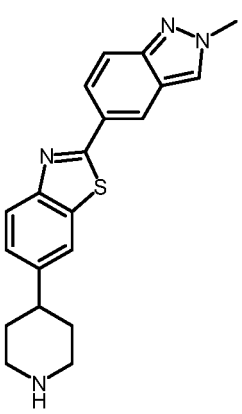

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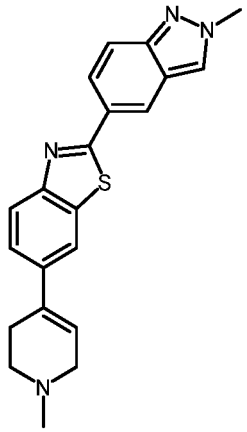

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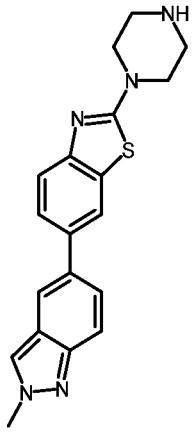

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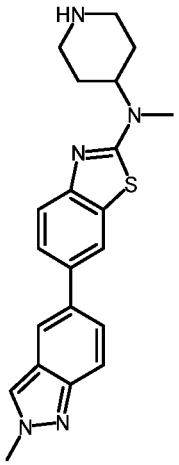

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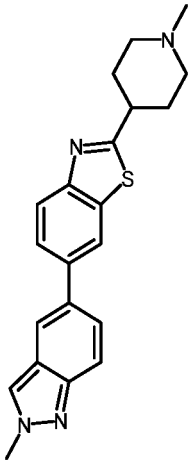

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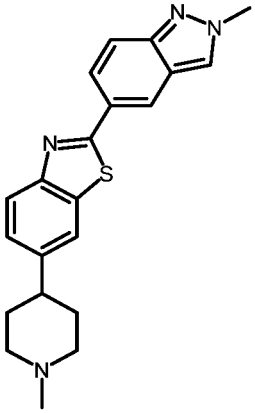

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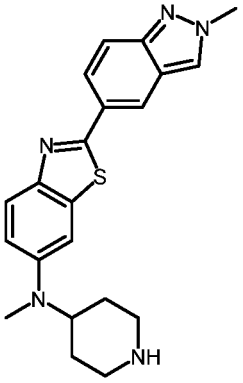

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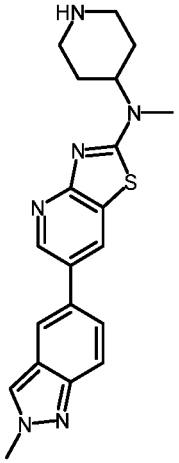

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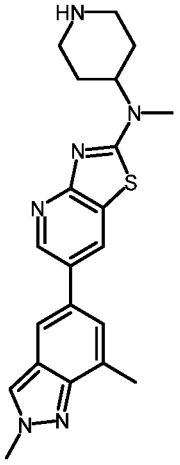

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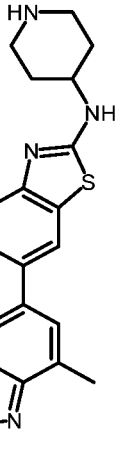

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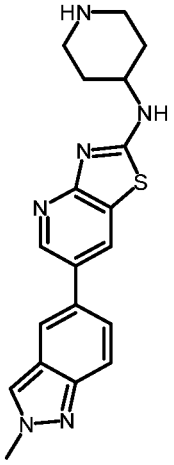

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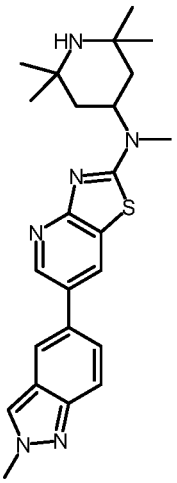

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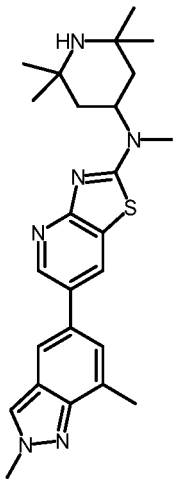

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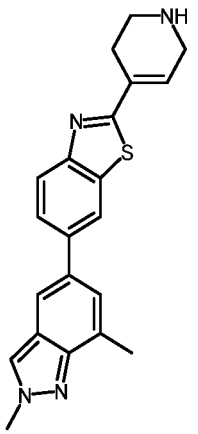

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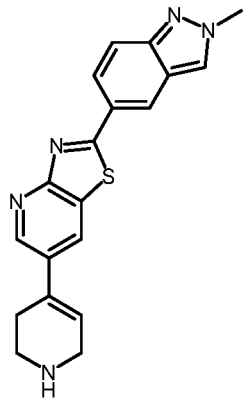

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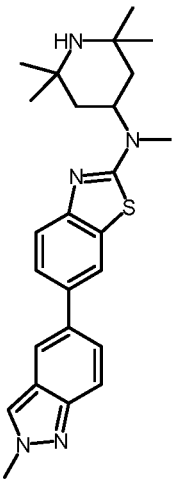

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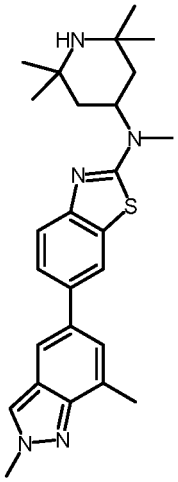

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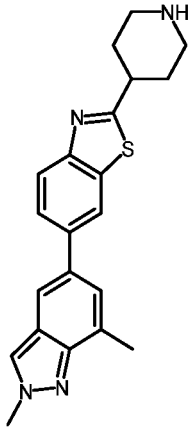

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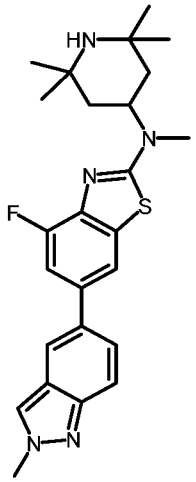

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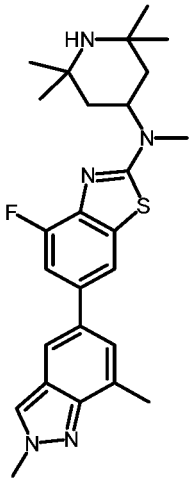

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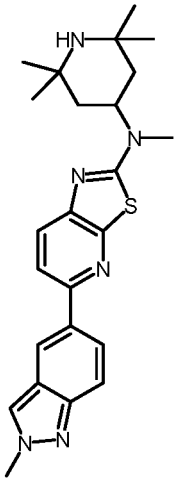

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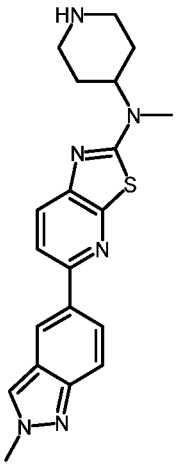

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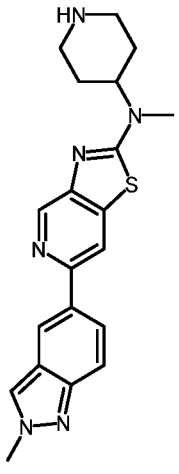

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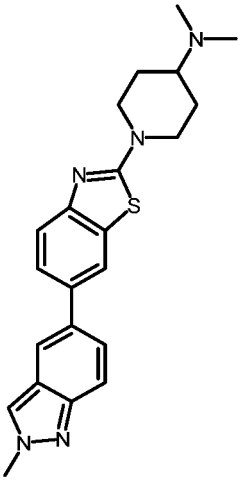

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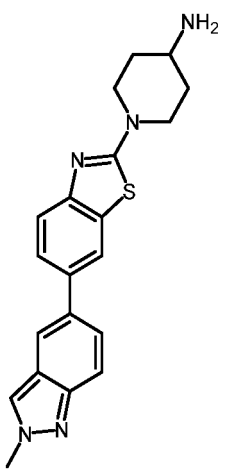

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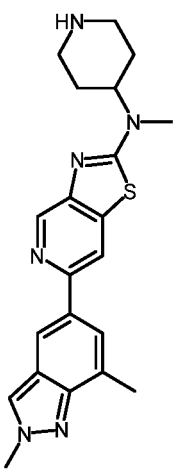

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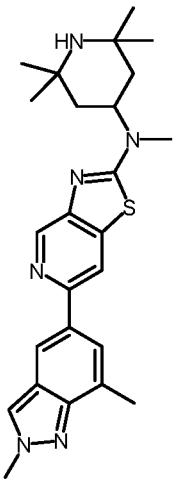

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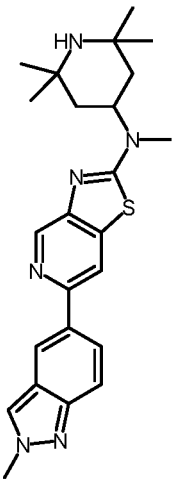

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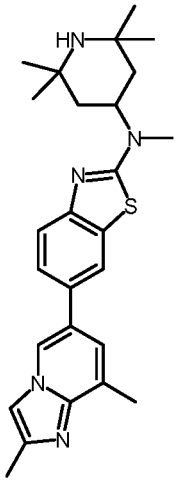

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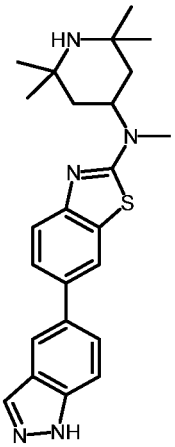

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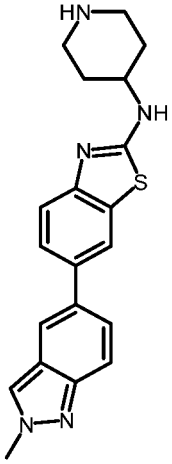

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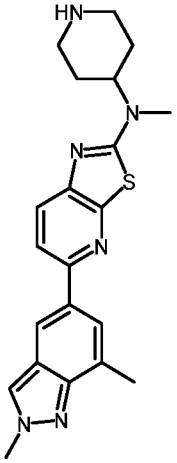

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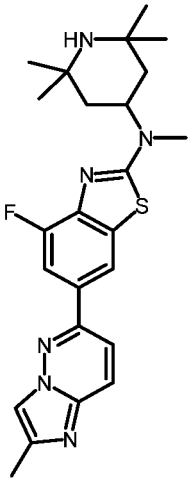

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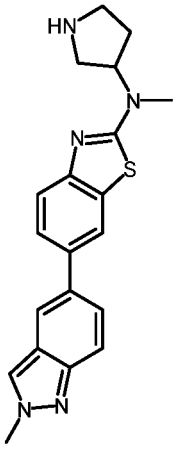

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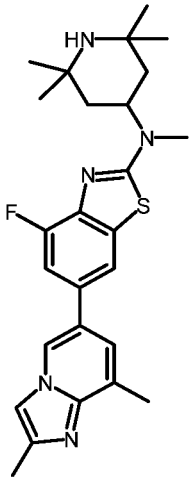

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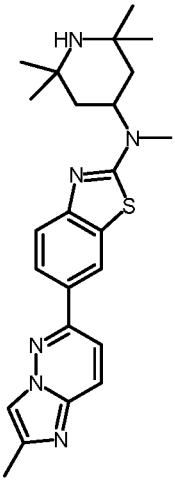

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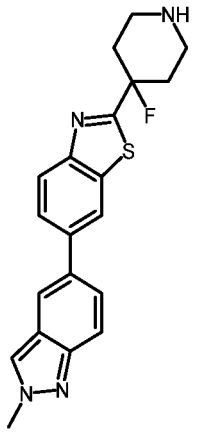

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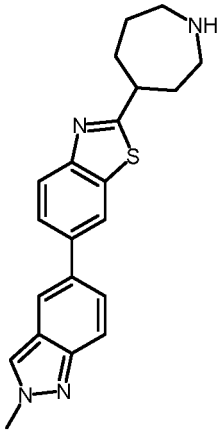

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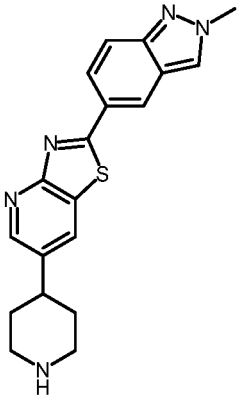

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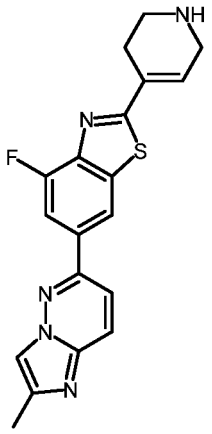

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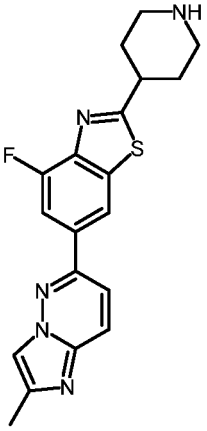

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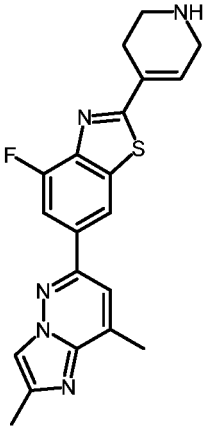

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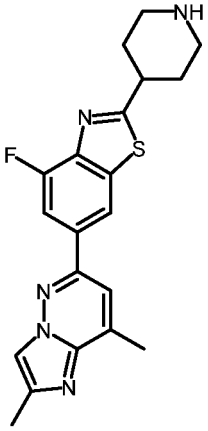

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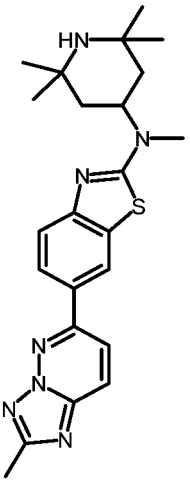

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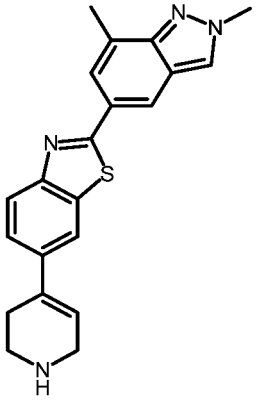

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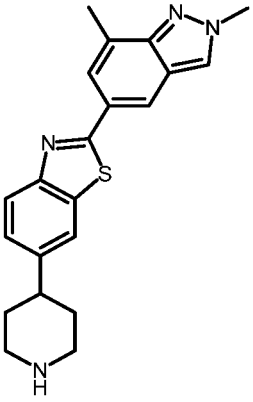

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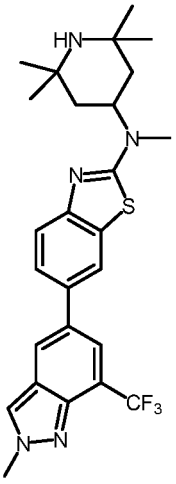

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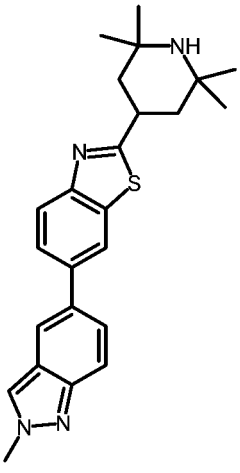

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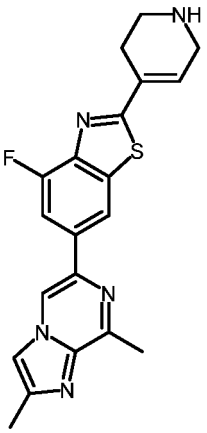

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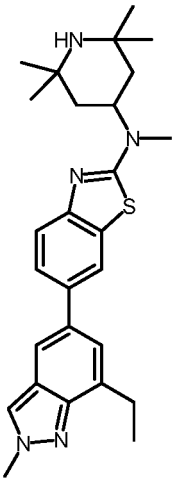

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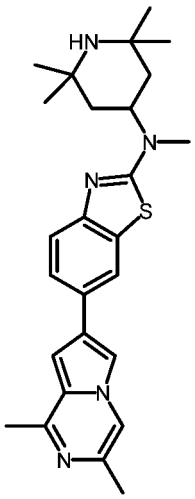

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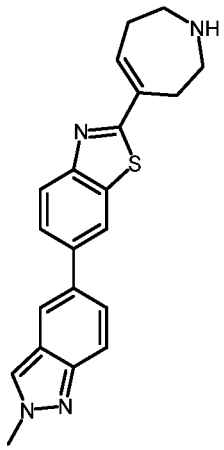

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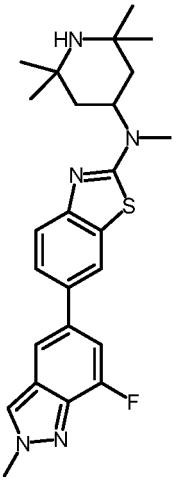

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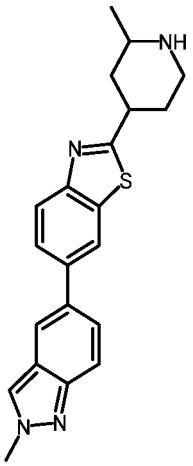

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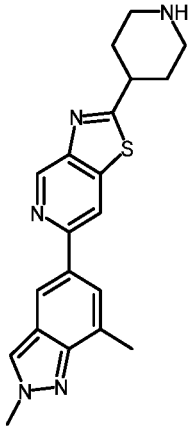

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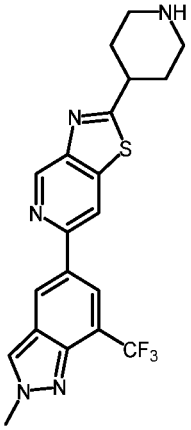

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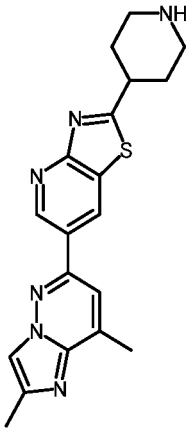

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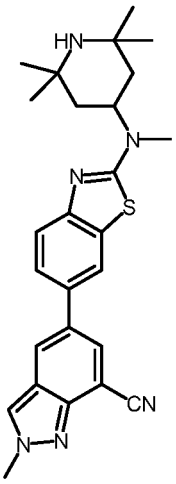

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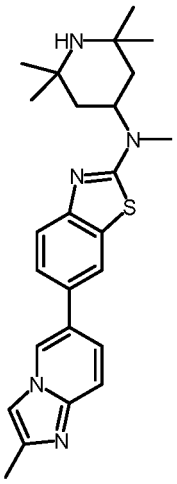

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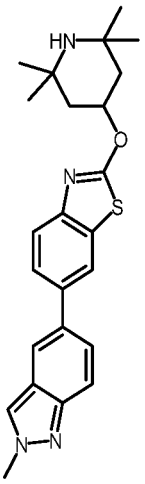

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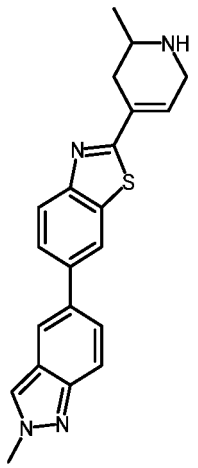

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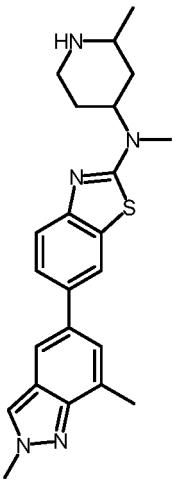

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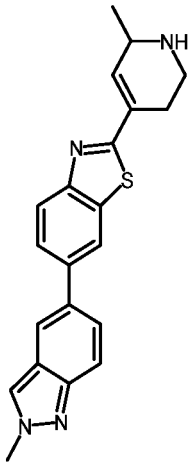

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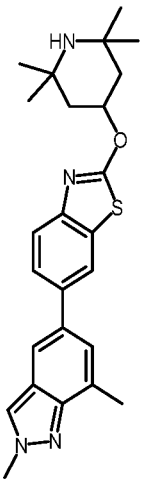

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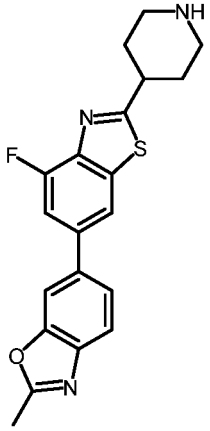

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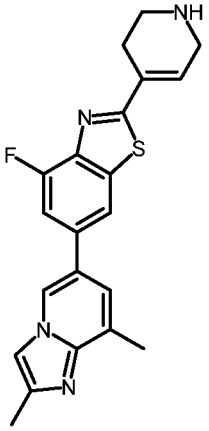

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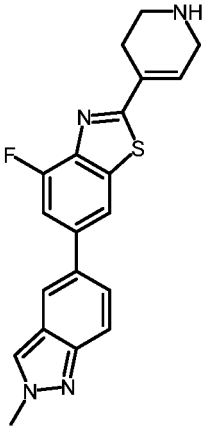

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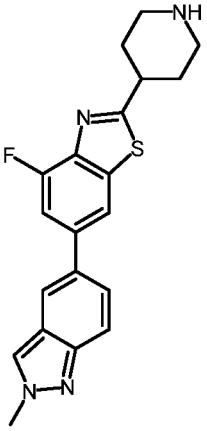

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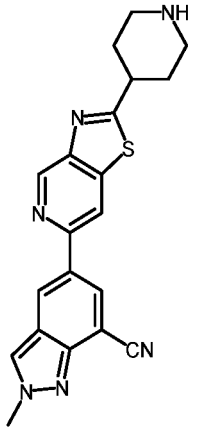

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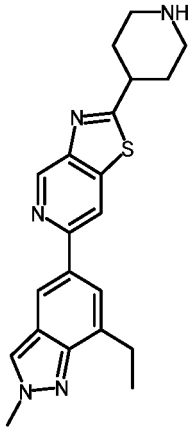

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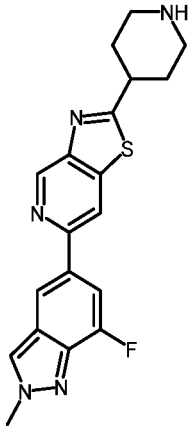

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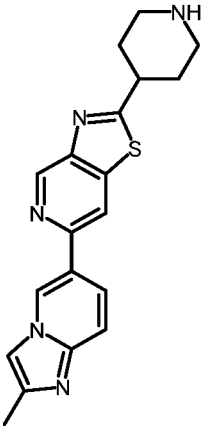

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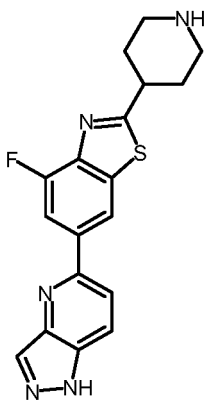

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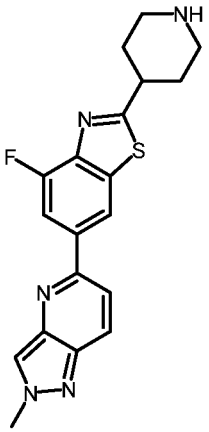

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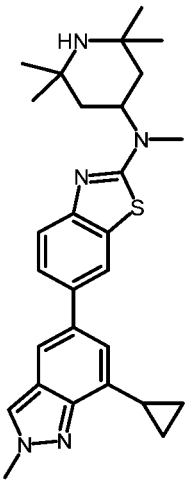

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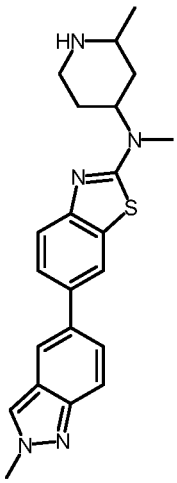

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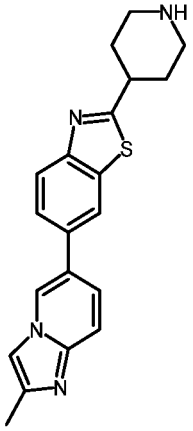

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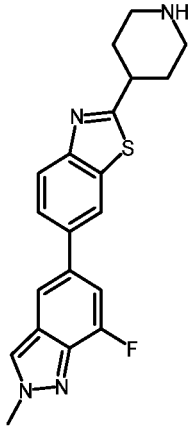

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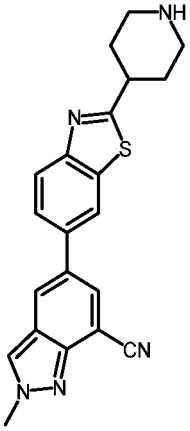

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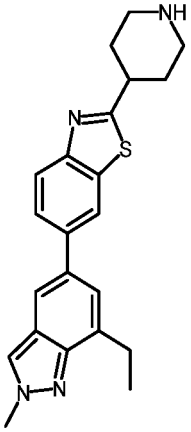

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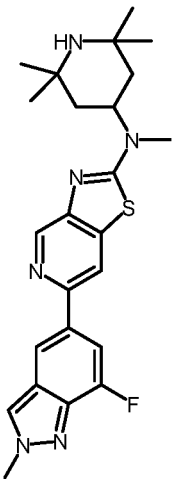

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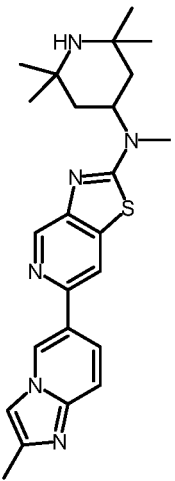

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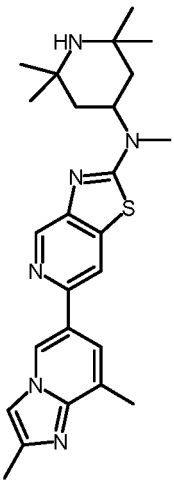

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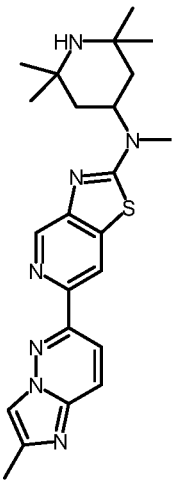

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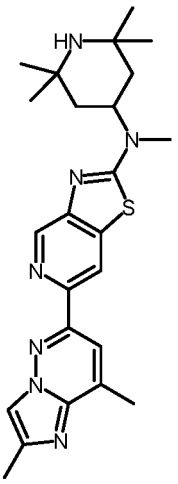

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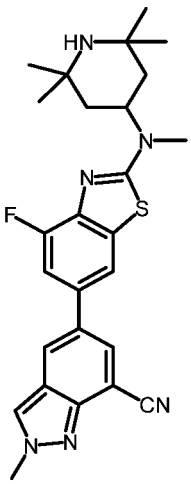

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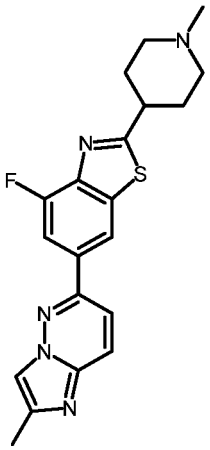

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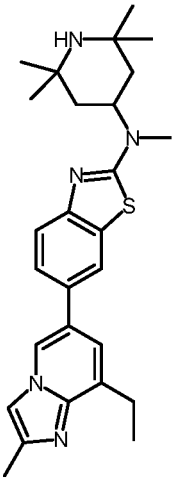

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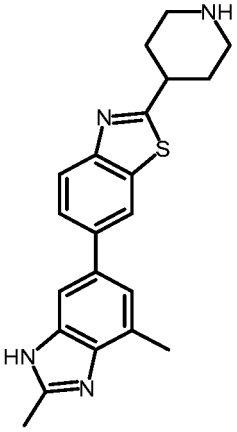

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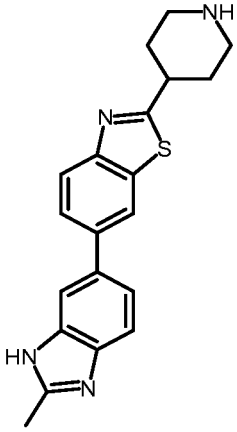

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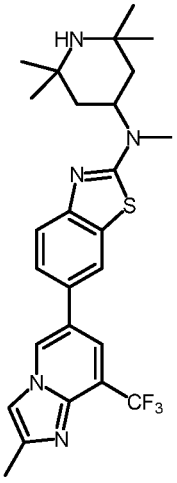

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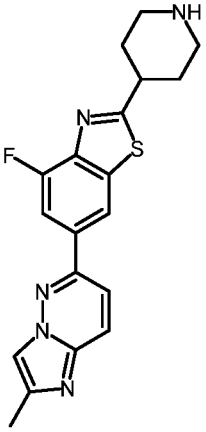

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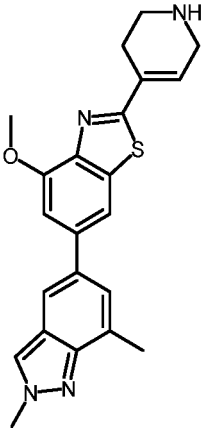

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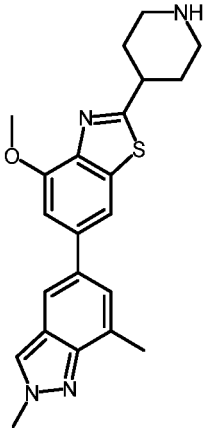

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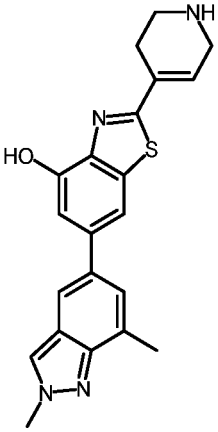

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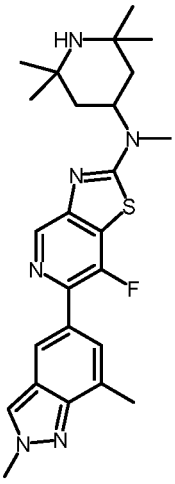

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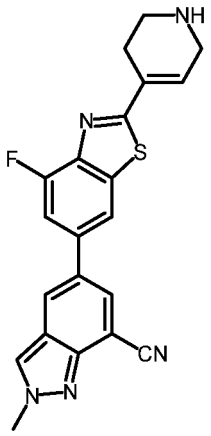

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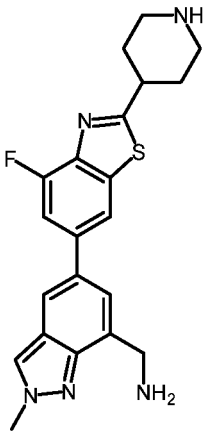

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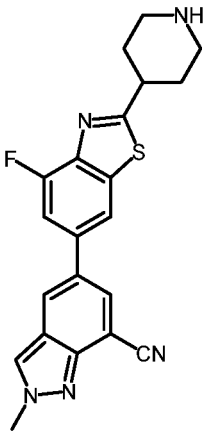

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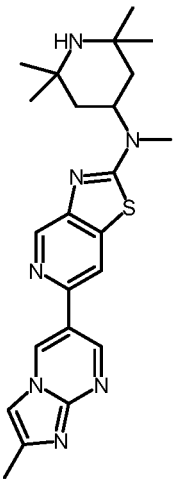

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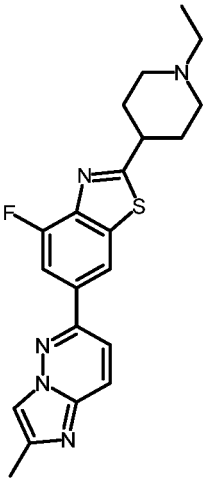

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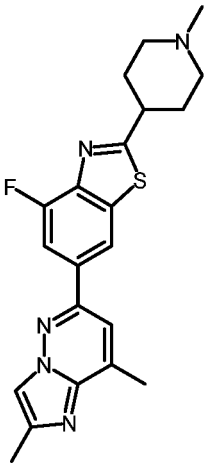

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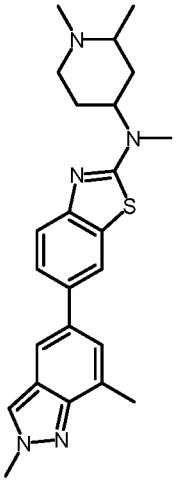

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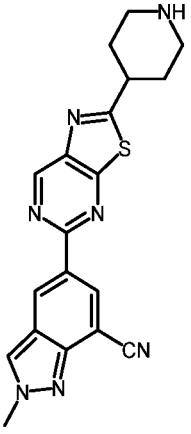

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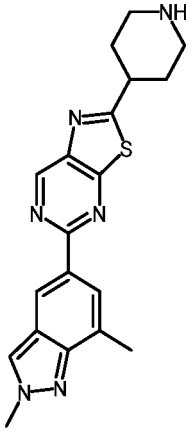

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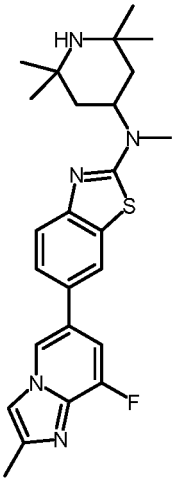

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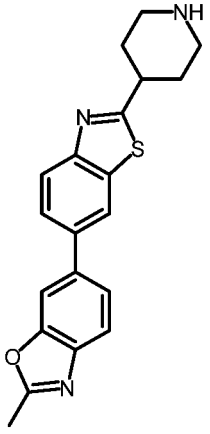

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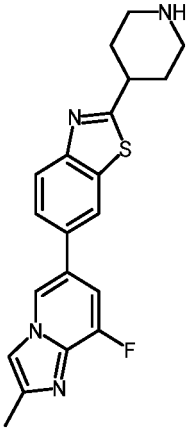

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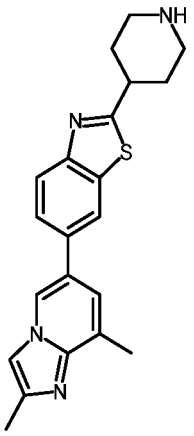

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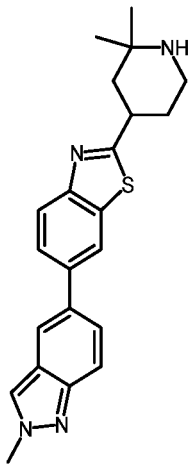

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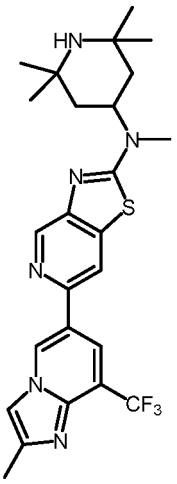

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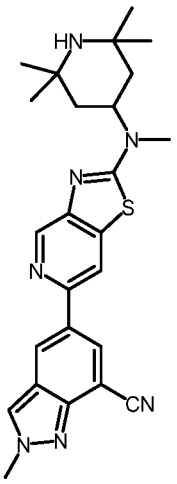

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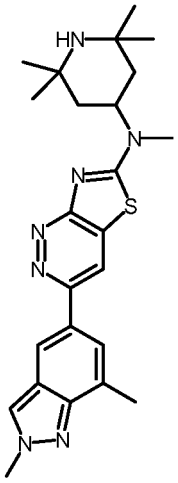

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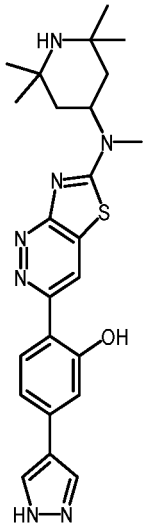

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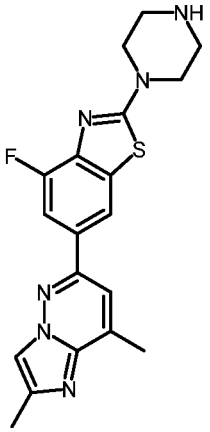

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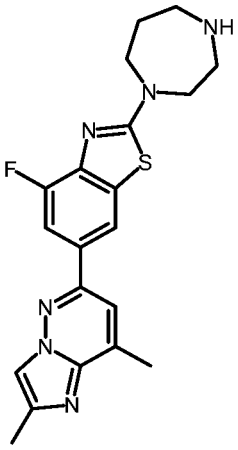

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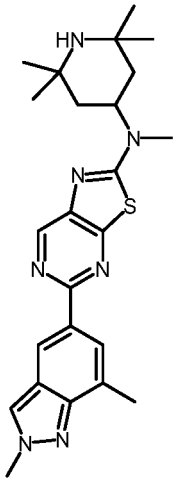

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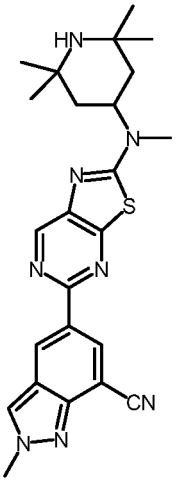

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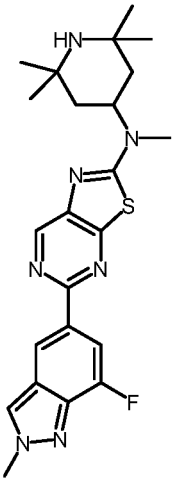

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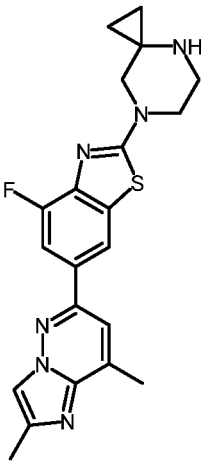

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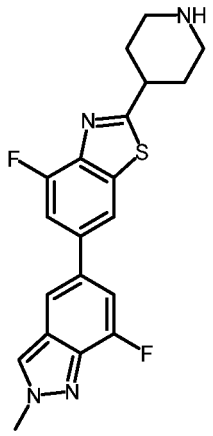

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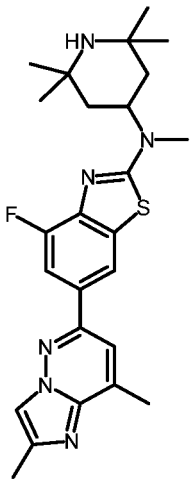

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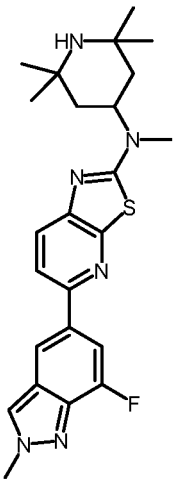

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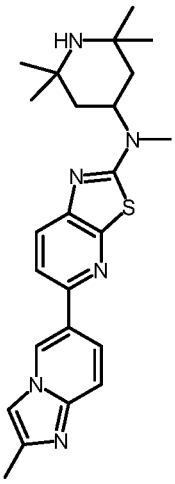

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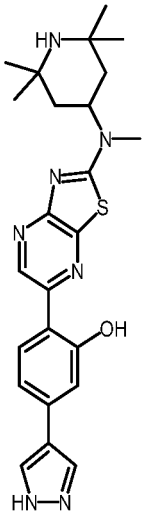

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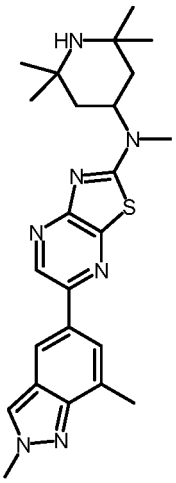

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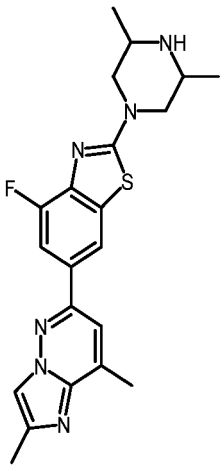

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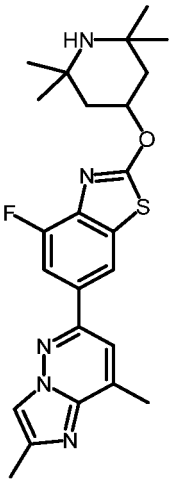

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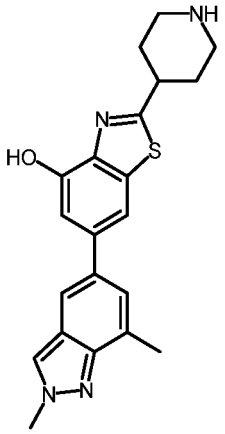

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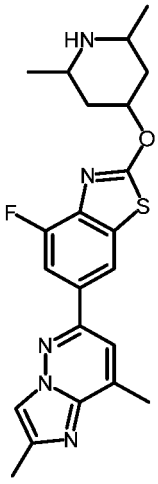

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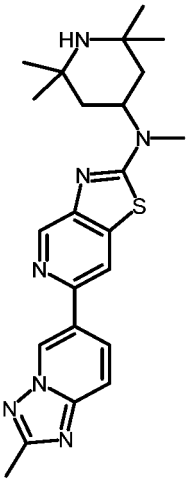

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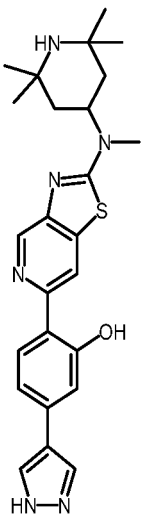

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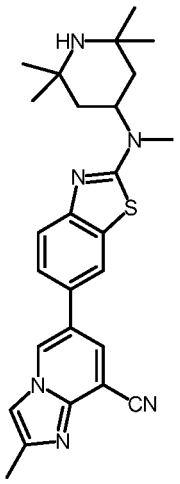

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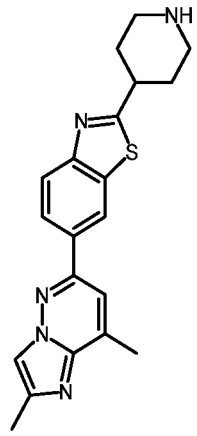

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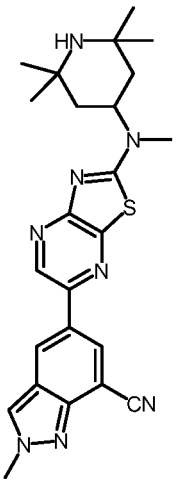

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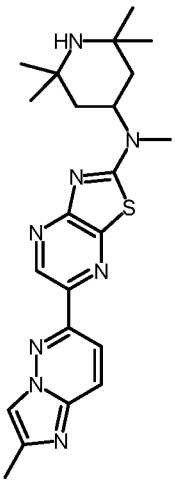

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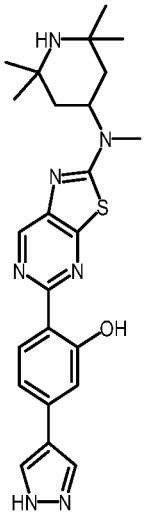

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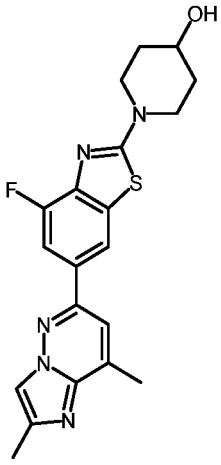

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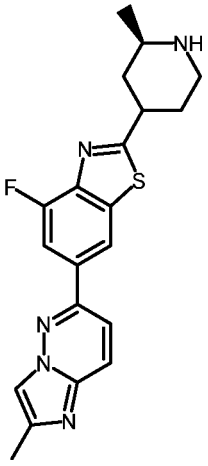

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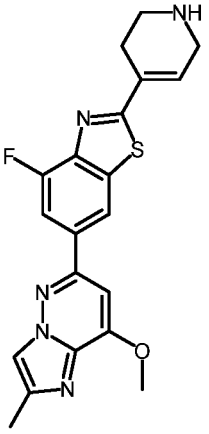

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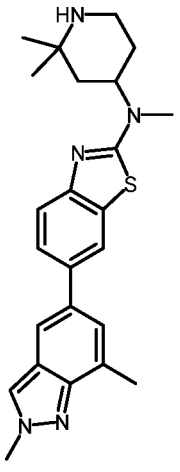

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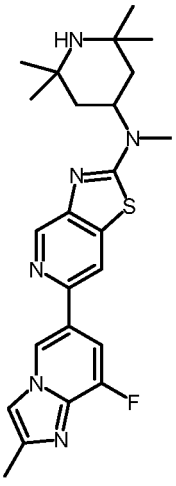

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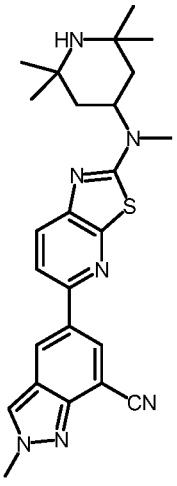

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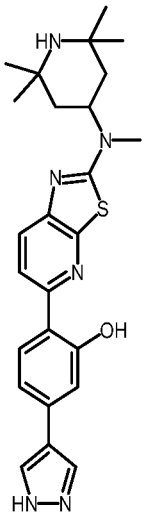

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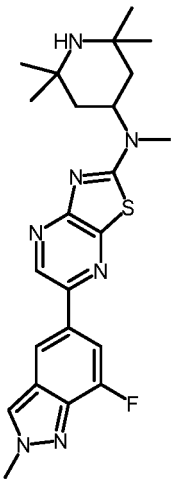

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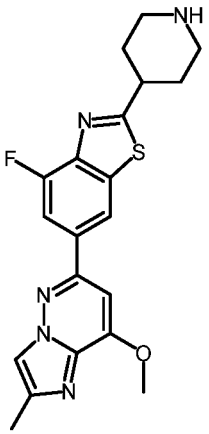

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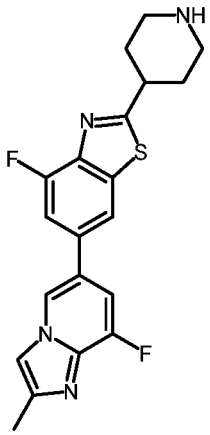

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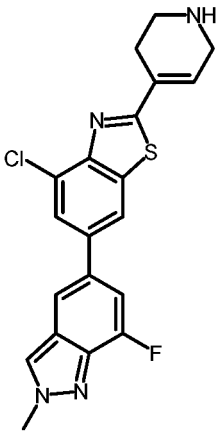

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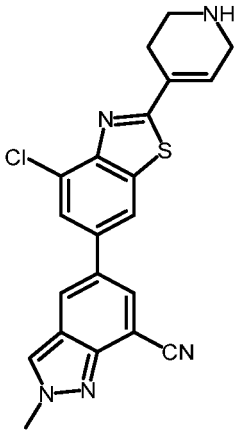

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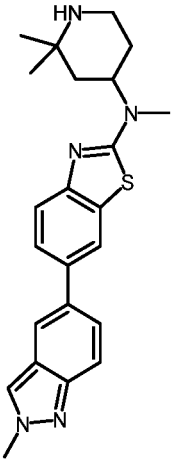

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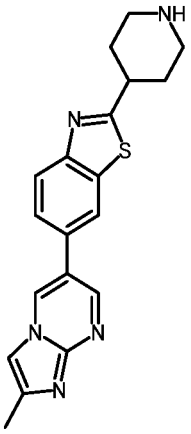

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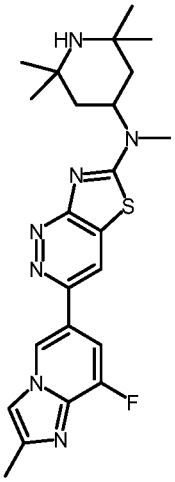

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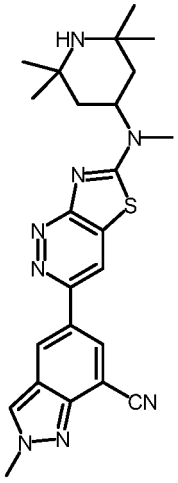

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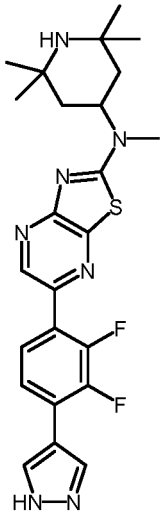

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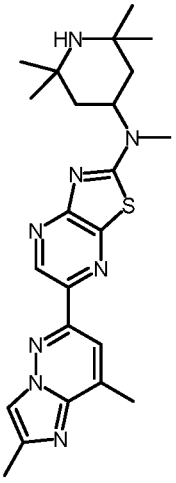

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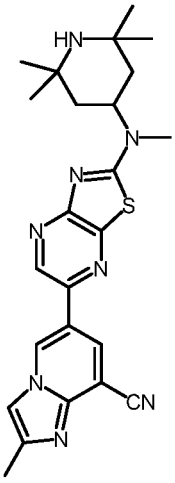

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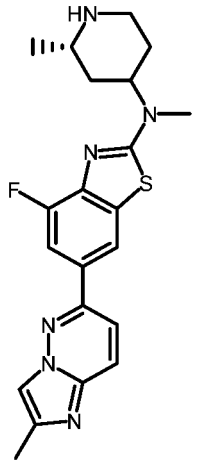

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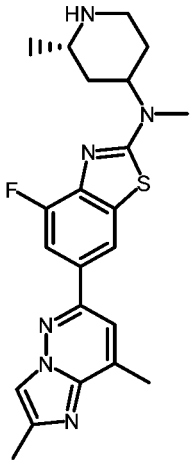

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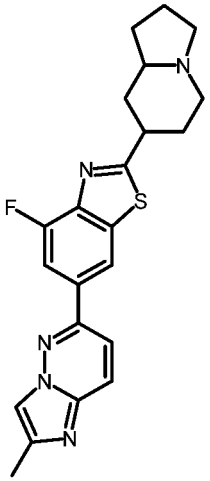

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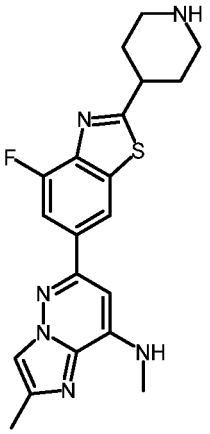

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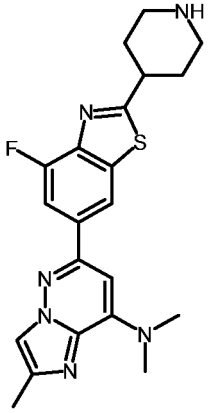

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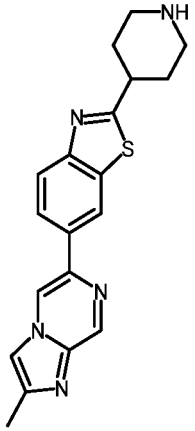

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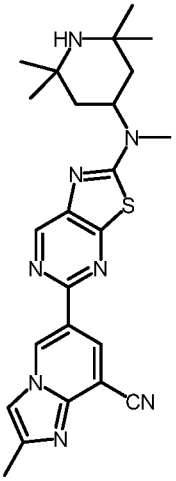

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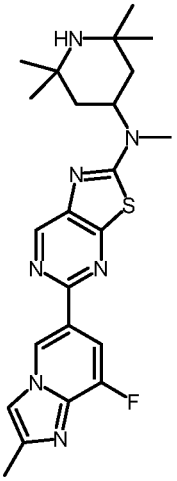

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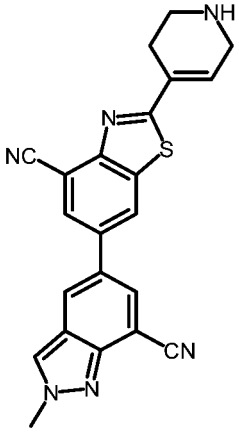

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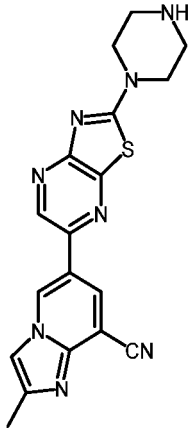

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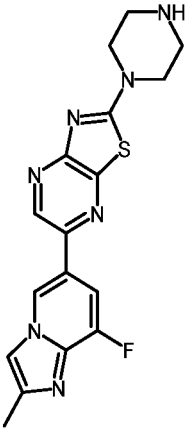

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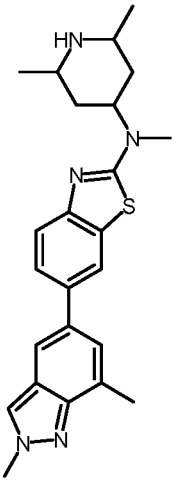

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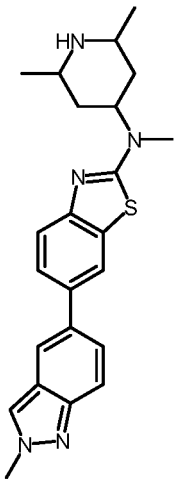

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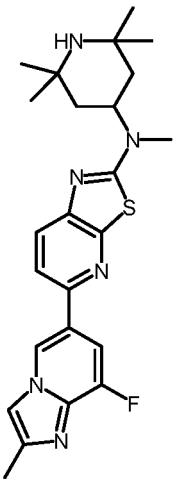

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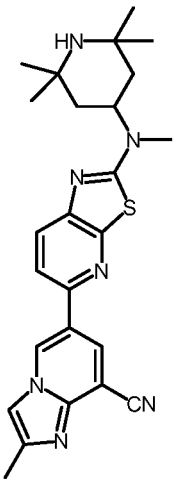

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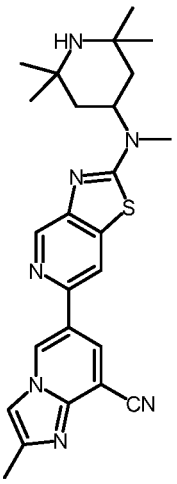

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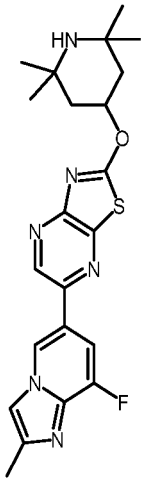

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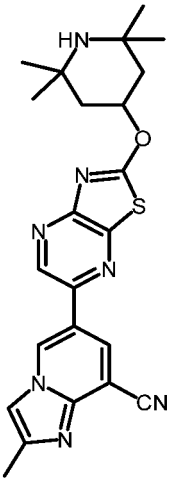

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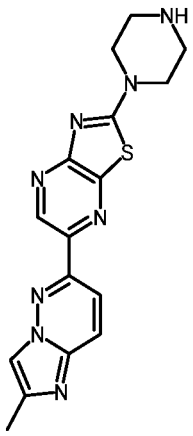

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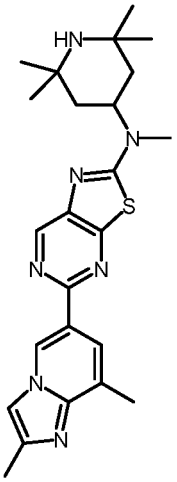

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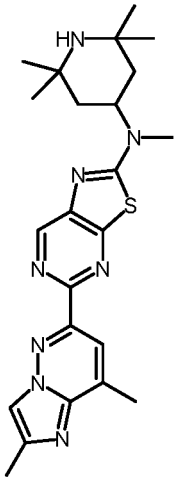

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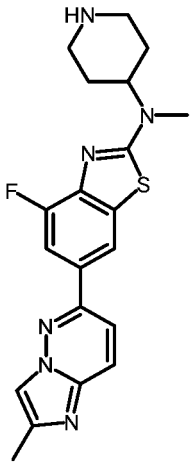

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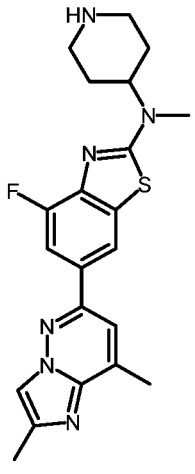

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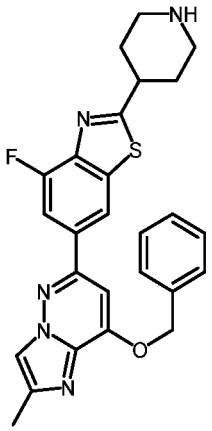

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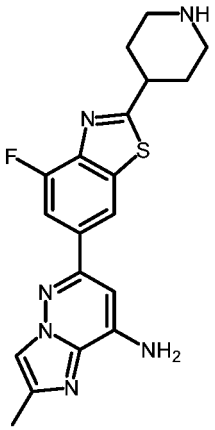

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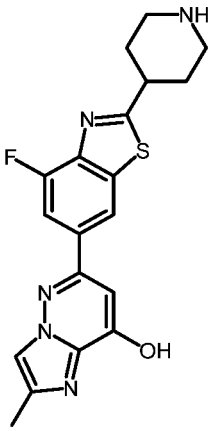

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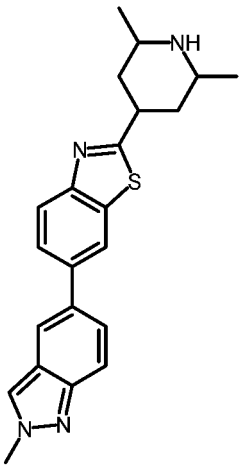

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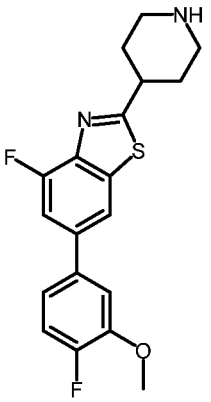

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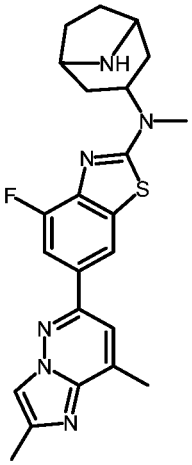

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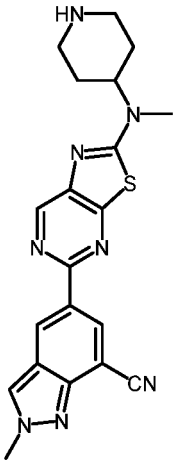

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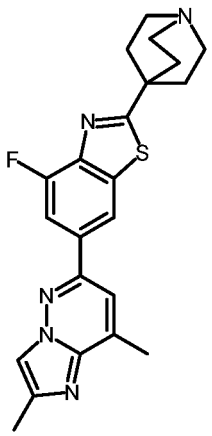

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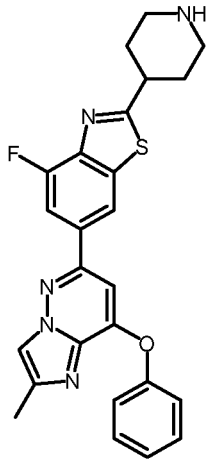

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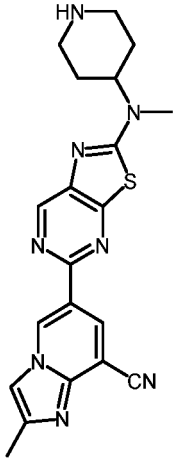

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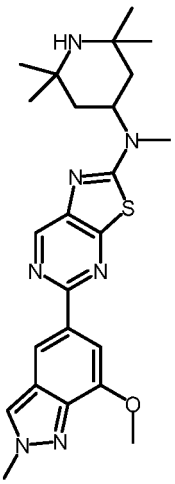

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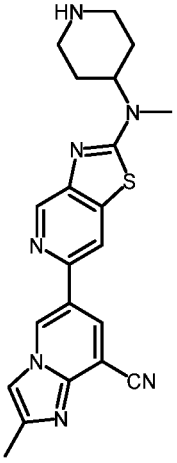

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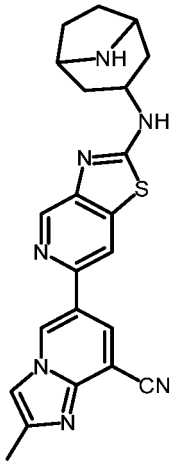

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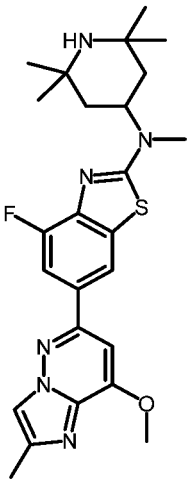

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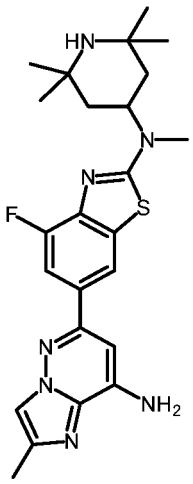

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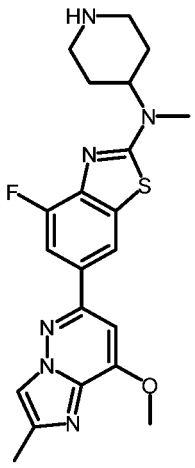

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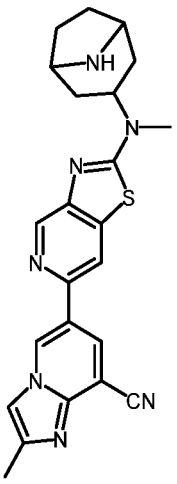

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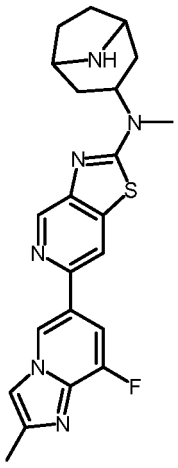

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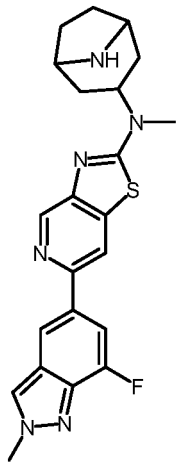

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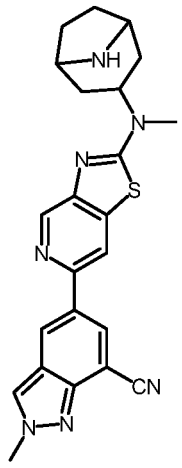

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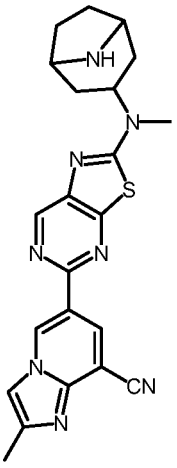

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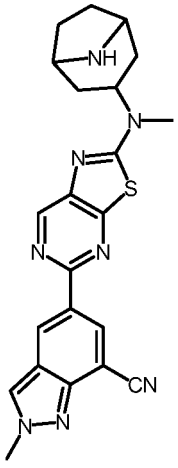

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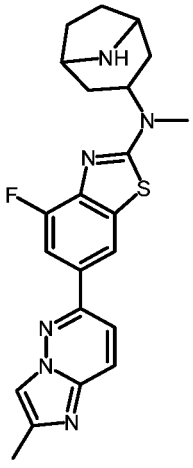

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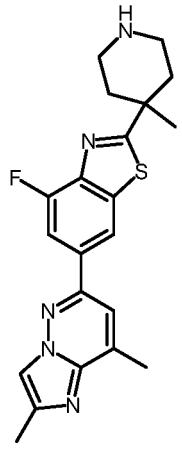

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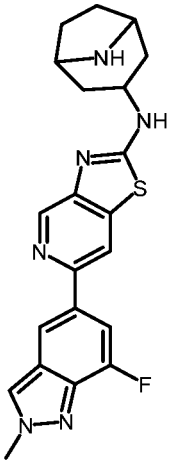

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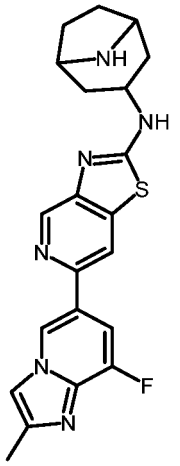

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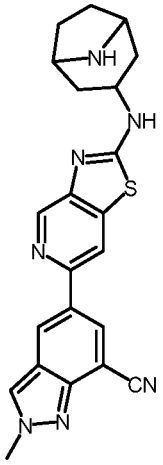

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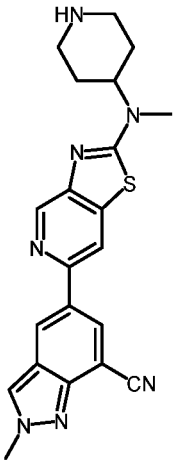

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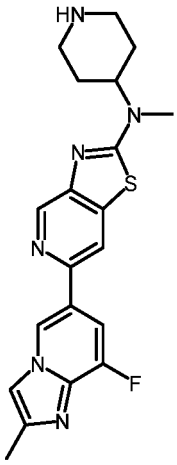

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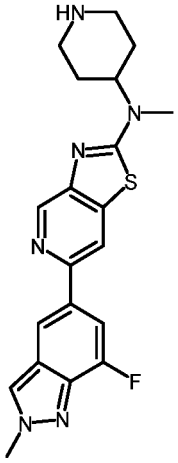

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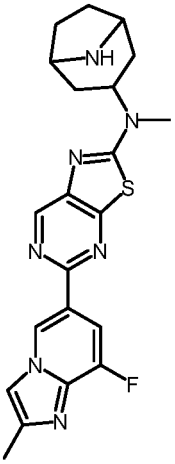

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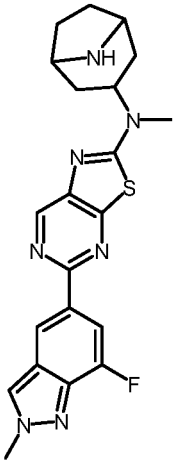

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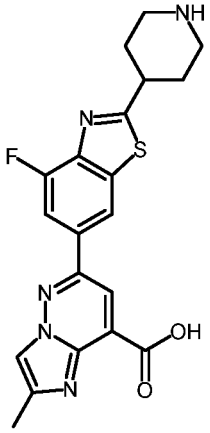

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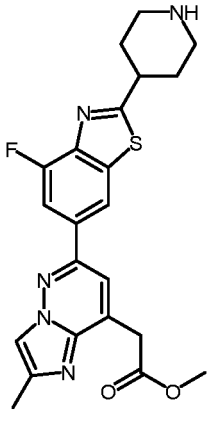

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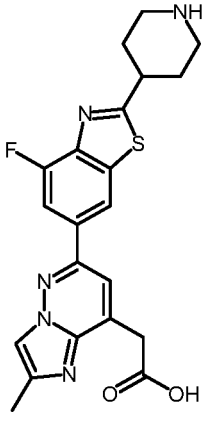

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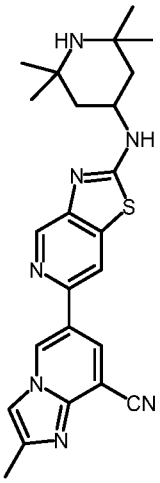

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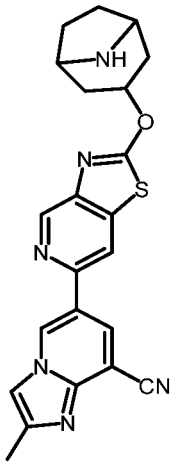

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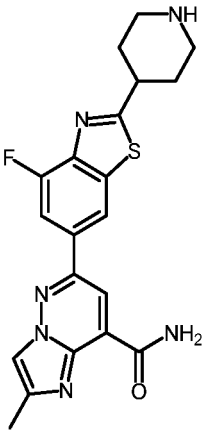

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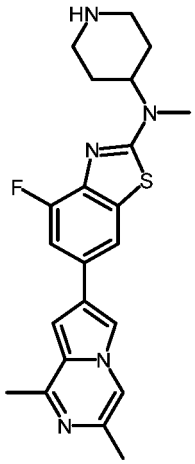

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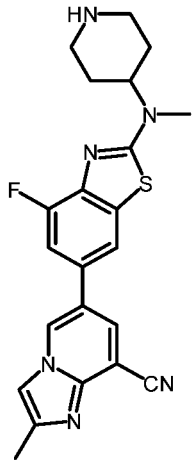

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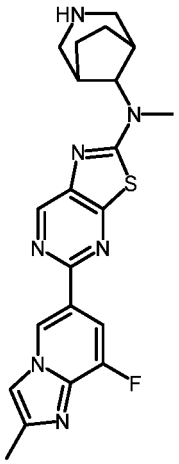

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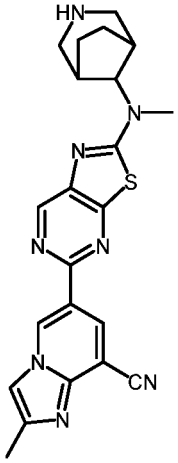

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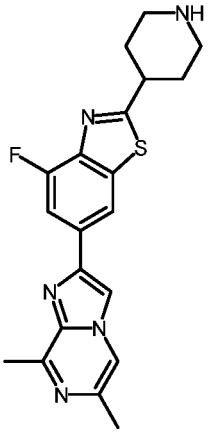

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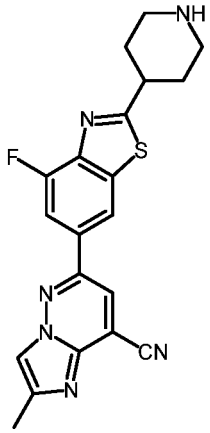

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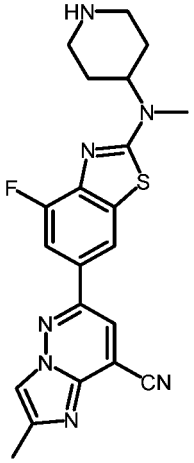

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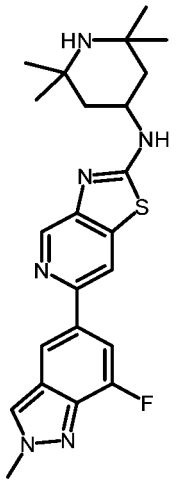

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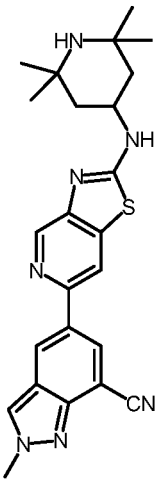

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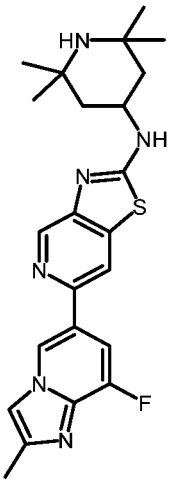

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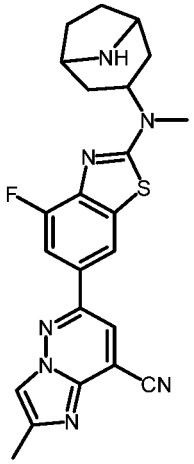

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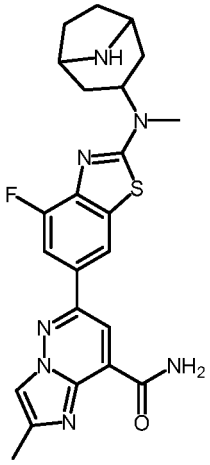

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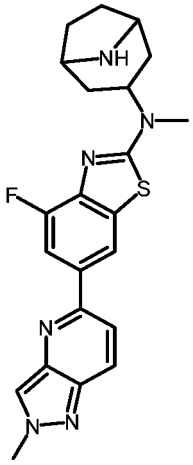

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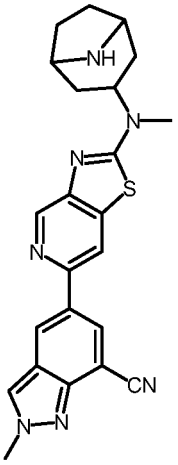

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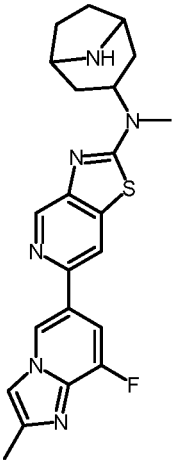

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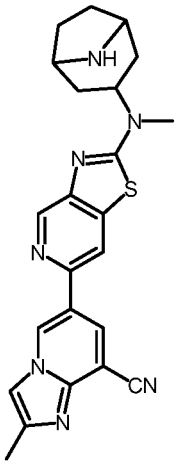

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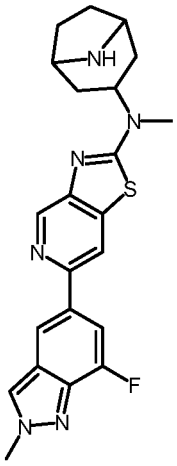

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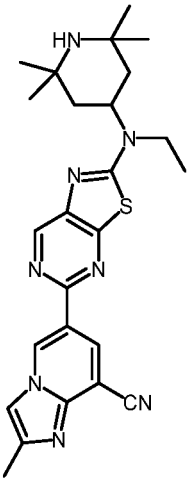

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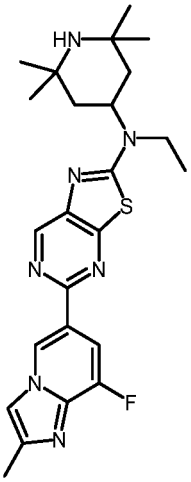

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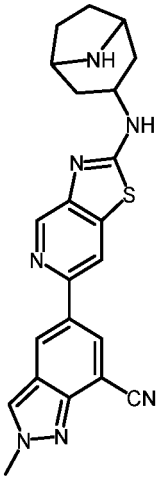

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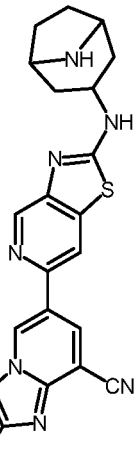

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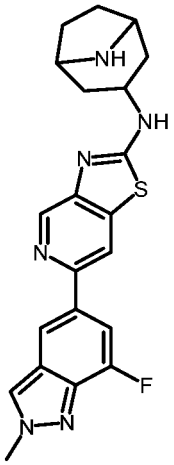

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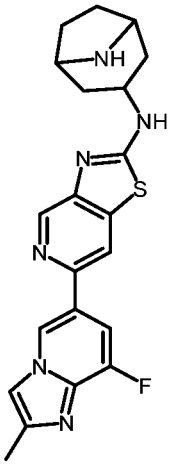

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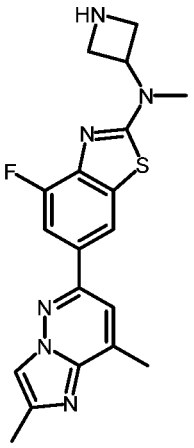

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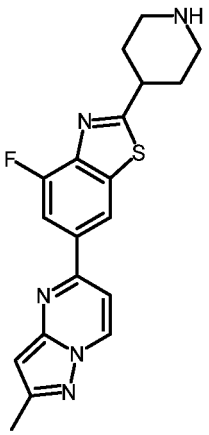

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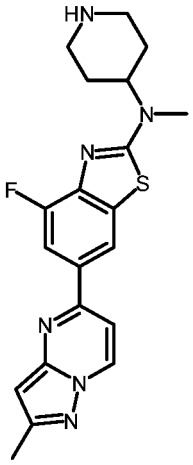

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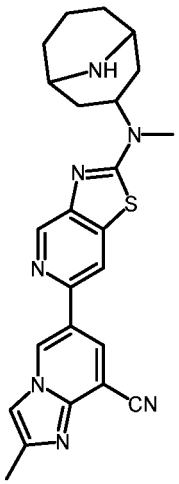

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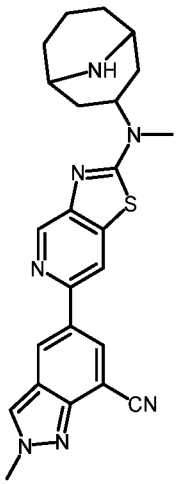

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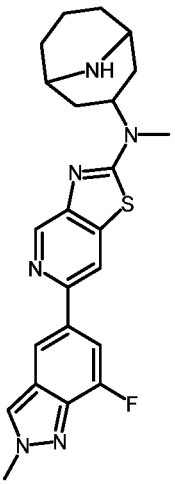

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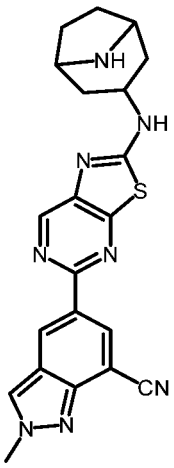

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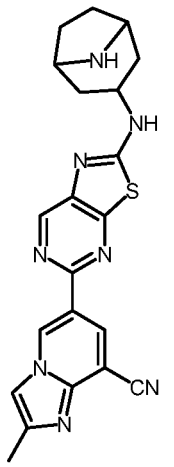

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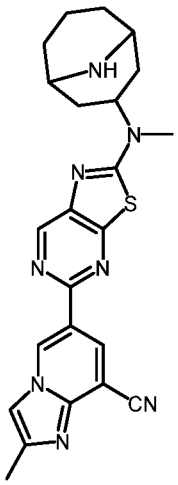

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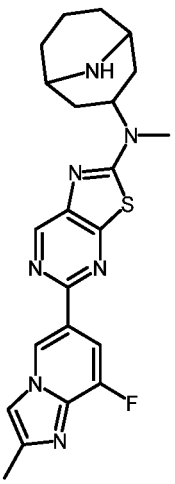

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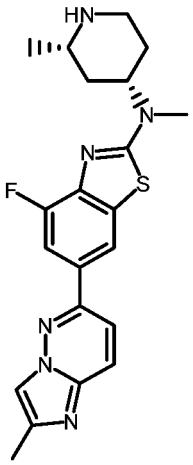

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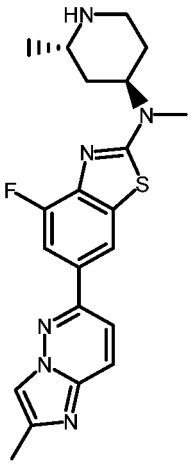

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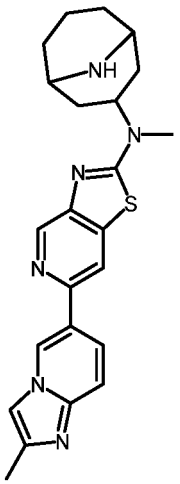

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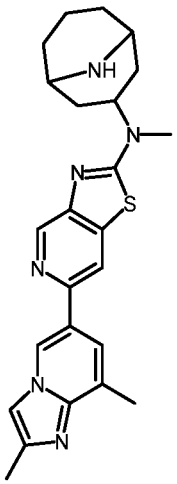

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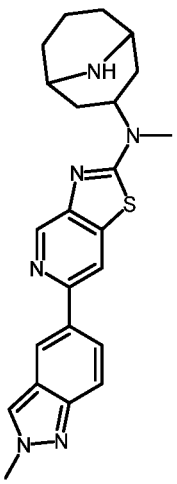

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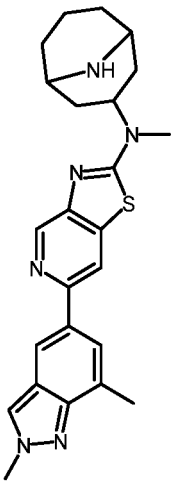

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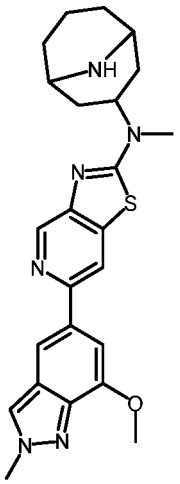

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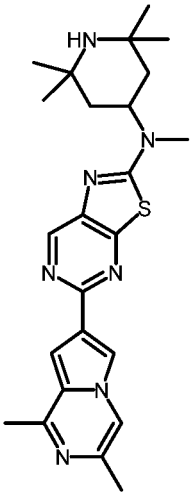

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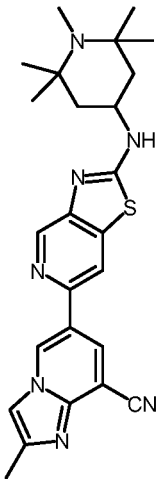

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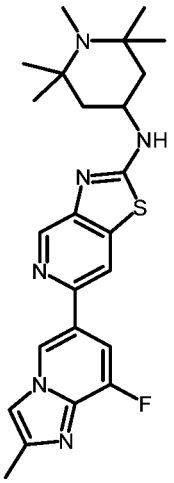

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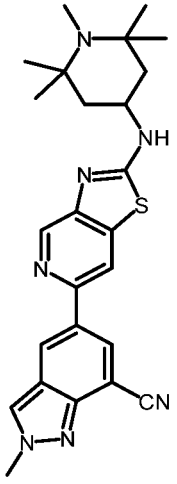

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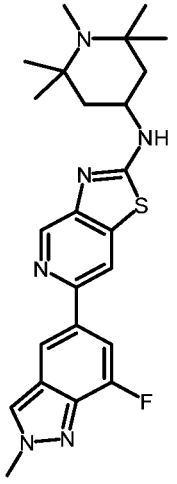

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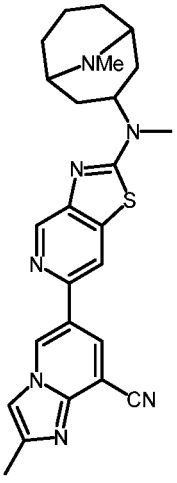

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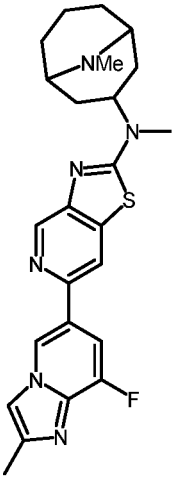

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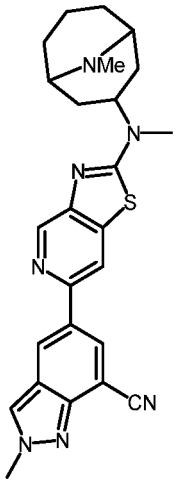

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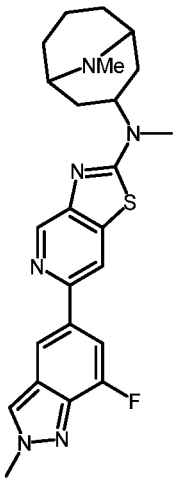

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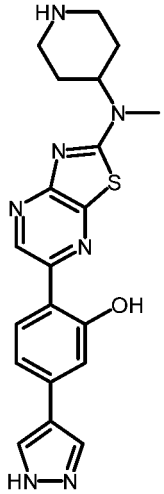

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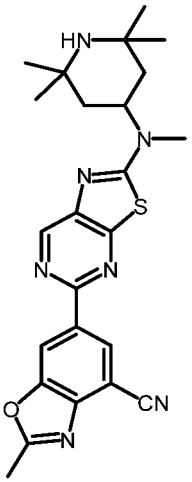

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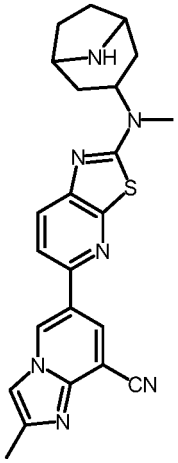

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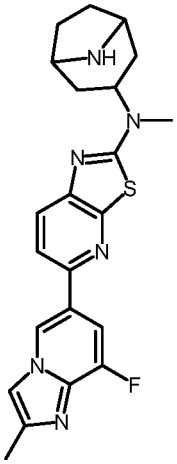

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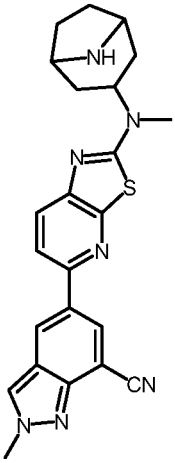

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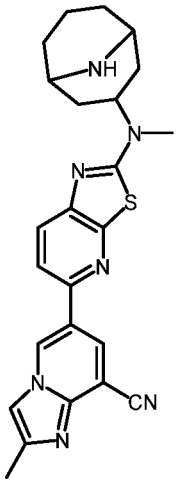

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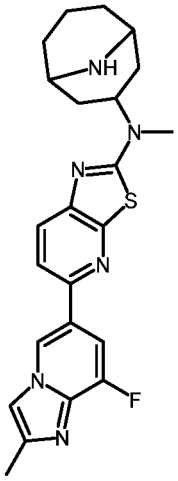

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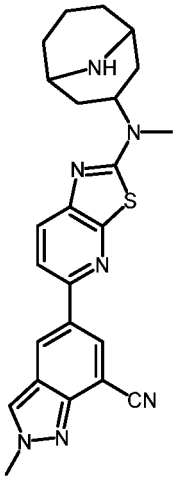

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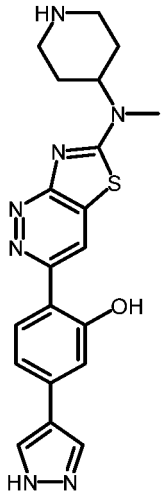

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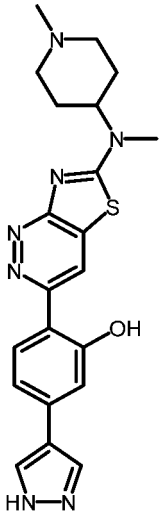

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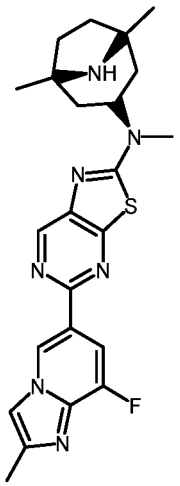

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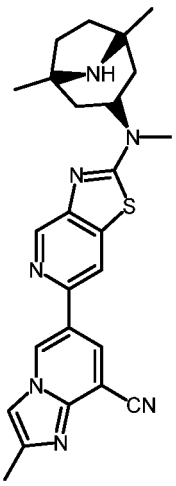

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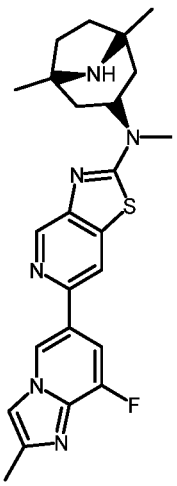

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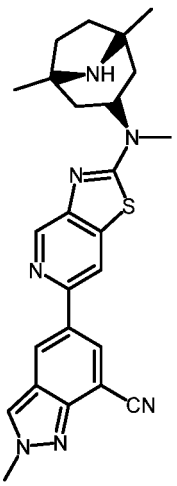

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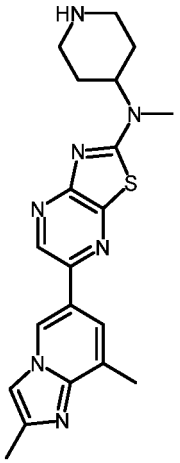

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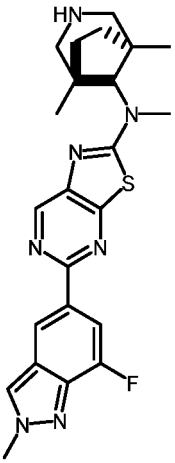

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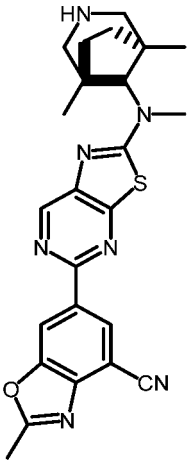

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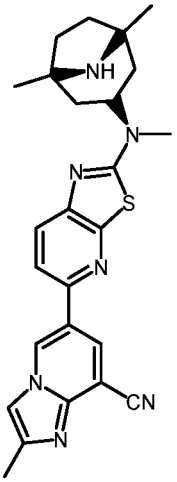

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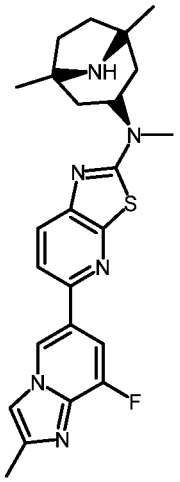

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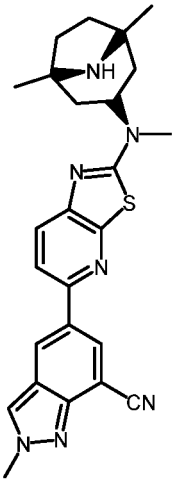

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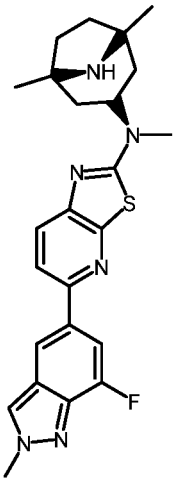

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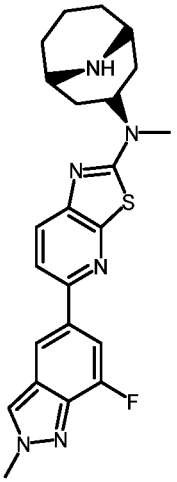

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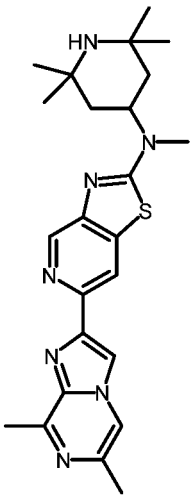

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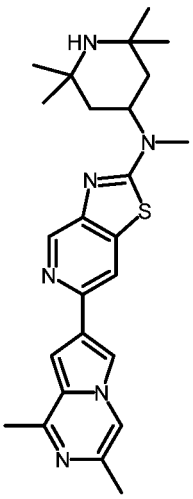

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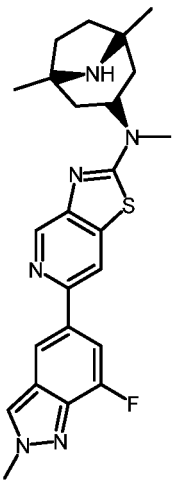

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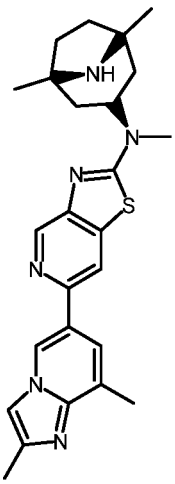

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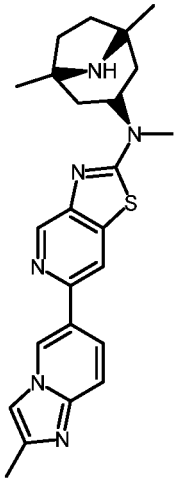

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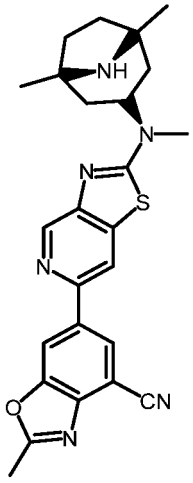

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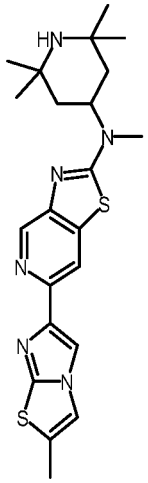

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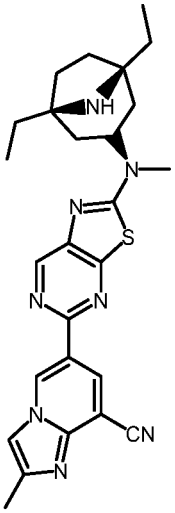

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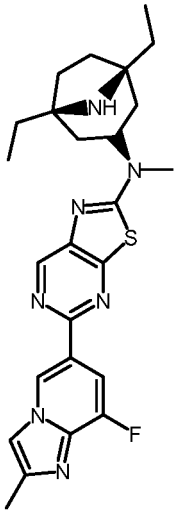

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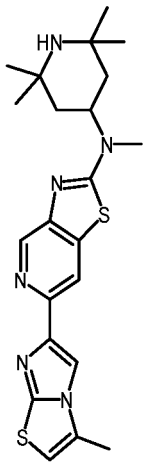

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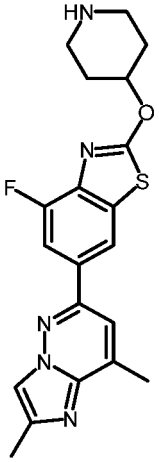

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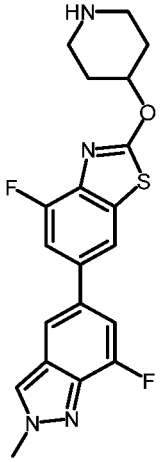

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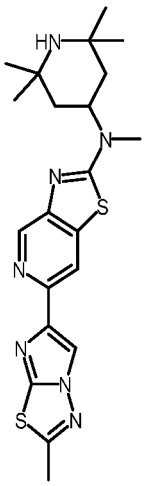

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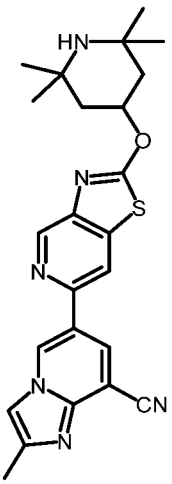

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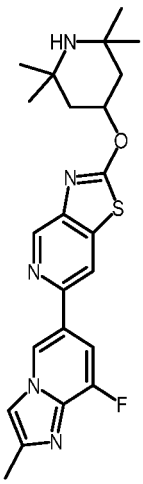

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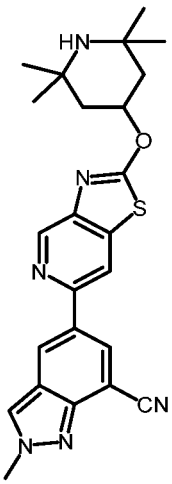

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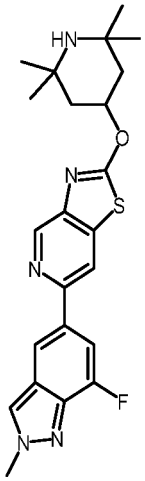

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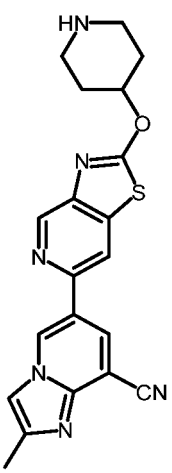

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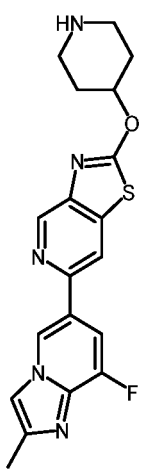

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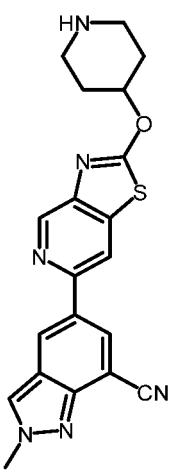

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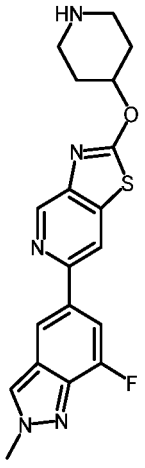

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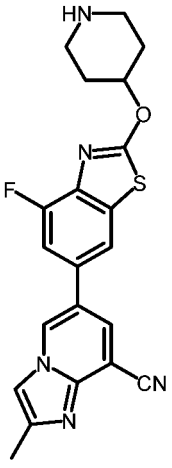

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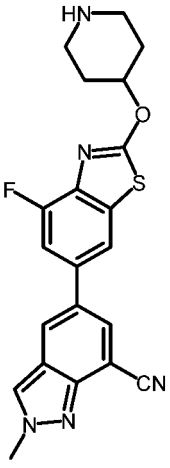

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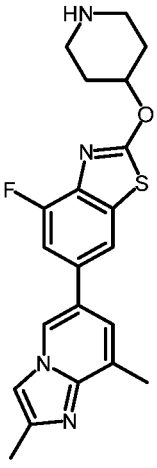

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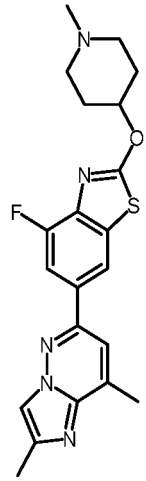

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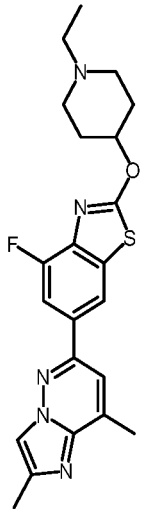

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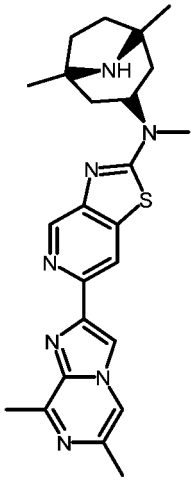

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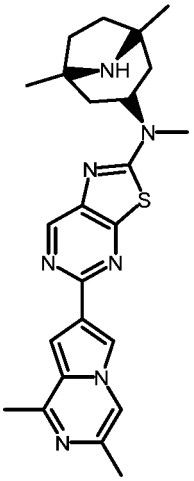

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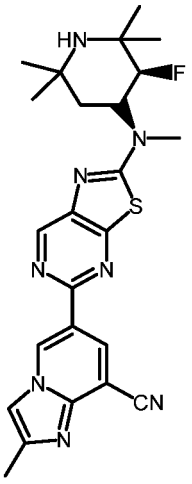

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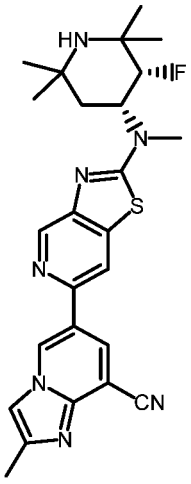

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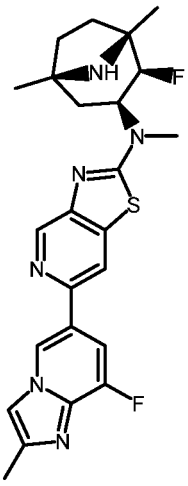

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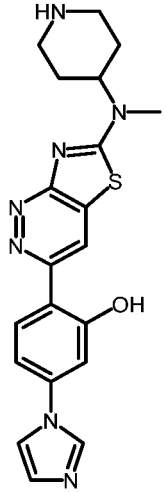

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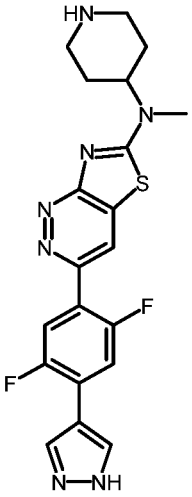

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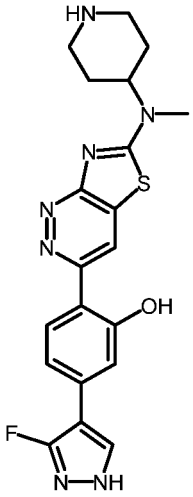

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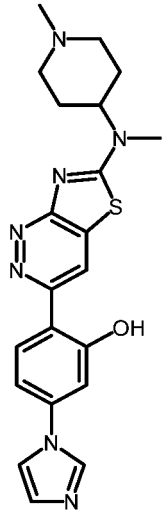

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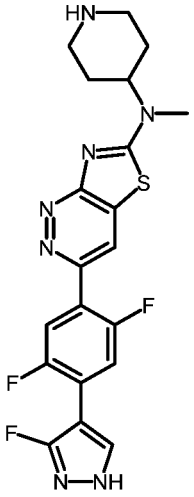

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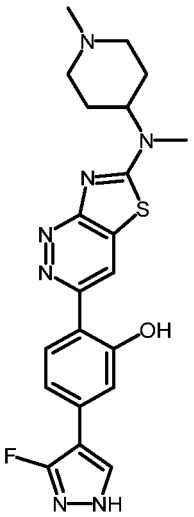

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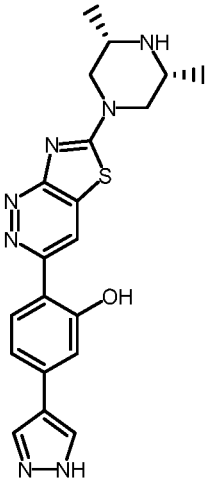

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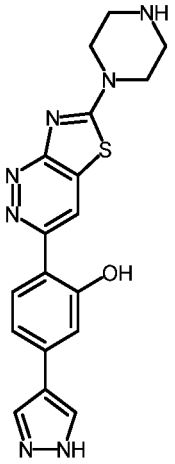

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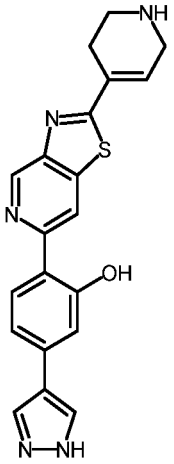

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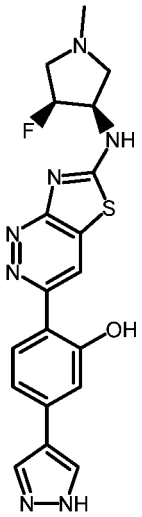

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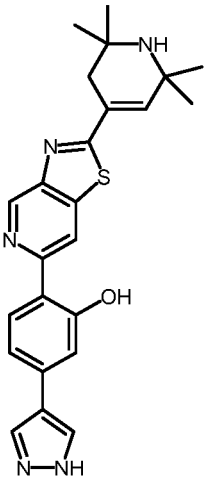

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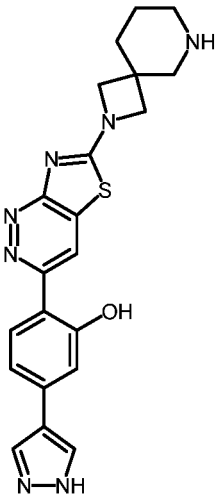

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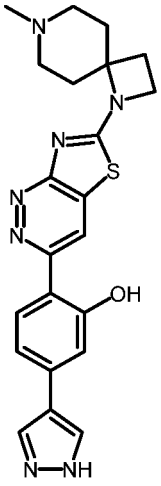

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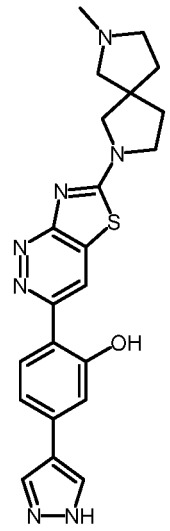

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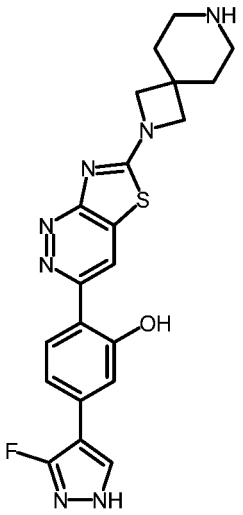

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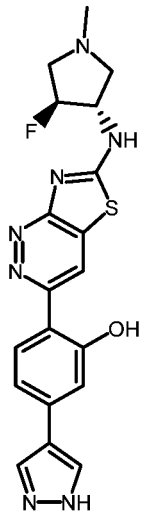

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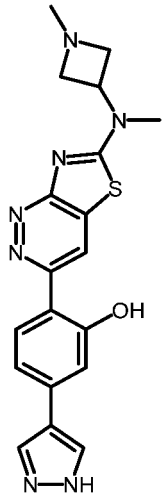

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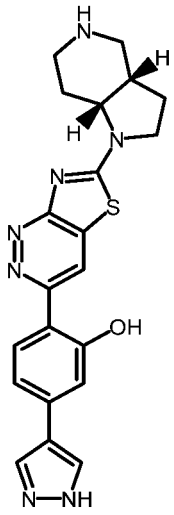

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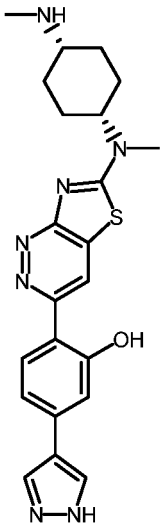

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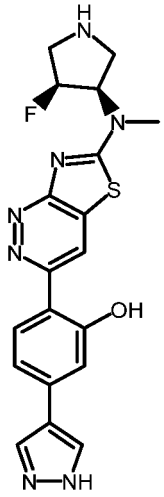

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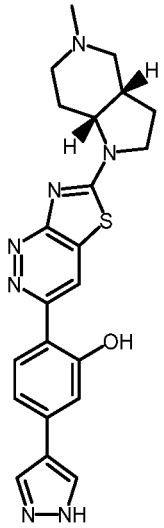

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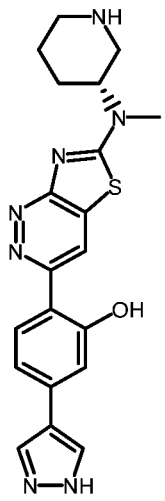

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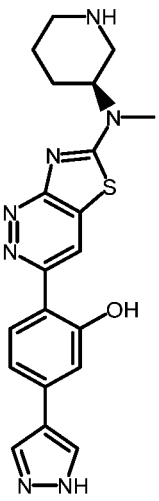

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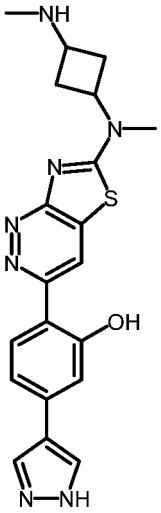

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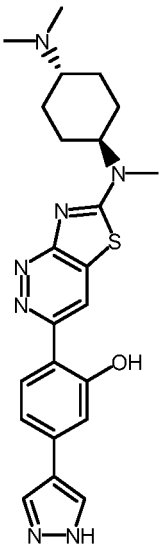

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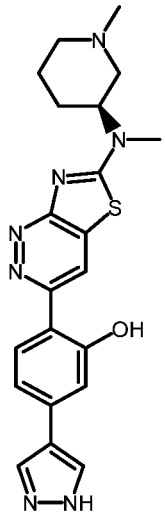

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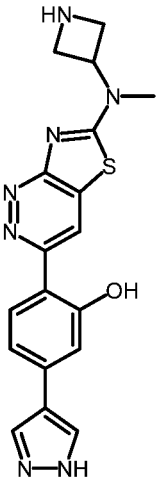

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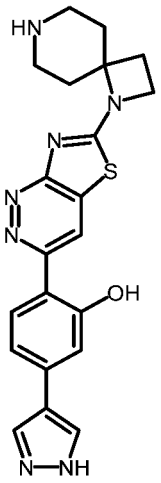

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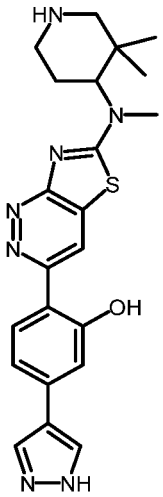

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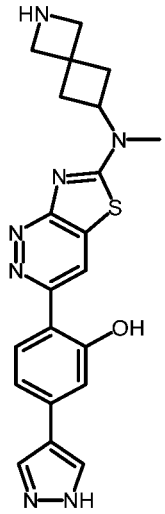

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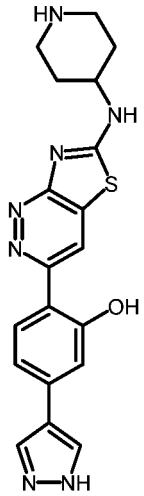

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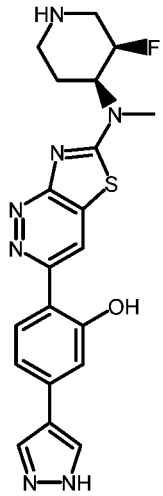

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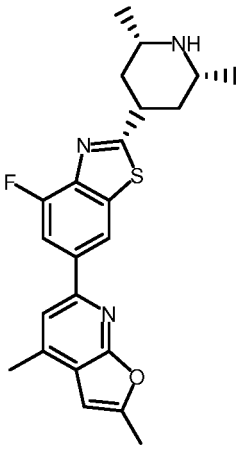

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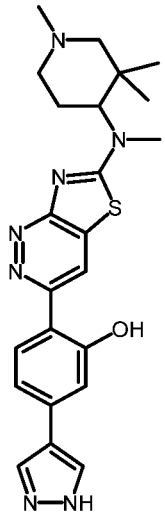

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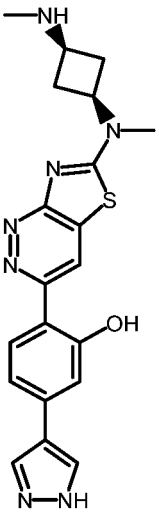

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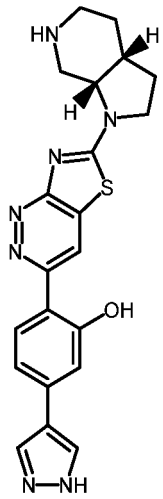

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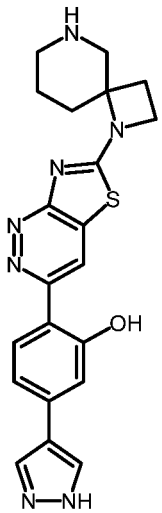

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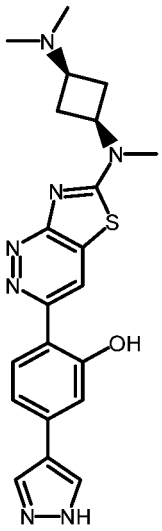

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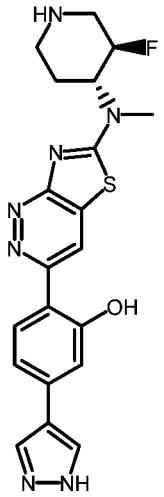

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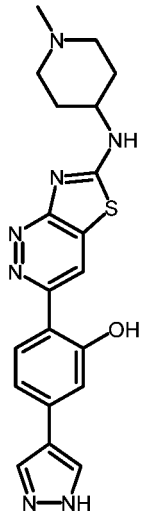

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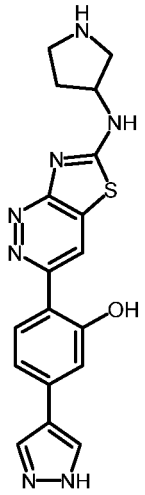

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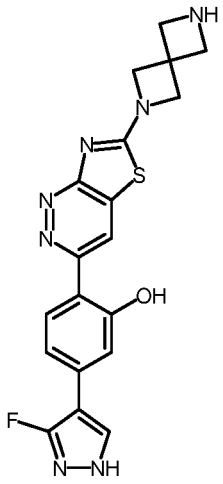

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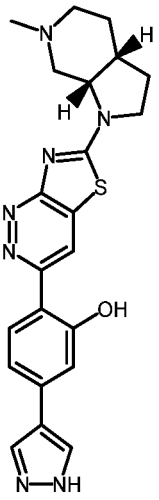

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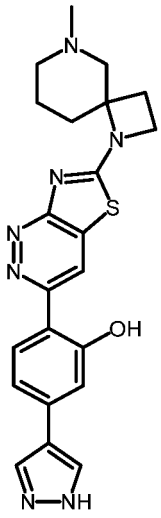

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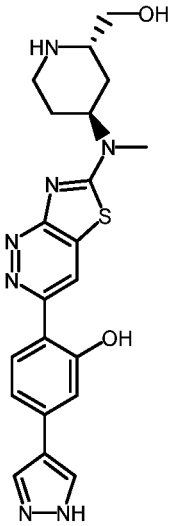

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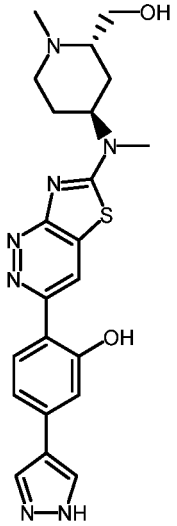

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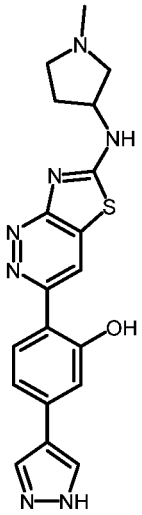

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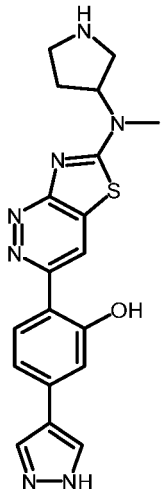

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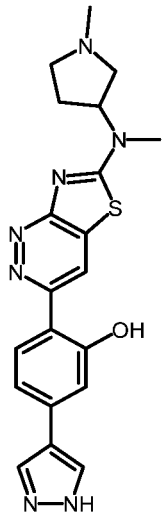

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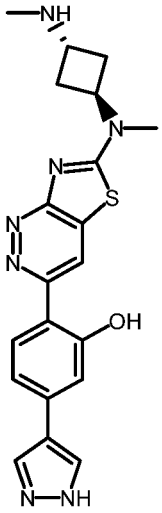

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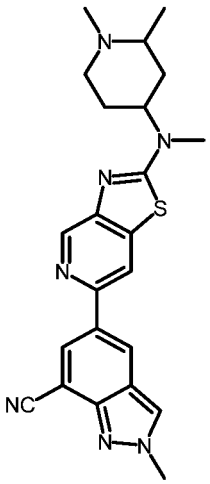

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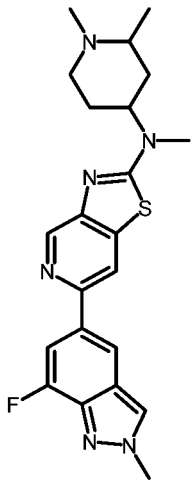

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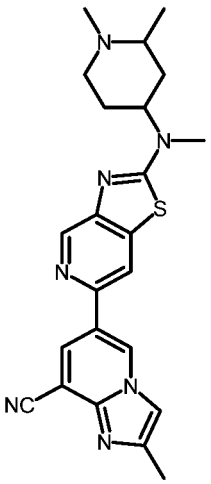

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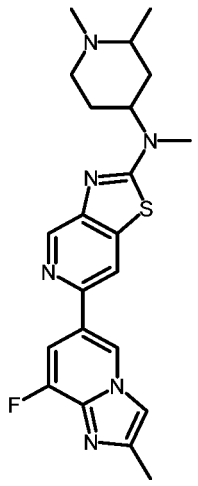

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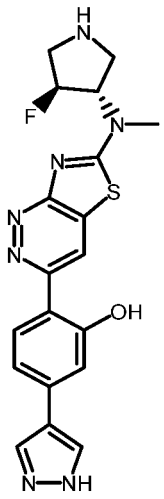

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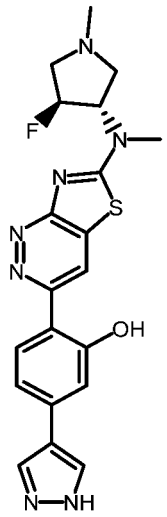

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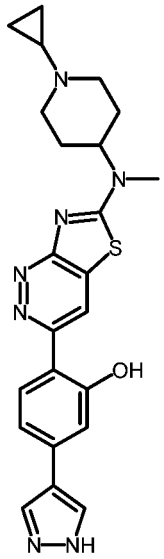

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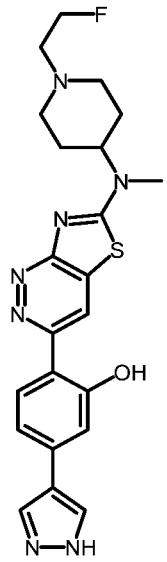

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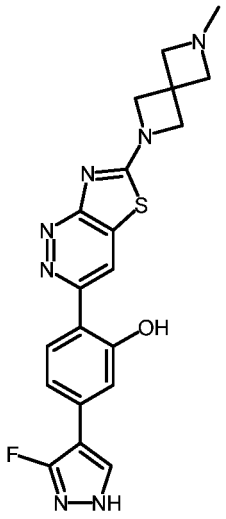

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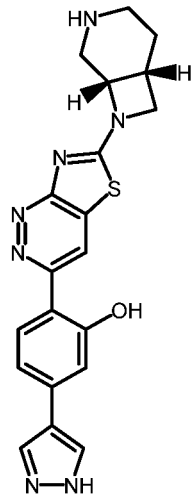

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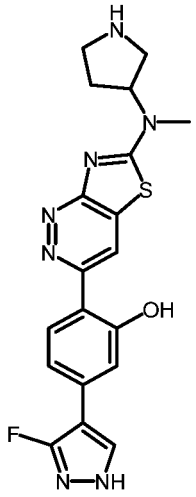

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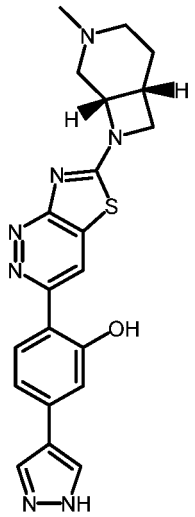

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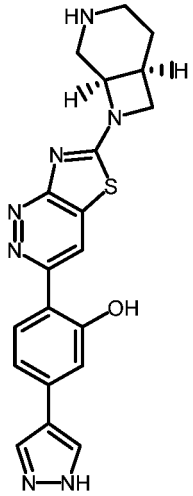

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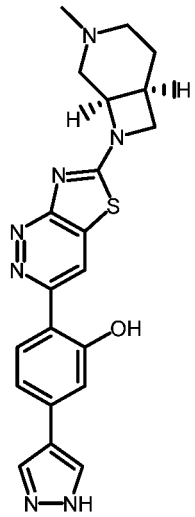

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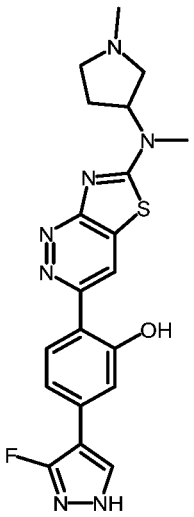

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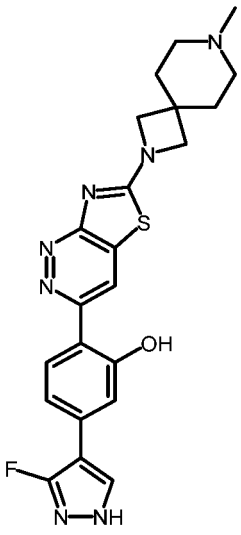

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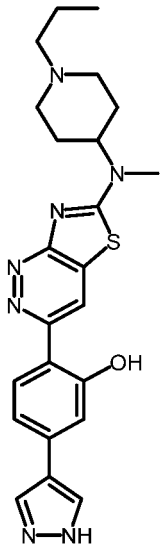

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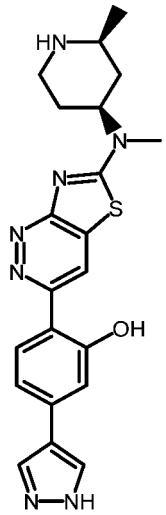

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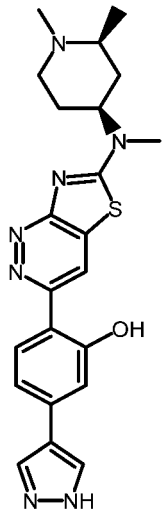

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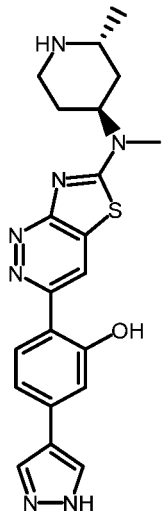

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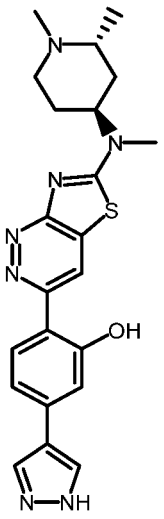

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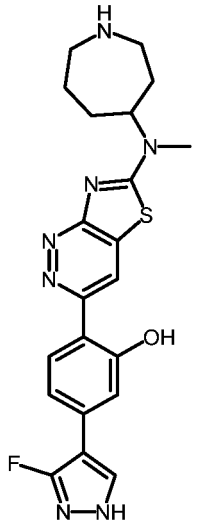

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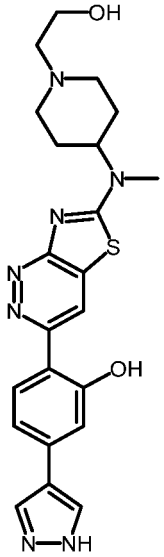


399;

wherein a form of the compound is selected from the group consisting of a salt, hydrate, solvate, racemate, enantiomer, diastereomer, stereoisomer, and tautomer form thereof.

An aspect the compound of Formula (I) or Formula (II) or a form thereof (wherein compound number (#[1]) indicates that the salt form was isolated) includes a compound selected from the group consisting of:

Cpd	Name
1	6-(2-methyl-2*H*-indazol-5-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole
2	6-(2-methyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)-1,3-benzothiazole
3	6-(2-methyl-2*H*-indazol-5-yl)-2-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole
4[1]	2-(2-methyl-2*H*-indazol-5-yl)-6-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole
5[1]	2-(2-methyl-2*H*-indazol-5-yl)-6-(piperidin-4-yl)-1,3-benzothiazole
6[1]	2-(2-methyl-2*H*-indazol-5-yl)-6-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole
7	6-(2-methyl-2*H*-indazol-5-yl)-2-(piperazin-1-yl)-1,3-benzothiazole
8[1]	*N*-methyl-6-(2-methyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)-1,3-benzothiazol-2-amine
9	6-(2-methyl-2*H*-indazol-5-yl)-2-(1-methylpiperidin-4-yl)-1,3-benzothiazole
10[1]	2-(2-methyl-2*H*-indazol-5-yl)-6-(1-methylpiperidin-4-yl)-1,3-benzothiazole
11[1]	*N*-methyl-2-(2-methyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)-1,3-benzothiazol-6-amine
12[1]	*N*-methyl-6-(2-methyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-b]pyridine-2-amine

Cpd	Name
13[1]	6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-b]pyridin-2-amine
14[1]	6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-b]pyridin-2-amine
15[1]	6-(2-methyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-b]pyridin-2-amine
16	*N*-methyl-6-(2-methyl-2*H*-indazol-5-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-b]pyridin-2-amine
17	6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-b]pyridin-2-amine
18[1]	6-(2,7-dimethyl-2*H*-indazol-5-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole
19[1]	2-(2-methyl-2*H*-indazol-5-yl)-6-(1,2,3,6-tetrahydropyridin-4-yl)[1,3]thiazolo[4,5-b]pyridine
20	*N*-methyl-6-(2-methyl-2*H*-indazol-5-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine
21	6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine
22[1]	6-(2,7-dimethyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)-1,3-benzothiazole
23	4-fluoro-*N*-methyl-6-(2-methyl-2*H*-indazol-5-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine
24	6-(2,7-dimethyl-2*H*-indazol-5-yl)-4-fluoro-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine
25[1]	*N*-methyl-5-(2-methyl-2*H*-indazol-5-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[5,4-b]pyridin-2-amine
26[1]	*N*-methyl-5-(2-methyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)[1,3]thiazolo[5,4-b]pyridin-2-amine
27[1]	*N*-methyl-6-(2-methyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine
28[1]	*N*,*N*-dimethyl-1-[6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazol-2-yl]piperidin-4-amine
29[1]	1-[6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazol-2-yl]piperidin-4-amine
30[1]	6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine
31	6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine
32	*N*-methyl-6-(2-methyl-2*H*-indazol-5-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine
33	6-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine
34[1]	6-(1*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine

Cpd	Name
35[1]	6-(2-methyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)-1,3-benzothiazol-2-amine
36[1]	5-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[5,4-b]pyridin-2-amine
37	4-fluoro-*N*-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine
38[1]	*N*-methyl-6-(2-methyl-2*H*-indazol-5-yl)-*N*-(pyrrolidin-3-yl)-1,3-benzothiazol-2-amine
39	6-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-4-fluoro-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine
40[1]	*N*-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine
41[1]	2-(4-fluoropiperidin-4-yl)-6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazole
42[1]	2-(azepan-4-yl)-6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazole
43[1]	2-(2-methyl-2*H*-indazol-5-yl)-6-(piperidin-4-yl)[1,3]thiazolo[4,5-b]pyridine
44[1]	6-[4-fluoro-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazine
45[1]	6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazine
46[1]	6-[4-fluoro-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazol-6-yl]-2,8-dimethylimidazo[1,2-b]pyridazine
47[1]	6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2,8-dimethylimidazo[1,2-b]pyridazine
48	*N*-methyl-6-(2-methyl[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine
49[1]	2-(2,7-dimethyl-2*H*-indazol-5-yl)-6-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole
50[1]	2-(2,7-dimethyl-2*H*-indazol-5-yl)-6-(piperidin-4-yl)-1,3-benzothiazole
51[1]	*N*-methyl-6-[2-methyl-7-(trifluoromethyl)-2*H*-indazol-5-yl]-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine
52	6-(2-methyl-2*H*-indazol-5-yl)-2-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazole
53[1]	6-[4-fluoro-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazol-6-yl]-2,8-dimethylimidazo[1,2-a]pyrazine
54	6-(7-ethyl-2-methyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine
55[1]	6-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine
56	6-(2-methyl-2*H*-indazol-5-yl)-2-(2,3,6,7-tetrahydro-1*H*-azepin-4-yl)-1,3-benzothiazole
57[1]	6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine
58[1]	6-(2-methyl-2*H*-indazol-5-yl)-2-(2-methylpiperidin-4-yl)-1,3-benzothiazole
59[1]	6-(2,7-dimethyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridine

Cpd	Name
60[1]	6-[2-methyl-7-(trifluoromethyl)-2*H*-indazol-5-yl]-2-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridine
61[1]	6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-(piperidin-4-yl)[1,3]thiazolo[4,5-b]pyridine
62[1]	2-methyl-5-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino]-1,3-benzothiazol-6-yl}-2*H*-indazole-7-carbonitrile
63[1]	*N*-methyl-6-(2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine
64	6-(2-methyl-2*H*-indazol-5-yl)-2-[(2,2,6,6-tetramethylpiperidin-4-yl)oxy]-1,3-benzothiazole
65[1]	6-(2-methyl-2*H*-indazol-5-yl)-2-(2-methyl-1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole
66[1]	6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2-methylpiperidin-4-yl)-1,3-benzothiazol-2-amine
67[1]	6-(2-methyl-2*H*-indazol-5-yl)-2-(6-methyl-1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole
68[1]	6-(2,7-dimethyl-2*H*-indazol-5-yl)-2-[(2,2,6,6-tetramethylpiperidin-4-yl)oxy]-1,3-benzothiazole
70[1]	6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methyl-1,3-benzoxazole
71[1]	6-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-4-fluoro-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole
72[1]	4-fluoro-6-(2-methyl-2*H*-indazol-5-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole
73[1]	4-fluoro-6-(2-methyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)-1,3-benzothiazole
74[1]	2-methyl-5-[2-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-6-yl]-2*H*-indazole-7-carbonitrile
75[1]	6-(7-ethyl-2-methyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridine
76[1]	6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridine
77[1]	6-(2-methylimidazo[1,2-a]pyridin-6-yl)-2-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridine
78[1]	5-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-1*H*-pyrazolo[4,3-b]pyridine
79[1]	5-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methyl-2*H*-pyrazolo[4,3-b]pyridine
80[1]	6-(7-cyclopropyl-2-methyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine
81[1]	*N*-methyl-6-(2-methyl-2*H*-indazol-5-yl)-*N*-(2-methylpiperidin-4-yl)-1,3-benzothiazol-2-amine
82	6-(2-methylimidazo[1,2-a]pyridin-6-yl)-2-(piperidin-4-yl)-1,3-benzothiazole
83	6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)-1,3-benzothiazole

Cpd	Name
84[1]	2-methyl-5-[2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2*H*-indazole-7-carbonitrile
85	6-(7-ethyl-2-methyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)-1,3-benzothiazole
86	6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine
87	*N*-methyl-6-(2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine
88	6-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine
89	*N*-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine
90	6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine
91	5-{4-fluoro-2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino]-1,3-benzothiazol-6-yl}-2-methyl-2*H*-indazole-7-carbonitrile
92	6-[4-fluoro-2-(1-methylpiperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazine
93[1]	6-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine
94[1]	6-(2,4-dimethyl-1*H*-benzimidazol-6-yl)-2-(piperidin-4-yl)-1,3-benzothiazole
95[1]	6-(2-methyl-1*H*-benzimidazol-6-yl)-2-(piperidin-4-yl)-1,3-benzothiazole
96	*N*-methyl-6-[2-methyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-6-yl]-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine
97[1]	2-methyl-6-[2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]imidazo[1,2-b]pyridazine
98[1]	6-(2,7-dimethyl-2*H*-indazol-5-yl)-4-methoxy-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole
99[1]	6-(2,7-dimethyl-2*H*-indazol-5-yl)-4-methoxy-2-(piperidin-4-yl)-1,3-benzothiazole
100[1]	6-(2,7-dimethyl-2*H*-indazol-5-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazol-4-ol
101	6-(2,7-dimethyl-2*H*-indazol-5-yl)-7-fluoro-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine
102[1]	5-[4-fluoro-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazol-6-yl]-2-methyl-2*H*-indazole-7-carbonitrile
103[1]	1-{5-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methyl-2*H*-indazol-7-yl}methanamine
104[1]	5-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methyl-2*H*-indazole-7-carbonitrile
105	*N*-methyl-6-(2-methylimidazo[1,2-a]pyrimidin-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine

Cpd	Name
106	6-[2-(1-ethylpiperidin-4-yl)-4-fluoro-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazine
107	6-[4-fluoro-2-(1-methylpiperidin-4-yl)-1,3-benzothiazol-6-yl]-2,8-dimethylimidazo[1,2-b]pyridazine
108	6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-(1,2-dimethylpiperidin-4-yl)-*N*-methyl-1,3-benzothiazol-2-amine
109[1]	2-methyl-5-[2-(piperidin-4-yl)[1,3]thiazolo[5,4-d]pyrimidin-5-yl]-2*H*-indazole-7-carbonitrile
110[1]	5-(2,7-dimethyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)[1,3]thiazolo[5,4-d]pyrimidine
111[1]	6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine
112	2-methyl-6-[2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-1,3-benzoxazole
113[1]	6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-(piperidin-4-yl)-1,3-benzothiazole
114[1]	6-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-2-(piperidin-4-yl)-1,3-benzothiazole
115[1]	2-(2,2-dimethylpiperidin-4-yl)-6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazole
116	*N*-methyl-6-[2-methyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-6-yl]-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine
117	2-methyl-5-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2*H*-indazole-7-carbonitrile
118	3-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridazin-6-amine
119[1]	2-{6-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol
120	6-[4-fluoro-2-(piperazin-1-yl)-1,3-benzothiazol-6-yl]-2,8-dimethylimidazo[1,2-b]pyridazine
121	6-[2-(1,4-diazepan-1-yl)-4-fluoro-1,3-benzothiazol-6-yl]-2,8-dimethylimidazo[1,2-b]pyridazine
122	5-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[5,4-d]pyrimidin-2-amine
123	2-methyl-5-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-2*H*-indazole-7-carbonitrile
124	5-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[5,4-d]pyrimidin-2-amine
125	6-[2-(4,7-diazaspiro[2.5]oct-7-yl)-4-fluoro-1,3-benzothiazol-6-yl]-2,8-dimethylimidazo[1,2-b]pyridazine
126	4-fluoro-6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)-1,3-benzothiazole
127	6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4-fluoro-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine

Cpd	Name
128	5-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[5,4-b]pyridin-2-amine
129	*N*-methyl-5-(2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[5,4-b]pyridin-2-amine
130[1]	2-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-b]pyrazin-6-yl}-5-(1*H*-pyrazol-4-yl)phenol
131	6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-b]pyrazin-2-amine
132[1]	6-[2-(3,5-dimethylpiperazin-1-yl)-4-fluoro-1,3-benzothiazol-6-yl]-2,8-dimethylimidazo[1,2-b]pyridazine
133[1]	6-{4-fluoro-2-[(2,2,6,6-tetramethylpiperidin-4-yl)oxy]-1,3-benzothiazol-6-yl}-2,8-dimethylimidazo[1,2-b]pyridazine
134	6-(2,7-dimethyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)-1,3-benzothiazol-4-ol
135[1]	6-{2-[(2,6-dimethylpiperidin-4-yl)oxy]-4-fluoro-1,3-benzothiazol-6-yl}-2,8-dimethylimidazo[1,2-b]pyridazine
136	*N*-methyl-6-(2-methyl[1,2,4]triazolo[1,5-a]pyridin-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine
137[1]	2-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-5-(1*H*-pyrazol-4-yl)phenol
138[1]	2-methyl-6-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino]-1,3-benzothiazol-6-yl}imidazo[1,2-a]pyridine-8-carbonitrile
139[1]	2,8-dimethyl-6-[2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]imidazo[1,2-b]pyridazine
140	2-methyl-5-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-b]pyrazin-6-yl}-2*H*-indazole-7-carbonitrile
141	*N*-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-b]pyrazin-2-amine
142[1]	2-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-5-(1*H*-pyrazol-4-yl)phenol
143	1-[6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4-fluoro-1,3-benzothiazol-2-yl]piperidin-4-ol
144[1]	6-{4-fluoro-2-[(2*R*)-2-methylpiperidin-4-yl]-1,3-benzothiazol-6-yl}-2-methylimidazo[1,2-b]pyridazine
145[1]	6-[4-fluoro-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazol-6-yl]-8-methoxy-2-methylimidazo[1,2-b]pyridazine
146[1]	6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-(2,2-dimethylpiperidin-4-yl)-*N*-methyl-1,3-benzothiazol-2-amine
147	6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine

Cpd	Name
148	2-methyl-5-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[5,4-b]pyridin-5-yl}-2*H*-indazole-7-carbonitrile
149[1]	2-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[5,4-b]pyridin-5-yl}-5-(1*H*-pyrazol-4-yl)phenol
150	6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-b]pyrazin-2-amine
151[1]	6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-8-methoxy-2-methylimidazo[1,2-b]pyridazine
152[1]	4-fluoro-6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-(piperidin-4-yl)-1,3-benzothiazole
153[1]	4-chloro-6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole
154[1]	5-[4-chloro-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazol-6-yl]-2-methyl-2*H*-indazole-7-carbonitrile
155[1]	*N*-(2,2-dimethylpiperidin-4-yl)-*N*-methyl-6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazol-2-amine
156	2-methyl-6-[2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]imidazo[1,2-a]pyrimidine
157	3-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridazin-6-amine
158	2-methyl-5-{6-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-2*H*-indazole-7-carbonitrile
161[1]	6-[2,3-difluoro-4-(1*H*-pyrazol-4-yl)phenyl]-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-b]pyrazin-2-amine
162	6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-b]pyrazin-2-amine
163	2-methyl-6-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-b]pyrazin-6-yl}imidazo[1,2-a]pyridine-8-carbonitrile
164[1]	4-fluoro-*N*-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-[(2*S*)-2-methylpiperidin-4-yl]-1,3-benzothiazol-2-amine
165[1]	6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4-fluoro-*N*-methyl-*N*-[(2*S*)-2-methylpiperidin-4-yl]-1,3-benzothiazol-2-amine
166[1]	6-[4-fluoro-2-(octahydroindolizin-7-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazine
167[1]	6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-*N*,2-dimethylimidazo[1,2-b]pyridazin-8-amine
168[1]	6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-*N*,*N*,2-trimethylimidazo[1,2-b]pyridazin-8-amine
169	2-methyl-6-[2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]imidazo[1,2-a]pyrazine

Cpd	Name
170	2-methyl-6-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}imidazo[1,2-a]pyridine-8-carbonitrile
171	5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[5,4-d]pyrimidin-2-amine
172[1]	6-(7-cyano-2-methyl-2*H*-indazol-5-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole-4-carbonitrile
173[1]	2-methyl-6-[2-(piperazin-1-yl)[1,3]thiazolo[4,5-b]pyrazin-6-yl]imidazo[1,2-a]pyridine-8-carbonitrile
174[1]	6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-(piperazin-1-yl)[1,3]thiazolo[4,5-b]pyrazine
175[1]	6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-(2,6-dimethylpiperidin-4-yl)-*N*-methyl-1,3-benzothiazol-2-amine
176[1]	*N*-(2,6-dimethylpiperidin-4-yl)-*N*-methyl-6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazol-2-amine
177	5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[5,4-b]pyridin-2-amine
178	2-methyl-6-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[5,4-b]pyridin-5-yl}imidazo[1,2-a]pyridine-8-carbonitrile
179	2-methyl-6-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}imidazo[1,2-a]pyridine-8-carbonitrile
180	6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-[(2,2,6,6-tetramethylpiperidin-4-yl)oxy][1,3]thiazolo[4,5-b]pyrazine
181	2-methyl-6-{2-[(2,2,6,6-tetramethylpiperidin-4-yl)oxy][1,3]thiazolo[4,5-b]pyrazin-6-yl}imidazo[1,2-a]pyridine-8-carbonitrile
182[1]	6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-2-(piperazin-1-yl)[1,3]thiazolo[4,5-b]pyrazine
183	5-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[5,4-d]pyrimidin-2-amine
184	5-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[5,4-d]pyrimidin-2-amine
185[1]	4-fluoro-*N*-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-(piperidin-4-yl)-1,3-benzothiazol-2-amine
186[1]	6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4-fluoro-*N*-methyl-*N*-(piperidin-4-yl)-1,3-benzothiazol-2-amine
187[1]	8-(benzyloxy)-6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazine
188[1]	6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazin-8-amine

Cpd	Name
189[1]	6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazin-8-ol
190[1]	2-(2,6-dimethylpiperidin-4-yl)-6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazole
191[1]	4-fluoro-6-(4-fluoro-3-methoxyphenyl)-2-(piperidin-4-yl)-1,3-benzothiazole
192[1]	*N*-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4-fluoro-*N*-methyl-1,3-benzothiazol-2-amine
193[1]	2-methyl-5-{2-[methyl(piperidin-4-yl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-2*H*-indazole-7-carbonitrile
194[1]	6-[2-(1-azabicyclo[2.2.2]oct-4-yl)-4-fluoro-1,3-benzothiazol-6-yl]-2,8-dimethylimidazo[1,2-b]pyridazine
195[1]	6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methyl-8-phenoxyimidazo[1,2-b]pyridazine
196[1]	2-methyl-6-{2-[methyl(piperidin-4-yl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}imidazo[1,2-a]pyridine-8-carbonitrile
197	5-(7-methoxy-2-methyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[5,4-d]pyrimidin-2-amine
198[1]	2-methyl-6-{2-[methyl(piperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}imidazo[1,2-a]pyridine-8-carbonitrile
199[1]	6-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-ylamino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile
200	4-fluoro-6-(8-methoxy-2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine
201[1]	6-{4-fluoro-2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino]-1,3-benzothiazol-6-yl}-2-methylimidazo[1,2-b]pyridazin-8-amine
202[1]	4-fluoro-6-(8-methoxy-2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-methyl-*N*-(piperidin-4-yl)-1,3-benzothiazol-2-amine
203[1]	6-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile
204[1]	*N*-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine
205[1]	*N*-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine
206[1]	5-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methyl-2*H*-indazole-7-carbonitrile
207[1]	6-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile
208[1]	5-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-2-methyl-2*H*-indazole-7-carbonitrile

Cpd	Name
209[1]	*N*-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-4-fluoro-*N*-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-1,3-benzothiazol-2-amine
210[1]	6-[4-fluoro-2-(4-methylpiperidin-4-yl)-1,3-benzothiazol-6-yl]-2,8-dimethylimidazo[1,2-b]pyridazine
211[1]	*N*-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine
212[1]	*N*-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine
213[1]	5-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-ylamino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methyl-2*H*-indazole-7-carbonitrile
214[1]	2-methyl-5-{2-[methyl(piperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2*H*-indazole-7-carbonitrile
215[1]	6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine
216[1]	6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine
217[1]	*N*-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[5,4-d]pyrimidin-2-amine
218[1]	*N*-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-5-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[5,4-d]pyrimidin-2-amine
219[1]	6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazine-8-carboxylic acid
220[1]	methyl {6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazin-8-yl}acetate
221[1]	{6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazin-8-yl}acetic acid
222	2-methyl-6-{2-[(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}imidazo[1,2-a]pyridine-8-carbonitrile
223[1]	6-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yloxy][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile
224[1]	6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazine-8-carboxamide
225	6-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-4-fluoro-*N*-methyl-*N*-(piperidin-4-yl)-1,3-benzothiazol-2-amine
226[1]	6-{4-fluoro-2-[methyl(piperidin-4-yl)amino]-1,3-benzothiazol-6-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile
227[1]	*N*-[(8-anti)-3-azabicyclo[3.2.1]oct-8-yl]-5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[5,4-d]pyrimidin-2-amine

Cpd	Name
228[1]	6-{2-[(8-anti)-3-azabicyclo[3.2.1]oct-8-yl(methyl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile
229[1]	2-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-6,8-dimethylimidazo[1,2-a]pyrazine
230[1]	6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazine-8-carbonitrile
231[1]	6-{4-fluoro-2-[methyl(piperidin-4-yl)amino]-1,3-benzothiazol-6-yl}-2-methylimidazo[1,2-b]pyridazine-8-carbonitrile
232[1]	6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine
233	2-methyl-5-{2-[(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2*H*-indazole-7-carbonitrile
234	6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine
235[1]	6-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino]-4-fluoro-1,3-benzothiazol-6-yl}-2-methylimidazo[1,2-b]pyridazine-8-carbonitrile
236[1]	6-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino]-4-fluoro-1,3-benzothiazol-6-yl}-2-methylimidazo[1,2-b]pyridazine-8-carboxamide
237[1]	*N*-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-4-fluoro-*N*-methyl-6-(2-methyl-2*H*-pyrazolo[4,3-b]pyridin-5-yl)-1,3-benzothiazol-2-amine
238	2-methyl-5-(2-{methyl[(3-exo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]amino}[1,3]thiazolo[4,5-c]pyridin-6-yl)-2*H*-indazole-7-carbonitrile
239	6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-[(3-exo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl][1,3]thiazolo[4,5-c]pyridin-2-amine
240	2-methyl-6-(2-{methyl[(3-exo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]amino}[1,3]thiazolo[4,5-c]pyridin-6-yl)imidazo[1,2-a]pyridine-8-carbonitrile
241	6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-[(3-exo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl][1,3]thiazolo[4,5-c]pyridin-2-amine
242	6-{2-[ethyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile
243	*N*-ethyl-5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[5,4-d]pyrimidin-2-amine
244	2-methyl-5-(2-{[(3-exo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]amino}[1,3]thiazolo[4,5-c]pyridin-6-yl)-2*H*-indazole-7-carbonitrile
245	2-methyl-6-(2-{[(3-exo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]amino}[1,3]thiazolo[4,5-c]pyridin-6-yl)imidazo[1,2-a]pyridine-8-carbonitrile
246	6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-[(3-exo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl][1,3]thiazolo[4,5-c]pyridin-2-amine

Cpd	Name
247	6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-[(3-exo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl][1,3]thiazolo[4,5-c]pyridin-2-amine
248[1]	*N*-(azetidin-3-yl)-6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4-fluoro-*N*-methyl-1,3-benzothiazol-2-amine
249[1]	5-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylpyrazolo[1,5-a]pyrimidine
250[1]	4-fluoro-*N*-methyl-6-(2-methylpyrazolo[1,5-a]pyrimidin-5-yl)-*N*-(piperidin-4-yl)-1,3-benzothiazol-2-amine
251[1]	6-{2-[9-azabicyclo[3.3.1]non-3-yl(methyl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile
252[1]	5-{2-[9-azabicyclo[3.3.1]non-3-yl(methyl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methyl-2*H*-indazole-7-carbonitrile
253[1]	*N*-(9-azabicyclo[3.3.1]non-3-yl)-6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine
254	5-{2-[(1,5-dimethyl-8-azabicyclo[3.2.1]oct-3-yl)(methyl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-2-methyl-2*H*-indazole-7-carbonitrile
255	6-(2-{[(1*R*)-1,5-dimethyl-8-azabicyclo[3.2.1]oct-3-yl](methyl)amino}[1,3]thiazolo[5,4-d]pyrimidin-5-yl)-2-methylimidazo[1,2-a]pyridine-8-carbonitrile
256[1]	6-{2-[(1*R*,5*S*)-9-azabicyclo[3.3.1]non-3-yl(methyl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile
257[1]	*N*-[(1*R*,5*S*)-9-azabicyclo[3.3.1]non-3-yl]-5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[5,4-d]pyrimidin-2-amine
258[1]	4-fluoro-*N*-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-[(2*S*,4*S*)-2-methylpiperidin-4-yl]-1,3-benzothiazol-2-amine
259[1]	4-fluoro-*N*-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-[(2*S*,4*R*)-2-methylpiperidin-4-yl]-1,3-benzothiazol-2-amine
260[1]	*N*-(9-azabicyclo[3.3.1]non-3-yl)-*N*-methyl-6-(2-methylimidazo[1,2-a]pyridin-6-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine
261[1]	*N*-(9-azabicyclo[3.3.1]non-3-yl)-6-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine
262[1]	*N*-(9-azabicyclo[3.3.1]non-3-yl)-*N*-methyl-6-(2-methyl-2*H*-indazol-5-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine
263[1]	*N*-(9-azabicyclo[3.3.1]non-3-yl)-6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine
264[1]	*N*-(9-azabicyclo[3.3.1]non-3-yl)-6-(7-methoxy-2-methyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine
265	5-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[5,4-d]pyrimidin-2-amine

Cpd	Name
266[1]	2-methyl-6-{2-[(1,2,2,6,6-pentamethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}imidazo[1,2-a]pyridine-8-carbonitrile
267[1]	6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-(1,2,2,6,6-pentamethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine
268[1]	2-methyl-5-{2-[(1,2,2,6,6-pentamethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2*H*-indazole-7-carbonitrile
269[1]	6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-(1,2,2,6,6-pentamethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine
270	2-methyl-6-{2-[methyl(9-methyl-9-azabicyclo[3.3.1]non-3-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}imidazo[1,2-a]pyridine-8-carbonitrile
271	6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(9-methyl-9-azabicyclo[3.3.1]non-3-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine
272	2-methyl-5-{2-[methyl(9-methyl-9-azabicyclo[3.3.1]non-3-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2*H*-indazole-7-carbonitrile
273	6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(9-methyl-9-azabicyclo[3.3.1]non-3-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine
274[1]	2-{2-[methyl(piperidin-4-yl)amino][1,3]thiazolo[4,5-b]pyrazin-6-yl}-5-(1*H*-pyrazol--yl)phenol
275	2-methyl-6-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-1,3-benzoxazole-4-carbonitrile
276[1]	6-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino][1,3]thiazolo[5,4-b]pyridin-5-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile
277[1]	*N*-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[5,4-b]pyridin-2-amine
278[1]	5-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino][1,3]thiazolo[5,4-b]pyridin-5-yl}-2-methyl-2*H*-indazole-7-carbonitrile
279[1]	6-{2-[(3-exo)-9-azabicyclo[3.3.1]non-3-yl(methyl)amino][1,3]thiazolo[5,4-b]pyridin-5-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile
280[1]	*N*-[(3-exo)-9-azabicyclo[3.3.1]non-3-yl]-5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[5,4-b]pyridin-2-amine
281[1]	5-{2-[(3-exo)-9-azabicyclo[3.3.1]non-3-yl(methyl)amino][1,3]thiazolo[5,4-b]pyridin-5-yl}-2-methyl-2*H*-indazole-7-carbonitrile
282[1]	2-{6-[methyl(piperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol
283[1]	2-{6-[methyl(1-methylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol
284	*N*-[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl]-5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[5,4-d]pyrimidin-2-amine

Cpd	Name
285	6-(2-{[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridin-6-yl)-2-methylimidazo[1,2-a]pyridine-8-carbonitrile
286[1]	*N*-[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl]-6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine
287	5-(2-{[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridin-6-yl)-2-methyl-2*H*-indazole-7-carbonitrile
288[1]	6-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-b]pyrazin-2-amine
289	*N*-[(1*R*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl]-5-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[5,4-d]pyrimidin-2-amine
290	6-(2-{[(1*R*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl](methyl)amino}[1,3]thiazolo[5,4-d]pyrimidin-5-yl)-2-methyl-1,3-benzoxazole-4-carbonitrile
291	6-(2-{[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl](methyl)amino}[1,3]thiazolo[5,4-b]pyridin-5-yl)-2-methylimidazo[1,2-a]pyridine-8-carbonitrile
292	*N*-[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl]-5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[5,4-b]pyridin-2-amine
293	5-(2-{[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl](methyl)amino}[1,3]thiazolo[5,4-b]pyridin-5-yl)-2-methyl-2*H*-indazole-7-carbonitrile
294	*N*-[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl]-5-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[5,4-b]pyridin-2-amine
295[1]	*N*-(9-azabicyclo[3.3.1]nonan-3-yl)-5-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[5,4-b]pyridin-2-amine
296[1]	6-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine
297[1]	6-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine
298	*N*-[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl]-6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine
299	*N*-[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl]-6-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine
300	*N*-[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl]-*N*-methyl-6-(2-methylimidazo[1,2-a]pyridin-6-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine
301[1]	6-(2-{[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridin-6-yl)-2-methyl-1,3-benzoxazole-4-carbonitrile

Cpd	Name
302[1]	*N*-methyl-6-(2-methylimidazo[2,1-b][1,3]thiazol-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine
303	6-(2-{[(1*R*,3*r*,5*S*)-1,5-diethyl-8-azabicyclo[3.2.1]octan-3-yl](methyl)amino}[1,3]thiazolo[5,4-d]pyrimidin-5-yl)-2-methylimidazo[1,2-a]pyridine-8-carbonitrile
304	*N*-[(1*R*,3*r*,5*S*)-1,5-diethyl-8-azabicyclo[3.2.1]octan-3-yl]-5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[5,4-d]pyrimidin-2-amine
305	*N*-methyl-6-(3-methylimidazo[2,1-b][1,3]thiazol-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine
306[1]	6-{4-fluoro-2-[(piperidin-4-yl)oxy]-1,3-benzothiazol-6-yl}-2,8-dimethylimidazo[1,2-b]pyridazine
307[1]	4-fluoro-6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-2-[(piperidin-4-yl)oxy]-1,3-benzothiazole
308[1]	*N*-methyl-6-(2-methylimidazo[2,1-b][1,3,4]thiadiazol-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine
309	2-methyl-6-{2-[(2,2,6,6-tetramethylpiperidin-4-yl)oxy][1,3]thiazolo[4,5-c]pyridin-6-yl}imidazo[1,2-a]pyridine-8-carbonitrile
310	6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-[(2,2,6,6-tetramethylpiperidin-4-yl)oxy][1,3]thiazolo[4,5-c]pyridine
311	2-methyl-5-{2-[(2,2,6,6-tetramethylpiperidin-4-yl)oxy][1,3]thiazolo[4,5-c]pyridin-6-yl}-2*H*-indazole-7-carbonitrile
312	6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-2-[(2,2,6,6-tetramethylpiperidin-4-yl)oxy][1,3]thiazolo[4,5-c]pyridine
313[1]	2-methyl-6-{2-[(piperidin-4-yl)oxy][1,3]thiazolo[4,5-c]pyridin-6-yl}imidazo[1,2-a]pyridine-8-carbonitrile
314[1]	6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-[(piperidin-4-yl)oxy][1,3]thiazolo[4,5-c]pyridine
315[1]	2-methyl-5-{2-[(piperidin-4-yl)oxy][1,3]thiazolo[4,5-c]pyridin-6-yl}-2*H*-indazole-7-carbonitrile
316[1]	6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-2-[(piperidin-4-yl)oxy][1,3]thiazolo[4,5-c]pyridine
317[1]	6-{4-fluoro-2-[(piperidin-4-yl)oxy]-1,3-benzothiazol-6-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile
318[1]	5-{4-fluoro-2-[(piperidin-4-yl)oxy]-1,3-benzothiazol-6-yl}-2-methyl-2*H*-indazole-7-carbonitrile
319[1]	6-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-4-fluoro-2-[(piperidin-4-yl)oxy]-1,3-benzothiazole
320	6-{4-fluoro-2-[(1-methylpiperidin-4-yl)oxy]-1,3-benzothiazol-6-yl}-2,8-dimethylimidazo[1,2-b]pyridazine

Cpd	Name
321	6-{2-[(1-ethylpiperidin-4-yl)oxy]-4-fluoro-1,3-benzothiazol-6-yl}-2,8-dimethylimidazo[1,2-b]pyridazine
322	*N*-[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl]-6-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine
323	*N*-[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl]-5-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-*N*-methyl[1,3]thiazolo[5,4-d]pyrimidin-2-amine
324[1]	6-(2-{[(3*R*,4*R*)-3-fluoro-2,2,6,6-tetramethylpiperidin-4-yl](methyl)amino}[1,3]thiazolo[5,4-d]pyrimidin-5-yl)-2-methylimidazo[1,2-a]pyridine-8-carbonitrile
325[1]	6-(2-{[(3*R*,4*R*)-3-fluoro-2,2,6,6-tetramethylpiperidin-4-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridin-6-yl)-2-methylimidazo[1,2-a]pyridine-8-carbonitrile
326[1]	*N*-[(1*R*,2*S*,3*S*,5*S*)-2-fluoro-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl]-6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine
327[1]	5-(1*H*-imidazol-1-yl)-2-{6-[methyl(piperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}phenol
328[1]	3-[2,5-difluoro-4-(1*H*-pyrazol-4-yl)phenyl]-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridazin-6-amine
329	5-(3-fluoro-1*H*-pyrazol-4-yl)-2-{6-[methyl(piperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}phenol
330	5-(1*H*-imidazol-1-yl)-2-{6-[methyl(1-methylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}phenol
331[1]	3-[2,5-difluoro-4-(3-fluoro-1*H*-pyrazol-4-yl)phenyl]-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridazin-6-amine
332	5-(3-fluoro-1*H*-pyrazol-4-yl)-2-{6-[methyl(1-methylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}phenol
333	2-{6-[(3*R*,5*S*)-3,5-dimethylpiperazin-1-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol
334[1]	2-[6-(piperazin-1-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(1*H*-pyrazol-4-yl)phenol
335[1]	5-(1*H*-pyrazol-4-yl)-2-[6-(1,2,3,6-tetrahydropyridin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-yl]phenol
336[1]	2-(6-{[(3*R*,4*S*)-4-fluoro-1-methylpyrrolidin-3-yl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol
337[1]	5-(1*H*-pyrazol-4-yl)-2-[6-(2,2,6,6-tetramethyl-1,2,3,6-tetrahydropyridin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-yl]phenol
338[1]	2-[6-(2,6-diazaspiro[3.5]nonan-2-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(1*H*-pyrazol-4-yl)phenol
339[1]	2-[6-(7-methyl-1,7-diazaspiro[3.5]nonan-1-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(1*H*-pyrazol-4-yl)phenol

Cpd	Name
340[1]	2-[6-(7-methyl-2,7-diazaspiro[4.4]nonan-2-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(1*H*-pyrazol-4-yl)phenol
341[1]	2-[6-(2,7-diazaspiro[3.5]nonan-2-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(3-fluoro-1*H*-pyrazol-4-yl)phenol
342[1]	2-(6-{[(3*S*,4*S*)-4-fluoro-1-methylpyrrolidin-3-yl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol
343	2-{6-[methyl(1-methylazetidin-3-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol
344[1]	2-{6-[(3a*S*,7a*R*)-octahydro-1*H*-pyrrolo[3,2-c]pyridin-1-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol
345[1]	2-(6-{methyl[(1*s*,4*s*)-4-(methylamino)cyclohexyl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol
346[1]	2-(6-{[(3*R*,4*S*)-4-fluoropyrrolidin-3-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol
347[1]	2-{6-[(3a*S*,7a*R*)-5-methyloctahydro-1*H*-pyrrolo[3,2-c]pyridin-1-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol
348[1]	2-(6-{methyl[(3*R*)-piperidin-3-yl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol
349[1]	2-(6-{methyl[(3*S*)-piperidin-3-yl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol
350[1]	2-(6-{methyl[3-(methylamino)cyclobutyl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol
351[1]	2-(6-{[(1*r*,4*r*)-4-(dimethylamino)cyclohexyl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol
352[1]	2-(6-{methyl[(3*S*)-1-methylpiperidin-3-yl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol
353[1]	2-{6-[(azetidin-3-yl)(methyl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol
354[1]	2-[6-(1,7-diazaspiro[3.5]nonan-1-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(1*H*-pyrazol-4-yl)phenol
355[1]	2-{6-[(3,3-dimethylpiperidin-4-yl)(methyl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol
356[1]	2-{6-[(2-azaspiro[3.3]heptan-6-yl)(methyl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol
357	2-{6-[(piperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol
358	2-(6-{[(3*R*,4*S*)-3-fluoropiperidin-4-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol

Cpd	Name
359[1]	5-{2-[(2*R*,4*r*,6*S*)-2,6-dimethylpiperidin-4-yl]-4-fluoro-1,3-benzothiazol-6-yl}-2,7-dimethyl[1,3]oxazolo[5,4-b]pyridine
360[1]	2-{6-[methyl(1,3,3-trimethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol
361[1]	2-(6-{methyl[(1*s*,3*s*)-3-(methylamino)cyclobutyl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol
362[1]	2-{6-[(3a*R*,7a*S*)-octahydro-1*H*-pyrrolo[2,3-c]pyridin-1-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol
363[1]	2-[6-(1,6-diazaspiro[3.5]nonan-1-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(1*H*-pyrazol-4-yl)phenol
364[1]	2-(6-{[(1*s*,3*s*)-3-(dimethylamino)cyclobutyl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol
365[1]	2-(6-{[(3*R*,4*R*)-3-fluoropiperidin-4-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol
366	2-{6-[(1-methylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol
367[1]	5-(1*H*-pyrazol-4-yl)-2-{6-[(pyrrolidin-3-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}phenol
368[1]	2-[6-(2,6-diazaspiro[3.3]heptan-2-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(3-fluoro-1*H*-pyrazol-4-yl)phenol
369[1]	2-{6-[(3a*R*,7a*S*)-6-methyloctahydro-1*H*-pyrrolo[2,3-c]pyridin-1-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol
370[1]	2-[6-(6-methyl-1,6-diazaspiro[3.5]nonan-1-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(1*H*-pyrazol-4-yl)phenol
371[1]	2-(6-{[(2*S*,4*S*)-2-(hydroxymethyl)piperidin-4-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol
372[1]	2-(6-{[(2*S*,4*S*)-2-(hydroxymethyl)-1-methylpiperidin-4-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol
373	2-{6-[(1-methylpyrrolidin-3-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol
374	2-{6-[methyl(pyrrolidin-3-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol
375	2-{6-[methyl(1-methylpyrrolidin-3-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol
376[1]	2-(6-{methyl[(1*r*,3*r*)-3-(methylamino)cyclobutyl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol
377	5-{2-[(1,2-dimethylpiperidin-4-yl)(methyl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methyl-2*H*-indazole-7-carbonitrile

Cpd	Name
378	*N*-(1,2-dimethylpiperidin-4-yl)-6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine
379	6-{2-[(1,2-dimethylpiperidin-4-yl)(methyl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile
380[1]	*N*-(1,2-dimethylpiperidin-4-yl)-6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine
381	2-(6-{[(3*S*,4*S*)-4-fluoropyrrolidin-3-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol
382	2-(6-{[(3*S*,4*S*)-4-fluoro-1-methylpyrrolidin-3-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol
383	2-{6-[(1-cyclopropylpiperidin-4-yl)(methyl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol
384	2-(6-{[1-(2-fluoroethyl)piperidin-4-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol
385	5-(3-fluoro-1*H*-pyrazol-4-yl)-2-[6-(6-methyl-2,6-diazaspiro[3.3]heptan-2-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]phenol
386[1]	2-{6-[(1*S*,6*R*)-3,8-diazabicyclo[4.2.0]octan-8-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol
387	5-(3-fluoro-1*H*-pyrazol-4-yl)-2-{6-[methyl(pyrrolidin-3-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}phenol
388[1]	2-{6-[(1*S*,6*R*)-3-methyl-3,8-diazabicyclo[4.2.0]octan-8-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol
389[1]	2-{6-[(1*R*,6*S*)-3,8-diazabicyclo[4.2.0]octan-8-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol
390[1]	2-{6-[(1*R*,6*S*)-3-methyl-3,8-diazabicyclo[4.2.0]octan-8-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol
391	5-(3-fluoro-1*H*-pyrazol-4-yl)-2-{6-[methyl(1-methylpyrrolidin-3-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}phenol
392	5-(3-fluoro-1*H*-pyrazol-4-yl)-2-[6-(7-methyl-2,7-diazaspiro[3.5]nonan-2-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]phenol
393	2-{6-[methyl(1-propylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol
394[1]	2-(6-{methyl[(2*S*,4*S*)-2-methylpiperidin-4-yl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol
395[1]	2-(6-{[(2*S*,4*S*)-1,2-dimethylpiperidin-4-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol
396[1]	2-(6-{methyl[(2*R*,4*S*)-2-methylpiperidin-4-yl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol

Cpd	Name
397[1]	2-(6-{[(2*R*,4*S*)-1,2-dimethylpiperidin-4-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol
398	2-{6-[(azepan-4-yl)(methyl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(3-fluoro-1*H*-pyrazol-4-yl)phenol, and
399	2-(6-{[1-(2-hydroxyethyl)piperidin-4-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol;

wherein a form of the compound is selected from the group consisting of a salt, hydrate, solvate, racemate, enantiomer, diastereomer, stereoisomer, and tautomer form thereof.

Another aspect of the compound of Formula (I) or Formula (II) or a form thereof is a compound salt selected from the group consisting of:

Cpd	Name
4	2-(2-methyl-2*H*-indazol-5-yl)-6-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole hydrochloride
5	2-(2-methyl-2*H*-indazol-5-yl)-6-(piperidin-4-yl)-1,3-benzothiazole hydrochloride
6	2-(2-methyl-2*H*-indazol-5-yl)-6-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole hydrochloride
8	*N*-methyl-6-(2-methyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride
10	2-(2-methyl-2*H*-indazol-5-yl)-6-(1-methylpiperidin-4-yl)-1,3-benzothiazole hydrochloride
11	*N*-methyl-2-(2-methyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)-1,3-benzothiazol-6-amine hydrochloride
12	*N*-methyl-6-(2-methyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-b]pyridin-2-amine hydrochloride
13	6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-b]pyridin-2-amine hydrochloride
14	6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-b]pyridin-2-amine hydrochloride
15	6-(2-methyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-b]pyridin-2-amine hydrochloride
18	6-(2,7-dimethyl-2*H*-indazol-5-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole hydrochloride
19	2-(2-methyl-2*H*-indazol-5-yl)-6-(1,2,3,6-tetrahydropyridin-4-yl)[1,3]thiazolo[4,5-b]pyridine hydrochloride
22	6-(2,7-dimethyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)-1,3-benzothiazole hydrochloride
25	*N*-methyl-5-(2-methyl-2*H*-indazol-5-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[5,4-b]pyridin-2-amine hydrochloride

Cpd	Name
26	*N*-methyl-5-(2-methyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)[1,3]thiazolo[5,4-b]pyridin-2-amine hydrochloride
27	*N*-methyl-6-(2-methyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride
28	*N*,*N*-dimethyl-1-[6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazol-2-yl]piperidin-4-amine hydrochloride
29	1-[6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazol-2-yl]piperidin-4-amine hydrochloride
30	6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride
34	6-(1*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride
35	6-(2-methyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride
36	5-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[5,4-b]pyridin-2-amine hydrochloride
38	*N*-methyl-6-(2-methyl-2*H*-indazol-5-yl)-*N*-(pyrrolidin-3-yl)-1,3-benzothiazol-2-amine hydrochloride
40	*N*-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride
41	2-(4-fluoropiperidin-4-yl)-6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazole hydrochloride
42	2-(azepan-4-yl)-6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazole hydrochloride
43	2-(2-methyl-2*H*-indazol-5-yl)-6-(piperidin-4-yl)[1,3]thiazolo[4,5-b]pyridine hydrochloride
44	6-[4-fluoro-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazine hydrochloride
45	6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazine hydrochloride
46	6-[4-fluoro-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazol-6-yl]-2,8-dimethylimidazo[1,2-b]pyridazine hydrochloride
47	6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2,8-dimethylimidazo[1,2-b]pyridazine hydrochloride
49	2-(2,7-dimethyl-2*H*-indazol-5-yl)-6-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole hydrochloride
50	2-(2,7-dimethyl-2*H*-indazol-5-yl)-6-(piperidin-4-yl)-1,3-benzothiazole hydrochloride
51	*N*-methyl-6-[2-methyl-7-(trifluoromethyl)-2*H*-indazol-5-yl]-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride
53	6-[4-fluoro-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazol-6-yl]-2,8-dimethylimidazo[1,2-a]pyrazine hydrochloride

Cpd	Name
55	6-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride
57	6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride
58	6-(2-methyl-2*H*-indazol-5-yl)-2-(2-methylpiperidin-4-yl)-1,3-benzothiazole hydrochloride
59	6-(2,7-dimethyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridine hydrochloride
60	6-[2-methyl-7-(trifluoromethyl)-2*H*-indazol-5-yl]-2-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridine hydrochloride
61	6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-(piperidin-4-yl)[1,3]thiazolo[4,5-b]pyridine hydrochloride
62	2-methyl-5-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino]-1,3-benzothiazol-6-yl}-2*H*-indazole-7-carbonitrile hydrochloride
63	*N*-methyl-6-(2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride
65	6-(2-methyl-2*H*-indazol-5-yl)-2-(2-methyl-1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole hydrochloride
66	6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2-methylpiperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride
67	6-(2-methyl-2*H*-indazol-5-yl)-2-(6-methyl-1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole hydrochloride
68	6-(2,7-dimethyl-2*H*-indazol-5-yl)-2-[(2,2,6,6-tetramethylpiperidin-4-yl)oxy]-1,3-benzothiazole hydrochloride
70	6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methyl-1,3-benzoxazole hydrochloride
71	6-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-4-fluoro-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole hydrochloride
72	4-fluoro-6-(2-methyl-2*H*-indazol-5-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole hydrochloride
73	4-fluoro-6-(2-methyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)-1,3-benzothiazole hydrochloride
74	2-methyl-5-[2-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-6-yl]-2*H*-indazole-7-carbonitrile hydrochloride
75	6-(7-ethyl-2-methyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridine hydrochloride
76	6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridine hydrochloride

Cpd	Name
77	6-(2-methylimidazo[1,2-a]pyridin-6-yl)-2-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridine hydrochloride
78	5-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-1*H*-pyrazolo[4,3-b]pyridine hydrochloride
79	5-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methyl-2*H*-pyrazolo[4,3-b]pyridine hydrochloride
80	6-(7-cyclopropyl-2-methyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride
81	*N*-methyl-6-(2-methyl-2*H*-indazol-5-yl)-*N*-(2-methylpiperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride
84	2-methyl-5-[2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2*H*-indazole-7-carbonitrile hydrochloride
93	6-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride
94	6-(2,4-dimethyl-1*H*-benzimidazol-6-yl)-2-(piperidin-4-yl)-1,3-benzothiazole hydrochloride
95	6-(2-methyl-1*H*-benzimidazol-6-yl)-2-(piperidin-4-yl)-1,3-benzothiazole dihydrochloride
97	2-methyl-6-[2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]imidazo[1,2-b]pyridazine hydrochloride
98	6-(2,7-dimethyl-2*H*-indazol-5-yl)-4-methoxy-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole hydrochloride
99	6-(2,7-dimethyl-2*H*-indazol-5-yl)-4-methoxy-2-(piperidin-4-yl)-1,3-benzothiazole hydrochloride
100	6-(2,7-dimethyl-2*H*-indazol-5-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazol-4-ol hydrobromide
102	5-[4-fluoro-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazol-6-yl]-2-methyl-2*H*-indazole-7-carbonitrile hydrochloride
103	1-{5-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methyl-2*H*-indazol-7-yl}methanamine dihydrochloride
104	5-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methyl-2*H*-indazole-7-carbonitrile hydrochloride
109	2-methyl-5-[2-(piperidin-4-yl)[1,3]thiazolo[5,4-d]pyrimidin-5-yl]-2*H*-indazole-7-carbonitrile hydrochloride
110	5-(2,7-dimethyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)[1,3]thiazolo[5,4-d]pyrimidine hydrochloride
111	6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride

Cpd	Name
113	6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-(piperidin-4-yl)-1,3-benzothiazole hydrochloride
114	6-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-2-(piperidin-4-yl)-1,3-benzothiazole hydrochloride
115	2-(2,2-dimethylpiperidin-4-yl)-6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazole hydrochloride
119	2-{6-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol hydrochloride
130	2-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-b]pyrazin-6-yl}-5-(1*H*-pyrazol-4-yl)phenol hydrochloride
132	6-[2-(3,5-dimethylpiperazin-1-yl)-4-fluoro-1,3-benzothiazol-6-yl]-2,8-dimethylimidazo[1,2-b]pyridazine hydrochloride
133	6-{4-fluoro-2-[(2,2,6,6-tetramethylpiperidin-4-yl)oxy]-1,3-benzothiazol-6-yl}-2,8-dimethylimidazo[1,2-b]pyridazine hydrochloride
135	6-{2-[(2,6-dimethylpiperidin-4-yl)oxy]-4-fluoro-1,3-benzothiazol-6-yl}-2,8-dimethylimidazo[1,2-b]pyridazine hydrochloride
137	2-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-5-(1*H*-pyrazol-4-yl)phenol hydrochloride
138	2-methyl-6-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino]-1,3-benzothiazol-6-yl}imidazo[1,2-a]pyridine-8-carbonitrile hydrochloride
139	2,8-dimethyl-6-[2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]imidazo[1,2-b]pyridazine hydrochloride
142	2-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-5-(1*H*-pyrazol-4-yl)phenol hydrochloride
144	6-{4-fluoro-2-[(2*R*)-2-methylpiperidin-4-yl]-1,3-benzothiazol-6-yl}-2-methylimidazo[1,2-b]pyridazine hydrochloride
145	6-[4-fluoro-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazol-6-yl]-8-methoxy-2-methylimidazo[1,2-b]pyridazine hydrochloride
146	6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-(2,2-dimethylpiperidin-4-yl)-*N*-methyl-1,3-benzothiazol-2-amine hydrochloride
149	2-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[5,4-b]pyridin-5-yl}-5-(1*H*-pyrazol-4-yl)phenol hydrochloride
151	6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-8-methoxy-2-methylimidazo[1,2-b]pyridazine hydrochloride
152	4-fluoro-6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-(piperidin-4-yl)-1,3-benzothiazole hydrochloride
153	4-chloro-6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole hydrochloride

Cpd	Name
154	5-[4-chloro-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazol-6-yl]-2-methyl-2*H*-indazole-7-carbonitrile hydrochloride
155	*N*-(2,2-dimethylpiperidin-4-yl)-*N*-methyl-6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazol-2-amine hydrochloride
161	6-[2,3-difluoro-4-(1*H*-pyrazol-4-yl)phenyl]-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-b]pyrazin-2-amine hydrochloride
164	4-fluoro-*N*-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-[(2*S*)-2-methylpiperidin-4-yl]-1,3-benzothiazol-2-amine hydrochloride
165	6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4-fluoro-*N*-methyl-*N*-[(2*S*)-2-methylpiperidin-4-yl]-1,3-benzothiazol-2-amine hydrochloride
166	6-[4-fluoro-2-(octahydroindolizin-7-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazine hydrochloride
167	6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-*N*,2-dimethylimidazo[1,2-b]pyridazin-8-amine hydrochloride
168	6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-*N*,*N*,2-trimethylimidazo[1,2-b]pyridazin-8-amine hydrochloride
172	6-(7-cyano-2-methyl-2*H*-indazol-5-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole-4-carbonitrile hydrochloride
173	2-methyl-6-[2-(piperazin-1-yl)[1,3]thiazolo[4,5-b]pyrazin-6-yl]imidazo[1,2-a]pyridine-8-carbonitrile hydrochloride
174	6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-(piperazin-1-yl)[1,3]thiazolo[4,5-b]pyrazine hydrochloride
175	6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-(2,6-dimethylpiperidin-4-yl)-*N*-methyl-1,3-benzothiazol-2-amine hydrochloride
176	*N*-(2,6-dimethylpiperidin-4-yl)-*N*-methyl-6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazol-2-amine hydrochloride
182	6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-2-(piperazin-1-yl)[1,3]thiazolo[4,5-b]pyrazine hydrochloride
185	4-fluoro-*N*-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-(piperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride
186	6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4-fluoro-*N*-methyl-*N*-(piperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride
187	8-(benzyloxy)-6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazine hydrochloride
188	6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazin-8-amine hydrochloride
189	6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazin-8-ol hydrochloride

Cpd	Name
190	2-(2,6-dimethylpiperidin-4-yl)-6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazole hydrochloride
191	4-fluoro-6-(4-fluoro-3-methoxyphenyl)-2-(piperidin-4-yl)-1,3-benzothiazole hydrochloride
192	*N*-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4-fluoro-*N*-methyl-1,3-benzothiazol-2-amine hydrochloride
193	2-methyl-5-{2-[methyl(piperidin-4-yl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-2*H*-indazole-7-carbonitrile hydrochloride
194	6-[2-(1-azabicyclo[2.2.2]oct-4-yl)-4-fluoro-1,3-benzothiazol-6-yl]-2,8-dimethylimidazo[1,2-b]pyridazine hydrochloride
195	6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methyl-8-phenoxyimidazo[1,2-b]pyridazine hydrochloride
196	2-methyl-6-{2-[methyl(piperidin-4-yl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}imidazo[1,2-a]pyridine-8-carbonitrile hydrochloride
198	2-methyl-6-{2-[methyl(piperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}imidazo[1,2-a]pyridine-8-carbonitrile hydrochloride
199	6-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-ylamino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile hydrochloride
201	6-{4-fluoro-2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino]-1,3-benzothiazol-6-yl}-2-methylimidazo[1,2-b]pyridazin-8-amine hydrochloride
202	4-fluoro-6-(8-methoxy-2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-methyl-*N*-(piperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride
203	6-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile hydrochloride
204	*N*-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride
205	*N*-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride
206	5-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methyl-2*H*-indazole-7-carbonitrile hydrochloride
207	6-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile hydrochloride
208	5-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-2-methyl-2*H*-indazole-7-carbonitrile hydrochloride
209	*N*-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-4-fluoro-*N*-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-1,3-benzothiazol-2-amine hydrochloride
210	6-[4-fluoro-2-(4-methylpiperidin-4-yl)-1,3-benzothiazol-6-yl]-2,8-dimethylimidazo[1,2-b]pyridazine hydrochloride

Cpd	Name
211	*N*-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride
212	*N*-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride
213	5-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-ylamino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methyl-2*H*-indazole-7-carbonitrile hydrochloride
214	2-methyl-5-{2-[methyl(piperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2*H*-indazole-7-carbonitrile hydrochloride
215	6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride
216	6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride
217	*N*-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[5,4-d]pyrimidin-2-amine hydrochloride
218	*N*-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-5-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[5,4-d]pyrimidin-2-amine hydrochloride
219	6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazine-8-carboxylic acid hydrochloride
220	methyl {6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazin-8-yl}acetate hydrochloride
221	{6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazin-8-yl}acetic acid hydrochloride
223	6-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yloxy][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile hydrochloride
224	6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazine-8-carboxamide trifluoroacetate
226	6-{4-fluoro-2-[methyl(piperidin-4-yl)amino]-1,3-benzothiazol-6-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile hydrochloride
227	*N*-[(8-anti)-3-azabicyclo[3.2.1]oct-8-yl]-5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[5,4-d]pyrimidin-2-amine hydrochloride
228	6-{2-[(8-anti)-3-azabicyclo[3.2.1]oct-8-yl(methyl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile hydrochloride
229	2-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-6,8-dimethylimidazo[1,2-a]pyrazine hydrochloride
230	6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazine-8-carbonitrile hydrochloride
231	6-{4-fluoro-2-[methyl(piperidin-4-yl)amino]-1,3-benzothiazol-6-yl}-2-methylimidazo[1,2-b]pyridazine-8-carbonitrile hydrochloride

Cpd	Name
232	6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride
235	6-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino]-4-fluoro-1,3-benzothiazol-6-yl}-2-methylimidazo[1,2-b]pyridazine-8-carbonitrile hydrochloride
236	6-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino]-4-fluoro-1,3-benzothiazol-6-yl}-2-methylimidazo[1,2-b]pyridazine-8-carboxamide hydrochloride
237	*N*-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-4-fluoro-*N*-methyl-6-(2-methyl-2*H*-pyrazolo[4,3-b]pyridin-5-yl)-1,3-benzothiazol-2-amine hydrochloride
248	*N*-(azetidin-3-yl)-6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4-fluoro-*N*-methyl-1,3-benzothiazol-2-amine hydrochloride
249	5-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylpyrazolo[1,5-a]pyrimidine hydrochloride
250	4-fluoro-*N*-methyl-6-(2-methylpyrazolo[1,5-a]pyrimidin-5-yl)-*N*-(piperidin-4-yl)-,3-benzothiazol-2-amine hydrochloride
251	6-{2-[9-azabicyclo[3.3.1]non-3-yl(methyl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile hydrochloride
252	5-{2-[9-azabicyclo[3.3.1]non-3-yl(methyl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methyl-2*H*-indazole-7-carbonitrile hydrochloride
253	*N*-(9-azabicyclo[3.3.1]non-3-yl)-6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride
256	6-{2-[(1*R*,5*S*)-9-azabicyclo[3.3.1]non-3-yl(methyl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile hydrochloride
257	*N*-[(1*R*,5*S*)-9-azabicyclo[3.3.1]non-3-yl]-5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[5,4-d]pyrimidin-2-amine hydrochloride
258	4-fluoro-*N*-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-[(2*S*,4*S*)-2-methylpiperidin-4-yl]-1,3-benzothiazol-2-amine hydrochloride
259	4-fluoro-*N*-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-[(2*S*,4*R*)-2-methylpiperidin-4-yl]-1,3-benzothiazol-2-amine hydrochloride
260	*N*-(9-azabicyclo[3.3.1]non-3-yl)-*N*-methyl-6-(2-methylimidazo[1,2-a]pyridin-6-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride
261	*N*-(9-azabicyclo[3.3.1]non-3-yl)-6-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride
262	*N*-(9-azabicyclo[3.3.1]non-3-yl)-*N*-methyl-6-(2-methyl-2*H*-indazol-5-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride
263	*N*-(9-azabicyclo[3.3.1]non-3-yl)-6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride
264	*N*-(9-azabicyclo[3.3.1]non-3-yl)-6-(7-methoxy-2-methyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride

Cpd	Name
266	2-methyl-6-{2-[(1,2,2,6,6-pentamethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}imidazo[1,2-a]pyridine-8-carbonitrile hydrochloride
267	6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-(1,2,2,6,6-pentamethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride
268	2-methyl-5-{2-[(1,2,2,6,6-pentamethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2*H*-indazole-7-carbonitrile hydrochloride
269	6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-(1,2,2,6,6-pentamethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride
274	2-{2-[methyl(piperidin-4-yl)amino][1,3]thiazolo[4,5-b]pyrazin-6-yl}-5-(1*H*-pyrazol-4-yl)phenol hydrochloride
276	6-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino][1,3]thiazolo[5,4-b]pyridin-5-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile hydrochloride
277	*N*-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[5,4-b]pyridin-2-amine hydrochloride
278	5-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino][1,3]thiazolo[5,4-b]pyridin-5-yl}-2-methyl-2*H*-indazole-7-carbonitrile hydrochloride
279	6-{2-[(3-exo)-9-azabicyclo[3.3.1]non-3-yl(methyl)amino][1,3]thiazolo[5,4-b]pyridin-5-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile hydrochloride
280	*N*-[(3-exo)-9-azabicyclo[3.3.1]non-3-yl]-5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[5,4-b]pyridin-2-amine hydrochloride
281	5-{2-[(3-exo)-9-azabicyclo[3.3.1]non-3-yl(methyl)amino][1,3]thiazolo[5,4-b]pyridin-5-yl}-2-methyl-2*H*-indazole-7-carbonitrile hydrochloride
282	2-{6-[methyl(piperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol hydrochloride
283	2-{6-[methyl(1-methylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol hydrochloride
286	*N*-[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl]-6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride
288	6-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-b]pyrazin-2-amine hydrochloride
295	*N*-(9-azabicyclo[3.3.1]nonan-3-yl)-5-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[5,4-b]pyridin-2-amine hydrochloride
296	6-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride
297	6-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride

Cpd	Name
301	6-(2-{[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridin-6-yl)-2-methyl-1,3-benzoxazole-4-carbonitrile trifluoroacetate
302	*N*-methyl-6-(2-methylimidazo[2,1-b][1,3]thiazol-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride
306	6-{4-fluoro-2-[(piperidin-4-yl)oxy]-1,3-benzothiazol-6-yl}-2,8-dimethylimidazo[1,2-b]pyridazine hydrochloride
307	4-fluoro-6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-2-[(piperidin-4-yl)oxy]-1,3-benzothiazole hydrochloride
308	*N*-methyl-6-(2-methylimidazo[2,1-b][1,3,4]thiadiazol-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride
313	2-methyl-6-{2-[(piperidin-4-yl)oxy][1,3]thiazolo[4,5-c]pyridin-6-yl}imidazo[1,2-a]pyridine-8-carbonitrile hydrochloride
314	6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-[(piperidin-4-yl)oxy][1,3]thiazolo[4,5-c]pyridine hydrochloride
315	2-methyl-5-{2-[(piperidin-4-yl)oxy][1,3]thiazolo[4,5-c]pyridin-6-yl}-2*H*-indazole-7-carbonitrile hydrochloride
316	6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-2-[(piperidin-4-yl)oxy][1,3]thiazolo[4,5-c]pyridine hydrochloride
317	6-{4-fluoro-2-[(piperidin-4-yl)oxy]-1,3-benzothiazol-6-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile hydrochloride
318	5-{4-fluoro-2-[(piperidin-4-yl)oxy]-1,3-benzothiazol-6-yl}-2-methyl-2*H*-indazole-7-carbonitrile hydrochloride
319	6-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-4-fluoro-2-[(piperidin-4-yl)oxy]-1,3-benzothiazole hydrochloride
324	6-(2-{[(3*R*,4*R*)-3-fluoro-2,2,6,6-tetramethylpiperidin-4-yl](methyl)amino}[1,3]thiazolo[5,4-d]pyrimidin-5-yl)-2-methylimidazo[1,2-a]pyridine-8-carbonitrile dihydrochloride
325	6-(2-{[(3*R*,4*R*)-3-fluoro-2,2,6,6-tetramethylpiperidin-4-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridin-6-yl)-2-methylimidazo[1,2-a]pyridine-8-carbonitrile dihydrochloride
326	*N*-[(1*R*,2*S*,3*S*,5*S*)-2-fluoro-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl]-6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine dihydrochloride
327	5-(1*H*-imidazol-1-yl)-2-{6-[methyl(piperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}phenol formate
328	3-[2,5-difluoro-4-(1*H*-pyrazol-4-yl)phenyl]-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridazin-6-amine formate
331	3-[2,5-difluoro-4-(3-fluoro-1*H*-pyrazol-4-yl)phenyl]-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridazin-6-amine formate

Cpd	Name
334	2-[6-(piperazin-1-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(1*H*-pyrazol-4-yl)phenol formate
335	5-(1*H*-pyrazol-4-yl)-2-[6-(1,2,3,6-tetrahydropyridin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-yl]phenol hydrochloride
336	2-(6-{[(3*R*,4*S*)-4-fluoro-1-methylpyrrolidin-3-yl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol formate
337	5-(1*H*-pyrazol-4-yl)-2-[6-(2,2,6,6-tetramethyl-1,2,3,6-tetrahydropyridin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-yl]phenol hydrochloride
338	2-[6-(2,6-diazaspiro[3.5]nonan-2-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride
339	2-[6-(7-methyl-1,7-diazaspiro[3.5]nonan-1-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride
340	2-[6-(7-methyl-2,7-diazaspiro[4.4]nonan-2-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride
341	2-[6-(2,7-diazaspiro[3.5]nonan-2-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(3-fluoro-1*H*-pyrazol-4-yl)phenol formate
342	2-(6-{[(3*S*,4*S*)-4-fluoro-1-methylpyrrolidin-3-yl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol formate
344	2-{6-[(3a*S*,7a*R*)-octahydro-1*H*-pyrrolo[3,2-c]pyridin-1-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride
345	2-(6-{methyl[(1*s*,4*s*)-4-(methylamino)cyclohexyl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride
346	2-(6-{[(3*R*,4*S*)-4-fluoropyrrolidin-3-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol formate
347	2-{6-[(3a*S*,7a*R*)-5-methyloctahydro-1*H*-pyrrolo[3,2-c]pyridin-1-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride
348	2-(6-{methyl[(3*R*)-piperidin-3-yl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride
349	2-(6-{methyl[(3*S*)-piperidin-3-yl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride
350	2-(6-{methyl[3-(methylamino)cyclobutyl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol ditrifluoroacetate
351	2-(6-{[(1*r*,4*r*)-4-(dimethylamino)cyclohexyl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride
352	2-(6-{methyl[(3*S*)-1-methylpiperidin-3-yl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride
353	2-{6-[(azetidin-3-yl)(methyl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride

Cpd	Name
354	2-[6-(1,7-diazaspiro[3.5]nonan-1-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride
355	2-{6-[(3,3-dimethylpiperidin-4-yl)(methyl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride
356	2-{6-[(2-azaspiro[3.3]heptan-6-yl)(methyl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride
359	5-{2-[(2*R*,4*r*,6*S*)-2,6-dimethylpiperidin-4-yl]-4-fluoro-1,3-benzothiazol-6-yl}-2,7-dimethyl[1,3]oxazolo[5,4-b]pyridine hydrochloride
360	2-{6-[methyl(1,3,3-trimethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride
361	2-(6-{methyl[(1*s*,3*s*)-3-(methylamino)cyclobutyl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride
362	2-{6-[(3a*R*,7a*S*)-octahydro-1*H*-pyrrolo[2,3-c]pyridin-1-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride
363	2-[6-(1,6-diazaspiro[3.5]nonan-1-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride
364	2-(6-{[(1*s*,3*s*)-3-(dimethylamino)cyclobutyl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride
365	2-(6-{[(3*R*,4*R*)-3-fluoropiperidin-4-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol formate
367	5-(1*H*-pyrazol-4-yl)-2-{6-[(pyrrolidin-3-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}phenol formate
368	2-[6-(2,6-diazaspiro[3.3]heptan-2-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(3-fluoro-1*H*-pyrazol-4-yl)phenol formate
369	2-{6-[(3a*R*,7a*S*)-6-methyloctahydro-1*H*-pyrrolo[2,3-c]pyridin-1-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride
370	2-[6-(6-methyl-1,6-diazaspiro[3.5]nonan-1-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride
371	2-(6-{[(2*S*,4*S*)-2-(hydroxymethyl)piperidin-4-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride
372	2-(6-{[(2*S*,4*S*)-2-(hydroxymethyl)-1-methylpiperidin-4-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride
376	2-(6-{methyl[(1*r*,3*r*)-3-(methylamino)cyclobutyl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride
380	*N*-(1,2-dimethylpiperidin-4-yl)-6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine trifluoroacetate
386	2-{6-[(1*S*,6*R*)-3,8-diazabicyclo[4.2.0]octan-8-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol trifluoroacetate

Cpd	Name
388	2-{6-[(1*S*,6*R*)-3-methyl-3,8-diazabicyclo[4.2.0]octan-8-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol trifluoroacetate
389	2-{6-[(1*R*,6*S*)-3,8-diazabicyclo[4.2.0]octan-8-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol trifluoroacetate
390	2-{6-[(1*R*,6*S*)-3-methyl-3,8-diazabicyclo[4.2.0]octan-8-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol trifluoroacetate
394	2-(6-{methyl[(2*S*,4*S*)-2-methylpiperidin-4-yl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol trifluoroacetate
395	2-(6-{[(2*S*,4*S*)-1,2-dimethylpiperidin-4-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol trifluoroacetate
396	2-(6-{methyl[(2*R*,4*S*)-2-methylpiperidin-4-yl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol trifluoroacetate, and
397	2-(6-{[(2*R*,4*S*)-1,2-dimethylpiperidin-4-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol trifluoroacetate;

wherein the form of the compound salt is selected from the group consisting of hydrate, solvate, racemate, enantiomer, diastereomer, stereoisomer, and tautomer form thereof.

An aspect of the present description includes a method for preventing, treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of a compound of Formula (I) or Formula (II) or a form thereof.

An aspect of the present description includes a method for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of a compound of Formula (I) or Formula (II) or a form thereof.

Another aspect of the present description includes a method for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of a compound salt of Formula (I) or Formula (II) or a form thereof.

An aspect of the present description includes a method for use of a compound of Formula (I) or Formula (II) or a form or composition thereof for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of the compound of Formula (I) or Formula (II) or a form or composition thereof.

Another aspect of the present description includes a method for use of a compound salt of Formula (I) or Formula (II) or a form or composition thereof for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of the compound salt of Formula (I) or Formula (II) or a form thereof.

An aspect of the present description includes a use for a compound of Formula (I) or Formula (II) or a form thereof for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of the compound of Formula (I) or Formula (II) or a form thereof.

Another aspect of the present description includes a use for a compound salt of Formula (I) or Formula (II) or a form thereof for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of the compound salt of Formula (I) or Formula (II) or a form thereof.

An aspect of the present description includes a use for a compound of Formula (I) or Formula (II) or a form thereof in the manufacture of a medicament for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of the medicament.

Another aspect of the present description includes a use for a compound salt of Formula (I) or Formula (II) or a form thereof in the manufacture of a medicament for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of the medicament.

An aspect of the present description includes a use for a compound of Formula (I) or Formula (II) or a form thereof in a combination product with one or more therapeutic agents for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of the compound of Formula (I) or Formula (II) or a form thereof in combination with an effective amount of the one or more agents.

Another aspect of the present description includes a use for a compound salt of Formula (I) or Formula (II) or a form thereof in a combination product with one or more therapeutic agents for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of the compound salt of Formula (I) or Formula (II) or a form thereof in combination with an effective amount of the one or more agents.

CHEMICAL DEFINITIONS

The chemical terms used above and throughout the d;escription herein, unless specifically defined otherwise, shall be understood by one of ordinary skill in the art to have the following indicated meanings.

As used herein, the term "C_{1-6}alkyl" generally refers to saturated hydrocarbon radicals having from one to eight carbon atoms in a straight or branched chain configuration, including, but not limited to, methyl, ethyl, n-propyl (also referred to as propyl or propanyl), isopropyl, n-butyl (also referred to as butyl or butanyl), isobutyl, sec-butyl, tert-butyl, n-pentyl (also referred to as pentyl or pentanyl), n-hexyl (also referred to as hexyl or hexanyl), and the like. In certain aspects, C_{1-6}alkyl includes, but is not limited to, C_{1-4}alkyl, C_{1-2}alkyl and the like. A C_{1-6}alkyl radical is optionally substituted with substituent species as described herein where allowed by available valences.

As used herein, the term "C_{2-8}alkenyl" generally refers to partially unsaturated hydrocarbon radicals having from two to eight carbon atoms in a straight or branched chain configuration and one or more carbon-carbon double bonds therein, including, but not limited to, ethenyl (also referred to as vinyl), allyl, propenyl and the like. In certain aspects, C_{2-8}alkenyl includes, but is not limited to, C_{2-6}alkenyl, C_{2-4}alkenyl and the like. A C_{2-8}alkenyl radical is optionally substituted with substituent species as described herein where allowed by available valences.

As used herein, the term "C_{2-8}alkynyl" generally refers to partially unsaturated hydrocarbon radicals having from two to eight carbon atoms in a straight or branched chain configuration and one or more carbon-carbon triple bonds therein, including, but not limited to, ethynyl, propynyl, butynyl and the like. In certain aspects, C_{2-8}alkynyl includes, but is not limited to, C_{2-6}alkynyl, C_{2-4}alkynyl and the like. A C_{2-8}alkynyl radical is optionally substituted with substituent species as described herein where allowed by available valences.

As used herein, the term "C_{1-6}alkoxy" generally refers to saturated hydrocarbon radicals having from one to eight carbon atoms in a straight or branched chain configuration of the formula: -O-C_{168}alkyl, including, but not limited to, methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, isobutoxy, sec-butoxy, tert-butoxy, n-pentoxy, n-hexoxy and the like. In certain aspects, C_{1-6}alkoxy includes, but is not limited to, C_{1-4}alkoxy, C_{1-2}alkoxy and the like. A C_{1-6}alkoxy radical is optionally substituted with substituent species as described herein where allowed by available valences.

As used herein, the term "C_{3-10}cycloalkyl" generally refers to a saturated or partially unsaturated monocyclic, bicyclic or polycyclic hydrocarbon radical, including, but not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclohexenyl, cycloheptyl, cyclooctyl,

1*H*-indanyl, indenyl, tetrahydro-naphthalenyl and the like. In certain aspects, $C_{3\text{-}10}$cycloalkyl includes, but is not limited to, $C_{3\text{-}8}$cycloalkyl, $C_{5\text{-}8}$cycloalkyl, and the like. A $C_{3\text{-}10}$cycloalkyl radical is optionally substituted with substituent species as described herein where allowed by available valences.

As used herein, the term "aryl" generally refers to a monocyclic, bicyclic or polycyclic aromatic carbon atom ring structure radical, including, but not limited to, phenyl, naphthyl, anthracenyl, fluorenyl, azulenyl, phenanthrenyl and the like. An aryl radical is optionally substituted with substituent species as described herein where allowed by available valences.

As used herein, the term "heteroaryl" generally refers to a monocyclic, bicyclic or polycyclic aromatic carbon atom ring structure radical in which one or more carbon atom ring members have been replaced, where allowed by structural stability, with one or more heteroatoms, such as an O, S or N atom, including, but not limited to, furanyl, thienyl, pyrrolyl, pyrazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxazolyl, 1,3-thiazolyl, triazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazinyl, indolyl, indazolyl, indolizinyl, isoindolyl, benzofuranyl, benzothienyl, benzoimidazolyl, 1,3-benzothiazolyl, 1,3-benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, 1,3-diazinyl, 1,2-diazinyl, 1,2-diazolyl, 1,4-diazanaphthalenyl, acridinyl, furo[3,2-*b*]pyridinyl, furo[3,2-*c*]pyridinyl, furo[2,3-*c*]pyridinyl, 6*H*-thieno[2,3-*b*]pyrrolyl, thieno[3,2-*c*]pyridinyl, thieno[2,3-*d*]pyrimidinyl, 1*H*-pyrrolo[2,3-*b*]pyridinyl, 1*H*-pyrrolo[2,3-*c*]pyridinyl, 1*H*-pyrrolo[3,2-*b*]pyridinyl, pyrrolo[1,2-*a*]pyrazinyl, pyrrolo[1,2-*b*]pyridazinyl, pyrazolo[1,5-*a*]pyridinyl, pyrazolo[1,5-*a*]pyrazinyl, imidazo[1,2-*a*]pyridinyl, 3*H*-imidazo[4,5-*b*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*c*]pyrimidinyl, imidazo[1,2-*b*]pyridazinyl, imidazo[1,2-*a*]pyrazinyl, imidazo[2,1-*b*][1,3]thiazolyl, imidazo[2,1-*b*][1,3,4]thiadiazolyl, [1,2,4]triazolo[1,5-*a*]pyridinyl, [1,2,4]triazolo[4,3-*a*]pyridinyl and the like. A heteroaryl radical is optionally substituted on a carbon or nitrogen atom ring member with substituent species as described herein where allowed by available valences.

In certain aspects, the nomenclature for a heteroaryl radical may differ, such as in non-limiting examples where furanyl may also be referred to as furyl, thienyl may also be referred to as thiophenyl, pyridinyl may also be referred to as pyridyl, benzothienyl may also be referred to as benzothiophenyl and 1,3-benzoxazolyl may also be referred to as 1,3-benzooxazolyl.

In certain other aspects, the term for a heteroaryl radical may also include other regioisomers, such as in non-limiting examples where the term pyrrolyl may also include 2*H*-pyrrolyl, 3*H*-pyrrolyl and the like, the term pyrazolyl may also include 1*H*-pyrazolyl and the like, the term imidazolyl may also include 1*H*-imidazolyl and the like, the term triazolyl may also include 1*H*-1,2,3-triazolyl and the like, the term oxadiazolyl may also include 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl and the like, the term tetrazolyl may also include 1*H*-tetrazolyl, 2*H*-tetrazolyl and the like, the term indolyl may also include 1*H*-indolyl and the like, the term indazolyl may also include 1*H*-indazolyl, 2*H*-indazolyl and the like, the term benzoimidazolyl may also include 1*H*-benzoimidazolyl and the term purinyl may also include 9*H*-purinyl and the like.

As used herein, the term "heterocyclyl" generally refers to a saturated or partially unsaturated monocyclic, bicyclic or polycyclic carbon atom ring structure radical in which one or more carbon atom ring members have been replaced, where allowed by structural stability, with a heteroatom, such as an O, S or N atom, including, but not limited to, oxiranyl, oxetanyl, azetidinyl, tetrahydrofuranyl, pyrrolinyl, pyrrolidinyl, pyrazolinyl, pyrazolidinyl, imidazolinyl, imidazolidinyl, isoxazolinyl, isoxazolidinyl, isothiazolinyl, isothiazolidinyl, oxazolinyl, oxazolidinyl, thiazolinyl, thiazolidinyl, triazolinyl, triazolidinyl, oxadiazolinyl, oxadiazolidinyl, thiadiazolinyl, thiadiazolidinyl, tetrazolinyl, tetrazolidinyl, pyranyl, dihydro-2*H*-pyranyl, thiopyranyl, 1,3-dioxanyl, 1,2,5,6-tetrahydropyridinyl, 1,2,3,6-tetrahydropyridinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, 1,4-diazepanyl, 1,3-benzodioxolyl, 1,4-benzodioxanyl, 2,3-dihydro-1,4-benzodioxinyl, hexahydropyrrolo[3,4-*b*]pyrrol-(1*H*)-yl, (3a*S*,6a*S*)-hexahydropyrrolo[3,4-*b*]pyrrol-(1*H*)-yl, (3a*R*,6a*R*)-hexahydropyrrolo[3,4-*b*]pyrrol-(1*H*)-yl, hexahydropyrrolo[3,4-*b*]pyrrol-(2*H*)-yl, (3a*S*,6a*S*)-hexahydropyrrolo[3,4-*b*]pyrrol-(2*H*)-yl, (3a*R*,6a*R*)-hexahydropyrrolo[3,4-*b*]pyrrol-(2*H*)-yl, hexahydropyrrolo[3,4-*c*]pyrrol-(1*H*)-yl, (3a*R*,6a*S*)-hexahydropyrrolo[3,4-*c*]pyrrol-(1*H*)-yl, (3a*R*,6a*R*)-hexahydropyrrolo[3,4-*c*]pyrrol-(1*H*)-yl, octahydro-5*H*-pyrrolo[3,2-*c*]pyridinyl, octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, (4a*R*,7a*R*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, (4a*S*,7a*S*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (7*R*,8a*S*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8a*S*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8a*R*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8a*S*)-octahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8a*R*)-octahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl,

hexahydropyrrolo[1,2-*a*]pyrazin-(2*H*)-one, octahydro-2*H*-pyrido[1,2-*a*]pyrazinyl, 3-azabicyclo[3.1.0]hexyl, (1*R*,5*S*)-3-azabicyclo[3.1.0]hexyl, 8-azabicyclo[3.2.1]octyl, (1*R*,5*S*)-8-azabicyclo[3.2.1]octyl, 8-azabicyclo[3.2.1]oct-2-enyl, (1*R*,5*S*)-8-azabicyclo[3.2.1]oct-2-enyl, 9-azabicyclo[3.3.1]nonyl, (1*R*,5*S*)-9-azabicyclo[3.3.1]nonyl, 2,5-diazabicyclo[2.2.1]heptyl, (1*S*,4*S*)-2,5-diazabicyclo[2.2.1]heptyl, 2,5-diazabicyclo[2.2.2]octyl, 3,8-diazabicyclo[3.2.1]octyl, (1*R*,5*S*)-3,8-diazabicyclo[3.2.1]octyl, 1,4-diazabicyclo[3.2.2]nonyl, azaspiro[3.3]heptyl, 2,6-diazaspiro[3.3]heptyl, 2,7-diazaspiro[3.5]nonyl, 5,8-diazaspiro[3.5]nonyl, 2,7-diazaspiro[4.4]nonyl, 6,9-diazaspiro[4.5]decyl and the like. A heterocyclyl radical is optionally substituted on a carbon or nitrogen atom ring member with substituent species as described herein where allowed by available valences.

In certain aspects, the nomenclature for a heterocyclyl radical may differ, such as in non-limiting examples where 1,3-benzodioxolyl may also be referred to as benzo[*d*][1,3]dioxolyl and 2,3-dihydro-1,4-benzodioxinyl may also be referred to as 2,3-dihydrobenzo[*b*][1,4]dioxinyl.

As used herein, the term "C_{1-6}alkoxy-C_{1-6}alkyl" refers to a radical of the formula: -C_{1-6}alkyl-O-C_{1-6}alkyl.

As used herein, the term "C_{1-6}alkoxy-carbonyl" refers to a radical of the formula: -C(O)-O-C_{1-6}alkyl.

As used herein, the term "C_{1-6}alkoxy-carbonyl-C_{1-6}alkyl" refers to a radical of the formula: -C_{1-6}alkyl-C(O)-O-C_{1-6}alkyl.

As used herein, the term "C_{1-6}alkoxy-carbonyl-amino" refers to a radical of the formula: -NH-C(O)-O-C_{1-6}alkyl.

As used herein, the term "C_{1-6}alkyl-amino" refers to a radical of the formula: -NH-C_{1-6}alkyl.

As used herein, the term "(C_{1-6}alkyl)$_2$-amino" refers to a radical of the formula: -N(C_{1-6}alkyl)$_2$.

As used herein, the term "C_{1-6}alkyl-carbonyl" refers to a radical of the formula: -C(O)-C_{1-6}alkyl.

As used herein, the term "C_{1-6}alkyl-carbonyl-amino" refers to a radical of the formula: -NH-C(O)-C_{1-6}alkyl.

As used herein, the term “amino-C_{1-6}alkyl” refers to a radical of the formula: -C_{1-6}alkyl-NH_2.

As used herein, the term "amino-carbonyl" refers to a radical of the formula: -C(O)-NH_2.

As used herein, the term “aryl-C_{1-6}alkoxy” refers to a radical of the formula: -O-C_{1-6}alkyl-aryl.

As used herein, the term “aryl-oxy” refers to a radical of the formula: -O-aryl.

As used herein, the term “aryl-C_{1-6}alkyl” refers to a radical of the formula: -C_{1-6}alkyl-aryl.

As used herein, the term “benzoxy-carbonyl” refers to a radical of the formula: -C(O)-O-CH_2-phenyl.

As used herein, the term “halo” or “halogen” generally refers to a halogen atom radical, including fluoro, chloro, bromo and iodo.

As used herein, the term “halo-C_{1-6}alkoxy” refers to a radical of the formula: -O-C_{1-6}alkyl-halo, wherein C_{1-6}alkyl is partially or completely substituted with one or more halogen atoms where allowed by available valences.

As used herein, the term “halo-C_{1-6}alkyl” refers to a radical of the formula: -C_{1-6}alkyl-halo, wherein C_{1-6}alkyl is partially or completely substituted with one or more halogen atoms where allowed by available valences.

As used herein, the term "carboxyl" refers to a radical of the formula: -COOH, -C(O)OH or -CO_2H.

As used herein, the term "C_{1-6}alkyl-carboxyl" refers to a radical of the formula: -C_{1-6}alkyl-COOH, -C_{1-6}alkyl-C(O)OH or -C_{1-6}alkyl-CO_2H.

As used herein, the term “hydroxy” refers to a radical of the formula: -OH.

As used herein, the term “hydroxy-C_{1-6}alkoxy-C_{1-6}alkyl” refers to a radical of the formula: -C_{1-6}alkyl-O-C_{1-6}alkyl-OH.

As used herein, the term “hydroxy-C_{1-6}alkyl” refers to a radical of the formula: -C_{1-6}alkyl-OH, wherein C_{1-6}alkyl is partially or completely substituted with one or more hydroxy radicals where allowed by available valences.

As used herein, the term “substituent” means positional variables on the atoms of a core molecule that are substituted at a designated atom position, replacing one or more hydrogens on the designated atom, provided that the designated atom’s normal valency is not exceeded, and that the substitution results in a stable compound. Combinations of substituents and/or variables are

permissible only if such combinations result in stable compounds. A person of ordinary skill in the art should note that any carbon as well as heteroatom with valences that appear to be unsatisfied as described or shown herein is assumed to have a sufficient number of hydrogen atom(s) to satisfy the valences described or shown. In certain instances, one or more substituents having a double bond (e.g., "oxo" or "=O") as the point of attachment may be described, shown or listed herein within a substituent group, wherein the structure may only show a single bond as the point of attachment to the core structure of Formula (I) or Formula (II). A person of ordinary skill in the art would understand that, while only a single bond is shown, a double bond is intended for those substituents.

As used herein, the term "and the like," with reference to the definitions of chemical terms provided herein, means that variations in chemical structures that could be expected by one skilled in the art include, without limitation, isomers (including chain, branching or positional structural isomers), hydration of ring systems (including saturation or partial unsaturation of monocyclic, bicyclic or polycyclic ring structures) and all other variations where allowed by available valences which result in a stable compound.

For the purposes of this description, where one or more substituent variables for a compound of Formula (I) or Formula (II) or a form thereof encompass functionalities incorporated into a compound of Formula (I) or Formula (II), each functionality appearing at any location within the disclosed compound may be independently selected, and as appropriate, independently and/or optionally substituted.

As used herein, the terms "independently selected," or "each selected" refer to functional variables in a substituent list that may occur more than once on the structure of Formula (I) or Formula (II), the pattern of substitution at each occurrence is independent of the pattern at any other occurrence. Further, the use of a generic substituent variable on any formula or structure for a compound described herein is understood to include the replacement of the generic substituent with species substituents that are included within the particular genus, *e.g.*, aryl may be replaced with phenyl or naphthalenyl and the like, and that the resulting compound is to be included within the scope of the compounds described herein.

As used herein, the terms "each instance of" or "in each instance, when present," when used preceding a phrase such as "…C_{3-10}cycloalkyl, C_{3-10}cycloalkyl-C_{1-4}alkyl, aryl, aryl-C_{1-4}alkyl, heteroaryl, heteroaryl-C_{1-4}alkyl, heterocyclyl and heterocyclyl-C_{1-4}alkyl," are intended to refer to

the C_{3-10}cycloalkyl, aryl, heteroaryl and heterocyclyl ring systems when each are present either alone or as a substituent.

As used herein, the term "optionally substituted" means optional substitution with the specified substituent variables, groups, radicals or moieties.

COMPOUND FORMS

As used herein, the term "form" means a compound of Formula (I) or Formula (II) having a form selected from the group consisting of a free acid, free base, prodrug, salt, hydrate, solvate, clathrate, isotopologue, racemate, enantiomer, diastereomer, stereoisomer, polymorph and tautomer form thereof.

In certain aspects described herein, the form of the compound of Formula (I) or Formula (II) is a free acid, free base or salt thereof.

In certain aspects described herein, the form of the compound of Formula (I) or Formula (II) is a salt thereof.

In certain aspects described herein, the form of the compound of Formula (I) or Formula (II) is an isotopologue thereof.

In certain aspects described herein, the form of the compound of Formula (I) or Formula (II) is a stereoisomer, racemate, enantiomer or diastereomer thereof.

In certain aspects described herein, the form of the compound of Formula (I) or Formula (II) is a tautomer thereof.

In certain aspects described herein, the form of the compound of Formula (I) or Formula (II) is a pharmaceutically acceptable form.

In certain aspects described herein, the compound of Formula (I) or Formula (II) or a form thereof is isolated for use.

As used herein, the term "isolated" means the physical state of a compound of Formula (I) or Formula (II) or a form thereof after being isolated and/or purified from a synthetic process (*e.g.*, from a reaction mixture) or natural source or combination thereof according to an isolation or purification process or processes described herein or which are well known to the skilled artisan (*e.g.*, chromatography, recrystallization and the like) in sufficient purity to be characterized by standard analytical techniques described herein or well known to the skilled artisan.

As used herein, the term "protected" means that a functional group in a compound of Formula (I) or Formula (II) or a form thereof is in a form modified to preclude undesired side reactions at the protected site when the compound is subjected to a reaction. Suitable protecting groups will be recognized by those with ordinary skill in the art as well as by reference to standard textbooks such as, for example, T.W. Greene *et al*, *Protective Groups in organic Synthesis* (1991), Wiley, New York. Such functional groups include hydroxy, phenol, amino and carboxylic acid. Suitable protecting groups for hydroxy or phenol include trialkylsilyl or diarylalkylsilyl (e.g., t-butyldimethylsilyl, t-butyldiphenylsilyl or trimethylsilyl), tetrahydropyranyl, benzyl, substituted benzyl, methyl, methoxymethanol, and the like. Suitable protecting groups for amino, amidino and guanidino include t-butoxycarbonyl, benzyloxycarbonyl, and the like. Suitable protecting groups for carboxylic acid include alkyl, aryl or arylalkyl esters. In certain instances, the protecting group may also be a polymer resin, such as a Wang resin or a 2-chlorotrityl-chloride resin. Protecting groups may be added or removed in accordance with standard techniques, which are well-known to those skilled in the art and as described herein. It will also be appreciated by those skilled in the art, although such protected derivatives of compounds described herein may not possess pharmacological activity as such, they may be administered to a subject and thereafter metabolized in the body to form compounds described herein which are pharmacologically active. Such derivatives may therefore be described as "prodrugs". All prodrugs of compounds described herein are included within the scope of the use described herein.

As used herein, the term "prodrug" means a form of an instant compound (*e.g.*, a drug precursor) that is transformed *in vivo* to yield an active compound of Formula (I) or Formula (II) or a form thereof. The transformation may occur by various mechanisms (*e.g.*, by metabolic and/or non-metabolic chemical processes), such as, for example, by hydrolysis and/or metabolism in blood, liver and/or other organs and tissues. A discussion of the use of prodrugs is provided by T. Higuchi and W. Stella, "Pro-drugs as Novel Delivery Systems," Vol. 14 of the A.C.S. Symposium Series, and in Bioreversible Carriers in Drug Design, ed. Edward B. Roche, American Pharmaceutical Association and Pergamon Press, 1987.

In one example, when a compound of Formula (I) or Formula (II) or a form thereof contains a carboxylic acid functional group, a prodrug can comprise an ester formed by the replacement of the hydrogen atom of the acid group with a functional group such as alkyl and the

like. In another example, when a compound of Formula (I) or Formula (II) or a form thereof contains a hydroxyl functional group, a prodrug form can be prepared by replacing the hydrogen atom of the hydroxyl with another functional group such as alkyl, alkylcarbonyl or a phosphonate ester and the like. In another example, when a compound of Formula (I) or Formula (II) or a form thereof contains an amine functional group, a prodrug form can be prepared by replacing one or more amine hydrogen atoms with a functional group such as alkyl or substituted carbonyl. Pharmaceutically acceptable prodrugs of compounds of Formula (I) or Formula (II) or a form thereof include those compounds substituted with one or more of the following groups: carboxylic acid esters, sulfonate esters, amino acid esters, phosphonate esters and mono-, di- or triphosphate esters or alkyl substituents, where appropriate. As described herein, it is understood by a person of ordinary skill in the art that one or more of such substituents may be used to provide a compound of Formula (I) or Formula (II) or a form thereof as a prodrug.

One or more compounds described herein may exist in unsolvated as well as solvated forms with pharmaceutically acceptable solvents such as water, ethanol, and the like, and the description herein is intended to embrace both solvated and unsolvated forms.

As used herein, the term “solvate” means a physical association of a compound described herein with one or more solvent molecules. This physical association involves varying degrees of ionic and covalent bonding, including hydrogen bonding. In certain instances the solvate will be capable of isolation, for example when one or more solvent molecules are incorporated in the crystal lattice of the crystalline solid. As used herein, “solvate” encompasses both solution-phase and isolatable solvates. Non-limiting examples of suitable solvates include ethanolates, methanolates, and the like.

As used herein, the term “hydrate” means a solvate wherein the solvent molecule is water.

The compounds of Formula (I) or Formula (II) can form salts, which are intended to be included within the scope of this description. Reference to a compound of Formula (I) or Formula (II) or a form thereof herein is understood to include reference to salt forms thereof, unless otherwise indicated. The term "salt(s)", as employed herein, denotes acidic salts formed with inorganic and/or organic acids, as well as basic salts formed with inorganic and/or organic bases. In addition, when a compound of Formula (I) or Formula (II) or a form thereof contains both a basic moiety, such as, without limitation an amine moiety, and an acidic moiety, such as,

but not limited to a carboxylic acid, zwitterions ("inner salts") may be formed and are included within the term "salt(s)" as used herein.

The term "pharmaceutically acceptable salt(s)", as used herein, means those salts of compounds described herein that are safe and effective (*i.e.*, non-toxic, physiologically acceptable) for use in mammals and that possess biological activity, although other salts are also useful. Salts of the compounds of the Formula (I) or Formula (II) may be formed, for example, by reacting a compound of Formula (I) or Formula (II) or a form thereof with an amount of acid or base, such as an equivalent amount, in a medium such as one in which the salt precipitates or in an aqueous medium followed by lyophilization.

Pharmaceutically acceptable salts include one or more salts of acidic or basic groups present in compounds described herein. Particular aspects of acid addition salts include, and are not limited to, acetate, ascorbate, benzoate, benzenesulfonate, bisulfate, bitartrate, borate, bromide, butyrate, chloride, citrate, camphorate, camphorsulfonate, ethanesulfonate, formate, fumarate, gentisinate, gluconate, glucaronate, glutamate, iodide, isonicotinate, lactate, maleate, methanesulfonate, naphthalenesulfonate, nitrate, oxalate, pamoate, pantothenate, phosphate, propionate, saccharate, salicylate, succinate, sulfate, tartrate, thiocyanate, toluenesulfonate (also known as tosylate), trifluoroacetate salts and the like. Certain particular aspects of acid addition salts include chloride or dichloride.

Additionally, acids which are generally considered suitable for the formation of pharmaceutically useful salts from basic pharmaceutical compounds are discussed, for example, by P. Stahl *et al*, Camille G. (eds.) *Handbook of Pharmaceutical Salts. Properties, Selection and Use.* (2002) Zurich: Wiley-VCH; S. Berge *et al*, *Journal of Pharmaceutical Sciences* (1977) 66(1) 1-19; P. Gould, *International J. of Pharmaceutics* (1986) 33, 201-217; Anderson *et al*, *The Practice of Medicinal Chemistry* (1996), Academic Press, New York; and in *The Orange Book* (Food & Drug Administration, Washington, D.C. on their website). These disclosures are incorporated herein by reference thereto.

Suitable basic salts include, but are not limited to, aluminum, ammonium, calcium, lithium, magnesium, potassium, sodium and zinc salts.

All such acid salts and base salts are intended to be included within the scope of pharmaceutically acceptable salts as described herein. In addition, all such acid and base salts are

considered equivalent to the free forms of the corresponding compounds for purposes of this description.

Compounds of Formula (I) or Formula (II) and forms thereof, may further exist in a tautomeric form. All such tautomeric forms are contemplated and intended to be included within the scope of the compounds of Formula (I) or Formula (II) or a form thereof as described herein.

The compounds of Formula (I) or Formula (II) or a form thereof may contain asymmetric or chiral centers, and, therefore, exist in different stereoisomeric forms. The present description is intended to include all stereoisomeric forms of the compounds of Formula (I) or Formula (II) as well as mixtures thereof, including racemic mixtures.

The compounds described herein may include one or more chiral centers, and as such may exist as racemic mixtures (*R/S*) or as substantially pure enantiomers and diastereomers. The compounds may also exist as substantially pure (*R*) or (*S*) enantiomers (when one chiral center is present). In one particular aspect, the compounds described herein are (*S*) isomers and may exist as enantiomerically pure compositions substantially comprising only the (*S*) isomer. In another particular aspect, the compounds described herein are (*R*) isomers and may exist as enantiomerically pure compositions substantially comprising only the (*R*) isomer. As one of skill in the art will recognize, when more than one chiral center is present, the compounds described herein may also exist as a (*R,R*), (*R,S*), (*S,R*) or (*S,S*) isomer, as defined by *IUPAC* Nomenclature Recommendations.

As used herein, the term "substantially pure" refers to compounds consisting substantially of a single isomer in an amount greater than or equal to 90%, in an amount greater than or equal to 92%, in an amount greater than or equal to 95%, in an amount greater than or equal to 98%, in an amount greater than or equal to 99%, or in an amount equal to 100% of the single isomer.

In one aspect of the description, a compound of Formula (I) or Formula (II) or a form thereof is a substantially pure (*S*) enantiomer form present in an amount greater than or equal to 90%, in an amount greater than or equal to 92%, in an amount greater than or equal to 95%, in an amount greater than or equal to 98%, in an amount greater than or equal to 99%, or in an amount equal to 100%.

In one aspect of the description, a compound of Formula (I) or Formula (II) or a form thereof is a substantially pure (*R*) enantiomer form present in an amount greater than or equal to 90%, in an amount greater than or equal to 92%, in an amount greater than or equal to 95%, in an

amount greater than or equal to 98%, in an amount greater than or equal to 99%, or in an amount equal to 100%.

As used herein, a "racemate" is any mixture of isometric forms that are not "enantiomerically pure", including mixtures such as, without limitation, in a ratio of about 50/50, about 60/40, about 70/30, or about 80/20.

In addition, the present description embraces all geometric and positional isomers. For example, if a compound of Formula (I) or Formula (II) or a form thereof incorporates a double bond or a fused ring, both the cis- and trans-forms, as well as mixtures, are embraced within the scope of the description. Diastereomeric mixtures can be separated into their individual diastereomers on the basis of their physical chemical differences by methods well known to those skilled in the art, such as, for example, by chromatography and/or fractional crystallization. Enantiomers can be separated by use of chiral HPLC column or other chromatographic methods known to those skilled in the art. Enantiomers can also be separated by converting the enantiomeric mixture into a diastereomeric mixture by reaction with an appropriate optically active compound (*e.g.*, chiral auxiliary such as a chiral alcohol or Mosher's acid chloride), separating the diastereomers and converting (*e.g.*, hydrolyzing) the individual diastereomers to the corresponding pure enantiomers. Also, some of the compounds of Formula (I) or Formula (II) may be atropisomers (*e.g.*, substituted biaryls) and are considered as part of this description.

All stereoisomers (for example, geometric isomers, optical isomers and the like) of the present compounds (including those of the salts, solvates, esters and prodrugs of the compounds as well as the salts, solvates and esters of the prodrugs), such as those which may exist due to asymmetric carbons on various substituents, including enantiomeric forms (which may exist even in the absence of asymmetric carbons), rotameric forms, atropisomers, and diastereomeric forms, are contemplated within the scope of this description, as are positional isomers (such as, for example, 4-pyridyl and 3-pyridyl). Individual stereoisomers of the compounds described herein may, for example, be substantially free of other isomers, or may be present in a racemic mixture, as described supra.

The use of the terms "salt", "solvate", "ester", "prodrug" and the like, is intended to equally apply to the salt, solvate, ester and prodrug of enantiomers, stereoisomers, rotamers, tautomers, positional isomers, racemates or isotopologues of the instant compounds.

The term "isotopologue" refers to isotopically-enriched compounds described herein which are identical to those recited herein, but for the fact that one or more atoms are replaced by an atom having an atomic mass or mass number different from the atomic mass or mass number usually found in nature. Examples of isotopes that can be incorporated into compounds described herein include isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorus, fluorine and chlorine, such as ^{2}H, ^{3}H, ^{13}C, ^{14}C, ^{15}N, ^{18}O, ^{17}O, ^{31}P, ^{32}P, ^{35}S, ^{18}F, ^{35}Cl and ^{36}Cl, respectively, each of which are also within the scope of this description.

Certain isotopically-enriched compounds described herein (*e.g.,* those labeled with ^{3}H and ^{14}C) are useful in compound and/or substrate tissue distribution assays. Tritiated (*i.e.*, ^{3}H) and carbon-14 (*i.e.*, ^{14}C) isotopes are particularly preferred for their ease of preparation and detectability. Further, substitution with heavier isotopes such as deuterium (*i.e.*, ^{2}H) may afford certain therapeutic advantages resulting from greater metabolic stability (*e.g.*, increased in vivo half-life or reduced dosage requirements) and hence may be preferred in some circumstances.

Polymorphic crystalline and amorphous forms of the compounds of Formula (I) or Formula (II) and of the salts, solvates, hydrates, esters and prodrugs of the compounds of Formula (I) or Formula (II) are further intended to be included in the present description.

COMPOUND USES

In accordance with the intended scope of the present description, aspects of the present description include compounds that have been identified and have been demonstrated to be useful in selectively preventing, treating or ameliorating HD and have been provided for use for preventing, treating or ameliorating HD.

An aspect of the present description includes a method for preventing, treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of a compound of Formula (I) or Formula (II) or a form thereof.

An aspect of the present description includes a method for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of a compound of Formula (I) or Formula (II) or a form thereof.

An aspect of the present description includes a method for preventing HD in a subject in need thereof comprising, administering to the subject an effective amount of a compound of Formula (I) or Formula (II) or a form thereof.

An aspect of the present description includes a method for treating HD in a subject in need thereof comprising, administering to the subject an effective amount of a compound of Formula (I) or Formula (II) or a form thereof.

An aspect of the present description includes a method for ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of a compound of Formula (I) or Formula (II) or a form thereof.

Another aspect of the present description includes a method for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of a compound salt of Formula (I) or Formula (II) or a form thereof.

An aspect of the present description includes a method for use of a compound of Formula (I) or Formula (II) or a form or composition thereof for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of the compound of Formula (I) or Formula (II) or a form or composition thereof.

Another aspect of the present description includes a method for use of a compound salt of Formula (I) or Formula (II) or a form or composition thereof for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of the compound salt of Formula (I) or Formula (II) or a form thereof.

An aspect of the present description includes a use for a compound of Formula (I) or Formula (II) or a form thereof for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of the compound of Formula (I) or Formula (II) or a form thereof.

Another aspect of the present description includes a use for a compound salt of Formula (I) or Formula (II) or a form thereof for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of the compound salt of Formula (I) or Formula (II) or a form thereof.

An aspect of the present description includes a use for a compound of Formula (I) or Formula (II) or a form thereof in the manufacture of a medicament for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of the medicament.

Another aspect of the present description includes a use for a compound salt of Formula (I) or Formula (II) or a form thereof in the manufacture of a medicament for treating or

ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of the medicament.

An aspect of the present description includes in vitro or in vivo use of the compound of Formula (I) or Formula (II) or a form thereof having activity toward HD.

An aspect of the present description includes a use of the compound of Formula (I) or Formula (II) or a form thereof in a combination therapy to provide additive or synergistic activity, thus enabling the development of a combination product for treating or ameliorating HD.

Another aspect of the present description includes a combination therapy comprising compounds described herein in combination with one or more known drugs or one or more known therapies may be used to treat HD regardless of whether HD is responsive to the known drug.

An aspect of the present description includes a use for a compound of Formula (I) or Formula (II) or a form thereof in a combination product with one or more therapeutic agents for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of the compound of Formula (I) or Formula (II) or a form thereof in combination with an effective amount of the one or more agents.

Another aspect of the present description includes a use for a compound salt of Formula (I) or Formula (II) or a form thereof in a combination product with one or more therapeutic agents for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of the compound salt of Formula (I) or Formula (II) or a form thereof in combination with an effective amount of the one or more agents.

In an aspect of a use or method provided herein, compounds of Formula (I) or Formula (II) or a form thereof used in combination with one or more additional agents can be administered to a subject or contacted with a subject or patient cell(s) prior to, concurrently with, or subsequent to administering to the subject or patient or contacting the cell with an additional agent(s). A compound(s) of Formula (I) or Formula (II) or a form thereof and an additional agent(s) can be administered to a subject or contacted with a cell in single composition or different compositions. In a specific aspect, a compound(s) of Formula (I) or Formula (II) or a form thereof is used in combination with gene therapy to inhibit HTT expression (using, *e.g.*, viral delivery vectors) or the administration of another small molecule HTT inhibitor. In another specific aspect, a compound(s) of Formula (I) or Formula (II) or a form thereof are used in combination with cell

replacement using differentiated non-mutant HTT stem cells. In another specific aspect, a compound(s) of Formula (I) or Formula (II) or a form thereof are used in combination with cell replacement using differentiated HTT stem cells.

In one aspect, provided herein is the use of compounds of Formula (I) or Formula (II) or a form thereof in combination with supportive standard of care therapies, including palliative care.

An aspect of the present description includes a use for a compound of Formula (I) or Formula (II) or a form thereof in the preparation of a kit for treating or ameliorating HD in a subject in need thereof comprising, the compound of Formula (I) or Formula (II) or a form thereof and instructions for administering an effective amount of the compound of Formula (I) or Formula (II) or a form thereof.

An aspect of the present description includes a use for a compound of Formula (I) or Formula (II) or a form thereof in the preparation of a kit for treating or ameliorating HD in a subject in need thereof comprising, the compound of Formula (I) or Formula (II) or a form thereof and instructions for administering an effective amount of the compound of Formula (I) or Formula (II) or a form thereof; and optionally, for administering to the subject an effective amount of the compound of Formula (I) or Formula (II) or a form thereof in a combination product with an effective amount of one or more therapeutic agents.

An aspect of the present description includes a use for a compound of Formula (I) or Formula (II) or a form thereof in the preparation of a kit for treating or ameliorating HD in a subject in need thereof comprising, the compound of Formula (I) or Formula (II) or a form thereof and instructions for administering an effective amount of the compound of Formula (I) or Formula (II) or a form thereof; and optionally, for administering to the subject an effective amount of the compound of Formula (I) or Formula (II) or a form thereof in a combination product with an effective amount of the one or more therapeutic agents; and optionally, for administering to the subject an effective amount of the compound of Formula (I) or Formula (II) or a form thereof in a combination product with an effective amount of the one or more therapeutic agents in a combination therapy with a standard of care supportive therapy, wherein the standard of care supportive therapy is palliative care.

In one respect, for each of such aspects, the subject is treatment naive. In another respect, for each of such aspects, the subject is not treatment naive.

As used herein, the term "preventing" refers to keeping a disease, disorder or condition from occurring in a subject that may be predisposed to the disease, disorder and/or condition but has not yet been diagnosed as having the disease, disorder and/or condition.

As used herein, the term "treating" refers to inhibiting the progression of a disease, disorder or condition in a subject already exhibiting the symptoms of the disease, disorder and/or condition, *i.e.*, arresting the development of a disease, disorder and/or condition that has already affected the subject.

As used herein, the term "ameliorating" refers to relieving the symptoms of a disease, disorder or condition in a subject already exhibiting the symptoms of the disease, disorder and/or condition, *i.e.*, causing regression of the disease, disorder and/or condition that has already affected the subject.

As used herein, the term "subject" refers to an animal or any living organism having sensation and the power of voluntary movement, and which requires oxygen and organic food. Nonlimiting examples include members of the human, primate, equine, porcine, bovine, murine, rattus, canine and feline specie. In certain aspects, the subject is a mammal or a warm-blooded vertebrate animal. In other aspects, the subject is a human. As used herein, the term "patient" may be used interchangeably with "subject" and "human".

As used herein, the terms "effective amount" or "therapeutically effective amount" mean an amount of compound of Formula (I) or Formula (II) or a form, composition or medicament thereof that achieves a target plasma concentration that is effective in treating or ameliorating HD as described herein and thus producing the desired therapeutic, ameliorative, inhibitory or preventative effect in a subject in need thereof. In one aspect, the effective amount may be the amount required to treat HD in a subject or patient, more specifically, in a human.

In another aspect, the concentration-biological effect relationships observed with regard to a compound of Formula (I) or Formula (II) or a form thereof indicate a target plasma concentration ranging from approximately 0.001 μg/mL to approximately 50 μg/mL, from approximately 0.01 μg/mL to approximately 20 μg/mL, from approximately 0.05 μg/mL to approximately 10 μg/mL, or from approximately 0.1 μg/mL to approximately 5 μg/mL. To achieve such plasma concentrations, the compounds described herein may be administered at doses that vary, such as, for example, without limitation, from 1.0 ng to 10,000 mg.

In one aspect, the dose administered to achieve an effective target plasma concentration may be administered based upon subject or patient specific factors, wherein the doses administered on a weight basis may be in the range of from about 0.001 mg/kg/day to about 3500 mg/kg/day, or about 0.001 mg/kg/day to about 3000 mg/kg/day, or about 0.001 mg/kg/day to about 2500 mg/kg/day, or about 0.001 mg/kg/day to about 2000 mg/kg/day, or about 0.001 mg/kg/day to about 1500 mg/kg/day, or about 0.001 mg/kg/day to about 1000 mg/kg/day, or about 0.001 mg/kg/day to about 500 mg/kg/day, or about 0.001 mg/kg/day to about 250 mg/kg/day, or about 0.001 mg/kg/day to about 200 mg/kg/day, or about 0.001 mg/kg/day to about 150 mg/kg/day, or about 0.001 mg/kg/day to about 100 mg/kg/day, or about 0.001 mg/kg/day to about 75 mg/kg/day, or about 0.001 mg/kg/day to about 50 mg/kg/day, or about 0.001 mg/kg/day to about 25 mg/kg/day, or about 0.001 mg/kg/day to about 10 mg/kg/day, or about 0.001 mg/kg/day to about 5 mg/kg/day, or about 0.001 mg/kg/day to about 1 mg/kg/day, or about 0.001 mg/kg/day to about 0.5 mg/kg/day, or about 0.001 mg/kg/day to about 0.1 mg/kg/day, or from about 0.01 mg/kg/day to about 3500 mg/kg/day, or about 0.01 mg/kg/day to about 3000 mg/kg/day, or about 0.01 mg/kg/day to about 2500 mg/kg/day, or about 0.01 mg/kg/day to about 2000 mg/kg/day, or about 0.01 mg/kg/day to about 1500 mg/kg/day, or about 0.01 mg/kg/day to about 1000 mg/kg/day, or about 0.01 mg/kg/day to about 500 mg/kg/day, or about 0.01 mg/kg/day to about 250 mg/kg/day, or about 0.01 mg/kg/day to about 200 mg/kg/day, or about 0.01 mg/kg/day to about 150 mg/kg/day, or about 0.01 mg/kg/day to about 100 mg/kg/day, or about 0.01 mg/kg/day to about 75 mg/kg/day, or about 0.01 mg/kg/day to about 50 mg/kg/day, or about 0.01 mg/kg/day to about 25 mg/kg/day, or about 0.01 mg/kg/day to about 10 mg/kg/day, or about 0.01 mg/kg/day to about 5 mg/kg/day, or about 0.01 mg/kg/day to about 1 mg/kg/day, or about 0.01 mg/kg/day to about 0.5 mg/kg/day, or about 0.01 mg/kg/day to about 0.1 mg/kg/day, or from about 0.1 mg/kg/day to about 3500 mg/kg/day, or about 0.1 mg/kg/day to about 3000 mg/kg/day, or about 0.1 mg/kg/day to about 2500 mg/kg/day, or about 0.1 mg/kg/day to about 2000 mg/kg/day, or about 0.1 mg/kg/day to about 1500 mg/kg/day, or about 0.1 mg/kg/day to about 1000 mg/kg/day, or about 0.1 mg/kg/day to about 500 mg/kg/day, or about 0.1 mg/kg/day to about 250 mg/kg/day, or about 0.1 mg/kg/day to about 200 mg/kg/day, or about 0.1 mg/kg/day to about 150 mg/kg/day, or about 0.1 mg/kg/day to about 100 mg/kg/day, or about 0.1 mg/kg/day to about 75 mg/kg/day, or about 0.1 mg/kg/day to about 50 mg/kg/day, or about 0.1 mg/kg/day to about 25 mg/kg/day, or about 0.1 mg/kg/day to about 10 mg/kg/day, or about 0.1 mg/kg/day to

about 5 mg/kg/day, or about 0.1 mg/kg/day to about 1 mg/kg/day, or about 0.1 mg/kg/day to about 0.5 mg/kg/day.

Effective amounts for a given subject may be determined by routine experimentation that is within the skill and judgment of a clinician or a practitioner skilled in the art in light of factors related to the subject. Dosage and administration may be adjusted to provide sufficient levels of the active agent(s) or to maintain the desired effect. Factors which may be taken into account include genetic screening, severity of the disease state, status of disease progression, general health of the subject, ethnicity, age, weight, gender, diet, time of day and frequency of administration, drug combination(s), reaction sensitivities, experience with other therapies, and tolerance/response to therapy.

The dose administered to achieve an effective target plasma concentration may be orally administered once (once in approximately a 24 hour period; i.e., "q.d."), twice (once in approximately a 12 hour period; i.e., "b.i.d." or "q.12h"), thrice (once in approximately an 8 hour period; i.e., "t.i.d." or "q.8h"), or four times (once in approximately a 6 hour period; i.e., "q.d.s.", "q.i.d." or "q.6h") daily.

In certain aspects, the dose administered to achieve an effective target plasma concentration may also be administered in a single, divided, or continuous dose for a patient or subject having a weight in a range of between about 40 to about 200 kg (which dose may be adjusted for patients or subjects above or below this range, particularly children under 40 kg). The typical adult subject is expected to have a median weight in a range of about 70 kg. Long-acting pharmaceutical compositions may be administered every 2, 3 or 4 days, once every week, or once every two weeks depending on half-life and clearance rate of the particular formulation.

The compounds and compositions described herein may be administered to the subject via any drug delivery route known in the art. Nonlimiting examples include oral, ocular, rectal, buccal, topical, nasal, sublingual, transdermal, subcutaneous, intramuscular, intraveneous (bolus and infusion), intracerebral, and pulmonary routes of administration.

In another aspect, the dose administered may be adjusted based upon a dosage form described herein formulated for delivery at about 0.02, 0.025, 0.03, 0.05, 0.06, 0.075, 0.08, 0.09, 0.10, 0.20, 0.25, 0.30, 0.50, 0.60, 0.75, 0.80, 0.90, 1.0, 1.10, 1.20, 1.25, 1.50, 1.75, 2.0, 3.0, 5.0, 10, 20, 30, 40, 50, 100, 150, 200, 250, 300, 400, 500, 1000, 1500, 2000, 2500, 3000 or 4000 mg/day.

For any compound, the effective amount can be estimated initially either in cell culture assays or in relevant animal models, such as a mouse, guinea pig, chimpanzee, marmoset or tamarin animal model. Relevant animal models may also be used to determine the appropriate concentration range and route of administration. Such information can then be used to determine useful doses and routes for administration in humans. Therapeutic efficacy and toxicity may be determined by standard pharmaceutical procedures in cell cultures or experimental animals, *e.g.*, ED_{50} (the dose therapeutically effective in 50% of the population) and LD_{50} (the dose lethal to 50% of the population). The dose ratio between therapeutic and toxic effects is therapeutic index, and can be expressed as the ratio, LD_{50}/ED_{50}. In certain aspects, the effective amount is such that a large therapeutic index is achieved. In further particular aspects, the dosage is within a range of circulating concentrations that include an ED_{50} with little or no toxicity. The dosage may vary within this range depending upon the dosage form employed, sensitivity of the patient, and the route of administration.

In one aspect, provided herein are methods for modulating the amount of HTT (huntingtin protein), comprising contacting a human cell with a compound of Formula (I) or Formula (II) or a form thereof. In a specific aspect, provided herein are methods for modulating the amount of HTT, comprising contacting a human cell with a compound of Formula (I) or Formula (II) or a form thereof that modulates the expression of HTT. The human cell can be contacted with a compound of Formula (I) or Formula (II) or a form thereof *in vitro*, or *in vivo*, *e.g.*, in a non-human animal or in a human. In a specific aspect, the human cell is from or in a human. In another specific aspect, the human cell is from or in a human with HD. In another specific aspect, the human cell is from or in a human with HD, caused by a CAG repeat in the Htt gene, resulting in a loss of HTT expression and/or function. In another aspect, the human cell is from a human with HD. In another aspect, the human cell is in a human with HD. In one aspect, the compound is a form of the compound of Formula (I) or Formula (II).

In a specific aspect, provided herein is a method for enhancing the inhibition of mutant HTT transcribed from the Htt gene, comprising contacting a human cell with a compound of Formula (I) or Formula (II) or a form thereof. The human cell can be contacted with a compound of Formula (I) or Formula (II) or a form thereof *in vitro*, or *in vivo*, *e.g.*, in a non-human animal or in a human. In a specific aspect, the human cell is from or in a human. In another specific aspect, the human cell is from or in a human with HD. In another specific aspect, the human cell is from

or in a human with HD, caused by a CAG repeat in the Htt gene, resulting in a loss of wild-type "normal" HTT expression and/or function. In another aspect, the human cell is from a human with HD. In another aspect, the human cell is in a human with HD. In one aspect, the compound is a form of the compound of Formula (I) or Formula (II).

In another aspect, provided herein is a method for modulating the inhibition of mutant HTT transcribed from the Htt gene, comprising administering to a non-human animal model for HD a compound of Formula (I) or Formula (II) or a form thereof. In a specific aspect, provided herein is a method for modulating the inhibition of mutant HTT transcribed from the Htt gene, comprising administering to a non-human animal model for HD a compound of Formula (I) or Formula (II) or a form thereof. In a specific aspect, the compound is a form of the compound of Formula (I) or Formula (II).

In another aspect, provided herein is a method for decreasing the amount of mutant HTT, comprising contacting a human cell with a compound of Formula (I) or Formula (II) or a form thereof. In a specific aspect, provided herein is a method for decreasing the amount of mutant HTT, comprising contacting a human cell with a compound of Formula (I) or Formula (II) that inhibits the transcription of mutant *HTT* (huntingtin mRNA) from the Htt gene. In another specific aspect, provided herein is a method for decreasing the amount of HTT, comprising contacting a human cell with a compound of Formula (I) or Formula (II) that inhibits the expression of mutant HTT transcribed from the Htt gene. The human cell can be contacted with a compound of Formula (I) or Formula (II) or a form thereof *in vitro*, or *in vivo*, *e.g.*, in a non-human animal or in a human. In a specific aspect, the human cell is from or in a human. In another specific aspect, the human cell is from or in a human with HD. In another specific aspect, the human cell is from or in a human with HD, caused by a CAG repeat in the Htt gene, resulting in a loss of HTT expression and/or function. In another aspect, the human cell is from a human with HD. In another aspect, the human cell is in a human with HD. In one aspect, the compound is a form of the compound of Formula (I) or Formula (II).

In certain aspects, treating or ameliorating HD with a compound of Formula (I) or Formula (II) or a form thereof (alone or in combination with an additional agent) has a therapeutic effect and/or beneficial effect. In a specific aspect, treating HD with a compound of Formula (I) or Formula (II) or a form thereof (alone or in combination with an additional agent) results in one, two or more of the following effects: (i) reduces or ameliorates the severity of HD; (ii) delays

onset of HD; (iii) inhibits the progression of HD; (iv) reduces hospitalization of a subject; (v) reduces hospitalization length for a subject; (vi) increases the survival of a subject; (vii) improves the quality of life for a subject; (viii) reduces the number of symptoms associated with HD; (ix) reduces or ameliorates the severity of a symptom(s) associated with HD; (x) reduces the duration of a symptom associated with HD; (xi) prevents the recurrence of a symptom associated with HD; (xii) inhibits the development or onset of a symptom of HD; and/or (xiii) inhibits of the progression of a symptom associated with HD.

METABOLITES

Another aspect included within the scope of the present description are the use of *in vivo* metabolic products of the compounds described herein. Such products may result, for example, from the oxidation, reduction, hydrolysis, amidation, esterification and the like of the administered compound, primarily due to enzymatic processes. Accordingly, the description includes the use of compounds produced by a process comprising contacting a compound described herein with a mammalian tissue or a mammal for a period of time sufficient to yield a metabolic product thereof.

Such products typically are identified by preparing a radio-labeled isotopologue (*e.g.*, ^{14}C or ^{3}H) of a compound described herein, administering the radio-labeled compound in a detectable dose (*e.g.*, greater than about 0.5 mg/kg) to a mammal such as a rat, mouse, guinea pig, dog, monkey or human, allowing sufficient time for metabolism to occur (typically about 30 seconds to about 30 hours), and identifying the metabolic conversion products from urine, bile, blood or other biological samples. The conversion products are easily isolated since they are "radiolabeled" by virtue of being isotopically-enriched (others are isolated by the use of antibodies capable of binding epitopes surviving in the metabolite). The metabolite structures are determined in conventional fashion, *e.g.*, by MS or NMR analysis. In general, analysis of metabolites may be done in the same way as conventional drug metabolism studies well-known to those skilled in the art. The conversion products, so long as they are not otherwise found *in vivo*, are useful in diagnostic assays for therapeutic dosing of the compounds described herein even if they possess no biological activity of their own.

PHARMACEUTICAL COMPOSITIONS

In accordance with the intended scope of the present description, aspects of the present description include compounds that have been identified and have been demonstrated to be useful in selectively preventing, treating or ameliorating HD and have been provided for use as one or more pharmaceutical compositions for preventing, treating or ameliorating HD.

An aspect of the present description includes a use for a compound of Formula (I) or Formula (II) or a form thereof in the preparation of a pharmaceutical composition for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of the compound of Formula (I) or Formula (II) or a form thereof in admixture with one or more pharmaceutically acceptable excipients.

An aspect of the present description includes a use for a pharmaceutical composition of the compound of Formula (I) or Formula (II) or a form thereof in the preparation of a kit for treating or ameliorating HD in a subject in need thereof comprising, the pharmaceutical composition of the compound of Formula (I) or Formula (II) or a form thereof and instructions for administering the pharmaceutical composition.

As used herein, the term "composition" means a product comprising the specified ingredients in the specified amounts, as well as any product which results, directly or indirectly, from combination of the specified ingredients in the specified amounts.

The pharmaceutical composition may be formulated to achieve a physiologically compatible pH, ranging from about pH 3 to about pH 11. In certain aspects, the pharmaceutical composition is formulated to achieve a pH of from about pH 3 to about pH 7. In other aspects, the pharmaceutical composition is formulated to achieve a pH of from about pH 5 to about pH 8.

The term "pharmaceutically acceptable excipient" refers to an excipient for administration of a pharmaceutical agent, such as the compounds described herein. The term refers to any pharmaceutical excipient that may be administered without undue toxicity. Pharmaceutically acceptable excipients may be determined in part by the particular composition being administered, as well as by the particular mode of administration and/or dosage form. Nonlimiting examples of pharmaceutically acceptable excipients include carriers, solvents, stabilizers, adjuvants, diluents, *etc.* Accordingly, there exists a wide variety of suitable formulations of pharmaceutical compositions for the instant compounds described herein (*see, e.g.*, Remington's Pharmaceutical Sciences).

Suitable excipients may be carrier molecules that include large, slowly metabolized macromolecules such as proteins, polysaccharides, polylactic acids, polyglycolic acids, polymeric amino acids, amino acid copolymers, and inactive antibodies. Other exemplary excipients include antioxidants such as ascorbic acid; chelating agents such as EDTA; carbohydrates such as dextrin, hydroxyalkylcellulose, hydroxyalkylmethylcellulose (*e.g.*, hydroxypropylmethylcellulose, also known as HPMC), stearic acid; liquids such as oils, water, saline, glycerol and ethanol; wetting or emulsifying agents; pH buffering substances; and the like. Liposomes are also included within the definition of pharmaceutically acceptable excipients.

The pharmaceutical compositions described herein may be formulated in any form suitable for the intended use described herein. Suitable formulations for oral administration include solids, liquid solutions, emulsions and suspensions, while suitable inhalable formulations for pulmonary administration include liquids and powders. Alternative formulations include syrups, creams, ointments, tablets, and lyophilized solids which can be reconstituted with a physiologically compatible solvent prior to administration.

When intended for oral use for example, tablets, troches, lozenges, aqueous or oil suspensions, non-aqueous solutions, dispersible powders or granules (including micronized particles or nanoparticles), emulsions, hard or soft capsules, syrups or elixirs may be prepared. Compositions intended for oral use may be prepared according to any method known to the art for the manufacture of pharmaceutical compositions, and such compositions may contain one or more agents including sweetening agents, flavoring agents, coloring agents, and preserving agents, in order to provide a palatable preparation.

Pharmaceutically acceptable excipients suitable for use in conjunction with tablets include, for example, inert diluents, such as celluloses, calcium or sodium carbonate, lactose, calcium or sodium phosphate; disintegrating agents, such as croscarmellose sodium, cross-linked povidone, maize starch, or alginic acid; binding agents, such as povidone, starch, gelatin or acacia; and lubricating agents, such as magnesium stearate, stearic acid, or talc. Tablets may be uncoated or may be coated by known techniques including microencapsulation to delay disintegration and adsorption in the gastrointestinal tract and thereby provide a sustained action over a longer period. For example, a time delay material such as glyceryl monostearate or glyceryl distearate alone or with a wax may be employed.

Formulations for oral use may be also presented as hard gelatin capsules where the active ingredient is mixed with an inert solid diluent, for example celluloses, lactose, calcium phosphate, or kaolin, or as soft gelatin capsules wherein the active ingredient is mixed with non-aqueous or oil medium, such as glycerin, propylene glycol, polyethylene glycol, peanut oil, liquid paraffin, or olive oil.

In other aspects, pharmaceutical compositions described herein may be formulated as suspensions comprising a compound of Formula (I) or Formula (II) or a form thereof in admixture with one or more pharmaceutically acceptable excipients suitable for the manufacture of a suspension. In yet other aspects, pharmaceutical compositions described herein may be formulated as dispersible powders and granules suitable for preparation of a suspension by the addition of one or more excipients.

Excipients suitable for use in connection with suspensions include suspending agents, such as sodium carboxymethylcellulose, methylcellulose, hydroxypropyl methylcelluose, sodium alginate, polyvinylpyrrolidone, gum tragacanth, gum acacia, dispersing or wetting agents such as a naturally occurring phosphatide (*e.g.*, lecithin), a condensation product of an alkylene oxide with a fatty acid (*e.g.*, polyoxyethylene stearate), a condensation product of ethylene oxide with a long chain aliphatic alcohol (*e.g.*, heptadecaethyleneoxycethanol), a condensation product of ethylene oxide with a partial ester derived from a fatty acid and a hexitol anhydride (*e.g.*, polyoxyethylene sorbitan monooleate); and thickening agents, such as carbomer, beeswax, hard paraffin, or cetyl alcohol. The suspensions may also contain one or more preservatives such as acetic acid, methyl and/or n-propyl p-hydroxy-benzoate; one or more coloring agents; one or more flavoring agents; and one or more sweetening agents such as sucrose or saccharin.

The pharmaceutical compositions described herein may also be in the form of oil-in-water emulsions. The oily phase may be a vegetable oil, such as olive oil or arachis oil, a mineral oil, such as liquid paraffin, or a mixture of these. Suitable emulsifying agents include naturally-occurring gums, such as gum acacia and gum tragacanth; naturally occurring phosphatides, such as soybean lecithin, esters or partial esters derived from fatty acids; hexitol anhydrides, such as sorbitan monooleate; and condensation products of these partial esters with ethylene oxide, such as polyoxyethylene sorbitan monooleate. The emulsion may also contain sweetening and flavoring agents. Syrups and elixirs may be formulated with sweetening agents, such as glycerol,

sorbitol or sucrose. Such formulations may also contain a demulcent, a preservative, a flavoring or a coloring agent.

Additionally, the pharmaceutical compositions described herein may be in the form of a sterile injectable preparation, such as a sterile injectable aqueous emulsion or oleaginous suspension. Such emulsion or suspension may be formulated according to the known art using those suitable dispersing or wetting agents and suspending agents which have been mentioned above. The sterile injectable preparation may also be a sterile injectable solution or suspension in a non-toxic parenterally acceptable diluent or solvent, such as a solution in 1,2-propanediol. The sterile injectable preparation may also be prepared as a lyophilized powder. Among the acceptable vehicles and solvents that may be employed are water, Ringer's solution and isotonic sodium chloride solution. In addition, sterile fixed oils may be employed as a solvent or suspending medium. For this purpose any bland fixed oil may be employed including synthetic mono- or di-glycerides. In addition, fatty acids such as oleic acid may likewise be used in the preparation of injectables.

The compounds described herein may be substantially insoluble in water and sparingly soluble in most pharmaceutically acceptable protic solvents and vegetable oils, but generally soluble in medium-chain fatty acids (*e.g.*, caprylic and capric acids) or triglycerides and in propylene glycol esters of medium-chain fatty acids. Thus, contemplated in the description are compounds which have been modified by substitutions or additions of chemical or biochemical moieties which make them more suitable for delivery (*e.g.*, increase solubility, bioactivity, palatability, decrease adverse reactions, *etc.*), for example by esterification, glycosylation, PEGylation, etc.

In certain aspects, the compound described herein is formulated for oral administration in a lipid-based composition suitable for low solubility compounds. Lipid-based formulations can generally enhance the oral bioavailability of such compounds. As such, pharmaceutical compositions described herein may comprise a effective amount of a compound of Formula (I) or Formula (II) or a form thereof, together with at least one pharmaceutically acceptable excipient selected from medium chain fatty acids or propylene glycol esters thereof (*e.g.*, propylene glycol esters of edible fatty acids such as caprylic and capric fatty acids) and pharmaceutically acceptable surfactants, such as polysorbate 20 or 80 (also referred to as Tween® 20 or Tween® 80, respectively) or polyoxyl 40 hydrogenated castor oil.

In other aspects, the bioavailability of low solubility compounds may be enhanced using particle size optimization techniques including the preparation of nanoparticles or nanosuspensions using techniques known to those skilled in the art. The compound forms present in such preparations include amorphous, partially amorphous, partially crystalline or crystalline forms.

In alternative aspects, the pharmaceutical composition may further comprise one or more aqueous solubility enhancer(s), such as a cyclodextrin. Nonlimiting examples of cyclodextrin include hydroxypropyl, hydroxyethyl, glucosyl, maltosyl and maltotriosyl derivatives of α-, β-, and γ-cyclodextrin, and hydroxypropyl-β-cyclodextrin (HPBC). In certain aspects, the pharmaceutical composition further comprises HPBC in a range of from about 0.1% to about 20%, from about 1% to about 15%, or from about 2.5% to about 10%. The amount of solubility enhancer employed may depend on the amount of the compound in the composition.

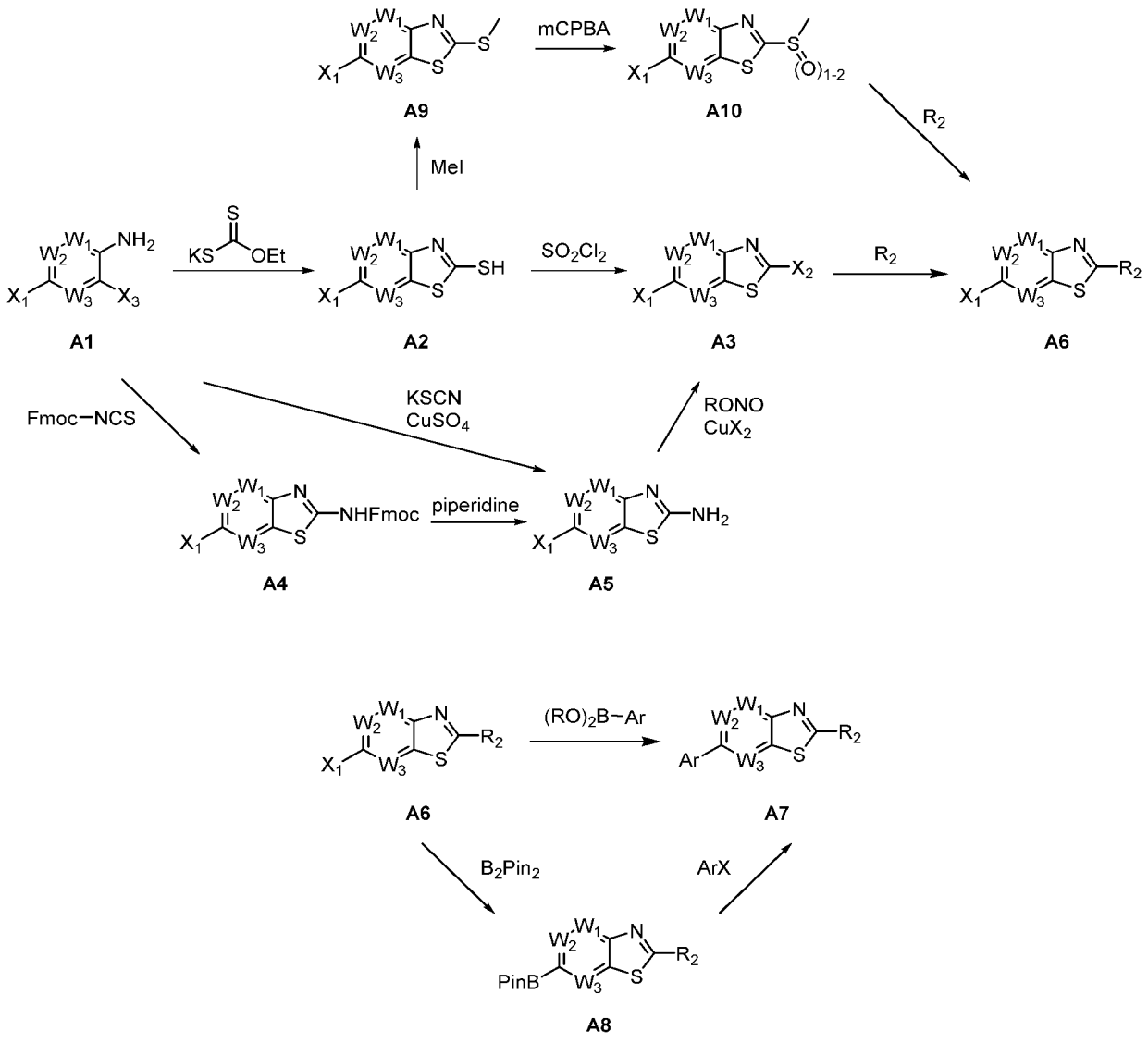
PREPARATION OF COMPOUNDS

GENERAL SYNTHETIC METHODS

As disclosed herein, general methods for preparing the compounds of Formula (I) or Formula (II) or a form thereof as described herein are available via standard, well-known synthetic methodology. Many of the starting materials are commercially available or, when not available, can be prepared using the routes described below using techniques known to those skilled in the art. The synthetic schemes provided herein comprise multiple reaction steps, each of which is intended to stand on its own and can be carried out with or without any preceding or succeeding step(s). In other words, each of the individual reaction steps of the synthetic schemes provided herein in isolation is contemplated.

Scheme A:

Compounds of Formula (I) or Formula (II), wherein R_1 and R_2 independently selected from C_{3-10}cycloalkyl, heterocyclyl, phenyl, or heteroaryl ring systems, may be prepared as described in Scheme A below.

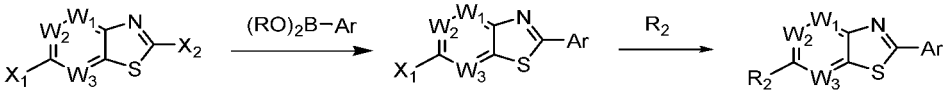


Compound **A1** (where X_1 and X_3 are independently bromine, chlorine, fluorine and the like; W_1, W_2, and W_3 are independently C-R_a or N, where R_a can be functional substituents for further derivatization using techniques known to a person of ordinary skill in the art) is converted to Compound **A2** by reacting with potassium ethyl xanthate in a suitable solvent (such as DMF and the like) at elevated temperature (such as 130 °C), which is further reacted with sulfuryl

chloride to give Compound **A3** (X_2=Cl). Alternatively, Compound **A1** is reacted with Fmoc-NCS to give Compound **A4** which is deprotected by an amine (such as piperidine and the like) to afford Compound **A5**. Alternatively, Compound **A1** is reacted with KNCS in the presence of $CuSO_4$ in a suitable solvent (such as MeOH and the like) to give Compound **A5**. Compound **A5** is then converted to **A3** (X_2=Cl, Br) by a Sandmeyer reaction using alkyl nitrite (such as t-butyl nitrite and the like) and copper (II) halide in a suitable solvent (such as acetonitrile and the like). Compound **A3** is converted to **A6** by a nucleophilic substitution with a primary or secondary amine or an alcohol in the presence of a suitable base (such as NaH, K_2CO_3 and the like) in a suitable solvent (such as DMF and the like). Alternatively, Compound **A2** can be reacted with iodomethane to give Compound **A9**, which can be oxidized by an oxidant like mCPBA to give Compound **A10**. Compound **A10** is converted to **A6** by a nucleophilic substitution with a primary or secondary amine or an alcohol in the presence of a suitable base (such as NaH, K_2CO_3 and the like) in a suitable solvent (such as DMF and the like).Compound **A6** is converted to Compound **A7** by a Suzuki coupling with an aryl- or heteroaryl-boronic acid (or pinacol boronic ester) in the presence of a catalyst (such as $Pd(dppf)Cl_2$ and the like) and base (such as aqueous K_2CO_3 and the like) in a suitable solvent (such as 1,4-dioxane and the like). Alternatively, compound **A6** is converted to compound **A8** by coupling with B_2Pin_2 in the presence of a catalyst (such as $Pd(dppf)Cl_2$ and the like) and base (such as KOAc and the like) in a suitable solvent (such as 1,4-dioxane and the like). Compound **A8** is further coupled with an aryl halide or heteroaryl halide in the presence of a catalyst (such as $Pd(dppf)Cl_2$ and the like) and base (such as aqueous K_2CO_3 and the like) in a suitable solvent (such as 1,4-dioxane and the like) to give Compound **A7**.

Scheme B:

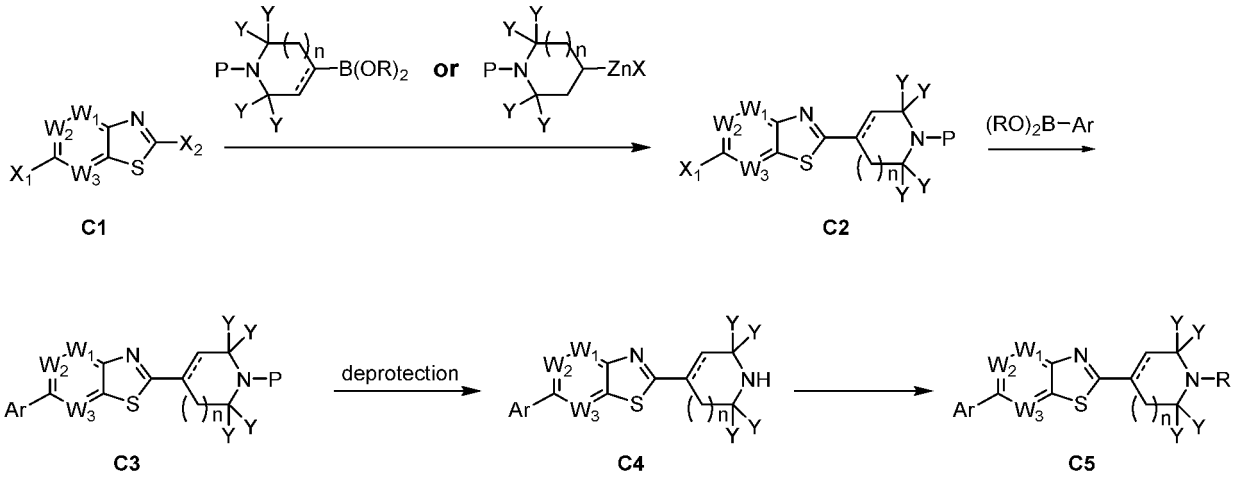
Compounds of Formula (II), wherein R_1 and R_2 independently selected from C_{3-10}cycloalkyl, heterocyclyl, phenyl, or heteroaryl ring systems, may be prepared as described in Scheme B below.



Compound **B1** (where X_1 and X_2 are independently bromine, chlorine and the like; W_1, W_2, and W_3 are independently C-R_a or N, where R_a can be functional substituents for further derivatization using techniques known to a person of ordinary skill in the art) is converted to **B2** by a Suzuki coupling with an aryl- or heteroaryl-boronic acid (or pinacol boronic ester) in the presence of a catalyst (such as $Pd(dppf)Cl_2$ and the like) and base (such as aqueous K_2CO_3 and the like) in a suitable solvent (such as 1,4-dioxane and the like). Compound **B2** is converted to Compound **B3** by a nucleophilic substitution with a primary or secondary amine in the presence of a suitable base (such as K_2CO_3 and the like) in a suitable solvent (such as DMF and the like), or by a Hartwig-Buchwald coupling in the presence of a catalyst (such as $Pd_2(dba)_3$/RuPhos and the like) and base (such as t-BuONa and the like) in a suitable solvent (such as 1,4-dioxane and the like).

Scheme C:

Compounds of Formula (I) or Formula (II), wherein R_1 and R_2 independently selected from $C_{3\text{-}10}$cycloalkyl, heterocyclyl, phenyl, or heteroaryl ring systems, may be prepared as described in Scheme C below.

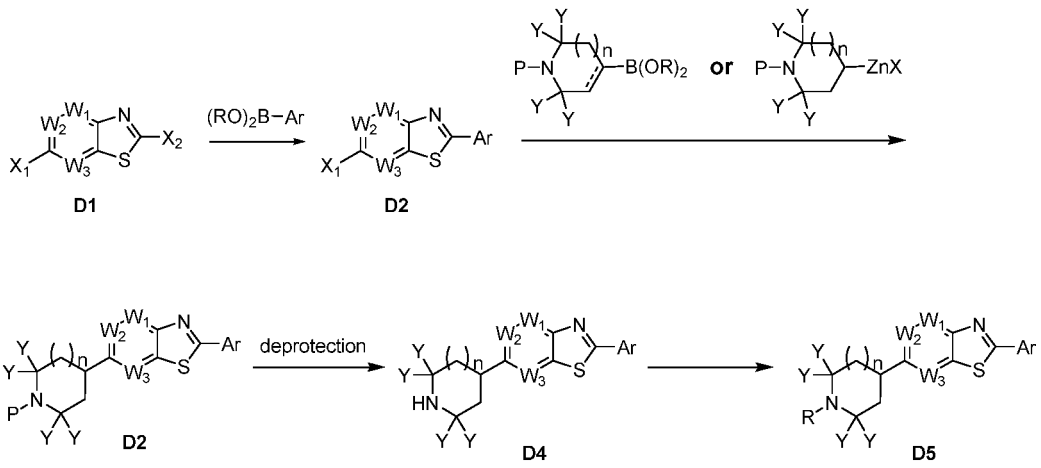


Compound **C1** (where X_1 and X_2 are independently bromine, chlorine and the like; W_1, W_2, and W_3 are independently C-R_a or N, where R_a can be functional substituents for further derivatization using techniques known to a person of ordinary skill in the art) is converted to Compound **C2** by a Suzuki coupling with an optionally substituted and appropriately protected amino-containing cycloalkyl/cycloalkenyl pinacol boronic ester (where Y is hydrogen or an

optionally substituted alkyl group and P is a protecting group such as Boc and the like) in the presence of a catalyst (such as $Pd(dppf)Cl_2$ and the like) and base (such as aqueous K_2CO_3 and the like) in a suitable solvent (such as 1,4-dioxane and the like). Alternatively, Compound **C1** is converted to Compound **C2** by a Negishi coupling with an optionally substituted and appropriately protected amino-containing cycloalkyl zinc halide in the presence of a catalyst (such as $Pd(dppf)Cl_2$ and the like) in a suitable solvent (such as 1,4-dioxane and the like). Compound **C2** is converted to Compound **C3** by a Suzuki coupling with an aryl- or heteroaryl-boronic acid (or pinacol boronic ester) in the presence of a catalyst (such as $Pd(dppf)Cl_2$ and the like) and base (such as aqueous K_2CO_3 and the like) in a suitable solvent (such as 1,4-dioxane and the like). Upon treatment with a deprotecting agent appropriate for the protecting group (such as HCl in dioxane for a Boc protecting group), Compound **C3** is converted to Compound **C4**. Compound **C4** is converted to Compound **C5** by reductive amination with a suitable aldehyde and reducing agent (such as $NaBH(OAc)_3$ and the like) in a suitable solvent (such as 1,2-dichloroethane and the like). Alternatively, Compound **C4** is converted to Compound **C5** by alkylation with an alkyl halide (such as 2-iodopropane and the like) in the presence of an appropriate base (such as K_2CO_3 and the like). In cases where unsaturation exists in the ring containing the basic amino group, the compound may be converted to the fully saturated analog under an atmosphere of H_2 in a suitable solvent (such as methanol and the like) and in the presence of catalyst (such as 10% Pd/C and the like).

Scheme D:

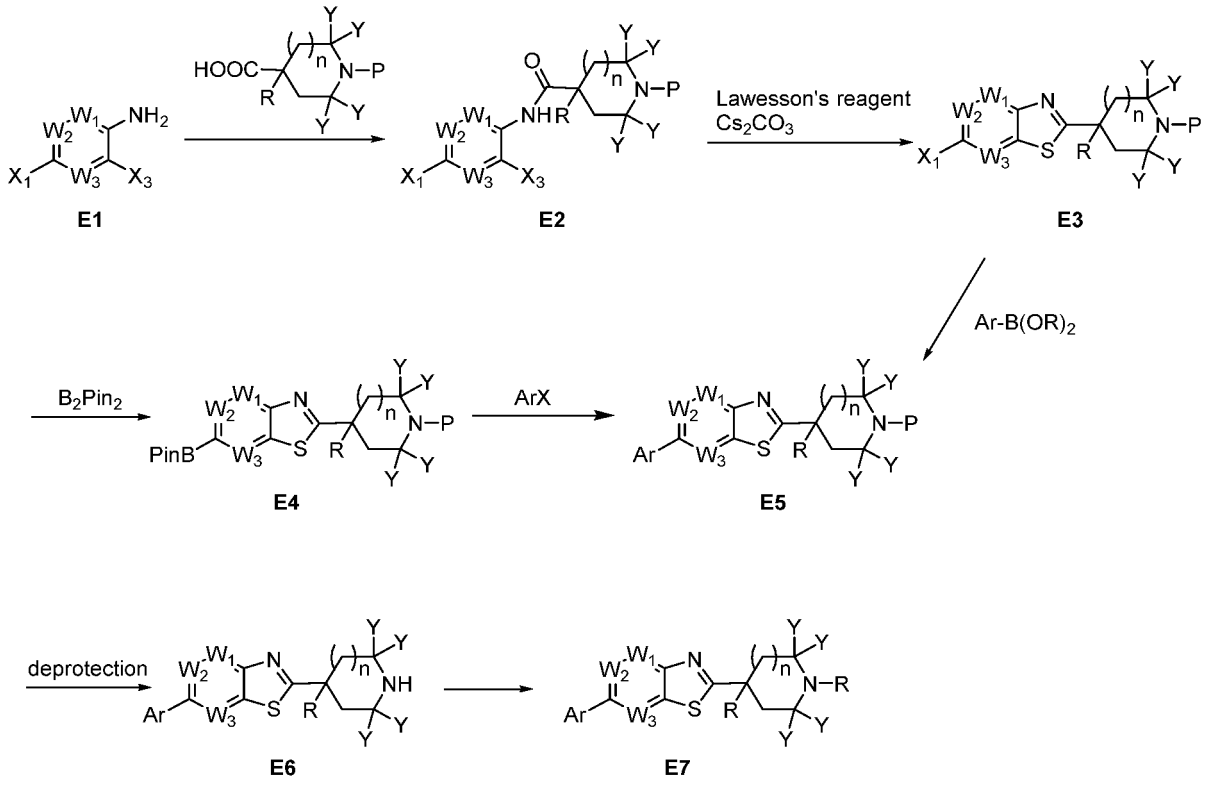
Compounds of Formula (II), wherein R_1 and R_2 independently selected from C_{3-10}cycloalkyl, heterocyclyl, phenyl, or heteroaryl ring systems, may be prepared as described in Scheme D below.



Compound **D1** can be converted to Compound **D4** and **D5** using the conditions described in Scheme C where steps 1 and 2 are reversed.

.Scheme E:

Compounds of Formula (I) or Formula (II), wherein R_1 and R_2 independently selected from C_{3-10}cycloalkyl, heterocyclyl, phenyl, or heteroaryl ring systems, may be prepared as described in Scheme E below.

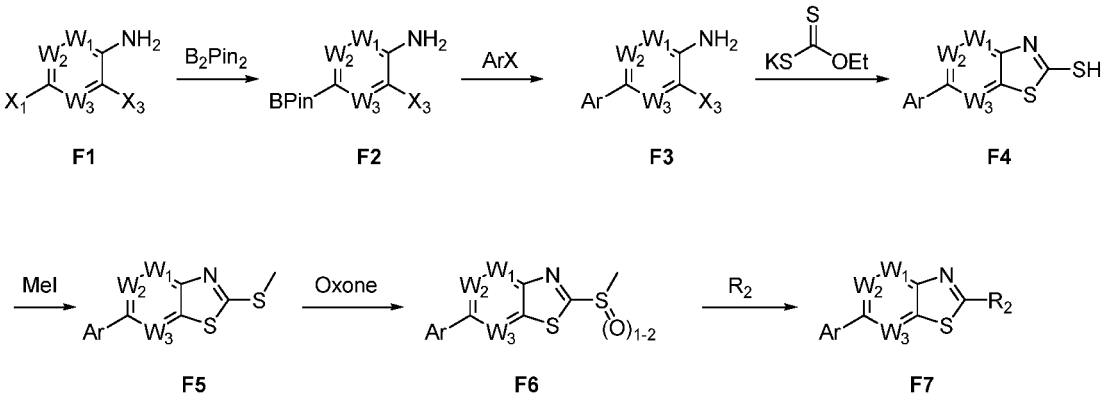


Compound **E1** (where X_1 and X_3 are independently bromine, chlorine, fluorine and the like; W_1, W_2, and W_3 are independently C-R_a or N, where R_a can be functional substituents for further derivatization using techniques known to a person of ordinary skill in the art) is converted to Compound **E2** by reacting with an optionally substituted and appropriately protected amino-containing cycloalkyl/cycloalkenyl carboxylic acid (where Y is hydrogen or an optionally substituted alkyl group, P is a protecting group such as Boc and the like and R is H, halogen or an optionally substituted alkyl group) in the presence of an activating reagent (such as oxalyl chloride and the like) and base (such as aqueous pyridine and the like) in a suitable solvent (such as dichloromethane and the like). Compound **E2** can be treated with Lawesson's Reagent in the presense of base (such as Cs_2CO_3 and the like) in a suitable solvent (such as toluene and the like) to give Compound **E3**. Compound **E3** is converted to compound **E4** by coupling with B_2Pin_2 in

the presence of a catalyst (such as $Pd(dppf)Cl_2$ and the like) and base (such as KOAc and the like) in a suitable solvent (such as 1,4-dioxane and the like). Compound **E4** is further coupled with an aryl halide or heteroaryl halide in the presence of a catalyst (such as $Pd(dppf)Cl_2$ and the like) and base (such as aqueous K_2CO_3 and the like) in a suitable solvent (such as 1,4-dioxane and the like) to give Compound **E5**. Alternatively, Compound **E3** is converted to Compound **E5** by a Suzuki coupling with an aryl- or heteroaryl-boronic acid (or pinacol boronic ester) in the presence of a catalyst (such as $Pd(dppf)Cl_2$ and the like) and base (such as aqueous K_2CO_3 and the like) in a suitable solvent (such as 1,4-dioxane and the like). Upon treatment with a deprotecting agent appropriate for the protecting group (such as HCl in dioxane for a Boc protecting group), Compound **E5** is converted to Compound **E6**. Compound **E6** is converted to Compound **E7** by reductive amination with a suitable aldehyde and reducing agent (such as $NaBH(OAc)_3$ and the like) in a suitable solvent (such as 1,2-dichloroethane and the like).

Scheme F:

Compounds of Formula (I) or Formula (II), wherein R_1 and R_2 independently selected from $C_{3\text{-}10}$cycloalkyl, heterocyclyl, phenyl, or heteroaryl ring systems, may be prepared as described in Scheme F below.



Compound **F1** (where X_1 and X_3 are independently bromine, chlorine, fluorine and the like; W_1, W_2, and W_3 are independently C-R_a or N, where R_a can be functional substituents for further derivatization using techniques known to a person of ordinary skill in the art) is converted to Compound **F2** by coupling with B_2Pin_2 in the presence of a catalyst (such as $Pd(dppf)Cl_2$ and the like) and base (such as KOAc and the like) in a suitable solvent (such as 1,4-dioxane and the like), which was further coupled with an aryl halide or heteroaryl halide in the presence of a

catalyst (such as $Pd(dppf)Cl_2$ and the like) and base (such as aqueous K_2CO_3 and the like) in a suitable solvent (such as 1,4-dioxane and the like) to give Compound **F3**. Compound **F3** is converted to Compound **F4** by reacting with potassium ethyl xanthate in a suitable solvent (such as DMF and the like) at elevated temperature (such as 130 °C), which is further reacted with iodomethane to give Compound **F5**. Oxidation of Compound **F5** by Oxone affords Compound **F6**. Compound **F6** is converted to Compound **F7** by a nucleophilic substitution with a primary or secondary amine in the presence of a suitable base (such as K_2CO_3 and the like) in a suitable solvent (such as DMF and the like).

SPECIFIC SYNTHETIC EXAMPLES

To describe in more detail and assist in understanding, the following non-limiting examples are offered to more fully illustrate the scope of compounds described herein and are not to be construed as specifically limiting the scope thereof. Such variations of the compounds described herein that may be now known or later developed, which would be within the purview of one skilled in the art to ascertain, are considered to fall within the scope of the compounds as described herein and hereinafter claimed. These examples illustrate the preparation of certain compounds. Those of skill in the art will understand that the techniques described in these examples represent techniques, as described by those of ordinary skill in the art, that function well in synthetic practice, and as such constitute preferred modes for the practice thereof. However, it should be appreciated that those of skill in the art should, in light of the present disclosure, appreciate that many changes can be made in the specific methods that are disclosed and still obtain a like or similar result without departing from the spirit and scope of the present description.

Other than in the following examples of the embodied compounds, unless indicated to the contrary, all numbers expressing quantities of ingredients, reaction conditions, experimental data, and so forth used in the specification and claims are to be understood as being modified by the term "about". Accordingly, all such numbers represent approximations that may vary depending upon the desired properties sought to be obtained by a reaction or as a result of variable experimental conditions. Therefore, within an expected range of experimental reproducibility, the term "about" in the context of the resulting data, refers to a range for data provided that may vary according to a standard deviation from the mean. As well, for experimental results provided, the

resulting data may be rounded up or down to present data consistently, without loss of significant figures. At the very least, and not as an attempt to limit the application of the doctrine of equivalents to the scope of the claims, each numerical parameter should be construed in light of the number of significant digits and rounding techniques used by those of skill in the art.

While the numerical ranges and parameters setting forth the broad scope of the present description are approximations, the numerical values set forth in the examples set forth below are reported as precisely as possible. Any numerical value, however, inherently contains certain errors necessarily resulting from the standard deviation found in their respective testing measurements.

COMPOUND EXAMPLES

As used above, and throughout the present description, the following abbreviations, unless otherwise indicated, shall be understood to have the following meanings:

Abbreviation	Meaning
Δ	heating (chemistry) or deletion (biology)
AcOH or HOAc	acetic acid
Ac_2O	acetic anhydride
Ag_2SO_4	silver sulfate
Ar	argon
ACN or CH_3CN	acetonitrile
atm	atmosphere(s)
BBr_3	boron tribromide
BnNHMe	benzyl methylamine
BnOH	benzyl alcohol
Boc	tert-butoxy-carbonyl
Boc_2O	di-tert-butyl dicarbonate
B_2pin_2	bis(pinacolato)diboron
BPin	4,4,5,5-tetramethyl-1,3,2-dioxaborolanyl
Br_2	bromine
Burgess Reagent	methyl *N*-(triethylammoniosulfonyl)carbamate
nBuLi or BuLi	*n*-butyl lithium
t-$BuNH_2$	t-butyl amine
BuOH	*n*-butanol

Abbreviation	Meaning
t-BuONa	sodium t-butoxide
$(t\text{-}Bu)_3P\ HBF_4$	Tri-*t*-butylphosphonium tetrafluoroborate
°C	degrees Centigrade
Cbz-Cl	benzyl chloroformate
CDI	1,1-carbonyldiimidazole or N,N'-carbonyldiimidazole
Celite® or Celite	diatomaceous earth
$(COCl)_2$	oxalyl chloride
$CO(OMe)_2$	dimethyl carbonate
CPME	cyclopropyl methyl ether
CS_2	carbon disulfide
Cs_2CO_3	cesium carbonate
CuI	copper(I) iodide
$CuBr_2$	copper(II) bromide
$CuCl_2$	copper(II) chloride
$CuSO_4$	copper(II) sulfate
d/h/hr/hrs/min/s	day(d)/hour(h, hr or hrs)/minute(min)/second(s)
DAST	(diethylamino)sulfur trifluoride
DCE	1,2-dichloroethane
DCM or CH_2Cl_2	dichloromethane
DDQ	2,3-dichloro-5,6-dicyano-*p*-benzoquinone
DIAD	diisopropyl azodicarboxylate
DIEA or DIPEA	N,*N*-diisopropylethylamine
DMA	dimethylacetamide
DMAP	4-(dimethylamino)pyridine
DME	1,2-dimethoxyethane
DMF	dimethylformamide
DMSO	dimethylsulfoxide
EDC or EDCI	*N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride
EtI	iodoethane
EtOAc	ethyl acetate
EtOH	ethanol
Et_2O	diethyl ether

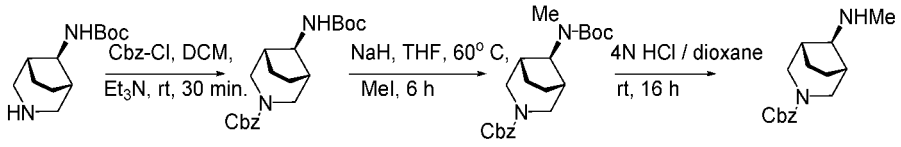
Abbreviation	Meaning
Fmoc-NCS	2-(9H-fluoren-9-yloxy)acetyl isothiocyanate
H_2	hydrogen
HCl	hydrochloric acid
H_2SO_4	sulfuric acid
HATU	1-[bis(dimethylamino)methylene]-1*H*-1,2,3-triazolo[4,5-*b*]pyridinium 3-oxid hexafluorophosphate
iPrI	2-iodopropane, isopropyl iodide
K_2CO_3	potassium carbonate
KOAc	potassium acetate
KOtBu	Potassium *t*-butoxide
KOH	potassium hydroxide
KSCN	potassium thiocyanate
Lawesson's Reagent	2,4-bis(4-methoxyphenyl)-2,4-dithioxo-1,3,2,4-dithiadiphosphetane, 2,4-Bis-(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane 2,4-disulfide
LAH	lithium aluminum hydride
LC/MS, LCMS or LC-MS	liquid chromatographic mass spectroscopy
LDA	lithium diisopropylamine
LHMDS	lithium bis(trimethylsilyl)amide or lithium hexamethyldisilazide
LiOH	lithium hydroxide
MeOH	methanol
MeI	iodomethane
$MeSO_3H$	methanesulfonic acid
Me-THF	2-methyltetrahydrofuran
$MgSO_4$	magnesium sulfate
MS	mass spectroscopy
NBS	*N*-bromosuccinimide
NCS	*N*-chlorosuccinimide
NFSI	*N*-fluorobenzenesulfonimide
NH_4Cl	ammonium chloride
NH_4OAc	ammonium acetate
$NaBH_4$	sodium borohydride

Abbreviation	Meaning
$NaBH(OAc)_3$	sodium triacetoxyborohydride
NaH	sodium hydride
$NaHCO_3$	sodium bicarbonate
NaHMDS	sodium bis(trimethylsilyl)amide or sodium hexamethyldisilazide
NaH	sodium hydride
NaOAc	sodium acetate
NaOH	sodium hydroxide
NaOMe	sodium methoxide
Na_2SO_4	sodium sulfate
N_2	nitrogen
NH_4Cl	ammoniuim chloride
NMP	*N*-methylpyrrolidone
NMR	nuclear magnetic resonance
$Pb(OAc)_4$	lead(IV) acetate or lead tetracetate
Pd	palladium
Pd/C	palladium on carbon
$Pd(dba)_2$	bis(dibenzylideneacetone)palladium
$Pd_2(dba)_3$ or Pd_2dba_3	tris(dibenzylideneacetone)dipalladium(0)
$PdCl_2(PhCN)_2$	trans-bis(benzonitrile)dichloropalladium(II)
$Pd(dppf)Cl_2$ or $Pd(dppf)Cl_2$-CH_2Cl_2	[1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane
$Pd(OAc)_2$	palladium(II) acetate
$Pd(OH)_2$	palladium hydroxide
$Pd(PPh_3)_4$ or $Pd(Ph_3P)_4$	tetrakis(triphenylphosphine)palladium(0)
$Pd(PPh_3)_2Cl_2$, $PdCl_2(PPh_3)_2$ or $PdCl_2(Ph_3P)_2$	bis(triphenylphosphine)palladium(II) dichloride
$PHBu_3BF_4$ or tBu_3PHBF_4	tri-tert-butylphosphonium tetrafluoroborate
PhI	iodobenzene
$PhI(OTFA)_2$	[bis(trifluoroacetoxy)iodo]benzene
PhMe	toluene

Abbreviation	Meaning
Ph-N(Tf)$_2$ or PhN(Tf)$_2$	*N*-phenyl triflimide, also referred to as *N*-phenyl-bis(trifluoromethanesulfonimide)
$POCl_3$	phosphoryl chloride or phosphorous(V) oxychloride
PPh_3	triphenylphosphine
P_2S_5	phosphorous pentasulfide
PhMe	toluene
Psi	pounds per square inch pressure
RT	retention time
RuPhos	2-dicyclohexylphosphino-2′,6′-diisopropoxybiphenyl
$SOCl_2$	thionly chloride
SO_2Cl_2	sulfuryl chloride
S-Phos, SPhos or Sphos	2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl
S-Phos-Pd G_2	chloro(2-dicyclohexylphosphino-2',6'-dimethoxy-1,1'-biphenyl)(2'-amino-1,1'-biphenyl-2-yl) palladium(II)
T_3P	propylphosphonic anhydride
TEA, Et_3N or NEt_3	triethylamine
Ti(OiPr)$_4$	titanium(IV) isopropoxide
Tf_2O	triflic anhydride
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TIPS	tiisopropylsilane
TLC	thin layer chromatography
TMEDA	tetramethylethylenediamine
TMS	trimethylsilane
TMSCl	trimethylchlorosilane or trimethylsilyl chloride
t-Bu	tert-butyl
TsOH, p-TsOH or *p*TSA	tosylic acid or *p*-toluenesulfonic acid
X-Phos	2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl
ZnCN	zinc cyanide

Intermediate 1

Benzyl (1*R*,5*S*,8*S*)-8-(Methylamino)-3-azabicyclo[3.2.1]octane-3-carboxylate



Step 1: tert-Butyl (1*R*,5*S*,8*S*)-3-azabicyclo[3.2.1]octan-8-yl)carbamate (500 mg, 2.21 mmol) was dissolved in CH_2Cl_2 (2.5 mL) and Et_3N (0.36 mL, 2.58 mmol) at 0 °C. Benzyl chloroformate (0.36 mL, 2.44 mmol) was added dropwise. The reaction mixture was then stirred at room temperature for 30 min. The precipitated triethylammonium hydrochloride was filtered off. The filtrate was purified by silica gel chromatography (10-20% EtOAc in CH_2Cl_2), yielding benzyl (1*R*,5*S*,8*S*)-8-((tert-butoxycarbonyl)amino)-3-azabicyclo[3.2.1]octane-3-carboxylate (718 mg, 90%) as a white solid.

^{1}H NMR (acetone-d_6) δ: 7.30-7.45 (m, 5H), 5.86 (br s, 1H), 5.08-5.18 (m, 2H), 3.90-3.96 (m, 2H), 3.61 (m, 1H), 3.09 (d, *J*= 12 Hz, 1H), 2.97 (d, *J*= 12 Hz, 1H), 2.22-2.27 (m, 2H), 1.86-1.89 (m, 2H), 1.43-1.49 (m, 2H), 1.41 (s, 9H).

Step 2: Benzyl (1*R*,5*S*,8*S*)-8-((tert-butoxycarbonyl)amino)-3-azabicyclo[3.2.1]octane-3-carboxylate (716 mg, 1.99 mmol), THF (12 mL), and NaH (60% oil suspension, 160 mg, 4 mmol) were stirred at room temperature for 30 min. MeI (375 µL, 6 mmol) was added. This mixture was heated at 60 °C for 6 h. This mixture was partitioned between EtOAc and H_2O. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. Purification by silica gel chromatography (10-20% EtOAc in CH_2Cl_2) yielded benzyl (1*R*,5*S*,8*S*)-8-((tert-butoxycarbonyl)(methyl)amino)-3-azabicyclo[3.2.1]octane-3-carboxylate (546 mg, 73%) as a clear oil.

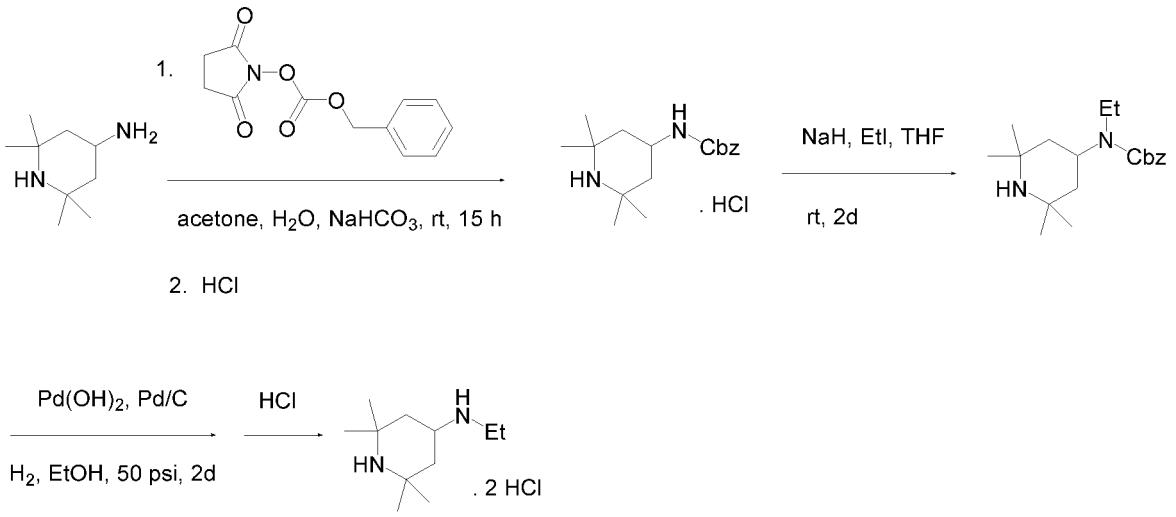
^{1}H NMR (acetone-d_6) δ: 7.30-7.45 (m, 5H), 5.10-5.16 (m, 2H), 3.92-3.97 (m, 2H), 3.78 (s, 1H), 3.13 (d, *J*= 12 Hz, 1H), 3.02 (d, *J*= 12 Hz, 1H), 2.84 (s, 3H), 2.42-2.46 (m, 2H), 1.78-1.83 (m, 2H), 1.53-1.59 (m, 2H), 1.47 (s, 9H).

Step 3: Benzyl (1*R*,5*S*,8*S*)-8-((tert-butoxycarbonyl)(methyl)amino)-3-azabicyclo[3.2.1]octane-3-carboxylate (510 mg, 1.36 mmol) was stirred in 4N HCl in dioxane (2 mL, 8 mmol) at room temperature for 16 h. The reaction mixture was diluted with ether and filtered to yield benzyl (1R,5S,8s)-8-(methylamino)-3-azabicyclo[3.2.1]octane-3-carboxylate hydrochloride (374 mg, 88%) as a white solid.

^{1}H NMR (methanol-d_4) δ: 7.31-7.41 (m, 5H), 5.11-5.20 (m, 2H), 4.04 (dd, J= 13 Hz, 3 Hz, 2H), 3.37 (s, 1H), 3.11 (d, J= 13 Hz, 1H), 3.01 (d, J= 13 Hz, 1H), 2.75 (s, 3H), 2.46-2.54 (m, 2H), 1.82-1.86 (m, 2H), 1.61-1.69 (m, 2H).

Intermediate 2

N-Ethyl-2,2,6,6-tetramethylpiperidin-4-amine Dihydrochloride



Step 1: 2,2,6,6-Tetramethylpiperidin-4-amine (1 g, 6.4 mmol), benzyl (2,5-dioxopyrrolidin-1-yl) carbonate (1.82 g, 7.3 mmol), $NaHCO_3$ (1M in H_2O, 14 mL, 14 mmol), and acetone (20 mL) were stirred at room temperature for 15 h. The product, which was very water-soluble, was extracted from the reaction mixture with ethyl acetate. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The concentrate was treated with HCl in ether and filtered to yield benzyl (2,2,6,6-tetramethylpiperidin-4-yl)carbamate hydrochloride (1.93 g, 92%) as a white solid.

^{1}H NMR (methanol-d_4) δ: 7.30-7.42 (m, 5H), 5.11 (s, 2H), 4.0-4.06 (m, 1H), 2.08 (dd, J= 14 Hz, 3.5 Hz, 2H), 1.54 (br s, 6H), 1.47 (m, 2H), 1.41 (s, 6H).

Step 2: Benzyl (2,2,6,6-tetramethylpiperidin-4-yl)carbamate hydrochloride (1.9 g, 5.8 mmol), THF (19 mL) and 60% NaH suspension (1.9 g, 48 mmol) were stirred at room temperature for 30 min. This was followed by addition of EtI (1.5 mL, 19 mmol). The reaction mixture was stirred at room temperature for 2 days. This mixture was partitioned between EtOAc and H_2O. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. Purification by silica gel chromatography (5-10% MeOH in CH_2Cl_2, with 0.1% NH_4OH modifier) was done. The product was dissolved in ether and was filtered to remove particulate impurities. The filtrate was

concentrated to yield benzyl ethyl(2,2,6,6-tetramethylpiperidin-4-yl)carbamate (701 mg, 38%) as a clear oil.

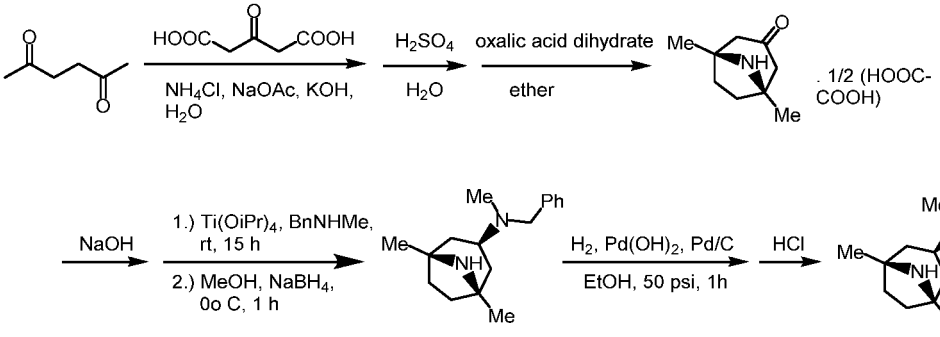
^{1}H NMR (acetone-d_6) δ: 7.30-7.50 (m, 5H), 5.15 (s, 2H), 4.48 (m, 1H), 3.25 (q, J= 7 Hz, 2H), 1.53-1.59 (m, 2H), 1.38 (t, J= 12 Hz, 2H), 1.21 (br 2, 6H), 1.13 (t, J= 7 Hz, 3H), 1.10 (s, 6H).

Step 3: Benzyl ethyl(2,2,6,6-tetramethylpiperidin-4-yl)carbamate (700 mg, 2.2 mmol), ethanol (12 mL), 20% $Pd(OH)_2$ on carbon (100 mg) and 10% Pd/C (100 mg) were hydrogenated at 50 psi for 2 days. The reaction mixture was filtered through Celite®. The filtrate was concentrated and then treated with ethereal HCl. The precipitates that formed were filtered and washed with ether to yield *N*-ethyl-2,2,6,6-tetramethylpiperidin-4-amine dihydrochloride (525 mg, 93%) as a white solid.

^{1}H NMR (methanol-d_4) δ: 8.48 (s, 1H), 3.69 (m, 1H), 3.12 (q, J= 7 Hz, 2H), 2.26 (dd, J= 14 Hz, 3.5 Hz, 2H), 1.67 (t, J= 13 Hz, 2H), 1.51 (s, 12H), 1.35 (t, J= 7 Hz, 3H).

Intermediate 3

(1*R*,3*S*,5*S*)-*N*,1,5-Trimethyl-8-azabicyclo[3.2.1]octan-3-amine Dihydrochloride



Step 1: Hexane-2,5-dione (10.8 mL, 92.1 mmol) and 3-oxopentanedioic acid (26 g, 178 mmol) were dissolved in H_2O (75 mL) at 0 °C. A solution of KOH (23.2 g, 414 mmol) in H_2O (15 mL) was added dropwise, followed by a solution of NaOAc (9 g, 109.7 mmol) and NH_4Cl (15 g, 280.4 mmol) in H_2O (135 mL). Aqueous 50% w/w KOH (8 mL) was added to adjust the pH to 9. More H_2O (60 mL) was added. This was stirred at room temperature over 5 days. The reaction mixture was then re-cooled to 0 °C. 50% w/w H_2SO_4 (120 mL) was added slowly until the pH was 2, resulting in CO_2 evolution. This mixture was then washed with CH_2Cl_2 (2x300 mL). The aqueous layer was made basic with solid KOH. This was extracted into EtOAc (5 x 300 mL). The EtOAc layer was back-washed with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum, yielding crude amine. This was treated with a solution of oxalic acid dihydrate (5.4 g) in 600 mL

of ether. The solid was filtered off, washed with ether, then EtOH, then ether again to yield (1*R*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-one hemi-oxalate (6.085 g, 27.2%) as an off-white solid.

^{1}H NMR (D_2O) δ: 2.79 (d, *J*= 12.5 Hz, 2H), 2.59 (d, *J*= 12.5 Hz, 2H), 1.98-2.06 (m, 4H), 1.50 (s, 6H).

Step 2: (1*R*,5*S*)-1,5-Dimethyl-8-azabicyclo[3.2.1]octan-3-one hemi-oxalate (500 mg) was partitioned between dilute aqueous NaOH and CH_2Cl_2. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum to yield free base (1*R*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-one (330 mg, 2.15 mmol) as a clear light orange liquid. This was dissolved in titanium isopropoxide (2.15 mL, 7.25 mmol) and benzyl methylamine (0.42 mL, 3.3 mmol), and stirred at room temperature for 15 h. The mixture was cooled to 0 °C. MeOH (8.4 mL) was added, followed by $NaBH_4$ (195 mg, 5.15 mmol) in one portion. This was stirred at 0 °C for 1 h. A 50% solution (w/w) of KOH (0.8 mL) was added, and the mixture was then diluted in CH_2Cl_2 and filtered through Celite. CH_2Cl_2/MeOH was used to wash the product off the Celite pad. The filtrate was concentrated under vacuum. Purification by silica gel chromatography (9/1/0.1 CH_2Cl_2/MeOH/NH_4OH) yielded (1*R*,3*S*,5*S*)-*N*-benzyl-N,1,5-trimethyl-8-azabicyclo[3.2.1]octan-3-amine (413 mg, 74%).

^{1}H NMR (methanol-d_4) δ: 7.25-7.40 (m, 5H), 3.61 (s, 2H), 2.92 (m, 1H), 2.23 (s, 3H), 1.72-1.77 (m, 2H), 1.55-1.70 (m, 4H), 1.48 (t, *J*= 12 Hz, 2H), 1.29 (s, 6H).

Step 3: (1*R*,3*S*,5*S*)-*N*-Benzyl-N,1,5-trimethyl-8-azabicyclo[3.2.1]octan-3-amine (395 mg, 1.53 mmol) was dissolved in EtOH (10 mL). Pd/C (10%, 100 mg) and $Pd(OH)_2$ (20% on carbon, 100 mg) were added, and the mixture was hydrogenated at 50 psi for 1 h. The reaction mixture was then filtered through Celite. The filtrate was concentrated under vacuum. The concentrate was triturated with ethereal HCl, and the resultant solids were filtered and washed with ether to yield (1R,3s,5S)-N,1,5-trimethyl-8-azabicyclo[3.2.1]octan-3-amine dihydrochloride (281 mg, 76%) as a white solid.

^{1}H NMR (methanol-d_4) δ: 3.66 (m, 1H), 2.77 (s, 3H), 2.31 (dd, *J*= 14 Hz, 5.5 Hz, 2H), 2.10-2.20 (m, 2H), 1.97-2.07 (m, 2H), 1.94 (t, *J*= 13 Hz, 2H), 1.58 (s, 6H).

Intermediate 3a

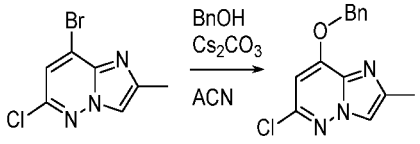
(1*R*,3*r*,5*S*)-1,5-Diethyl-*N*-methyl-8-azabicyclo[3.2.1]octan-3-amine

Intermediate 3a was prepared in a similar manner to Intermediate 3.

^{1}H NMR (methanol-d_4) δ: 3.64 (m, 1H), 2.80 (s, 3H), 2.36 (dd, *J*= 13.5, 4.5 Hz, 2H), 2.14 (m, 2H), 1.85-2.0 (m, 8H), 1.09 (t, *J*= 7.5 Hz, 6H).

Intermediate 4

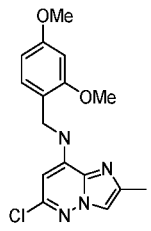
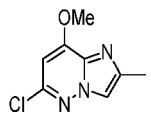
8-(Benzyloxy)-6-chloro-2-methylimidazo[1,2-b]pyridazine

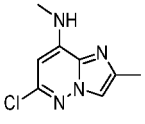
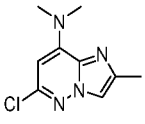


A mixture of 8-bromo-6-chloro-2-methyl-imidazo[1,2-b]pyridazine (100 mg, 0.41 mmol, 1.0 eq.), benzyl alcohol (89 mg, 0.085 mL, 0.81 mmol, 2.0 eq.) and Cs_2CO_3 (400 mg, 1.2 mmol, 3.0 eq.) in acetonitrile (1.0 mL) was stirred at 88 °C overnight, then cooled, diluted with ethyl acetate and filtered through Celite. The filtrate was concentrated and purified over silica with ethyl acetate in CH_2Cl_2 (0 to 10% gradient) to give 8-benzyloxy-6-chloro-2-methyl-imidazo[1,2-b]pyridazine (81 mg, 73%).

^{1}H NMR ($CDCl_3$) δ: 7.62 (d, *J*= 0.6 Hz, 1H), 7.46 - 7.53 (m, 2H), 7.36 - 7.44 (m, 3H), 6.41 (s, 1H), 5.39 (s, 2H), 2.48 (d, *J*= 0.6 Hz, 3H).

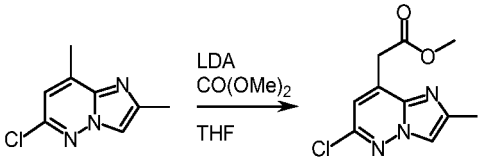
Using the procedures described above, additional intermediates described herein may be prepared by substituting the appropriate starting material, suitable reagents and reaction conditions, obtaining compounds such as those selected from:

Structure	Name and Data
	6-Chloro-*N*-(2,4-dimethoxybenzyl)-2-methylimidazo[1,2-b]pyridazin-8-amine ^{1}H NMR ($CDCl_3$) δ: 7.49 (d, *J*= 0.6 Hz, 1H), 7.18 (d, *J*= 8.2 Hz, 1H), 6.50 (d, *J*= 2.2 Hz, 1H), 6.46 (dd, *J*= 8.2, 2.2 Hz, 1H), 6.11 (br. s., 1H), 6.08 (s, 1H), 4.41 (d, *J*= 6.0 Hz, 2H), 3.86 (s, 3H), 3.83 (s, 3H), 2.41 (d, *J*= 0.9 Hz, 3H).
	6-Chloro-8-methoxy-2-methylimidazo[1,2-b]pyridazine ^{1}H NMR ($CDCl_3$) δ: 7.61 (d, *J*= 0.9 Hz, 1H), 6.38 (s, 1H), 4.09 (s, 3H), 2.47 (d, *J*= 0.6 Hz, 3H).

Structure	Name and Data
	6-Chloro-*N*,2-dimethylimidazo[1,2-b]pyridazin-8-amine ^{1}H NMR ($CDCl_3$) δ: 7.50 (d, *J*= 0.6 Hz, 1H), 5.90 - 6.04 (m, 2H), 3.03 (d, *J*= 5.0 Hz, 3H), 2.42 (d, *J*= 0.6 Hz, 3H).
	6-Chloro-*N*,*N*,2-trimethylimidazo[1,2-b]pyridazin-8-amine ^{1}H NMR ($CDCl_3$) δ: 7.49 (d, *J*= 0.9 Hz, 1H), 5.84 (s, 1H), 3.50 (s, 6H), 2.42 (d, *J*= 0.6 Hz, 3H)

Intermediate 5

Methyl 2-(6-chloro-2-methylimidazo[1,2-b]pyridazin-8-yl)acetate

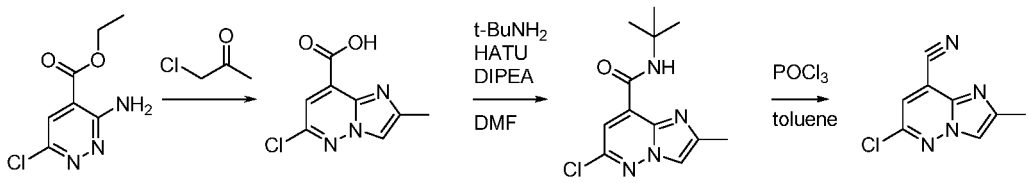


To a solution of 6-chloro-2,8-dimethyl-imidazo[1,2-b]pyridazine (50 mg, 0.28 mmol, 1.0 eq.) in THF (1.2 mL) cooled at -45 °C was added LDA (2.0 M) (0.17 mL, 0.33 mmol, 1.2 eq.) and the mixture was stirred at -45 °C for 30 min before dimethyl carbonate (38 mg, 0.035 mL, 0.41 mmol, 1.5 eq.) was added. After 30 min, the temperature was raised to 0 °C and the mixture was stirred for 2 h before being quenched with saturated NH_4Cl. The mixture was extracted with ethyl acetate, then dried and evaporated. The residue was purified over silica gel with methanol in dichloromethane (0 to 5% gradient) to give methyl 2-(6-chloro-2-methyl-imidazo[1,2-b]pyridazin-8-yl)acetate (48 mg, 0.20 mmol, 0.73 eq., 73%).

^{1}H NMR ($CDCl_3$) δ: 7.63 (d, *J*= 0.6 Hz, 1H), 6.97 (s, 1H), 4.00 (d, *J*= 0.6 Hz, 2H), 3.70 (s, 3H), 2.42 (s, 3H).

Intermediate 6

6-Chloro-2-methylimidazo[1,2-b]pyridazine-8-carbonitrile



Step 1: A mixture of ethyl 3-amino-6-chloro-pyridazine-4-carboxylate (360 mg, 1.8 mmol, 1.0 eq.) and chloroacetone (3.0 mL) was stirred at 100 °C for 48 h, then cooled, diluted with ether and

filtered. The solid was dissolved in methanol and purified with a C18 column to give 6-chloro-2-methyl-imidazo[1,2-b]pyridazine-8-carboxylic acid (150 mg, 40%).

^{1}H NMR (methanol-d_4) δ: 8.36 (br s, 1H), 8.24 (d, J= 7.6 Hz, 1H), 2.64 (s, 3H).

Step 2: To a solution of 6-chloro-2-methyl-imidazo[1,2-b]pyridazine-8-carboxylic acid (150 mg, 0.71 mmol, 1.0 eq.) in DMF (4.0 mL) was added HATU (560 mg, 1.4 mmol, 2.0 eq.). After 10 min, tert-butylamine (78 mg, 0.11 mL, 1.1 mmol, 1.5 eq.) was added followed by DIPEA (280 mg, 0.37 mL, 2.1 mmol, 3.0 eq.). The mixture was then stirred at room temperature for 5 min at which time LC/MS showed a complete reaction. Aqueous work up followed by purification over silica gel with ethyl acetate in hexanes (2 to 20% gradient) provided *N*-tert-butyl-6-chloro-2-methyl-imidazo[1,2-b]pyridazine-8-carboxamide (111 mg, 59%).

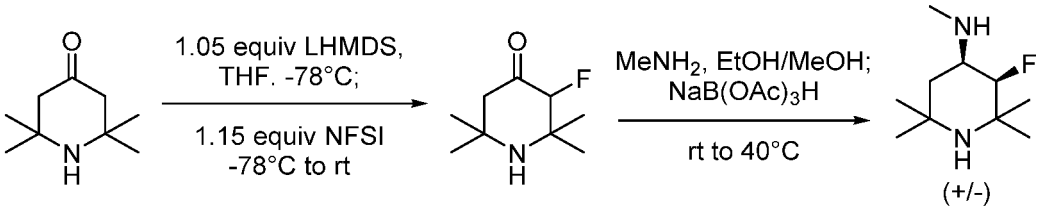
^{1}H NMR ($CDCl_3$) δ: 9.82 - 9.95 (br. s., 1H), 7.81 (s, 1H), 7.76 (d, J= 0.6 Hz, 1H), 2.52 (d, J= 0.6 Hz, 3H), 1.56 (s, 9H).

Step 3: A mixture of *N*-tert-butyl-6-chloro-2-methyl-imidazo[1,2-b]pyridazine-8-carboxamide (102 mg, 0.382 mmol, 0.54 eq.) and $POCl_3$ (0.80 mL, 8.5 mmol, 12 eq.) in toluene (2.0 mL) was stirred at 110 °C for 48 h and then cooled and filtered. The solid was collected as pure 6-chloro-2-methyl-imidazo[1,2-b]pyridazine-8-carbonitrile (110 mg, 81%).

^{1}H NMR ($CDCl_3$) δ: 7.88 (s, 1H), 7.36 (s, 1H), 2.60 (d, J= 0.6 Hz, 3H).

Intermediate 7

rac (3*R*,4*R*)-3-Fluoro-N,2,2,6,6-pentamethylpiperidin-4-amine



Step 1: To an oven-dried vial was added 2,2,6,6-tetramethylpiperidin-4-one (2.60 g, 16.78 mmol), which was cycled under nitrogen. THF (10 mL) was added, and the stirred reaction was cooled to −78 °C. LHMDS (1 mol/L) in THF (17.7 mL, 17.7 mmol) was added dropwise over 5 min. The solution was stirred at −78 °C for 30 min. *N*-Fluorobenzenesulfonimide (6.13 g, 19.45 mmol) was added to the stirred solution at −78 °C portionwise over 5 min. Stirring was continued for 4 h at −78 °C then the reaction was allowed to warm slowly to 23 °C over 16 h. Methanol (20 mL) was

added and the reaction was concentrated to dryness. The residue was purified by silica gel flash column chromatography with dichloromethane in methanol (0-10% gradient) to afford a white solid (1.26 g, 43%).

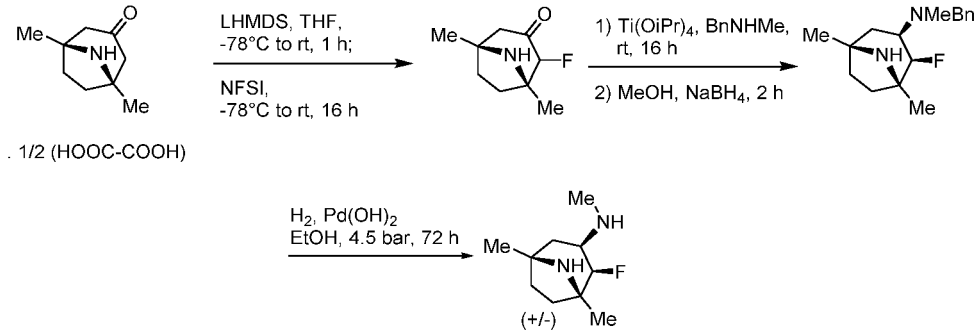
MS *m/z* 174.3 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 4.77 (d, *J*= 0.9 Hz, 1H), 2.60 (d, *J*= 12.5 Hz, 1H), 2.42 (dd, *J*= 12.8, 4.6 Hz, 1H), 1.32 (s, 3H), 1.29 (s, 3H), 1.22 (s, 3H), 1.15 (d, *J*= 3.4 Hz, 3H).

Step 2: To an oven-dried vial was added 3-fluoro-2,2,6,6-tetramethyl-piperidin-4-one (601.4 mg, 3.47 mmol), followed by methanol (15 mL) and methylamine (33 mass% in ethanol) (6 mL, 48.2 mmol). This solution was stirred at 23 °C for 45 min. To this solution was added sodium triacetoxyborohydride (3.01 g, 14.2 mmol) portionwise at room temperature and the solution was stirred for 3 h. The temperature was increased to 40 °C and another portion of sodium triacetoxyborohydride (4.0 equiv., 13.8 mmol) was added portionwise, followed by another 3 h of stirring at 40 °C. A third portion of sodium triacetoxyborohydride (4.0 equiv., 13.8 mmol) was added portionwise while stirring at 40 °C and the reaction was allowed to continue stirring at 40 °C for 16 h. The reaction was concentrated to dryness. The residue was partitioned between dichloromethane/methanol (9/1) and sodium hydroxide solution (1.0 N, aqueous). The layers were separated, and the aqueous layer was subsequently extracted once with dichloromethane/methanol (9/1) and then twice with dichloromethane. The combined organic layers were dried over sodium sulfate, filtered and concentrated to afford a light tan solid in a brown liquid that solidified completely after sitting for 2-3 weeks (519.3 mg, 79%).

MS *m/z* 189.3 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 4.42 (dd, *J*= 50.7, 1.2 Hz, 1H), 3.01 (dddd, *J*= 30.2, 12.5, 4.3, 1.5 Hz, 1H), 2.48 (s, 3H), 1.70 (dd, *J*= 12.8, 4.3 Hz, 1H), 1.36 (t, *J*= 12.7 Hz, 1H), 1.24 (s, 3H), 1.23 (d, *J*= 1.8 Hz, 3H), 1.20 (d, *J*= 2.4 Hz, 3H), 1.19 (s, 3H), NH protons not observed.

Intermediate 8

Rac (1*S*,2*R*,3*R*,5*R*)-2-Fluoro-N,1,5-trimethyl-8-azabicyclo[3.2.1]octan-3-amine



Step 1: To an oven-dried vial was added 1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-one ½ oxalate (491 mg, 2.87 mmol, 1.0 eq.) and THF (5 mL), which was cooled to -78°C. Lithium bis(trimethylsilyl)amide (1.0 M in THF, 11 mL, 11.0 mmol, 3.83 eq.) was added dropwise, and then the suspension was allowed to warm to room temperature over 1 h. The suspension was cooled to -78 °C and then *N*-fluorobenzenesulfonimide (1.98 g, 6.27 mmol, 2.18 eq.) was added portionwise. After complete addition, the reaction was warmed to room temperature over 16 h. The reaction was concentrated under reduced pressure, and then the solid was triturated with CH_2Cl_2/MeOH (1:1). The suspension was filtered and the orange filtrate was concentrated. The residue was purified by column chromatography eluting with 0-40% MeOH in CH_2Cl_2 to yield impure racemic 4-fluoro-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-one (491.3 mg, 57% by mass). MS *m/z* 172.3 $[M+H]^+$.

Step 2: To an oven-dried vial was added impure racemic 4-fluoro-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-one (373 mg, 2.18 mmol, 1.0 eq.), followed by titanium(IV) isopropoxide (3.4 mL, 11 mmol, 5.2 eq.) and *N*-methyl-1-phenyl-methylamine (0.71 mL, 5.5 mmol, 2.5 eq.). The reaction was stirred at room temperature for 16 h. Methanol (10 mL) was added, followed by sodium borohydride (802 mg, 20.7 mmol, 9.53 eq.). Stirring was continued for 2 h at room temperature. The reaction was quenched with aqueous sodium hydroxide (0.2 N, 35 mL). The reaction was then diluted with CH_2Cl_2/MeOH (9:1) and filtered through Celite to remove the emulsions. The layers were then separated, and the aqueous layer was extracted twice with CH_2Cl_2/MeOH (9:1). The combined organic phases were dried over sodium sulfate, filtered and concentrated. The residue was purified by column chromatography, eluting with 0-15%

MeOH in $CH_2Cl_2$to yield rac (1*S*,3*S*,4*S*,5*R*)-*N*-benzyl-4-fluoro-N,1,5-trimethyl-8-azabicyclo[3.2.1]octan-3-amine (40.5 mg, 7%).

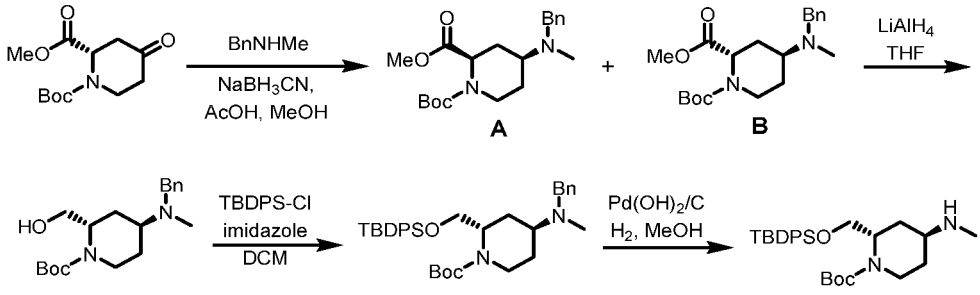
MS *m/z* 277.4 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 7.23-7.42 (m, 5H), 4.60 (dd, *J*= 50.7, 2.4 Hz, 1H), 3.78 (d, *J*= 13.1 Hz, 1H), 3.70 (d, *J*= 13.4 Hz, 1H), 2.85 (dddd, *J*= 36.0, 10.1, 8.2, 2.4 Hz, 1H), 2.34 (s, 3H), 1.77 (br d, *J*= 9.2 Hz, 2H), 1.65-1.71 (m, 2H), 1.56-1.64 (m, 2H), 1.33 (d, *J*= 2.4 Hz, 6H); 1 NH not observed.

Step 3: Rac (1*S*,3*S*,4*S*,5*R*)-*N*-Benzyl-4-fluoro-N,1,5-trimethyl-8-azabicyclo[3.2.1]octan-3-amine (40.5 mg, 0.147 mmol, 1.0 eq.), palladium hydroxide (20% w/w on carbon)(19.4 mg, 0.0276 mmol, 0.19 eq.), and ethanol (5 mL) were combined and shaken under a hydrogen atmosphere at 4.5 atm for 72 h. The reaction was filtered through Celite, and rinsed with EtOH. The filtrate was concentrated to yield rac (1*S*,3*S*,4S,5*R*)-4-fluoro-N,1,5-trimethyl-8-azabicyclo[3.2.1]octan-3-amine (23.3 mg, 85%).

MS *m/z* 187.3 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 4.40 (dd, *J*= 50.7, 3.1 Hz, 1H), 2.93 (dddd, *J*= 30.5, 12.2, 6.1, 3.1 Hz, 1H), 2.41 (s, 3H), 1.77 (dd, *J*= 13.0, 6.0 Hz, 1H), 1.62-1.71 (m, 2H), 1.53-1.61 (m, 2H), 1.27-1.32 (m, 1H), 1.24 (s, 3H), 1.19 (s, 3H); 2 NHs not observed.

Intermediate 9

(±) 2,4-*trans* *tert*-Butyl 2-[[*tert*-butyl(dimethyl)silyl]oxymethyl]-4-(methylamino)piperidine-1-carboxylate



Step 1: (±) 1-(*tert*-Butyl) 2-methyl (*R*)-4-oxopiperidine-1,2-dicarboxylate (10 g, 38.9 mmol) was dissolved in MeOH (50 mL). *N*-Methylbenzylamine (8 mL, 62 mmol) was added, followed by acetic acid (1 mL, 17.4 mmol). The reaction was stirred at room temperature for 1 h. After cooling the mixture to 0 °C, $NaBH_3CN$ (3.7 g, 59 mmol) was added in one portion. The reaction was warmed to room temperature and stirred for 15 h. The mixture was partitioned between EtOAc and H_2O. The organic layer was dried over $MgSO_4$, filtered, and then concentrated under vacuum. Purification by silica chromatography (20-50% EtOAc in hexanes) yielded (±)1-(*tert*-butyl) 2-methyl (*cis*)-4-(benzyl(methyl)amino)piperidine-1,2-dicarboxylate (A) (3.96 g, 28%) as

the second-highest major component on TLC (when visualized with iodine stain), and (±) 1-(*tert*-butyl) 2-methyl (*trans*)-4-(benzyl(methyl)amino)piperidine-1,2-dicarboxylate (B) (2.49 g, 18%) as the lowest major non-baseline TLC component.

A: ^{1}H NMR (methanol-d_4) δ: 7.20-7.40 (m, 5H), 4.49 (m, 1H), 3.70-3.85 (m, 2H), 3.67 (s, 3H), 3.35-3.50 (m, 1H), 3.30 (m, 1H), 2.45-2.60 (m, 2H), 2.10 (m, 1H), 2.07 (s, 3H), 1.93-2.00 (m, 1H), 1.70-1.78 (m, 1H), 1.47 (s, 9H).

B: ^{1}H NMR (methanol-d_4) 1:1 mixture of rotamers δ: 7.33 (d, *J*=4.3 Hz, 4H), 7.23-7.29 (m, 1H), 4.89-4.99 (m, 1H), 4.03-4.09 (m, 1H), 3.67-3.72 (m, 3H), 3.63 (s, 2H), 2.84-3.05 (m, 1H), 2.39-2.50 (m, 2H), 2.23 (s, 3H), 1.70-1.92 (m, 2H), 1.51-1.57 (m, 1H), 1.46 (br d, 9H)

Step 2: The (±) 2,4-*trans* O^1-*tert*-butyl O^2-methyl 4-[benzyl(methyl)amino]piperidine-1,2-dicarboxylate (2.49 g, 6.87 mmol) was dissolved in anhydrous THF (45 mL) in an oven-dried 100-mL round-bottomed flask. An oven-dried Teflon-coated stir bar was added. The tube was fitted with a septum cap and the headspace was swept with dry N_2. The flask was then submerged in an ice bath and the reaction mixture was cooled to 0 °C. A 1.0 M solution of $LiAlH_4$ in THF (6.3 mL, 6.3 mmol, 0.92 eq.) was added dropwise, under N2, at room temperature and the reaction mixture (a clear solution) was stirred at 0 °C for 1 h. The reaction mixture was then diluted with anhydrous Et_2O (20 mL) and quenched by the Fieser method with vigorous stirring, at 0 °C, under sweeping N_2. The reaction mixture was then stirred at room temperature for 1 h**.** The reaction mixture was then filtered through Celite (45 x 15 mm bed), and the Celite was washed with 1:1 Et_2O/EtOAc (150 mL). The clear, colorless filtrate was concentrated on a rotovap, then under high vacuum (0.3 mm Hg, room temperature) to afford crude (±) 2,4-*trans tert*-butyl 4-[benzyl(methyl)amino]-2-(hydroxymethyl)piperidine-1-carboxylate (2.22 g, 97% yield) as a clear, light-amber, flowing oil.

^{1}H NMR ($CDCl_3$) δ: 7.34 – 7.27 (m, 4H), 7.26 – 7.21 (m, 1H), 4.49 (d, *J*=50.4 Hz, 1H), 4.13 (d, *J*= 56.5 Hz, 1H), 3.73 (t, *J*=10.0 Hz, 1H), 3.63 – 3.48 (m, 3H), 2.95 – 2.77 (m, 1H), 2.71 (t, *J*=11.8 Hz, 1H), 2.18 (s, 3H), 1.89 (d, *J*=13.1 Hz, 1H), 1.81 (d, *J*=10.5 Hz, 1H), 1.65 (td, *J*=12.8, 6.2 Hz, 1H), 1.52 – 1.40 (m, 10H); OH proton not observed.

Step 3: A 100-mL, round-bottom flask was charged with a solution of (±) 2,4-*trans tert*-butyl 4-[benzyl(methyl)amino]-2-(hydroxymethyl)piperidine-1-carboxylate (2.22 g, 6.64 mmol) in CH_2Cl_2 (50 mL), a Teflon-coated stir bar, and crystalline imidazole (0.610 g, 8.96 mmol, 1.35 eq.). Once the imidazole had completely dissolved, *tert*-butyldiphenylchlorosilane (1.90 mL, 7.33 mmol, 1.10 eq.) was added to the solution, eliciting precipitation within ~5 minutes. The reaction

mixture was stirred gently at room temperature for 1 h. After this time, the reaction mixture was diluted with CH_2Cl_2 (30 mL), transferred to a 125 mL separatory funnel, and washed with water (50 mL) and sat. aq. $NaHCO_3$ (50 mL). The organic phase was then dried over anhydrous Na_2SO_4, filtered, and the clear colorless filtrate was concentrated on a rotovap to afford a thick, clear, colorless oil. The crude product was purified by silica gel column chromatography on an ISCO system: 80-g silica gel cartridge (CH_2Cl_2-equilibrated), CH_2Cl_2isocratic elution (10 minutes) followed by CH_2Cl_2/EtOAc gradient elution (1:0 to 1:9 over 40 minutes, 60 mL/min), 50-mL fractions. The product-containing fractions were combined and concentrated on a rotovap and further dried under high vacuum (0.3 mm Hg, room temperature, overnight) to afford (±) 2,4-*trans tert*-butyl 4-[benzyl(methyl)amino]-2-[[*tert*-butyl(diphenyl)silyl]oxymethyl]piperidine-1-carboxylate (2.76 g, 73% yield) as a clear, colorless, viscous oil.

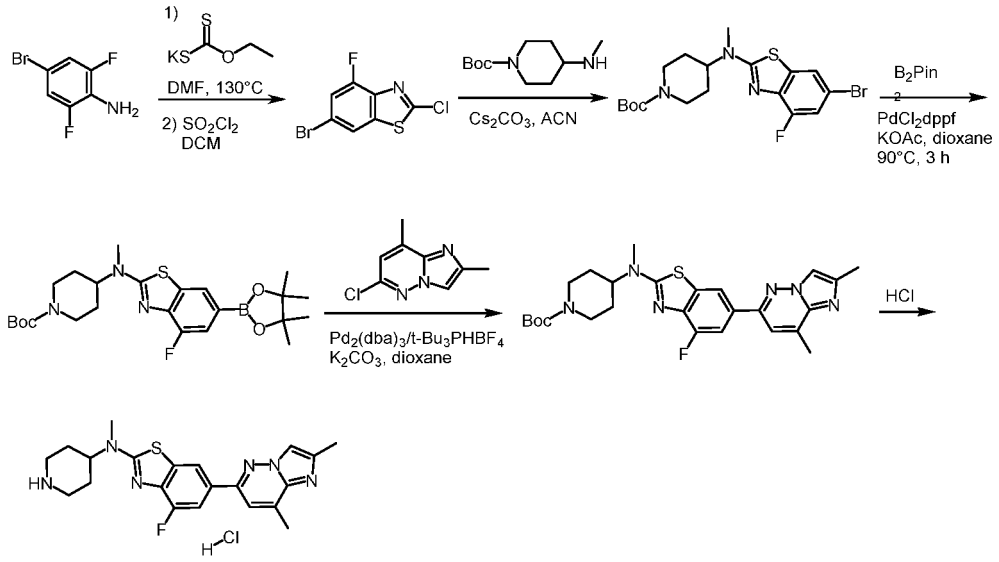
^{1}H NMR ($CDCl_3$) δ: 7.66 (d, *J*=7.0 Hz, 4H), 7.45 – 7.36 (m, 6H), 7.36 – 7.26 (m, 4H), 7.26 – 7.20 (m, 1H), 4.74 – 4.36 (m, 1H), 4.24 – 3.93 (m, 1H), 3.73 – 3.45 (m, 4H), 2.88 – 2.59 (m, 2H), 2.32 – 2.05 (m, 4H), 1.86 – 1.68 (m, 1H), 1.68 – 1.54 (m, 1H), 1.53 – 1.37 (m, 10H), 1.06 (s, 9H).

Step 4: The (±) 2,4-*trans tert*-butyl 4-[benzyl(methyl)amino]-2-[[*tert*-butyl(diphenyl)silyl]oxymethyl]piperidine-1-carboxylate (2.35 g, 4.10 mmol), was dissolved in MeOH (30 mL) in a 100-mL Parr bomb reactor. The solution was sparged with argon for 5 minutes, then 20% $Pd(OH)_2$/C (0.30 g, 0.43 mmol, 0.10 eq.) was added. The bomb was fitted to a Parr shaker apparatus, purged with H_2 (5 x 20 psi), then charged to a final H_2 pressure of 50 psi. The reaction mixture was shaken at room temperature for 50 h. The reaction mixture was then filtered through a 45 x 20 mm bed of Celite, and the Celite bed was washed with MeOH (200 mL). The clear, colorless filtrate was concentrated on a rotovap to afford a clear, very light amber oil. The crude product was purified by Kugelrohr distillation (260 °C, 0.8 mm Hg) to afford the desired (±) 2,4-*trans tert*-butyl 2-[[*tert*-butyl(dimethyl)silyl]oxymethyl]-4-(methylamino)piperidine-1-carboxylate (1.22 g, 83% yield) as a clear, colorless, thick oil.

^{1}H NMR ($CDCl_3$) δ 7.70 – 7.60 (m, 4H), 7.47 – 7.34 (m, 6H), 4.63 – 4.31 (m, 1H), 4.20 – 3.87 (m, 1H), 3.73 – 3.59 (m, 2H), 2.70 (br s, 1H), 2.56 (br s, 1H), 2.41 (s, 3H), 2.20 (br s, 1H), 1.83 (br s, 1H), 1.42 (s, 9H), 1.31 – 1.19 (m, 2H), 1.05 (s, 9H).

Example 1

Preparation of Compound 186



Step 1: A mixture of 4-bromo-2,6-difluoro-aniline (4.16 g, 20.0 mmol, 1.00 eq.) and ethoxycarbothioylsulfanyl potassium (7.69 g, 48.0 mmol, 2.40 eq.) in DMF (25 mL) was stirred at 130°C overnight, then cooled to room temperature, diluted with 1 N HCl (150 mL) and stirred at room temperature for 1 h. The resulting solid was filtered and washed with water and dried. The resulting material was suspended in CH_2Cl_2 (25 mL) and SO_2Cl_2 (27.5 g, 16.5 mL, 200 mmol, 10.0 eq.) was added slowly and stirred at room temperature for 48 h. Water was added slowly at 0° C to quenched the reaction. The resulting precipitate was collected by filtration and purified over silica with ethyl acetate in hexanes (2 to 10% gradient) to give 6-bromo-2-chloro-4-fluoro-1,3-benzothiazole (5.08 g, 95.3%). MS *m/z* 266.1, 268.0, 270.0 $[M+H]^+$.

Step 2: A mixture of 4-(methylamino)piperidine-1-carboxylate (88 mg, 0.41 mmol, 1.1 eq.), 6-bromo-2-chloro-4-fluoro-1,3-benzothiazole (100 mg, 0.38 mmol, 1.0 eq.) and Cs_2CO_3 (240 mg, 0.75 mmol, 2.0 eq.) in acetonitrile (1.0 mL) was stirred at 90 °C overnight, then cooled, diluted with ethyl acetate and concentrated. The residue was purified over silica with ethyl acetate in hexanes (2 to 10% gradient) to give tert-butyl 4-[(6-bromo-4-fluoro-1,3-benzothiazol-2-yl)-methyl-amino]piperidine-1-carboxylate (94 mg, 56%). MS *m/z* 388.2, 390.0 $[M+H]^+$.

Step 3: A mixture of tert-butyl 4-[(6-bromo-4-fluoro-1,3-benzothiazol-2-yl)-methyl-amino]piperidine-1-carboxylate (94 mg, 0.21 mmol, 1.0 eq.), B_2Pin_2 (81 mg, 0.32 mmol, 1.5 eq.), $PdCl_2(dppf)$ (16 mg, 0.021 mmol, 0.10 eq.) and KOAc (63 mg, 0.63 mmol, 3.0 eq.) in dioxane

(2.0 mL) was stirred at 90 °C for 3 h under an Ar atmosphere, then cooled, diluted with ethyl acetate and concentrated. The residue was purified over silica with ethyl acetate in hexanes (3 to 50% gradient) to give tert-butyl 4-[[4-fluoro-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3-benzothiazol-2-yl]-methyl-amino]piperidine-1-carboxylate (96 mg, 92%). MS *m/z* 492.1 $[M+H]^+$.

Step 4**:** A mixture of tert-butyl 4-[[4-fluoro-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3-benzothiazol-2-yl]-methyl-amino]piperidine-1-carboxylate (48 mg, 0.1 mmol, 1.1 eq.), 6-chloro-2,8-dimethyl-imidazo[1,2-b]pyridazine (16 mg, 0.088 mmol, 1.0 eq.), $Pd_2(dba)_3$ (4.1 mg, 0.0044 mmol, 0.05 eq.), $(t\text{-}Bu)_3P\ HBF_4$ (2.6 mg, 0.0088 mmol, 0.1 eq.) and 2.0 M aq. K_2CO_3 (0.13 mL, 0.26 mmol, 3.0 eq.) in dioxane (1.0 mL) was stirred at 90 °C for 3 h under an Ar atmosphere, then cooled and diluted with ethyl acetate. The mixture was washed with water, brine and the organic layer was dried over sodium sulfate and evaporated. The residue was purified over silica gel with ethyl acetate in dichloromethane (10 to 100% gradient) to provide tert-butyl 4-[[6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4-fluoro-1,3-benzothiazol-2-yl]-methyl-amino]piperidine-1-carboxylate (12 mg, 27%). MS *m/z* 511.4 $[M+H]^+$.

Step 5: To a solution of tert-butyl 4-[[6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4-fluoro-1,3-benzothiazol-2-yl]-methyl-amino]piperidine-1-carboxylate in CH_2Cl_2 (1.0 mL) was added TFA (1.0 mL). The mixture was stirred at room temperature for 1 h and then the organic volatiles were removed by a stream of nitrogen. The residue was purified by C18 chromatography to give 6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4-fluoro-*N*-methyl-*N*-(4-piperidyl)-1,3-benzothiazol-2-amine hydrochloride (24 mg) after treatment with HCl in ether.

MS *m/z* 411.4 $[M+H]^+$; ^{1}H NMR (methanol-d_4) δ: 8.41 (s, 1H), 8.31 (d, *J*=0.9 Hz, 1H), 8.28 (d, *J*=0.9 Hz, 1H), 7.95 - 8.01 (m, 1H), 4.67 - 4.77 (m, 1H), 3.57 - 3.64 (m, 2H), 3.24 - 3.31 (m, 2H), 3.23 (s, 3H), 2.80 (d, *J*=0.6 Hz, 3H), 2.67 (d, *J*=0.9 Hz, 3H), 2.09 - 2.29 (m, 4H).

Using the procedure described for Example 1, above, additional compounds described herein were prepared by substituting the appropriate starting material, suitable reagents and reaction conditions, obtaining compounds such as those selected from:

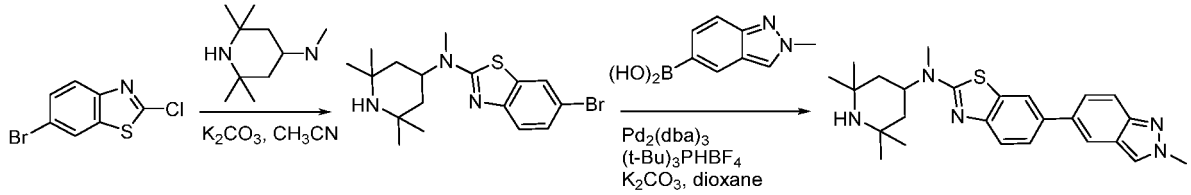
Cpd	Data
132	MS *m/z* 411.2 $[M+H]^+$; ^{1}H NMR (DMSO-d_6) δ: 9.59 - 9.70 (m, 1H), 9.22 - 9.34 (m, 1H), 8.51 (d, *J*= 1.6 Hz, 1H), 8.36 (s, 1H), 8.21 (br. s., 1H), 7.96 (dd, *J*= 12.3, 1.6 Hz, 1H), 4.20 - 4.32 (m, 2H), 3.50 (br. s., 2H), 3.31 (dd, *J*= 13.6, 11.7 Hz, 2H), 2.70 (d, *J*= 0.6 Hz, 3H), 2.54 (s, 3H), 1.37 (d, *J*= 6.6 Hz, 6H).

Cpd	Data
164	MS *m/z* 411.3 $[M+H]^+$; ^{1}H NMR (methanol-d_4) δ: 8.23 (s, 1H), 8.18 (s, 1H), 8.12 (s, 1H), 7.76 - 7.81 (m, 1H), 7.61 (s, 1H), 4.60 - 4.67 (m, 1H), 3.40 - 3.48 (m, 1H), 3.28 - 3.39 (m, 1H), 3.09 - 3.17 (m, 1H), 3.05 (s, 3H), 2.53 (s, 3H), 1.98 - 2.05 (m, 3H), 1.79 - 1.89 (m, 1H), 1.31 (d, *J*= 6.3 Hz, 3H).
165	MS *m/z* 425.4 $[M+H]^+$; ^{1}H NMR (methanol-d_4) δ: 8.23 (d, *J*= 1.6 Hz, 1H), 8.15 (d, *J*= 0.9 Hz, 1H), 8.11 (d, *J*= 1.3 Hz, 1H), 7.80 (dd, *J*= 12.1, 1.7 Hz, 1H), 4.57 - 4.68 (m, 1H), 3.43 - 3.48 (m, 1H), 3.32 - 3.40 (m, 1H), 3.10 - 3.17 (m, 1H), 3.05 (s, 3H), 2.65 (d, *J*= 0.9 Hz, 3H), 2.52 (d, *J*= 0.9 Hz, 3H), 1.96 - 2.09 (m, 3H), 1.77 - 1.87 (m, 1H), 1.30 (d, *J*= 6.3 Hz, 3H).
185	MS *m/z* 397.3 $[M+H]^+$; ^{1}H NMR (methanol-d_4) δ: 8.27 - 8.34 (m, 3H), 8.21 (s, 1H), 7.88 (d, *J*= 11.7 Hz, 1H), 4.51 (br. s., 1H), 3.42 – 3.52 (m, 2H), 3.10 - 3.20 (m, 5H), 2.53 (s, 3H), 2.01 - 2.22 (m, 4H).
192	MS *m/z* 437.4 $[M+H]^+$; ^{1}H NMR (methanol-d_4) δ: 8.29 (s, 1H), 8.17 (s, 1H), 8.14 (s, 1H), 7.85 (d, *J*= 12.0 Hz, 1H), 4.60 - 4.72 (m, 1H), 4.05 (br s, 2H), 3.11 (s, 3H), 2.66 (s, 3H), 2.51 - 2.59 (m, 5H), 2.04 - 2.17 (m, 4H), 1.90 – 1.98 (m, 2H).
202	MS *m/z* 427.2 $[M+H]^+$;^{1}H NMR (methanol-d_4) δ: 8.28 (d, *J*= 1.6 Hz, 1H), 8.11 (d, *J*= 1.3 Hz, 1H), 7.83 (dd, *J*= 12.0, 1.6 Hz, 1H), 7.65 (s, 1H), 4.55 - 4.64 (m, 1H), 4.24 (s, 3H), 3.46 (d, *J*= 12.9 Hz, 2H), 3.14 (td, *J*= 12.9, 3.2 Hz, 2H), 3.07 (s, 3H), 2.49 (d, *J*= 0.9 Hz, 3H), 1.97 - 2.15 (m, 4H).
209	MS *m/z* 423.4 $[M+H]^+$; ^{1}H NMR (methanol-d_4) δ: 8.25 (d, *J*= 1.9 Hz, 1H), 8.23 (s, 2H), 8.16 (d, *J*= 0.9 Hz, 1H), 7.83 (dd, *J*= 12.0, 1.6 Hz, 1H), 4.75 (m, 1H), 4.06 (br. s., 2H), 3.04 (s, 3H), 2.47 (d, *J*= 0.9 Hz, 3H), 2.13 – 2.25 (m, 2H), 2.08 (br s, 4H), 1.86 - 1.95 (m, 2H).
225	MS *m/z* 410.4 $[M+H]^+$; ^{1}H NMR ($CDCl_3$) δ: 7.66 (d, *J*= 1.6 Hz, 1H), 7.55 (d, *J*= 1.3 Hz, 2H), 7.35 (dd, *J*= 12.0, 1.6 Hz, 1H), 6.94 (s, 1H), 4.18 - 4.35 (m,1H), 3.30 (d, *J*= 12.3 Hz, 2H), 3.14 (s, 3H), 2.86 (td, *J*= 12.1, 2.8 Hz, 2H), 2.70 (s, 3H), 2.41 (d, *J*= 0.6 Hz, 3H), 1.83 - 1.94 (m, 4H).
226	MS *m/z* 421.3 $[M+H]^+$; ^{1}H NMR (methanol-d_4) δ: 9.18 (d, *J*= 1.6 Hz, 1H), 8.66 (d, *J*= 1.6 Hz, 1H), 7.99 (d, *J*= 1.3 Hz, 1H), 7.84 (d, *J*= 1.6 Hz, 1H), 7.41 - 7.47 (m,1H), 4.44 - 4.54 (m, 1H), 3.37 - 3.45 (m, 2H), 3.04 - 3.11 (m, 2H), 3.03 (s, 3H), 2.45 (d, *J*= 0.9 Hz, 3H), 1.94 - 2.09 (m, 4H).
231	MS *m/z* 422.4 $[M+H]^+$; ^{1}H NMR (methanol-d_4) δ: 8.80 - 8.84 (m, 1H), 8.41 - 8.43 (m, 1H), 8.38 - 8.40 (m, 1H), 7.93 - 8.00 (m, 1H), 4.70 - 4.77 (m, 1H), 3.56 - 3.63(m, 2H), 3.23 - 3.30 (m, 2H), 3.21 (s, 3H), 2.67 (s, 3H), 2.13 - 2.27 (m, 4H).
235	MS *m/z* 448.5 $[M+H]^+$; ^{1}H NMR (methanol-d_4) δ: 8.81 - 9.09 (m, 1H), 8.46 (br s, 2H), 7.98 (br s, 1H), 4.90 (m, 1H), 4.23 (br s, 2H), 3.20 (br s, 3H), 2.71 (br s, 3H), 1.92 - 2.44 (m, 8H).
236	MS *m/z* 466.4 $[M+H]^+$; ^{1}H NMR (methanol-d_4) δ: 8.67 (s, 1H), 8.31 - 8.34 (m, 1H), 8.24 - 8.27 (m, 1H), 7.86 - 7.92 (m, 1H), 4.84 - 4.95 (m, 1H), 4.07 - 4.14 (m, 2H), 3.05 (s, 3H), 2.55 (d, *J*= 0.6 Hz, 3H), 2.14 (br s, 6H), 1.92 - 1.99 (m, 2H).

Cpd	Data
237	MS *m/z* 423.4 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.88 (d, *J*= 8.8 Hz, 1H), 8.82 (s, 1H), 8.36 (s, 1H), 8.21 (d, *J*= 8.8 Hz, 1H), 7.92 (d, *J*= 11.3 Hz, 1H), 4.95 (m, 1H), 4.43 (s, 3H), 4.24 (br s, 2H), 3.22 (s, 3H), 2.39 (br s, 2H), 2.26 (s, 4H), 2.08 (d, *J*= 10.7 Hz, 2H).
248	MS *m/z* 383.3 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.43 (d, *J*= 1.9 Hz, 1H), 8.30 (d, *J*= 0.9 Hz, 1H), 8.26 (d, *J*= 1.3 Hz, 1H), 7.97 (dd, *J*= 11.8, 1.7 Hz, 1H), 5.24 (t, *J*= 8.0 Hz, 1H), 4.62 - 4.72 (m, 2H), 4.39 - 4.51 (m, 2H), 3.33 (s, 3H), 2.79 (d, *J*= 0.9 Hz, 3H), 2.60 - 2.71 (m, 3H).
250	MS *m/z* 397.1 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.72 (d, *J*= 7.6 Hz, 1H), 8.28 (d, *J*= 1.6 Hz, 1H), 7.85 - 7.91 (m, 1H), 7.41 (d, *J*= 7.6 Hz, 1H), 6.45 (s, 1H), 4.45 - 4.56 (m, 1H), 3.42 - 3.50 (m, 2H), 3.10 (s, 5H), 2.39 (s, 3H), 2.00 - 2.14 (m, 4H).
258	MS *m/z* 411.2 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.25 - 8.32 (m, 3H), 8.20 (s, 1H), 7.86 (d, *J*= 12.0 Hz, 1H), 4.54 (br. s., 1H), 3.45 (m, 1H), 3.33 -3.42 (m, 1H), 3.07 - 3.16 (m, 4H), 2.52 (s, 3H), 1.99 - 2.11 (m, 3H), 1.88 (m, 1H), 1.31 (d, *J*= 6.3 Hz, 3H).
259	MS *m/z* 411.2 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.26 - 8.32 (m, 3H), 8.21 (s, 1H), 7.86 (dd, *J*= 12.0, 0.9 Hz, 1H), 4.54 (br s, 1H), 3.89 (br s, 1H), 3.37 (d, *J*= 2.8 Hz, 1H), 3.30 (br. s., 1H), 3.09 (s, 3H), 2.53 (s, 3H), 2.26 (m, 1H), 2.04 (m, 2H), 1.89 (d, *J*= 13.9 Hz, 1H), 1.47 (d, *J*= 6.9 Hz, 3H).

Example 2

Preparation of Compound 20



Step 1: A mixture of 6-bromo-2-chloro-1,3-benzothiazole (600 mg, 2.4 mmol, 1.0 eq.), N,2,2,6,6-pentamethylpiperidin-4-amine (490 mg, 0.54 mL, 2.9 mmol, 1.2 eq.) and K_2CO_3 (1000 mg, 7.2 mmol, 3.0 eq.) in acetonitrile (6.0 mL) was stirred at 100 °C overnight, and then cooled, diluted with ethyl acetate and filtered. The filtrate was concentrated to give 6-bromo-*N*-methyl-*N*-(2,2,6,6-tetramethyl-4-piperidyl)-1,3-benzothiazol-2-amine, which was used without further purification.

Step 2: A mixture of 6-bromo-*N*-methyl-*N*-(2,2,6,6-tetramethyl-4-piperidyl)-1,3-benzothiazol-2-amine (60 mg, 0.16 mmol, 1.0 eq.), (2-methylindazol-5-yl)boronic acid (36 mg, 0.20 mmol, 1.3 eq.), $Pd_2(dba)_3$ (7.3 mg, 0.0078 mmol, 0.050 eq.), $(t\text{-}Bu)_3P\ HBF_4$ (4.6 mg, 0.016 mmol, 0.10 eq.)

and K_2CO_3 (2.0 M aq.) (0.24 mL, 0.47 mmol, 3.0 eq.) in dioxane (1.0 mL) was stirred at 100 °C for 1 h, and then cooled, diluted with ethyl acetate and washed with water and brine. The organic layer was separated, dried over sodium sulfate and evaporated. The residue was purified over basic alumina with ethyl acetate in hexanes (10 to 100% gradient) to provide *N*-methyl-6-(2-methylindazol-5-yl)-*N*-(2,2,6,6-tetramethyl-4-piperidyl)-1,3-benzothiazol-2-amine (57 mg, 84%).

MS *m/z* 434.4 $[M+H]^+$; ^1H NMR ($CDCl_3$) δ: 7.85 (s, 1H), 7.78 (d, *J*= 1.3 Hz, 1H), 7.73 - 7.75 (m, 1H), 7.68 (d, *J*= 9.1 Hz, 1H), 7.47 - 7.55 (m, 3H), 4.20 - 4.34 (m, 1H), 4.17 (s, 3H), 3.04 (s, 3H), 1.74 (dd, *J*= 12.5, 3.3 Hz, 2H), 1.36 (d, *J*= 10.7 Hz, 2H), 1.27 - 1.33 (m, 6H), 1.10 - 1.21 (m, 6H).

Using the procedure described for Example 2, above, additional compounds described herein were prepared by substituting the appropriate starting material, suitable reagents and reaction conditions, obtaining compounds such as those selected from:

Cpd	Data
7	^1H NMR (DMSO-d_6) δ: 8.36 (s, 1H), 8.10 (d, *J*= 1.9 Hz, 1H), 7.94 (d, *J*= 0.6 Hz, 1H), 7.63 - 7.68 (m, 1H), 7.59 (ddd, *J*= 10.8, 8.7, 1.9 Hz, 2H), 7.50 (d, *J*= 8.2 Hz, 1H), 4.18 (s, 3H), 3.47 - 3.54 (m, 4H), 2.79 - 2.86 (m, 4H).
8	MS *m/z* 378.0 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.27 (br s, 2H), 8.44 (s, 1H), 8.28 (d, *J*= 1.5 Hz, 1H), 8.00 (s, 1H), 7.67 - 7.83 (m, 3H), 7.61 (dd, *J*= 9.0, 1.6 Hz, 1H), 4.57 (br. s., 1H), 4.20 (s, 3H), 3.42 (d, *J*= 12.0 Hz, 2H), 3.04 - 3.22 (m, 5H), 2.15 - 2.30 (m, 2H), 2.01 (d, *J*= 11.7 Hz, 2H).
21	MS *m/z* 448.4 $[M+H]^+$; ^1H NMR ($CDCl_3$) δ: 7.93 (s, 1H), 7.87 (d, *J*= 1.3 Hz, 1H), 7.68 (d, *J*= 0.9 Hz, 1H), 7.57 - 7.64 (m, 2H), 7.35 - 7.40 (m, 1H), 4.30 - 4.41 (m, 1H), 4.27 (s, 3H), 3.14 (s, 3H), 2.71 (s, 3H), 1.83 (dd, *J*= 12.5, 3.3 Hz, 2H), 1.35 - 1.50 (m, 8H), 1.24 (br s, 6H).
23	MS *m/z* 452.0 $[M+H]^+$; ^1H NMR ($CDCl_3$) δ: 7.86 (s, 1H), 7.71 - 7.75 (m, 1H), 7.68 (d, *J*= 8.8 Hz, 1H), 7.55 (d, *J*= 1.6 Hz, 1H), 7.45 - 7.49 (m, 1H), 7.26 (dd, *J*= 12.0, 1.6 Hz, 1H), 4.29 (br. s., 1H), 4.17 (s, 3H), 3.07 (s, 3H), 1.75 (dd, *J*= 12.5, 3.3 Hz, 2H), 1.43 - 1.54 (m, 2H), 1.31 - 1.37 (m, 6H), 1.21 (d, *J*= 4.1 Hz, 6H).
24	MS *m/z* 466.0 $[M+H]^+$; ^1H NMR ($CDCl_3$) δ: 7.93 (s, 1H), 7.65 (dd, *J*= 6.3, 1.3 Hz, 2H), 7.31 - 7.38 (m, 2H), 4.25 - 4.37 (m, 4H), 3.17 (s, 3H), 2.71 (s, 3H), 1.83 (dd, *J*= 12.5, 3.3 Hz, 2H), 1.42 - 1.52 (m, 2H), 1.39 (s, 6H), 1.21 - 1.28 (m, 6H).
28	MS *m/z* 392.1 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.23 - 9.93 (m, 1H), 8.37 (s, 1H), 8.13 (d, *J*= 1.6 Hz, 1H), 7.95 (s, 1H), 7.64 - 7.68 (m, 1H), 7.62 (dd, *J*= 8.5, 1.6 Hz, 1H), 7.56 - 7.60 (m, 1H), 7.52 (d, *J*= 8.2 Hz, 1H), 4.18 (s, 5H), 3.21 (t, *J*= 12.0 Hz, 3H), 2.70 (br s, 6H), 2.09 (d, *J*= 11.7 Hz, 2H), 1.68 (d, *J*= 8.2 Hz, 2H).

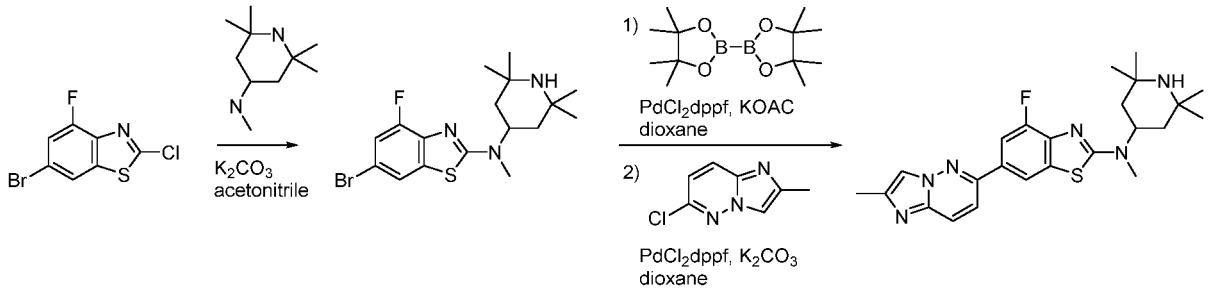
Cpd	Data
29	MS *m/z* 364.1 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.39 (s, 1H), 8.28 (br s, 3H), 8.17 (d, *J*= 1.6 Hz, 1H), 7.96 (s, 1H), 7.64 - 7.69 (m, 2H), 7.59 (dd, *J*= 9.1, 1.6 Hz, 1H), 7.56 (d, *J*= 8.5 Hz, 1H), 4.19 (s, 3H), 4.14 (d, *J*= 12.9 Hz, 2H), 3.27 - 3.42 (m, 3H), 2.08 (d, *J*= 10.7 Hz, 2H), 1.67 (dd, *J*= 11.8, 3.6 Hz, 2H).
33	MS *m/z* 448.5 $[M+H]^+$; ^1H NMR ($CDCl_3$) δ: 8.11 (d, *J*= 0.9 Hz, 1H), 7.78 (d, *J*= 1.9 Hz, 1H), 7.61 (d, *J*= 8.2 Hz, 1H), 7.48 (dd, *J*= 8.2, 1.9 Hz, 1H), 7.38 (d, *J*= 0.6 Hz, 1H), 7.23 (dd, *J*= 1.6, 0.9 Hz, 1H), 4.29 - 4.44 (m, 1H), 3.13 (s, 3H), 2.67 (s, 3H), 2.51 (s, 3H), 1.83 (dd, *J*= 12.5, 3.3 Hz, 2H), 1.46 (t, *J*= 12.0 Hz, 2H), 1.39 (d, *J*= 2.5 Hz, 6H), 1.24 (br s, 6H).
34	MS *m/z* 420.4 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.41 (d, *J*= 9.8 Hz, 1H), 8.38 (d, *J*= 10.7 Hz, 1H), 8.02 - 8.18 (m, 2H), 7.96 (s, 1H), 7.50 - 7.69 (m, 4H), 4.60 (br s, 1H), 3.03 (s, 3H), 2.05 (t, *J*= 12.5 Hz, 2H), 1.81 (d, *J*= 11.7 Hz, 2H), 1.37 - 1.55 (m, 12H).
35	MS *m/z* 364.1 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 10.25 - 10.81 (m, 1H), 9.09 (br s, 2H), 8.42 (s, 1H), 8.21 (s, 1H), 7.97 (s, 1H), 7.75 (d, *J*= 8.5 Hz, 1H), 7.66 - 7.72 (m, 2H), 7.57 (dd, *J*= 9.0, 1.4 Hz, 1H), 4.28 (br s, 1H), 4.19 (s, 3H), 3.32 - 3.44 (m, 2H), 3.04 (br s, 2H), 2.22 (d, *J*= 10.7 Hz, 2H), 1.79 - 1.96 (m, 2H).
38	MS *m/z* 364.2 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 10.02 (br s, 1H), 9.71 (br s, 1H), 8.44 (br s, 1H), 8.25 (br s, 1H), 7.99 (br s, 1H), 7.56 - 7.78 (m, 4H), 5.10 (br s, 1H), 4.20 (br s, 3H), 3.13 - 3.60 (m, 7H), 2.33 (br s, 1H), 2.18 (br s, 1H).
51	MS *m/z* 502.2 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.82 - 8.90 (m, 1H), 8.61 (s, 1H), 8.30 (s, 1H), 8.23 (d, *J*= 1.9 Hz, 1H), 7.94 (s, 1H), 7.84 - 7.91 (m, 1H), 7.67 (d, *J*= 1.9 Hz, 1H), 7.55 (d, *J*= 8.5 Hz, 1H), 4.56 - 4.70 (m, 1H), 4.26 (s, 3H), 3.06 (s, 3H), 1.90 - 1.96 (m, 4H), 1.52 (s, 6H), 1.44 (s, 6H).
54	MS *m/z* 462.3 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.33 (s, 1H), 8.09 - 8.13 (m, 1H), 7.75 (s, 1H), 7.58 - 7.62 (m, 1H), 7.48 - 7.52 (m, 1H), 7.36 (s, 1H), 4.39 - 4.55 (m, 1H), 4.18 (s, 3H), 3.04 (s, 3H), 2.94 - 3.01 (m, 2H), 1.68 - 1.83 (m, 4H), 1.34 - 1.44 (m, 9H), 1.30 (br s, 6H).
55	MS *m/z* 448.3 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.81 - 8.90 (m, 1H), 8.63 - 8.70 (m, 1H), 8.31 - 8.43 (m, 2H), 8.09 - 8.17 (m, 1H), 7.86 - 7.95 (m, 1H), 7.79 - 7.85 (m, 1H), 7.52 - 7.60 (m, 1H), 4.59 - 4.73 (m, 1H), 3.06 (s, 3H), 2.88 (s, 3H), 2.43 (s, 3H), 1.84 - 1.98 (m, 4H), 1.51 (s, 6H), 1.44 (s, 6H).
57	MS *m/z* 452.1 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.87 - 8.95 (m, 1H), 8.49 - 8.53 (m, 1H), 8.17 - 8.19 (m, 1H), 7.81 - 7.84 (m, 1H), 7.64 - 7.68 (m, 1H), 7.50 - 7.54 (m, 1H), 7.39 - 7.45 (m, 1H), 4.55 - 4.66 (m, 1H), 4.21 (s, 3H), 3.06 (s, 3H), 1.86 - 1.99 (m, 4H), 1.51 (s, 6H), 1.45 (s, 6H).
62	MS *m/z* 459.2 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.81 - 8.88 (m, 1H), 8.65 (s, 1H), 8.38 (s, 1H), 8.26 (s, 2H), 7.81 - 7.89 (m, 1H), 7.68 - 7.72 (m, 1H), 7.52 - 7.56 (m, 1H), 4.58 - 4.68 (m, 1H), 4.26 (s, 3H), 3.06 (s, 3H), 1.88 - 1.96 (m, 4H), 1.52 (s, 6H), 1.44 (s, 6H).

Cpd	Data
63	MS *m/z* 434.1 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.23 - 9.26 (m, 1H), 9.04 - 9.11 (m, 1H), 8.23 - 8.29 (m, 2H), 8.03 - 8.08 (m, 2H), 7.96 - 8.00 (m, 1H), 7.69 - 7.73 (m, 1H), 7.60 - 7.64 (m, 1H), 4.57 - 4.72 (m, 1H), 3.07 (s, 3H), 2.52 (s, 3H), 1.95 - 2.03 (m, 2H), 1.86 - 1.93 (m, 2H), 1.52 (s, 6H), 1.47 (s, 6H).
64	MS *m/z* 421.2 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.26 (s, 1H), 8.04 (s, 1H), 7.95 (s, 1H), 7.63 - 7.76 (m, 4H), 5.59 - 5.69 (m, 1H), 4.25 (s, 3H), 2.30 (dd, *J*= 12.3, 3.5 Hz, 2H), 1.51 (br. s., 2H), 1.40 (s, 6H), 1.30 (s, 6H).
68	MS *m/z* 435.0 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.94 (s, 1H), 8.14 (s, 1H), 8.09 (s, 1H), 7.95 (s, 1H), 7.78 (d, *J*= 3.2 Hz, 2H), 5.69 - 5.81 (m, 1H), 4.48 (s, 3H), 2.72 (s, 3H), 2.54 (dd, *J*= 13.7, 3.9 Hz, 2H), 1.96 (dd, *J*= 13.4, 10.9 Hz, 2H), 1.63 - 1.69 (m, 6H), 1.56 - 1.62 (m, 6H).
80	MS *m/z* 474.3 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.77 - 8.84 (m, 1H), 8.32 (s, 1H), 8.13 (s, 1H), 7.79 - 7.87 (m, 1H), 7.70 (s, 1H), 7.60 (s, 1H), 7.50 (d, *J*= 8.5 Hz, 1H), 7.11 (s, 1H), 4.55 - 4.66 (m, 1H), 4.18 (s, 3H), 3.05 (s, 3H), 2.40 - 2.44 (m, 1H), 1.89 - 1.95 (m, 4H), 1.51 (s, 6H), 1.43 (s, 6H), 0.98 - 1.18 (m, 4H).
81	MS *m/z* 392.0 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.09 - 9.25 (m, 2H), 8.40 (s, 1H), 8.20 (s, 1H), 7.97 (s, 1H), 7.65 - 7.72 (m, 2H), 7.60 (dd, *J*= 8.5, 5.0 Hz, 2H), 4.54 (br. s., 1H), 4.19 (s, 3H), 3.38 (d, *J*= 10.4 Hz, 2H), 3.05 - 3.17 (m, 4H), 2.15 (dd, *J*= 12.5, 3.6 Hz, 1H), 1.90 - 2.02 (m, 3H), 1.32 (d, *J*= 6.3 Hz, 3H).
91	MS *m/z* 477.4 $[M+H]^+$; ^1H NMR ($CDCl_3$) δ: 8.10 (s, 1H), 8.06 (d, *J*= 1.6 Hz, 1H), 7.99 (d, *J*= 1.6 Hz, 1H), 7.60 (d, *J*= 1.6 Hz, 1H), 7.29 (dd, *J*= 10.0, 1.6 Hz, 1H), 4.35 - 4.50 (br s, 1H), 4.34 (s, 3H), 3.17 (s, 3H), 1.84 (dd, *J*= 12.5, 3.3 Hz, 2H), 1.45 - 1.60 (m, 2H), 1.42 (br s, 6H), 1.30 (br s, 6H).
93	MS *m/z* 462.0 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.10 (s, 1H), 8.99 (d, *J*= 11.3 Hz, 1H), 8.28 (s, 1H), 8.09 - 8.20 (m, 2H), 8.06 (s, 1H), 7.73 (d, *J*= 8.5 Hz, 1H), 7.61 (d, *J*= 8.2 Hz, 1H), 4.61 - 4.74 (m, 1H), 3.08 (s, 3H), 3.01 (q, *J*= 7.6 Hz, 2H), 2.53 (s, 3H), 1.96 - 2.05 (m, 2H), 1.87 - 1.94 (m, 2H), 1.52 (s, 6H), 1.45 (s, 6H), 1.36 (t, *J*= 7.6 Hz, 3H).
96	MS *m/z* 502.2 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.09 - 9.12 (m, 1H), 8.19 - 8.22 (m, 1H), 7.92 - 7.95 (m, 1H), 7.84 - 7.87 (m, 1H), 7.63 - 7.67 (m, 1H), 7.51 - 7.55 (m, 1H), 4.26 - 4.33 (m, 1H), 3.04 (s, 3H), 2.40 (s, 3H), 1.60 - 1.65 (m, 2H), 1.43 - 1.50 (m, 2H), 1.24 (s, 6H), 1.10 (s, 6H).
111	MS *m/z* 452.0 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.92 - 9.08 (m, 2H), 8.25 (d, *J*= 1.6 Hz, 1H), 8.00 - 8.18 (m, 3H), 7.71 (dd, *J*= 8.5, 1.9 Hz, 1H), 7.60 (d, *J*= 8.5 Hz, 1H), 4.56 - 4.75 (m, 1H), 3.07 (s, 3H), 2.49 (s, 3H), 1.86 - 2.03 (m, 4H), 1.52 (s, 6H), 1.45 (s, 6H).
127	^1H NMR (DMSO-d_6) δ: 9.37 - 9.48 (m, 1H), 8.47 (d, *J*= 1.6 Hz, 1H), 8.39 (br. s., 2H), 8.20 - 8.31 (m, 1H), 7.95 (dd, *J*= 12.3, 1.6 Hz, 1H), 4.55 - 4.83 (m, 1H), 3.11 (s, 3H), 2.71 (s, 3H), 2.55 (s, 3H), 2.04 - 2.13 (m, 2H), 1.89 (d, *J*= 10.1 Hz, 2H), 1.49 - 1.56 (m, 12H).

Cpd	Data
138	MS *m/z* 459.8 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.20 (s, 1H), 8.75 - 8.84 (m, 1H), 8.37 (s, 1H), 8.22 (s, 1H), 7.89 (s, 1H), 7.79 - 7.87 (m, 1H), 7.69 (d, *J*= 8.5 Hz, 1H), 7.57 (d, *J*= 8.2 Hz, 1H), 4.59 - 4.70 (m, 1H), 3.06 (s, 3H), 2.42 (s, 3H), 1.87 - 1.98 (m, 4H), 1.51 (s, 6H), 1.43 (s, 6H).
146	MS *m/z* 420.2 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.40 (br s, 1H), 9.24 (d, *J*= 9.1 Hz, 1H), 8.38 (s, 1H), 8.22 (s, 1H), 7.79 (s, 1H), 7.70 - 7.75 (m, 1H), 7.64 - 7.69 (m, 1H), 7.38 (s, 1H), 4.56 - 4.77 (m, 1H), 4.19 (s, 3H), 3.34 (d, *J*= 11.7 Hz, 1H), 3.22 - 3.29 (m, 1H), 3.12 (s, 3H), 2.57 (s, 3H), 2.18 (dd, *J*= 12.0, 4.1 Hz, 1H), 2.10 (t, *J*= 12.9 Hz, 1H), 1.95 (d, *J*= 13.9 Hz, 1H), 1.85 (d, *J*= 11.0 Hz, 1H), 1.47 (s, 3H), 1.44 (s, 3H).
155	MS *m/z* 406.2 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.46 (br s, 1H), 9.30 (br s, 1H), 8.42 (s, 1H), 8.26 (s, 1H), 7.98 (s, 1H), 7.73 - 7.78 (m, 1H), 7.67 - 7.73 (m, 2H), 7.60 (d, *J*= 8.8 Hz, 1H), 4.69 (br s, 1H), 4.19 (s, 3H), 3.30 - 3.40 (m, 1H), 3.25 (d, *J*= 10.4 Hz, 1H), 3.13 (s, 3H), 2.08 - 2.25 (m, 2H), 1.96 (d, *J*= 12.0 Hz, 1H), 1.86 (d, *J*= 12.6 Hz, 1H), 1.48 (s, 3H), 1.45 (s, 3H).
175	MS *m/z* 420.0 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.20 - 9.62 (m, 2H), 8.40 (s, 1H), 8.23 - 8.29 (m, 1H), 7.66 - 7.82 (m, 3H), 7.40 (s, 1H), 4.48 - 4.90 (m, 1H), 4.20 (s, 3H), 3.34 - 3.88 (m, 2H), 3.16 (s, 3H), 2.57 (s, 3H), 1.80 - 2.43 (m, 4H), 1.30 - 1.53 (m, 6H).
176	MS *m/z* 406.0 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.15 - 9.63 (m, 2H), 8.42 (d, *J*= 2.5 Hz, 1H), 8.22 - 8.29 (m, 1H), 7.98 (s, 1H), 7.63 - 7.79 (m, 3H), 7.60 (d, *J*= 8.8 Hz, 1H), 4.54 - 4.83 (m, 1H), 4.19 (s, 3H), 3.37 - 3.89 (m, 2H), 3.13 (s, 3H), 1.77 - 2.41 (m, 4H), 1.31 - 1.49 (m, 6H).

Example 3

Preparation of Compound 37



Step 1: A mixture of 6-bromo-2-chloro-4-fluoro-1,3-benzothiazole (530 mg, 2.0 mmol, 1.0 eq.), N,2,2,6,6-pentamethylpiperidin-4-amine (410 mg, 0.45 mL, 2.4 mmol, 1.2 eq.) and K_2CO_3 (840 mg, 6.0 mmol, 3.0 eq.) in acetonitrile (5.0 mL) was stirred at 100 °C for 4 h, and then cooled, diluted with ethyl acetate and filtered through Celite. The filtrate was concentrated to give 6-

bromo-4-fluoro-*N*-methyl-*N*-(2,2,6,6-tetramethyl-4-piperidyl)-1,3-benzothiazol-2-amine (840 mg, 100%), which was used directly in next step without further purification.

Step 2: A mixture of 6-bromo-4-fluoro-*N*-methyl-*N*-(2,2,6,6-tetramethyl-4-piperidyl)-1,3-benzothiazol-2-amine (78 mg, 0.19 mmol, 1.0 eq.), 4,4,5,5-tetramethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3,2-dioxaborolane (54 mg, 0.21 mmol, 1.1 eq.), $PdCl_2$dppf dichloromethane complex (16 mg, 0.019 mmol, 0.10 eq.) and KOAc (58 mg, 0.58 mmol, 3.0 eq.) in dioxane (1.0 mL) was stirred at 90 °C for 4 h. LC/MS showed a complete conversion to the pinacol boronate. To the mixture was added 6-chloro-2-methyl-imidazo[1,2-b]pyridazine (26 mg, 0.16 mmol, 0.80 eq.) and $PdCl_2$dppf dichloromethane complex (16 mg, 0.019 mmol, 0.10 eq.), followed by K_2CO_3 (2.0 M aq.) (0.29 mL, 0.58 mmol, 3.0 eq.). The mixture was heated at 90 °C overnight, and then cooled, diluted with ethyl acetate and washed with water and brine. The organic layer was separated, dried over sodium sulfate, and evaporated. The residue was purified over basic alumina with ethyl acetate in hexanes (10 to 100% gradient) to provide 4-fluoro-*N*-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-(2,2,6,6-tetramethyl-4-piperidyl)-1,3-benzothiazol-2-amine (40 mg, 45%).

MS *m/z* 453.4 $[M+H]^+$; ^{1}H NMR ($CDCl_3$) δ: 7.92 (d, *J*= 1.9 Hz, 1H), 7.80 (d, *J*= 9.5 Hz, 1H), 7.70 (s, 1H), 7.59 (dd, *J*= 11.8, 1.7 Hz, 1H), 7.33 (d, *J*= 9.5 Hz, 1H), 4.19 - 4.49 (m, 1H), 3.09 (s, 3H), 2.46 (s, 3H), 1.76 (dd, *J*= 12.3, 3.2 Hz, 2H), 1.40 - 1.70 (m, 2H), 1.29 - 1.39 (m, 6H), 1.18 - 1.28 (m, 6H).

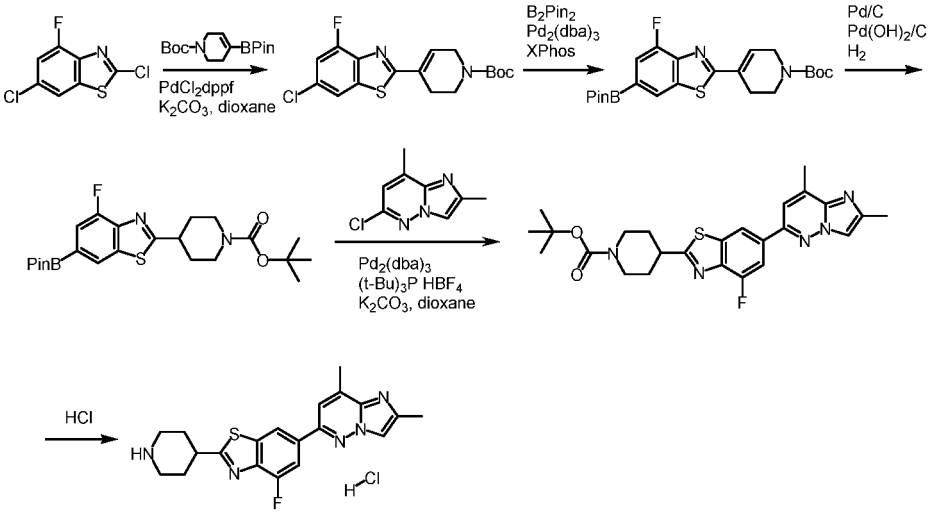
Using the procedure described for Example 3, above, additional compounds described herein were prepared by substituting the appropriate starting material, suitable reagents and reaction conditions, obtaining compounds such as those selected from:

Cpd	Data
39	MS *m/z* 466.4 $[M+H]^+$; ^{1}H NMR ($CDCl_3$) δ: 8.10 (d, *J*= 0.9 Hz, 1H), 7.56 (d, *J*= 1.6 Hz, 1H), 7.39 (s, 1H), 7.24 (dd, *J*= 11.8, 1.7 Hz, 1H), 7.19 (d, *J*= 0.9 Hz, 1H), 4.22 - 4.44 (m, 1H), 3.17 (s, 3H), 2.67 (s, 3H), 2.52 (s, 3H), 1.83 (dd, *J*= 12.5, 3.3 Hz, 2H), 1.40 - 1.52 (m, 2H), 1.35 - 1.41 (m, 6H), 1.21 - 1.30 (m, 6H).
40	MS *m/z* 435.4 $[M+H]^+$; ^{1}H NMR (DMSO-d_6) δ: 9.72 (br s, 1H), 8.32 - 8.82 (m, 5H), 8.08 (br s, 1H), 7.66 (br s, 1H), 4.71 (br s, 1H), 3.09 (br s, 3H), 2.55 (br s, 3H), 2.16 (br s, 2H), 1.81 (br s, 2H), 1.53 (br s, 12H).

Cpd	Data
48	MS *m/z* 436.4 $[M+H]^+$; ^1H NMR ($CDCl_3$) δ: 8.39 (d, *J*= 1.6 Hz, 1H), 8.05 (d, *J*= 9.5 Hz, 1H), 7.94 (dd, *J*= 8.5, 1.9 Hz, 1H), 7.84 (d, *J*= 9.5 Hz, 1H), 7.65 (d, *J*= 8.2 Hz, 1H), 4.34 - 4.53 (m, 1H), 3.15 (s, 3H), 2.70 (s, 3H), 1.83 (dd, *J*= 12.5, 3.3 Hz, 2H), 1.49 (br s, 2H), 1.41 (s, 6H), 1.27 (br s, 6H).
200	MS *m/z* 483.4 $[M+H]^+$; ^1H NMR ($CDCl_3$) δ: 8.00 (d, *J*= 1.6 Hz, 1H), 7.71 (d, *J*= 0.6 Hz, 1H), 7.64 (dd, *J*= 11.8, 1.7 Hz, 1H), 6.71 (s, 1H), 4.17 (s, 3H), 3.51 (s, 1H), 3.18 (s, 3H), 2.52 (d, *J*= 0.6 Hz, 3H), 1.86 (dd, *J*= 12.3, 2.8 Hz, 2H), 1.22 - 1.72 (m, 14H).

Example 4

Preparation of Compound 47



Step 1: A mixture of 2,6-dichloro-4-fluoro-1,3-benzothiazole (3.54 g, 15.9 mmol, 1.00 eq., prepared according to Example 1 step 1 starting from 4-chloro-2,6-difluoroaniline), tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,6-dihydro-2*H*-pyridine-1-carboxylate (5.91 g, 19.1 mmol, 1.20 eq.), $PdCl_2$(dppf) (1.2 g, 1.59 mmol, 0.1 eq.) and K_2CO_3 (2.0 M aq.) (24 mL, 47.8 mmol, 3.00 eq.) in dioxane (50 mL) was heated at 90 °C for 2 h, and then cooled, diluted with ethyl acetate and washed with water and brine. The organic layer was separated, dried over sodium sulfate and evaporated. The residue was purified over silica gel with ethyl acetate and hexanes (3 to 20%) to give tert-butyl 4-(6-chloro-4-fluoro-1,3-benzothiazol-2-yl)-3,6-dihydro-2*H*-pyridine-1-carboxylate (5.58 g, 94.9%).

^1H NMR ($CDCl_3$) δ: 7.63 (dd, *J*= 1.7, 0.8 Hz, 1H), 7.21 (dd, *J*= 9.8, 1.9 Hz, 1H), 6.72 (br. s., 1H), 4.21 (d, *J*= 2.5 Hz, 2H), 3.68 (t, *J*= 5.5 Hz, 2H), 2.84 (dd, *J*= 4.3, 2.7 Hz, 2H), 1.52 (s, 9H).

Step 2: A mixture of tert-butyl 4-(6-chloro-4-fluoro-1,3-benzothiazol-2-yl)-3,6-dihydro-2*H*-

pyridine-1-carboxylate (4.0 g, 10.8 mmol, 1.0 eq.), 4,4,5,5-tetramethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3,2-dioxaborolane (5.5 g, 21.7 mmol, 2.0 eq.), $Pd_2(dba)_3$ (0.5 g, 0.542 mmol, 0.05 eq.), X-Phos (1.06 g, 2.17 mmol, 0.2 eq.) and KOAc (3.23 g, 32.5 mmol, 3.0 eq.) in dioxane (100 mL) was heated at 110 °C overnight, and then cooled, diluted with ethyl acetate, filtered, and concentrated. The crude product was purified over silica gel to give tert-butyl 4-[4-fluoro-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3-benzothiazol-2-yl]-3,6-dihydro-2*H*-pyridine-1-carboxylate (5.1 g, 100%).

^{1}H NMR ($CDCl_3$) δ: 8.09 (d, *J*= 0.6 Hz, 1H), 7.57 (dd, *J*= 10.7, 0.6 Hz, 1H), 6.76 (s, 1H), 4.21 (br. s., 4H), 3.68 (br. s., 2H), 2.86 (d, *J*= 1.6 Hz, 2H), 1.52 (s, 9H), 1.39 (s, 12H).

Step 3: A mixture of tert-butyl 4-[4-fluoro-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3-benzothiazol-2-yl]-3,6-dihydro-2*H*-pyridine-1-carboxylate (1.0 g, 2.2 mmol, 1.0 eq.), 5% Pd/C (0.5 g, 0.2 mmol, 0.1 eq.) and 10% $Pd(OH)_2$/C (0.5 g, 0.4 mmol, 0.2 eq.) in MeOH (200 mL) and CH_2Cl_2 (20 mL) was hydrogenated overnight at 60 psi. The mixture was then filtered thru Celite and purified over silica gel with ethyl acetate in hexanes (5 to 20% gradient) to give tert-butyl 4-[4-fluoro-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3-benzothiazol-2-yl]piperidine-1-carboxylate (0.75 g, 75%).

^{1}H NMR ($CDCl_3$) δ: 8.12 (d, *J*= 0.9 Hz, 1H), 7.57 (d, *J*= 10.7 Hz, 1H), 4.19 - 4.34 (m, 2H), 3.28 - 3.38 (m, 1H), 2.86 - 2.99 (m, 2H), 2.15 - 2.25 (m, 2H), 1.81 - 1.94 (m, 2H), 1.50 (s, 9H), 1.39 (s, 12H).

Step 4: tert-Butyl 4-[4-fluoro-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3-benzothiazol-2-yl]piperidine-1-carboxylate (520 mg, 1.1 mmol, 1.0 eq.) was combined with 6-chloro-2,8-dimethyl-imidazo[1,2-b]pyridazine (204 mg, 1.1 mmol, 1.0 eq.), $Pd_2(dba)_3$ (52 mg, 0.056 mmol, 0.05 eq.) and $(t\text{-}Bu)_3P$ HBF_4 (33 mg, 0.11 mmol, 0.1 equiv.). The vessel was purged with N_2. To the vessel was added dioxane (7.0 mL) and K_2CO_3 (2.0 M aq.) (3.5 mL, 7.0 mmol). The mixture was heated at 80 °C for 1 h, then cooled and partitioned between EtOAc and H_2O. The organic layer was concentrated and chromatographed on silica gel, eluting with 30-100% EtOAc in CH_2Cl_2 to give the desired tert-butyl 4-[6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4-fluoro-1,3-benzothiazol-2-yl]piperidine-1-carboxylate (500 mg, 92%). MS *m/z* 482.2 $[M+H]^+$.

Step 5: tert-Butyl 4-[6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4-fluoro-1,3-benzothiazol-2-yl]piperidine-1-carboxylate (500 mg, 1.0 mmol) was suspended in 4.0 M HCl in 1,4-dioxane (3 mL, 12 mmol). The mixture was stirred for 30 min, then diluted with Et_2O (10 mL) and filtered.

The solid was partitioned between CH_2Cl_2 and aqueous K_2CO_3 (1M). The organic layer was then separated and concentrated. The residue was chromatographed on silica gel, eluting with 0-10% MeOH (2 N NH_3) in CH_2Cl_2. The purified material was dissolved in 1.25 M HCl in MeOH (3 mL) followed by the removal of volatiles to give 6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4-fluoro-2-(piperidin-4-yl)benzo[d]thiazole hydrochloride (340 mg, 72%).

MS *m/z* 382.3 $[M+H]^+$. ^1H NMR (methanol-d_4) δ: 8.49 (d, *J*= 1.9 Hz, 1H), 7.98 (dd, *J*= 11.9, 1.9 Hz, 1H), 7.95 (s, 1H), 7.66 (d, *J*= 1.3 Hz, 1H), 3.52 (m, 1H), 3.44 (m, 2H), 3.09 (td, *J*= 12.6, 3.2 Hz, 2H), 2.69 (s, 3H), 2.51 (s, 3H), 2.38 (m, 2H), 2.09 (m, 2H).

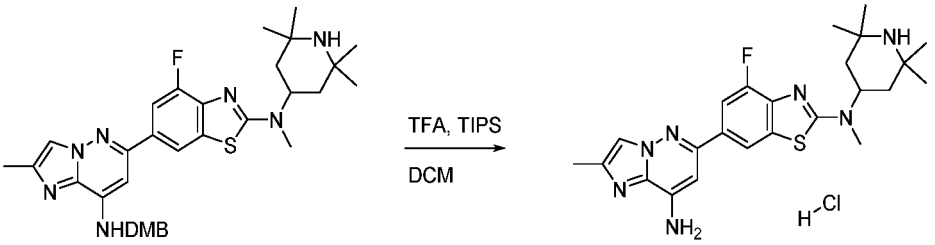
Using the procedure described for Example 4, above, additional compounds described herein were prepared by substituting the appropriate starting material, suitable reagents and reaction conditions, obtaining compounds such as those selected from:

Cpd	Data
78	MS *m/z* 354.2 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.42 (d, *J*= 1.6 Hz, 1H), 8.21 (d, *J*= 0.9 Hz, 1H), 8.05 (dd, *J*= 9.0, 1.1 Hz, 1H), 7.91 - 7.97 (m, 2H), 3.45 - 3.55 (m, 3H), 3.12 - 3.22 (m, 2H), 2.34 - 2.41 (m, 2H), 2.06 - 2.16 (m, 2H).
79	MS *m/z* 368.3 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.73 - 8.84 (m, 2H), 8.60 (d, *J*= 1.6 Hz, 1H), 8.20 (d, *J*= 9.1 Hz, 1H), 8.04 (dd, *J*= 11.3, 1.9 Hz, 1H), 4.44 (s, 3H), 3.65 - 3.73 (m, 1H), 3.61 (d, *J*= 13.2 Hz, 2H), 3.28 - 3.35 (m, 2H), 2.46 - 2.55 (m, 2H), 2.20 - 2.30 (m, 2H).
126	MS *m/z* 385.3 $[M+H]^+$; ^1H NMR ($CDCl_3$) δ: 8.04 (d, *J*= 2.5 Hz, 1H), 7.86 (d, *J*= 1.6 Hz, 1H), 7.66 (d, *J*= 1.3 Hz, 1H), 7.45 (dd, *J*= 11.3, 1.6 Hz, 1H), 7.25 (dd, *J*= 12.3, 1.3 Hz, 1H), 4.31 (s, 3H), 3.32 - 3.42 (m, 3H), 2.91 (td, *J*= 12.0, 2.5 Hz, 2H), 2.30 (dd, *J*= 13.1, 2.4 Hz, 2H), 1.96 - 2.04 (m, 2H).
151	MS *m/z* 398.3 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.73 (s, 1H), 8.31 (s, 1H), 8.13 (d, *J*= 11.3 Hz, 1H), 7.88 (s, 1H), 4.40 (s, 3H), 3.63 - 3.72 (m, 1H), 3.60 (d, *J*= 12.9 Hz, 2H), 3.28 (t, *J*= 7.4 Hz, 2H), 2.64 (s, 3H), 2.50 (d, *J*= 12.3 Hz, 2H), 2.20 - 2.30 (m, 2H).
152	MS *m/z* 385.3 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.93 (d, *J*= 1.3 Hz, 1H), 8.10 - 8.18 (m, 2H), 8.03 (d, *J*= 1.3 Hz, 1H), 7.61 (dd, *J*= 11.5, 1.7 Hz, 1H), 3.42 - 3.56 (m, 3H), 3.14 (td, *J*= 12.6, 2.8 Hz, 2H), 2.50 (d, *J*= 0.9 Hz, 3H), 2.35 (dd, *J*= 14.5, 2.8 Hz, 2H), 2.05 - 2.15 (m, 2H).
167	MS *m/z* 397.4 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.61 (br. s., 1H), 8.12 (s, 1H), 8.04 (d, *J*= 11.7 Hz, 1H), 7.18 (s, 1H), 3.65 - 3.70 (m, 1H), 3.59 (d, *J*= 11.3 Hz, 2H), 3.20 - 3.30 (m, 2H), 3.24 (s, 3H), 2.63 (s, 3H), 2.50 (d, *J*= 13.9 Hz, 2H), 2.18 - 2.30 (m, 2H).

Cpd	Data
168	MS *m/z* 411.4 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.60 (br. s., 1H), 8.15 (br s, 1H), 8.00 (d, *J*= 11.3 Hz, 1H), 7.14 (br. s., 1H), 3.52 - 3.60 (m, 3H), 3.46 (s, 6H), 3.20 - 3.26 (m, 2H), 2.62 (s, 3H), 2.40 - 2.50 (m, 2H), 2.23 (br s, 2H).
187	MS *m/z* 474.3 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.72 (d, *J*= 1.3 Hz, 1H), 8.31 (d, *J*= 1.3 Hz, 1H), 8.14 (dd, *J*= 11.7, 1.6 Hz, 1H), 8.01 (s, 1H), 7.67 (dd, *J*= 8.0, 1.4 Hz, 2H), 7.46 - 7.54 (m, 3H), 5.69 (s, 2H), 3.65 - 3.70 (m, 1H), 3.58 -3.63 (m, 2H), 3.25 - 3.31 (m, 2H), 2.61 (d, *J*= 0.9 Hz, 3H), 2.45 - 2.53 (m, 2H), 2.20 - 2.30 (m, 2H).
191	MS *m/z* 361.3 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.08 (s, 1H), 7.55 - 7.61 (m, 1H), 7.38 - 7.43 (m, 1H), 7.18 - 7.28 (m, 2H), 3.99 (s, 3H), 3.55 - 3.65 (m, 3H), 3.23 - 3.30 (m, 2H), 2.43 - 2.51 (m, 2H), 2.16 - 2.27 (m, 2H).
195	MS *m/z* 460.3 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.41 (dd, *J*= 4.1, 0.9 Hz, 2H), 7.92 (dd, *J*= 11.7, 0.9 Hz, 1H), 7.61 - 7.69 (m, 2H), 7.44 - 7.54 (m, 3H), 7.33 (s, 1H), 3.53 – 3.67 (m, 3H), 3.20 - 3.24 (m, 2H), 2.69 (s, 3H), 2.40 – 2.46 (m, 2H), 2.14 - 2.25 (m, 2H).
219	MS *m/z* 412.4 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.69 (s, 1H), 8.57 (d, *J*= 1.3 Hz, 1H), 8.31 (d, *J*= 0.9 Hz, 1H), 7.94 - 8.02 (m, 1H), 3.44 - 3.52 (m, 1H), 3.37 - 3.44 (m, 2H), 3.04 - 3.11 (m, 2H), 2.52 (d, *J*= 0.9 Hz, 3H), 2.26 - 2.34 (m, 2H), 2.00 – 2.10 (m, 2H).
220	MS *m/z* 440.4 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.54 (d, *J*= 1.6 Hz, 1H), 8.32 (s, 1H), 8.27 (d, *J*= 0.9 Hz, 1H), 7.94 - 8.00 (m, 1H), 4.18 (s, 2H), 3.69 (s, 3H), 3.48 - 3.56 (m, 1H), 3.40-3.45 (m, 2H), 3.13 – 3.18 (m, 2H), 2.54 (d, *J*= 0.9 Hz, 3H), 2.31 - 2.38 (m, 2H), 2.04 - 2.15 (m, 2H).
221	MS *m/z* 426.4 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.66 (s, 1H), 8.44 (s, 1H), 8.38 (s, 1H), 8.06 - 8.14 (m, 1H), 4.27 (s, 2H), 3.62 - 3.70 (m, 1H), 3.54 - 3.61 (m, 2H), 3.22 - 3.29 (m, 2H), 2.66 (s, 3H), 2.44 - 2.51 (m, 2H), 2.18 - 2.28 (m, 2H).
230	MS *m/z* 393.3 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.85 (s, 1H), 8.57 (s, 1H), 8.38 (s, 1H), 7.97 - 8.04 (m, 1H), 3.51 - 3.59 (m, 1H), 3.42 - 3.50 (m, 2H), 3.11 - 3.17 (m, 2H), 2.57 (s, 3H), 2.33 - 2.40 (m, 2H), 2.06 - 2.17 (m, 2H).
249	MS *m/z* 368.0 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.88 (d, *J*= 7.3 Hz, 1H), 8.66 (d, *J*= 1.6 Hz, 1H), 8.11 - 8.17 (m, 1H), 7.61 (d, *J*= 7.3 Hz, 1H), 6.60 (s, 1H), 3.55 - 3.69 (m, 3H), 3.23 - 3.31 (m, 2H), 2.54 (s, 3H), 2.45 - 2.52 (m, 2H), 2.18 - 2.28 (m, 2H).

Example 5

Preparation of Compound 201



A mixture of 6-[8-[(2,4-dimethoxyphenyl)methylamino]-2-methyl-imidazo[1,2-b]pyridazin-6-yl]-4-fluoro-*N*-methyl-*N*-(2,2,6,6-tetramethyl-4-piperidyl)-1,3-benzothiazol-2-amine (10 mg, 0.016 mmol, 1.0 eq., prepared according to the procedure in Example 3) and triisopropylsilane (0.2 mL) in CH_2Cl_2 (1.0 mL) and TFA (1.0 mL) was stirred at room temperature for 1 h. The mixture was then concentrated and purified with a C18 column to give 6-(8-amino-2-methyl-imidazo[1,2-b]pyridazin-6-yl)-4-fluoro-*N*-methyl-*N*-(2,2,6,6-tetramethyl-4-piperidyl)-1,3-benzothiazol-2-amine hydrochloride (5.0 mg, 61%) after treatment with HCl in MeOH.

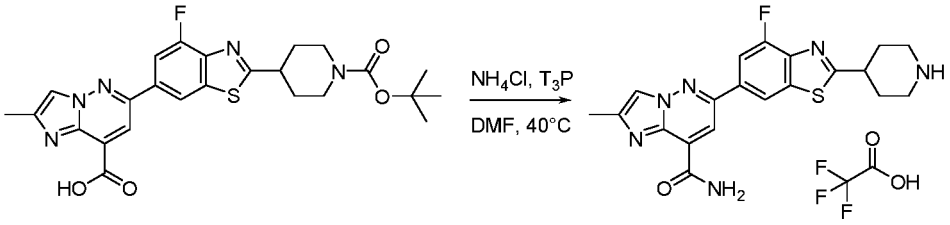
MS *m/z* 468.4 $[M+H]^+$. ^1H NMR (methanol-d_4) δ: 8.23 (d, *J*= 1.3 Hz, 1H), 8.11 (s, 1H), 7.75 - 7.83 (m, 1H), 7.25 (s, 1H), 4.98 - 5.08 (m, 1H), 3.19 (s, 3H), 2.63 (s, 3H), 2.01 - 2.13 (m, 4H), 1.68 (s, 6H), 1.57 (s, 6H).

Using the procedure described for Example 5, above, additional compounds described herein were prepared by substituting the appropriate starting material, suitable reagents and reaction conditions, obtaining compounds such as those selected from:

Cpd	Data
188	MS *m/z* 383.5 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.34 (d, *J*= 1.6 Hz, 1H), 7.98 (d, *J*= 0.9 Hz, 1H), 7.80 (dd, *J*= 11.7, 1.3 Hz, 1H), 7.11 (s, 1H), 3.41 - 3.54 (m, 3H), 3.09 - 3.17 (m, 2H), 2.49 (d, *J*= 0.9 Hz, 3H), 2.35 (dd, *J*= 14.3, 2.4 Hz, 2H), 2.09 (d, *J*= 12.0 Hz, 2H).
189	MS *m/z* 384.3 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.41 (br s, 1H), 8.07 (br s, 1H), 7.79 - 7.89 (m, 1H), 7.30 (br. s., 1H), 3.43 - 3.57 (m, 3H), 3.15 (td, *J*= 12.5, 2.5 Hz, 2H), 2.49 (s, 3H), 2.32 - 2.39 (m, 2H), 2.05 – 2.17 (m, 2H).

Example 6

Preparation of Compound 224

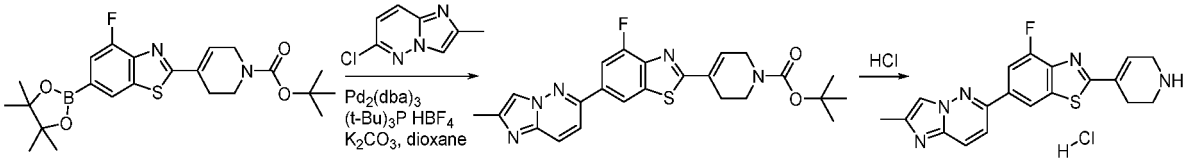


To a solution of 6-[2-(1-tert-butoxycarbonyl-4-piperidyl)-4-fluoro-1,3-benzothiazol-6-yl]-2-methyl-imidazo[1,2-b]pyridazine-8-carboxylic acid (17 mg, 0.033 mmol, 1.0 eq.) in DMF (0.5 mL) was added TEA (20 mg, 0.028 mL, 0.20 mmol, 6.0 eq.), after 10 min ammonium chloride (5.4 mg, 0.10 mmol, 3.0 eq.) was added followed by 1-propanephosphonic anhydride (50 mass%) in DMF (63 mg, 0.10 mmol, 3.0 eq.). The mixture was stirred at 40 °C overnight, then basified with aq. K_2CO_3, filtered, and the solid was collected and was further purified over C18 to give 6-[4-fluoro-2-(4-piperidyl)-1,3-benzothiazol-6-yl]-2-methyl-imidazo[1,2-b]pyridazine-8-carboxamide;2,2,2-trifluoroacetic acid (10.0 mg, 57%).

MS *m/z* 411.3 $[M+H]^+$. ^1H NMR (methanol-d_4) δ: 8.50 (d, *J*= 5.7 Hz, 2H), 8.17 (s, 1H), 7.94 (d, *J*= 11.3 Hz, 1H), 3.43-3.55 (m, 3H), 3.10 - 3.18 (m, 2H), 2.51(s, 3H), 2.32 - 2.40 (m, 2H), 2.05-2.15 (m, 2H).

Example 7

Preparation of Compound 44



Step 1: A mixture of tert-butyl 4-[4-fluoro-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3-benzothiazol-2-yl]-3,6-dihydro-2*H*-pyridine-1-carboxylate (prepared in example 4 step 2, 66 mg, 0.14 mmol, 1.2 eq.), 6-chloro-2-methyl-imidazo[1,2-b]pyridazine (20 mg, 0.12 mmol, 1.0 eq.), $Pd_2(dba)_3$ (5.5 mg, 0.0060 mmol, 0.05 eq.), $(t\text{-}Bu)_3P$ HBF_4 (3.5 mg, 0.012 mmol, 0.10 eq.) and K_2CO_3 (2.0 M aq.) (0.18 mL, 0.36 mmol, 3.0 eq.) in dioxane (1.0 mL) was stirred at 100 °C for 1 h. The reaction mixture was then cooled, diluted with ethyl acetate and washed with brine and

then dried over sodium sulfate and concentrated. The residue was purified over silica gel with methanol in dichloromethane (0 to 8% gradient) to give tert-butyl 4-[4-fluoro-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-1,3-benzothiazol-2-yl]-3,6-dihydro-2*H*-pyridine-1-carboxylate (59 mg, 100%). MS *m/z* 466.2 $[M+H]^+$.

Step 2: To a suspension of tert-butyl 4-[4-fluoro-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-1,3-benzothiazol-2-yl]-3,6-dihydro-2*H*-pyridine-1-carboxylate (15 mg, 0.032 mmol, 1.0 eq.) in dioxane (0.2 mL) was added HCl (4 M in dioxane) (1.0 mL). The mixture was stirred at room temperature for 1 h, then diluted with ether and filtered to give 4-fluoro-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole hydrochloride (12 mg, 85%).

MS *m/z* 366.3 $[M+H]^+$; ^{1}H NMR (DMSO-d_6) δ: 9.70 (br s, 1H), 9.61 (br s, 1H), 8.80 (d, *J*= 1.3 Hz, 1H), 8.49 (d, *J*= 9.5 Hz, 1H), 8.42 (s, 1H), 8.30 (d, *J*= 9.5 Hz, 1H), 8.13 (dd, *J*= 12.0, 1.3 Hz, 1H), 6.94 (br s, 1H), 3.90 (br s, 2H), 3.37 (d, *J*= 4.4 Hz, 2H), 2.95 (br s, 2H), 2.54 (s, 3H).

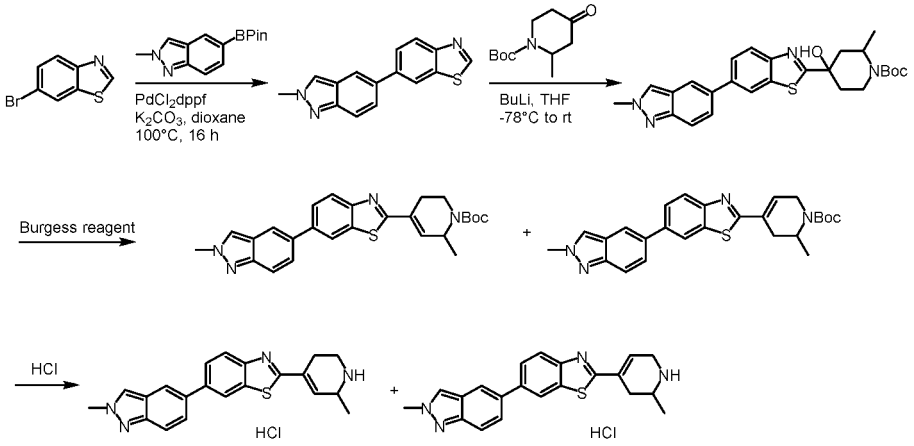
Using the procedure described for Example 7, above, additional compounds described herein were prepared by substituting the appropriate starting material, suitable reagents and reaction conditions, obtaining compounds such as those selected from:

Cpd	Data
1	MS *m/z* 347.1 $[M+H]^+$; ^{1}H NMR (DMSO-d_6) δ: 8.41 (s, 1H), 8.38 (s, 1H), 8.06 (s, 1H), 8.00 (d, *J*= 8.5 Hz, 1H), 7.82 (d, *J*= 8.5 Hz, 1H), 7.62 - 7.73 (m, 2H), 6.83 (br s, 1H), 4.19 (s, 3H), 3.49 (br s, 2H), 2.96 (t, *J*= 5.5 Hz, 2H), 2.59 (br s, 2H).
18	MS *m/z* 361.1 $[M+H]^+$; ^{1}H NMR (DMSO-d_6) δ: 9.09 (br s, 2H), 8.43 (d, *J*= 1.6 Hz, 1H), 8.39 (s, 1H), 8.04 (d, *J*= 8.5 Hz, 1H), 7.88 (s, 1H), 7.86 (dd, *J*= 8.5, 1.9 Hz, 1H), 7.45 (s, 1H), 6.81 (br s, 1H), 4.20 (s, 3H), 3.91 (br s, 2H), 3.40 (d, *J*= 4.4 Hz, 2H), 2.92 (br s, 2H), 2.58 (s, 3H).
46	MS *m/z* 380.1 $[M+H]^+$; ^{1}H NMR (DMSO-d_6) δ: 9.57 (br s, 2H), 8.68 (s, 1H), 8.34 (s, 1H), 8.22 (br s, 1H), 8.03 (d, *J*= 11.7 Hz, 1H), 6.86 (br s, 1H), 3.82 (br s, 2H), 3.24 - 3.35 (m, 2H), 2.87 (br s, 2H), 2.66 (s, 3H), 2.49 (s, 3H).
53	MS *m/z* 380.3 $[M+H]^+$; ^{1}H NMR (DMSO-d_6) δ: 9.57 (br s, 2H), 9.43 (s, 1H), 8.68 (s, 1H), 8.12 (s, 1H), 8.05 (d, *J*= 12.3 Hz, 1H), 6.88 (br s, 1H), 3.89 (br s, 2H), 3.37 (d, *J*= 6.9 Hz, 2H), 2.85 - 2.95 (m, 2H), 2.91 (s, 3H), 2.55 (s, 3H).
71	MS *m/z* 379.3 $[M+H]^+$; ^{1}H NMR (DMSO-d_6) δ: 9.56 (br s, 2H), 9.20 (s, 1H), 8.36 (d, *J*= 1.6 Hz, 1H), 8.15 (s, 1H), 8.02 (d, *J*= 0.9 Hz, 1H), 7.81 (dd, *J*= 12.0, 1.6 Hz, 1H), 6.80 - 6.86 (m, 1H), 3.88 - 3.92 (m, 2H), 3.24 - 3.33 (m, 2H), 2.87 (br. s., 2H), 2.60 (s, 3H), 2.48 (d, *J*= 0.9 Hz, 3H).

Cpd	Data
72	MS *m/z* 365.3 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.22 - 9.35 (m, 2H), 8.38 (s, 1H), 8.25 (d, *J*= 1.6 Hz, 1H), 8.07 (s, 1H), 7.71 (dd, *J*= 12.3, 1.6 Hz, 1H), 7.59 - 7.67 (m, 2H), 6.78 (br s, 1H), 4.13 (s, 3H), 3.78 - 3.85 (m, 2H), 3.25 - 3.33 (m, 2H), 2.87 (br s, 2H).
102	MS *m/z* 390.3 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.37 - 8.42 (m, 1H), 8.23 - 8.28 (m, 1H), 8.05 - 8.08 (m, 1H), 7.97 - 8.00 (m, 1H), 7.49 - 7.55 (m, 1H), 6.71 - 6.76 (m, 1H), 4.23 (s, 3H), 3.86 - 3.93 (m, 2H), 3.41 - 3.46 (m, 2H), 3.00 - 3.06 (m, 2H).
145	MS *m/z* 396.3 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.72 (d, *J*= 1.6 Hz, 1H), 8.31 (d, *J*= 0.9 Hz, 1H), 8.14 (dd, *J*= 11.7, 1.6 Hz, 1H), 7.88 (s, 1H), 6.96 (s, 1H), 4.40 (s, 3H), 4.04 (d, *J*= 3.2 Hz, 2H), 3.58 (t, *J*= 6.1 Hz, 2H), 3.15 (d, *J*= 1.9 Hz, 2H), 2.64 (d, *J*= 0.6 Hz, 3H).

Example 8

Preparation of Compound 65 and Compound 67



Step 1: A mixture of 6-bromobenzo[d]thiazole (2.12 g), 2-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2*H*-indazole (1.2 eq.), $PdCl_2dppf$ (0.1 eq.) and K_2CO_3 (2.5 eq.) in dioxane and water was heated at 100 °C for 16 h under N_2 atmosphere, then cooled, diluted with ethyl acetate and washed with water and brine. The organic layer was separated, dried over sodium sulfate and concentrated. The residue was purified by flash silica gel chromatography to afford 6-(2-methyl-2*H*-indazol-5-yl)benzo[d]thiazole (1.3 g, 48%). MS *m/z* 266.1, 268.1 $[M+H]^+$.

Step 2: To a solution of 6-(2-methyl-2*H*-indazol-5-yl)benzo[d]thiazole (700 mg) in THF at -78°C was added slowly a solution of n-BuLi (3.0 eq.) in hexanes. After 30 min, a solution of tert-butyl 2-methyl-4-oxopiperidine-1-carboxylate (2.0 eq.) in THF was added and the temperature was allowed to rise slowly to room temperature over 16 h. The mixture was treated with saturated

NH_4Cl solution and extracted with ethyl acetate. The organic extracts were combined, dried over sodium sulfate and evaporated. The residue was purified by silica gel flash column chromatography to afford tert-butyl 4-hydroxy-2-methyl-4-(6-(2-methyl-2*H*-indazol-5-yl)benzo[d]thiazol-2-yl)piperidine-1-carboxylate (0.56 g, 43%). MS *m/z* 479.2 $[M+H]^+$.

Step 3: A mixture of tert-butyl 4-hydroxy-2-methyl-4-(6-(2-methyl-2*H*-indazol-5-yl)benzo[d]thiazol-2-yl)piperidine-1-carboxylate (0.56 g) and Burgess reagent (2.0 eq.) in THF was stirred at 90 °C for 48 h, then cooled, diluted with ice-water, and basified with concentrated ammonium hydroxide. The mixture was extracted with ethyl acetate. The organic extracts were combined, dried over sodium sulfate and then concentrated. The residue was purified by silica gel flash column chromatography to give a mixture of tert-butyl 6-methyl-4-(6-(2-methyl-2*H*-indazol-5-yl)benzo[d]thiazol-2-yl)-3,6-dihydropyridine-1(2H)-carboxylate and tert-butyl 2-methyl-4-(6-(2-methyl-2*H*-indazol-5-yl)benzo[d]thiazol-2-yl)-3,6-dihydropyridine-1(2H)-carboxylate (410 mg, 76%). MS *m/z* 461.2 $[M+H]^+$.

Step 4: The mixture of tert-butyl 6-methyl-4-(6-(2-methyl-2*H*-indazol-5-yl)benzo[d]thiazol-2-yl)-3,6-dihydropyridine-1(2H)-carboxylate and tert-butyl 2-methyl-4-(6-(2-methyl-2*H*-indazol-5-yl)benzo[d]thiazol-2-yl)-3,6-dihydropyridine-1(2H)-carboxylate (300 mg) was stirred in 4.0 N HCl in dioxane for 16 h, then concentrated and the residue was purified over chiral prep-HPLC and C18 prep-HPLC to give 2-(6-methyl-1,2,3,6-tetrahydropyridin-4-yl)-6-(2-methyl-2*H*-indazol-5-yl)benzo[d]thiazole hydrochloride (21 mg).

MS *m/z* 361.1 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.81 - 9.93 (m, 1H), 9.25 - 9.38 (m, 1H), 8.45 (d, *J*= 8.5 Hz, 2H), 8.02 - 8.12 (m, 2H), 7.87 (dd, *J*= 8.7, 1.7 Hz, 1H), 7.64 - 7.74 (m, 2H), 6.74 (br s, 1H), 4.20 (br s, 3H), 3.44 - 3.54 (m, 1H), 3.20 - 3.33 (m, 1H), 2.93 (br s, 2H), 1.47 (d, *J*= 7.3 Hz, 3H)

and 2-(2-methyl-1,2,3,6-tetrahydropyridin-4-yl)-6-(2-methyl-2*H*-indazol-5-yl)benzo[d]thiazole hydrochloride (11 mg).

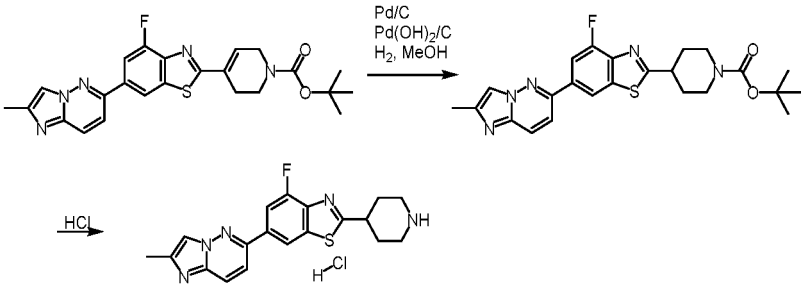
MS *m/z* 361.2 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.73 - 9.83 (m, 1H), 9.46 - 9.56 (m, 1H), 8.44 (d, *J*= 1.9 Hz, 2H), 8.08 (s, 1H), 8.05 (d, *J*= 8.5 Hz, 1H), 7.83 - 7.90 (m, 1H), 7.69 - 7.73 (m, 1H), 7.65 - 7.69 (m, 1H), 6.80 (br s, 1H), 4.20 (s, 3H), 3.89 (br s, 2H), 3.45 - 3.55 (m, 1H), 3.11 (d, *J*= 14.8 Hz, 1H), 2.60 - 2.69 (m, 1H), 1.44 (d, *J*= 6.3 Hz, 3H).

Using the procedure described for Example 8, above, additional compounds described herein were prepared by substituting the appropriate starting material, suitable reagents and reaction conditions, obtaining compounds such as those selected from:

Cpd	Data
56	MS *m/z* 361.2 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.42 (s, 1H), 8.38 (d, *J*= 1.3 Hz, 1H), 8.07 (s, 1H), 7.99 (d, *J*= 8.5 Hz, 1H), 7.82 (dd, *J*= 8.5, 1.6 Hz, 1H), 7.68 - 7.73 (m, 1H), 7.63 - 7.68 (m, 1H), 6.97 (t, *J*= 6.1 Hz, 1H), 4.20 (s, 3H), 3.16 (d, *J*= 4.7 Hz, 2H), 3.08 - 3.13 (m, 2H), 3.01 - 3.07 (m, 2H), 2.64 (d, *J*= 4.1 Hz, 2H).

Example 9

Preparation of Compound 45



Step 1: To a solution of tert-butyl 4-[4-fluoro-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-1,3-benzothiazol-2-yl]-3,6-dihydro-2*H*-pyridine-1-carboxylate (prepared according to example 7 step 1, 48 mg, 0.10 mmol, 1.0 eq.) in MeOH (30 mL) was added 10% Pd/C (40 mg, 0.038 mmol, 0.36 eq.) and 10% $Pd(OH)_2/C$ (30 mg, 0.021 mmol, 0.21 eq.) followed by one drop of 1N HCl. The mixture was shaken under a H_2 atmosphere at 50 psi in a Parr shaker for 16 h. LC/MS indicated complete reaction. The mixture was filtered through Celite, concentrated and purified over silica gel with methanol in dichloromethane (0 to 6% gradient) to give tert-butyl 4-[4-fluoro-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-1,3-benzothiazol-2-yl]piperidine-1-carboxylate (39 mg, 81%). MS *m/z* 468.1 $[M+H]^+$.

Step 2: To a suspension of tert-butyl 4-[4-fluoro-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-1,3-benzothiazol-2-yl]piperidine-1-carboxylate (15 mg, 0.032 mmol, 1.0 eq.) in dioxane (0.2 mL) was added HCl (4 M in dioxane) (1.0 mL). The mixture was stirred at room temperature for 1 h, then diluted with ether and filtered to give 4-fluoro-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-2-(4-piperidyl)-1,3-benzothiazole hydrochloride (25 mg, 74%).

MS *m/z* 368.3 $[M+H]^+$. ^1H NMR (DMSO-d_6) δ: 9.33 (br s, 1H), 9.20 (br s, 1H), 8.82 (d, *J*= 1.3 Hz, 1H), 8.56 (d, *J*= 9.5 Hz, 1H), 8.50 (s, 1H), 8.40 (d, *J*= 9.8 Hz, 1H), 8.13 (dd, *J*= 11.8, 1.1 Hz, 1H), 3.57 - 3.65 (m, 1H), 3.33 - 3.42 (m, 2H), 3.02 - 3.12 (m, 2H), 2.56 (s, 3H), 2.31 (d, *J*= 12.3 Hz, 2H), 2.06 - 2.17 (m, 2H).

Using the procedure described for Example 9, above, additional compounds described herein were prepared by substituting the appropriate starting material, suitable reagents and reaction conditions, obtaining compounds such as those selected from:

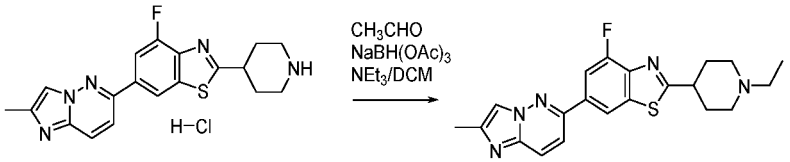
Cpd	Data
2	MS *m/z* 349.1 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.16 (s, 2H), 7.87 - 7.94 (m, 2H), 7.73 (dd, *J*= 8.5, 1.6 Hz, 1H), 7.59 (d, *J*= 3.5 Hz, 2H), 4.14 (s, 3H), 3.41 - 3.50 (m, 3H), 3.13 (td, *J*= 12.5, 2.7 Hz, 2H), 2.34 (d, *J*= 12.0 Hz, 2H), 2.07 (d, *J*= 12.0 Hz, 2H).
22	MS *m/z* 363.1 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.93 - 9.11 (m, 1H), 8.72 - 8.90 (m, 1H), 8.41 (d, *J*= 1.6 Hz, 1H), 8.38 (s, 1H), 8.01 (d, *J*= 8.5 Hz, 1H), 7.86 (s, 1H), 7.83 (dd, *J*= 8.5, 1.9 Hz, 1H), 7.43 (s, 1H), 4.20 (s, 3H), 3.52 (s, 1H), 3.39 (d, *J*= 12.6 Hz, 2H), 3.03 - 3.14 (m, 2H), 2.58 (s, 3H), 2.29 (d, *J*= 11.3 Hz, 2H), 2.05 (d, *J*= 11.3 Hz, 2H).
42	MS *m/z* 363.1 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.37 (br s, 1H), 9.22 (br s, 1H), 8.40 - 8.45 (m, 2H), 8.05 (s, 1H), 8.00 (d, *J*= 8.5 Hz, 1H), 7.83 (dd, *J*= 8.5, 1.9 Hz, 1H), 7.68 - 7.72 (m, 1H), 7.63 - 7.67 (m, 1H), 4.20 (s, 3H), 3.50 - 3.58 (m, 1H), 3.33 (br s, 1H), 3.10 - 3.27 (m, 3H), 2.41 (d, *J*= 14.8 Hz, 1H), 2.24 - 2.33 (m, 2H), 1.89 - 2.05 (m, 3H).
52	MS *m/z* 405.2 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.29 (s, 1H), 8.26 - 8.27 (m, 1H), 7.99 - 8.03 (m, 2H), 7.82 - 7.86 (m, 1H), 7.69 - 7.74 (m, 2H), 4.26 (s, 3H), 3.69 - 3.81 (m, 1H), 2.11 - 2.21 (m, 2H), 1.60 - 1.70 (m, 2H), 1.41 (s, 6H), 1.30 (s, 6H).
58	MS *m/z* 363.2 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.94 - 9.71 (m, 2H), 8.43 (d, *J*= 3.2 Hz, 2H), 8.05 (s, 1H), 8.02 (d, *J*= 8.5 Hz, 1H), 7.84 (dd, *J*= 8.5, 1.6 Hz, 1H), 7.68 - 7.73 (m, 1H), 7.62 - 7.67 (m, 1H), 4.20 (s, 3H), 3.50 - 3.59 (m, 1H), 3.02 - 3.12 (m, 1H), 2.51 (br s, 2H), 2.23 - 2.36 (m, 2H), 2.05 (dd, *J*= 12.8, 3.3 Hz, 1H), 1.88 (d, *J*= 12.9 Hz, 1H), 1.35 (d, *J*= 6.3 Hz, 3H).
66	MS *m/z* 406.2 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.74 - 8.99 (m, 2H), 8.33 (s, 1H), 8.11 (s, 1H), 7.75 (s, 1H), 7.60 (d, *J*= 9.8 Hz, 1H), 7.49 (d, *J*= 8.5 Hz, 1H), 7.37 (s, 1H), 4.43 - 4.58 (m, 1H), 4.18 (s, 3H), 3.35 - 3.43 (m, 2H), 3.08 - 3.17 (m, 1H), 3.03 (s, 3H), 2.56 (s, 3H), 2.00 - 2.12 (m, 1H), 1.85 - 1.98 (m, 3H), 1.29 (d, *J*= 6.3 Hz, 3H).
70	MS *m/z* 368.3 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.65 - 8.78 (m, 1H), 8.39 - 8.53 (m, 1H), 8.29 (d, *J*= 1.6 Hz, 1H), 8.04 (t, *J*= 1.1 Hz, 1H), 7.72 - 7.78 (m, 1H), 7.69 (d, *J*= 1.3 Hz, 2H), 3.45 - 3.53 (m, 1H), 3.32 - 3.38 (m, 2H), 2.97 - 3.08 (m, 2H), 2.59 (s, 3H), 2.20 - 2.28 (m, 2H), 1.91 - 2.02 (m, 2H).

Cpd	Data
73	MS *m/z* 367.3 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.96 - 9.07 (m, 1H), 8.69 - 8.83 (m, 1H), 8.45 (s, 1H), 8.31 (d, *J*= 1.6 Hz, 1H), 8.09 - 8.13 (m, 1H), 7.76 (dd, *J*= 12.3, 1.6 Hz, 1H), 7.70 - 7.73 (m, 1H), 7.68 (d, *J*= 1.9 Hz, 1H), 4.21 (s, 3H), 3.53 - 3.60 (m, 1H), 3.38 - 3.43 (m, 2H), 3.03 - 3.15 (m, 2H), 2.27 - 2.35 (m, 2H), 2.00 - 2.12 (m, 2H).
82	MS *m/z* 349.2 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.91 (s, 1H), 8.41 (d, *J*= 1.3 Hz, 1H), 8.03 (d, *J*= 8.5 Hz, 1H), 7.81 (dd, *J*= 8.5, 1.6 Hz, 1H), 7.71 (s, 1H), 7.58 - 7.63 (m, 1H), 7.52 - 7.57 (m, 1H), 3.25 (br. s., 1H), 3.08 (d, *J*= 12.3 Hz, 2H), 2.68 (t, *J*= 11.3 Hz, 2H), 2.36 (s, 3H), 2.07 (d, *J*= 11.3 Hz, 2H), 1.72 (dd, *J*= 12.0, 3.5 Hz, 2H).
83	MS *m/z* 367.1 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.55 (br s, 1H), 8.42 (br s, 1H), 7.99 (d, *J*= 7.6 Hz, 1H), 7.91 (br s, 1H), 7.84 (d, *J*= 7.3 Hz, 1H), 7.49 (d, *J*= 12.9 Hz, 1H), 4.23 (br. s., 3H), 3.22 (br s, 1H), 3.05 (d, *J*= 10.1 Hz, 2H), 2.64 (t, *J*= 11.0 Hz, 2H), 2.04 (d, *J*= 11.3 Hz, 2H), 1.69 (d, *J*= 10.4 Hz, 2H).
84	MS *m/z* 374.2 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.71 (s, 2H), 8.53 (d, *J*= 1.6 Hz, 1H), 8.49 (d, *J*= 1.6 Hz, 2H), 8.33 (d, *J*= 1.6 Hz, 1H), 8.06 (d, *J*= 8.5 Hz, 1H), 7.92 (dd, *J*= 8.4, 1.7 Hz, 1H), 4.28 (s, 3H), 3.50 - 3.58 (m, 1H), 3.42 (d, *J*= 12.6 Hz, 2H), 3.05 - 3.17 (m, 2H), 2.31 (d, *J*= 12.6 Hz, 2H), 1.95 - 2.06 (m, 2H).
85	MS *m/z* 377.2 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.38 (br s, 2H), 7.98 (d, *J*= 7.6 Hz, 1H), 7.83 (d, *J*= 18.6 Hz, 2H), 7.42 (br s, 1H), 4.20 (br s, 3H), 3.20 (br s, 1H), 2.94 - 3.10 (m, 4H), 2.62 (t, *J*= 10.4 Hz, 2H), 2.03 (d, *J*= 10.7 Hz, 2H), 1.67 (d, *J*= 11.0 Hz, 2H), 1.37 (br s, 3H).
94	MS *m/z* 363.2 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 15.14 - 15.48 (m, 2H), 9.39 (br. s., 1H), 9.28 (br s, 1H), 8.49 (s, 1H), 8.06 (d, *J*= 8.5 Hz, 1H), 7.79 - 7.93 (m, 2H), 7.72 (s, 1H), 3.54 (t, *J*= 11.2 Hz, 1H), 3.33 - 3.41 (m, 2H), 3.08 (q, *J*= 11.6 Hz, 2H), 2.86 (s, 3H), 2.67 (s, 3H), 2.29 (d, *J*= 12.9 Hz, 2H), 2.04 - 2.18 (m, 2H).
95	MS *m/z* 349.2 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 15.18 (br s, 2H), 9.23 (br s, 1H), 9.11 (d, *J*= 8.8 Hz, 1H), 8.53 (s, 1H), 8.02 - 8.13 (m, 2H), 7.81 - 7.95 (m, 3H), 3.48 - 3.60 (m, 1H), 3.38 (d, *J*= 10.7 Hz, 2H), 3.00 - 3.14 (m, 2H), 2.84 (s, 3H), 2.29 (d, *J*= 12.6 Hz, 2H), 2.00 - 2.17 (m, 2H).
97	MS *m/z* 350.0 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.19 - 9.28 (m, 1H), 9.08 - 9.18 (m, 1H), 8.96 (s, 1H), 8.59 (d, *J*= 9.5 Hz, 1H), 8.54 (s, 1H), 8.45 (d, *J*= 9.8 Hz, 1H), 8.28 (d, *J*= 8.8 Hz, 1H), 8.19 (d, *J*= 8.5 Hz, 1H), 3.58 (t, *J*= 11.2 Hz, 1H), 3.33 - 3.43 (m, 2H), 3.02 - 3.13 (m, 2H), 2.57 (s, 3H), 2.26 - 2.34 (m, 2H), 2.03 - 2.15 (m, 2H).
103	MS *m/z* 396.3 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.23 (s, 1H), 7.95 (dd, *J*= 13.9, 1.3 Hz, 2H), 7.58 (s, 1H), 7.43 - 7.49 (m, 1H), 4.39 (s, 2H), 4.13 (s, 3H), 3.36 - 3.47 (m, 3H), 3.03 - 3.11 (m, 2H), 2.23 - 2.34 (m, 2H), 1.97 - 2.11 (m, 2H).
104	MS *m/z* 392.3 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.53 (s, 1H), 8.37 (d, *J*= 1.6 Hz, 1H), 8.19 (d, *J*= 1.9 Hz, 1H), 8.14 (d, *J*= 1.6 Hz, 1H), 7.63 - 7.67 (m, 1H), 4.33 (s, 3H), 3.57 - 3.66 (m, 3H), 3.23 - 3.31 (m, 2H), 2.44 - 2.52 (m, 2H), 2.17 - 2.28 (m, 2H).

Cpd	Data
112	MS *m/z* 350.2 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.46 (s, 1H), 8.00 - 8.08 (m, 2H), 7.82 - 7.88 (m, 1H), 7.70 - 7.78 (m, 2H), 3.17 - 3.25 (m, 1H), 3.00 - 3.08 (m, 2H), 2.66 (s, 3H), 2.60 - 2.64 (m, 2H), 2.02 - 2.08 (m, 2H), 1.62 - 1.74 (m, 2H).
113	MS *m/z* 367.2 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 9.02 (s, 1H), 8.48 (s, 1H), 8.26 (d, *J*= 11.0 Hz, 1H), 8.13 - 8.18 (m, 2H), 7.92 (d, *J*= 8.5 Hz, 1H), 3.58 - 3.67 (m, 2H), 3.27 - 3.25 (m, 3H), 2.62 (s, 3H), 2.43 - 2.52 (m, 2H), 2.14 - 2.25 (m, 2H).
114	MS *m/z* 363.2 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.18 (s, 1H), 8.84 (br s, 1H), 8.61 (d, *J*= 10.1 Hz, 1H), 8.56 (s, 1H), 8.20 (s, 1H), 8.14 (d, *J*= 8.8 Hz, 1H), 8.08 (s, 1H), 7.92 (d, *J*= 8.5 Hz, 1H), 3.35 - 3.43 (d, *J*= 12.6 Hz, 1H), 3.05 - 3.16 (m, 2H), 2.65 (s, 3H), 2.54 (s, 3H), 2.31 (d, *J*= 12.3 Hz, 2H), 1.96 - 2.08 (m, 2H).
115	MS *m/z* 377.0 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.51 (d, *J*= 10.1 Hz, 1H), 9.35 (br s, 1H), 8.44 (d, *J*= 9.5 Hz, 2H), 8.07 (s, 1H), 8.02 (d, *J*= 8.5 Hz, 1H), 7.84 (d, *J*= 8.8 Hz, 1H), 7.64 - 7.74 (m, 2H), 4.21 (s, 3H), 3.63 - 3.73 (m, 1H), 3.22 (br s, 2H), 2.23 (d, *J*= 12.6 Hz, 1H), 2.16 (d, *J*= 13.2 Hz, 1H), 1.94 - 2.10 (m, 2H), 1.45 (d, *J*= 3.2 Hz, 6H).
139	MS *m/z* 364.2 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.18 (br s, 1H), 9.08 (br s, 1H), 8.90 (s, 1H), 8.43 (br s, 1H), 8.29 (br s, 1H), 8.22 - 8.27 (m, 1H), 8.17 (d, *J*= 8.8 Hz, 1H), 3.54 - 3.61 (m, 1H), 3.34 - 3.43 (m, 2H), 3.02 - 3.14 (m, 2H), 2.73 (s, 3H), 2.56 (s, 3H), 2.24 - 2.35 (m, 2H), 2.03 - 2.15 (m, 2H).
144	MS *m/z* 382.1 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.57 (d, *J*= 1.6 Hz, 1H), 8.35 (m, 2H), 8.27 (s, 1H), 7.98 - 8.02 (m, 1H), 3.46 - 3.51 (m, 1H), 3.31 - 3.38 (m, 2H), 3.11 - 3.16 (m, 2H), 2.55 (d, *J*= 0.9 Hz, 3H), 2.34 - 2.41 (m, 2H), 1.96 - 2.08 (m, 1H), 1.32 (d, *J*= 6.6 Hz, 3H).
156	MS *m/z* 350.2 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 9.12 (d, *J*= 2.2 Hz, 1H), 8.88 (d, *J*= 2.2 Hz, 1H), 8.34 (s, 1H), 8.07 (d, *J*= 8.5 Hz, 1H), 7.82 - 7.87 (m, 1H), 7.67 (s, 1H), 3.35 - 3.41 (m, 1H), 3.20 - 3.27 (m, 2H), 2.81 - 2.89 (m, 2H), 2.49 (s, 3H), 2.18 - 2.27 (m, 2H), 1.85 - 1.97 (m, 2H).
166	MS *m/z* 408.2 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.55 (d, *J*= 1.3 Hz, 1H), 8.31 (d, *J*= 0.9 Hz, 2H), 8.24 (s, 1H), 7.99 (dd, *J*= 11.7, 1.3 Hz, 1H), 3.72 - 3.88 (m, 1H), 3.50 - 3.65 (m, 2H), 3.23 - 3.49 (m, 2H), 2.96 - 3.15 (m, 2H), 2.54 (s, 3H), 2.19 - 2.33 (m, 2H), 2.05 - 2.17 (m, 3H), 1.94 - 2.04 (m, 2H).
169	MS *m/z* 350.1 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.96 - 9.00 (m, 2H), 8.62 (d, *J*= 1.6 Hz, 1H), 8.09 - 8.14 (m, 1H), 8.03 (s, 1H), 7.86 (s, 1H), 3.36 - 3.45 (m, 1H), 3.29 - 3.32 (m, 2H), 2.91 - 2.99 (m, 2H), 2.52 (s, 3H), 2.24 - 2.32 (m, 2H), 1.92 - 2.04 (m, 2H).
190	MS *m/z* 377.0 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.95 - 9.71 (m, 2H), 8.42 - 8.46 (m, 2H), 8.06 (s, 1H), 8.02 (d, *J*= 8.5 Hz, 1H), 7.84 (dd, *J*= 8.4, 1.7 Hz, 1H), 7.69 - 7.73 (m, 1H), 7.64 - 7.68 (m, 1H), 4.21 (s, 3H), 3.48 - 3.85 (m, 2H), 3.34 (br s, 1H), 2.18 - 2.35 (m, 2H), 1.77 - 2.14 (m, 2H), 1.31 - 1.50 (m, 6H).

Example 10

Preparation of Compound 106



To a mixture of 4-fluoro-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-2-(4-piperidyl)-1,3-benzothiazole hydrochloride (prepared according to Example 9 step 2, 100 mg, 0.25 mmol, 1.0 eq.) in CH_2Cl_2 (5.0 mL) was added NEt_3 (25 mg, 0.035 mL, 0.25 mmol, 1.0 eq.) followed by acetaldehyde (0.36 mL, 2.5 mmol, 10 eq.) followed by $NaBH(OAc)_3$ (160 mg, 0.74 mmol, 3.0 eq.). The mixture was stirred at room temperature for 2 h, after which LC/MS showed complete conversion. The mixture was treated with aq. K_2CO_3, and then extracted with ethyl acetate, dried and concentrated. The residue was purified over silica gel with methanol in CH_2Cl_2 (3 to 20% gradient) to give 2-(1-ethyl-4-piperidyl)-4-fluoro-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-1,3-benzothiazole (80 mg, 82%).

MS *m/z* 396.2 $[M+H]^+$; ^1H NMR ($CDCl_3$) δ: 8.26 (d, *J*= 1.3 Hz, 1H), 7.94 (d, *J*= 9.5 Hz, 1H), 7.80 - 7.86 (m, 2H), 7.47 (d, *J*= 9.5 Hz, 1H), 3.51 (d, *J*= 5.4 Hz, 3H), 3.28 (br s, 1H), 3.18 (d, *J*= 10.1 Hz, 2H), 2.50 - 2.65 (m, 2H), 2.01 - 2.41 (m, 6H), 1.14 - 1.25 (m, 3H).

Using the procedure described for Example 10, above, additional compounds described herein were prepared by substituting the appropriate starting material, suitable reagents and reaction conditions, obtaining compounds such as those selected from:

Cpd	Data
3	MS *m/z* 361.0 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.28 (s, 2H), 8.01 - 8.08 (m, 2H), 7.83 - 7.88 (m, 1H), 7.71 (s, 2H), 6.76 - 6.81 (m, 1H), 4.25 (s, 3H), 3.96 - 4.19 (m, 2H), 3.47 - 3.79 (m, 2H), 3.13 - 3.25 (m, 2H), 3.07 (s, 3H).
6	MS *m/z* 361.0 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 11.00 - 11.13 (m, 1H), 8.57 (s, 1H), 8.52 (s, 1H), 8.26 (d, *J*= 1.3 Hz, 1H), 7.95 - 8.05 (m, 2H), 7.75 (d, *J*= 9.1 Hz, 1H), 7.70 (dd, *J*= 8.5, 1.6 Hz, 1H), 6.34 (br s, 1H), 4.23 (s, 3H), 3.95 - 4.02 (m, 1H), 3.74 - 3.83 (m, 1H), 3.58 - 3.66 (m, 1H), 3.23 - 3.35 (m, 1H), 2.93 - 3.05 (m, 1H), 2.87 (m, 4H).
9	MS *m/z* 363.1 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.23 - 8.33 (m, 2H), 7.98 - 8.07 (m, 2H), 7.85 (dd, *J*= 8.5, 1.9 Hz, 1H), 7.66 - 7.76 (m, 2H), 4.26 (s, 3H), 3.72 (d, *J*= 12.8 Hz, 2H), 3.47 - 3.58 (m, 1H), 3.25 (d, *J*= 2.5 Hz, 2H), 2.98 (s, 3H), 2.51 (br. s., 2H), 2.13 - 2.28 (m, 2H).

Cpd	Data
10	MS *m/z* 363.2 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.97 - 9.35 (m, 1H), 8.42 (s, 1H), 8.37 (s, 1H), 7.82 - 7.91 (m, 3H), 7.62 (d, *J*= 9.1 Hz, 1H), 7.29 (d, *J*= 7.9 Hz, 1H), 4.09 (s, 3H), 3.32 - 3.48 (m, 2H), 2.99 (br. s., 2H), 2.79 - 2.88 (m, 1H), 2.71 (s, 3H), 1.91 - 2.03 (m, 2H), 1.71 - 1.85 (m, 2H).
92	MS *m/z* 382.3 $[M+H]^+$; ^1H NMR ($CDCl_3$) δ: 8.27 (d, *J*= 1.3 Hz, 1H), 7.95 (d, *J*= 9.5 Hz, 1H), 7.82 - 7.88 (m, 2H), 7.48 (d, *J*= 9.5 Hz, 1H), 3.11 - 3.38 (m, 3H), 2.57 (s, 3H), 2.10 - 2.53 (m, 9H).
107	MS *m/z* 396.3 $[M+H]^+$; ^1H NMR ($CDCl_3$) δ: 8.25 (d, *J*= 1.6 Hz, 1H), 7.82 (dd, *J*= 11.3, 1.6 Hz, 1H), 7.80 (d, *J*= 0.9 Hz, 1H), 7.30 (d, *J*= 0.9 Hz, 1H), 3.20 - 3.31 (m, 1H), 2.75 (d, *J*= 0.9 Hz, 3H), 2.56 (d, *J*= 0.6 Hz, 3H), 2.44 (br. s., 3H), 2.04 - 2.40 (m, 8H).
108	MS *m/z* 420.4 $[M+H]^+$; ^1H NMR ($CDCl_3$) δ: 7.93 (s, 1H), 7.88 (t, *J*= 1.1 Hz, 1H), 7.67 (d, *J*= 0.9 Hz, 1H), 7.60 (d, *J*= 0.9 Hz, 2H), 7.36 - 7.39 (m, 1H), 4.37 - 4.58 (m, 1H), 4.27 (s, 3H), 3.19 - 3.34 (m, 1H), 3.11 (s, 3H), 2.71 (s, 3H), 2.55 (br. s., 5H), 2.22 - 2.45 (m, 1H), 1.96 (d, *J*= 10.4 Hz, 3H), 1.37 (br. s., 3H).
330	MS *m/z* $[M+H]^+$ 422.1; ^1H NMR (methanol-*d4*) δ: 8.76 (s, 1H), 8.26 (s, 1H), 8.03 (d, *J*= 8.4 Hz, 1H), 7.67 (s, 1H), 7.23 – 7.19 (m, 3H), 3.24 (s, 3H), 3.33 (m, 1H), 3.14 (d, *J*= 12.0 Hz, 2H), 2.45 (s, 3H), 2.44 – 2.40 (m, 2H), 2.11 – 2.04 (m, 2H), 1.97 – 1.95 (m, 2H), OH proton not observed.
332	MS *m/z* $[M+H]^+$ 440.2; ^1H NMR (DMSO-*d6*) δ: 13.79 (s, 1H), 12.69 (s, 1H), 8.95 (s, 1H), 8.30 (s, 1H), 7.94 (d, *J*= 8.8 Hz, 1H), 7.24 – 7.18 (m, 2H), 3.35 – 3.31 (m, 1H), 3.16 (s, 3H), 3.05 (d, *J*= 12 Hz, 2H), 2.36 – 2.32 (m, 5H), 2.01 – 1.93 (m, 2H),1.83 – 1.81 (m, 2H).
336	MS *m/z* $[M+H]^+$ 412.0; ^1H NMR (DMSO-*d6*) δ: 8.76 (s, 1H), 8.14 (s, 2H), 7.88 (d, *J*= 8.4 Hz, 1H), 7.31 (d, *J*= 6.8Hz, 1H), 7.26 (s, 1H), 5.64 - 5.51 (m, 1H), 5.15 (br s, 1H), 4.30 - 3.54 (m, 4H), 3.01 (s, 3H), 2 NH and OH protons not observed.
339	MS *m/z* $[M+H]^+$ 434.4; ^1H NMR (DMSO-*d6*) δ: 10.45 (s, 1H), 9.10 (s, 1H), 8.15 (s, 2H), 7.75 (d, *J*= 8.2 Hz, 1H), 7.33 (s, 1H), 7.29 (d, *J*= 8.1 Hz, 1H), 4.25 (s, 2H), 3.49 (d, *J*= 11.2 Hz, 2H), 3.09 (q, *J*= 11.6, 11.1 Hz, 2H), 2.84 – 2.70 (m, 5H), 2.49 – 2.46 (m, 2H), 2.24 (d, *J*= 12.7 Hz, 2H), NH proton not observed.
340	MS *m/z* $[M+H]^+$ 434.4; ^1H NMR (DMSO-*d6*) δ: 11.42 – 11.05 (m, 1H), 9.05 (s, 1H), 8.14 (s, 2H), 7.83 – 7.76 (m, 1H), 7.32 – 7.25 (m, 2H), 4.00 – 3.81 (m, 2H), 3.75 – 3.56 (m, 4H), 3.27 – 3.06 (m, 2H), 2.82 (d, *J*= 4.5 Hz, 3H), 2.35 – 1.98 (m, 4H), 1 NH not observed.
342	MS *m/z* $[M+H]^+$ 412.2; ^1H NMR (DMSO-*d6*) δ: 8.74 (s, 1H), 8.17 (s, 1H), 8.10 (s, 2H), 7.85 (d, *J*= 8.3 Hz, 1H), 7.28 – 7.18 (m, 2H), 5.10 (d, *J*= 53.2 Hz, 1H), 4.63 – 4.41 (m, 1H), 3.23 (m, 1H), 2.95 – 2.74 (m, 2H), 2.41 (m, 1H), 2.32 (s, 3H), NH proton not observed.

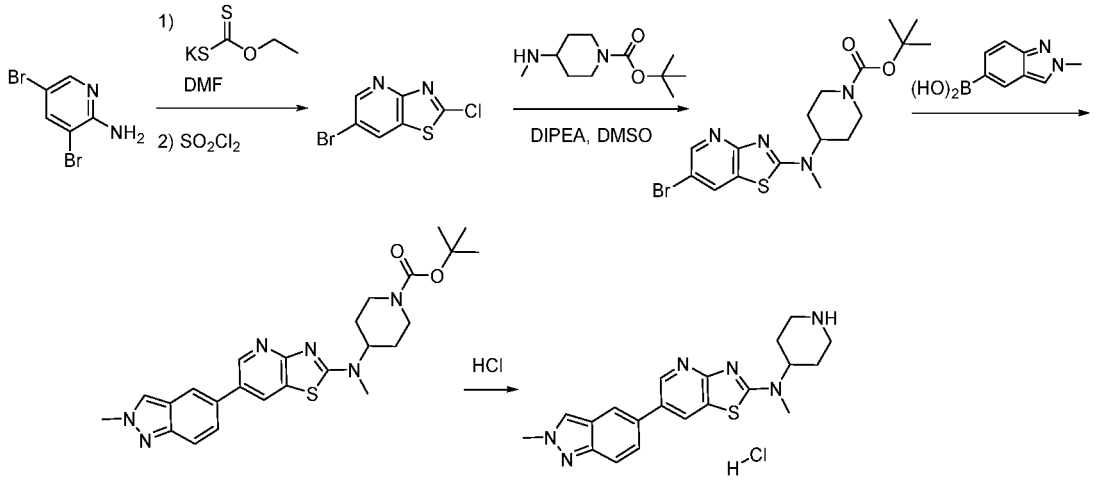
Cpd	Data
343	MS *m/z* $[M+H]^+$ 494.3; ^{1}H NMR (DMSO-d_6) δ: 2:1 mixture of rotamers δ: 11.08 (br s, 0.3H), 10.93 (br s, 0.7H), 9.09 (s, 1H), 8.16 (s, 2H), 7.83 (d, *J*= 8.3 Hz, 1H), 7.31 – 7.26 (m, 2H), 5.58 (bs, 0.3H), 5.12 (s, 0.7H), 4.70 – 4.59 (m, 1H), 4.52 – 4.36 (m, 3H), 4.32 – 4.22 (m, 1H), 3.45 (s, 1H), 3.32 (s, 2H), 2.96 – 2.91 (m, 3H).
347	MS *m/z* $[M+H]^+$ 434.3; ^{1}H NMR (DMSO-d_6) δ: 10.50 (br s, 1H), 9.03 (s, 1H), 8.15 (s, 2H), 7.90 – 7.75 (m, 1H), 7.27 (s, 2H), 4.61 – 4.04 (m, 1H), 4.02 – 3.53 (m, 3H), 3.49 – 3.23 (m, 2H), 3.26 – 2.84 (m, 1H), 2.77 (s, 6H), 2.12 (d, *J*= 6.2 Hz, 1H), 1.97 – 1.76 (m, 1H), NH proton not observed.
351	MS *m/z* $[M+H]^+$ 450.4; ^{1}H NMR (DMSO-d_6) δ: 11.29 (br s, 1H), 9.11 (s, 1H), 8.14 (s, 2H), 7.72 (d, *J*= 8.1 Hz, 1H), 7.35 (s, 1H), 7.28 (d, *J*= 8.0 Hz, 1H), 4.61 (br s, 1H), 3.33 – 3.07 (m, 4H), 2.69 (d, *J*= 4.0 Hz, 6H), 2.22 (d, *J*= 9.7 Hz, 2H), 1.99 – 1.90 (m, 2H), 1.90 – 1.80 (m, 2H), 1.79 – 1.66 (m, 2H), 1 NH proton not observed.
352	MS *m/z* $[M+H]^+$ 422.4; ^{1}H NMR (DMSO-d_6) δ: 9.11 (s, 1H), 8.16 (s, 2H), 7.81 (d, *J*= 7.1 Hz, 1H), 7.33 – 7.25 (m, 2H), 5.02 (br s, 1H), 3.52 – 3.33 (m, 3H), 3.23 (s, 3H), 2.99 – 2.88 (m, 1H), 2.79 (s, 3H), 2.06 – 1.86 (m, 4H), NH and OH protons not observed.
360	MS *m/z* $[M+H]^+$ 450.4; ^{1}H NMR (DMSO-d_6) δ: 10.06 (s, 1H), 9.04 (s, 1H), 8.15 (s, 2H), 7.86 (d, *J*= 8.4 Hz, 1H), 7.27 (s, 2H), 5.03 – 4.90 (m, 1H), 3.47 (d, *J*= 16.1 Hz, 1H), 3.33 – 3.08 (m, 6H), 2.75 (s, 3H), 2.47 – 2.38 (m, 1H), 1.98 (d, *J*= 16.1 Hz, 1H), 1.29 (s, 3H), 1.02 (s, 3H), NH proton not observed.
364	MS *m/z* $[M+H]^+$ 422.3; ^{1}H NMR (DMSO-d_6) δ: 11.40 (br s, 1H), 9.04 (s, 1H), 8.15 (s, 2H), 7.83 (d, *J*= 8.7 Hz, 1H), 7.35 – 7.22 (m, 2H), 4.80 (br s, 1H), 3.59 – 3.48 (m, 1H), 3.38 (s, 3H), 2.78 (q, *J*= 9.4 Hz, 2H), 2.69 (d, *J*= 4.8 Hz, 6H), 2.69 – 2.63 (m, 2H), 1 NH proton not observed.
366	MS *m/z* $[M+H]^+$ 408.0; ^{1}H NMR (DMSO-d_6) δ: 8.83 (s, 1H), 8.29 (br s, 1H), 8.01 (br s, 1H), 7.86 (d, *J*= 8.8 Hz, 1H), 7.28 – 7.22 (m, 2H), 3.89 (br s, 1H), 3.44 (m, 1H), 2.80 – 2.68 (m, 2H), 2.18 (s, 3H), 2.12 – 1.94 (m, 3H), 1.63 – 1.50 (m, 2H), 2 NH and OH protons not observed.
369	MS *m/z* $[M+H]^+$ 434.4; ^{1}H NMR (DMSO-d_6) δ: 1:1 mixture of rotamers δ: 11.19 – 10.61 (m, 2H), 9.07 (s, 1H), 8.15 (s, 2H), 7.81 (d, *J*= 8.3 Hz, 1H), 7.31 – 7.26 (m, 2H), 4.79 – 4.48 (m, 1H), 3.86 – 3.59 (m, 3H), 3.36 – 3.28 (m, 1H), 3.20 – 3.09 (m, 1H), 3.08 – 2.95 (m, 1H), 2.83 – 2.72 (m, 3H), 2.72 – 2.59 (m, 1H), 2.44 – 2.23 (m, 2H), 2.21 – 2.03 (m, 1H), 1.96 (d, *J*= 14.9 Hz, 1H).
370	MS *m/z* $[M+H]^+$ 434.4; ^{1}H NMR (DMSO-d_6) δ: 11.07 (s, 1H), 9.05 (s, 1H), 8.16 (s, 2H), 7.80 (d, *J*= 8.2 Hz, 1H), 7.30 (s, 1H), 7.28 (d, *J*= 8.2 Hz, 1H), 4.29 – 4.16 (m, 2H), 3.93 (d, *J*= 11.5 Hz, 1H), 3.61 (dd, *J*= 10.5 Hz, 1H), 3.31 (d, *J*= 11.1 Hz, 1H), 3.06 – 2.91 (m, 2H), 2.81 (d, *J*= 4.3 Hz, 3H), 2.45 – 2.33 (m, 2H), 2.16 (d, *J*= 12.3 Hz, 1H), 2.03 – 1.93 (m, 1H), 1.90 – 1.77 (m, 1H), NH proton not observed.

Cpd	Data
372	MS *m/z* $[M+H]^+$ 452.3; ^{1}H NMR (methanol-*d*$_4$) δ: 1:1 mixture of rotamers δ: 9.08 (s, 0.5H), 9.07 (s, 0.5H), 8.30 (s, 2H), 7.77 (d, *J*= 8.1 Hz, 1H), 7.38 (d, *J*= 8.1 Hz, 1H), 7.31 (s, 1H), 5.41 (br s, 0.5H), 4.22 (br s, 0.5H), 4.15 – 3.89 (m, 2H), 3.83 – 3.68 (m, 2H), 3.60 – 3.32 (m, 4H), 3.17 (s, 1.5H), 3.01 (s, 1.5H), 2.72 – 2.15 (m, 3H), 2.15 – 2.07 (m, 1H), NH and OH protons not observed.
373	MS *m/z* $[M+H]^+$ 393.9; ^{1}H NMR (DMSO-*d*$_6$) δ: 8.82 (s, 1H), 8.14 (s, 2H), 7.86 (d, *J*= 8.8 Hz, 1H), 7.28 – 7.21 (m, 2H), 4.50 (br s, 1H), 3.45 (m, 1H), 2.77 – 2.55 (m, 3H), 2.37 – 2.29 (m, 2H), 2.28 (s, 3H), 1.80 – 1.66 (m, 1H), NH and OH protons not observed.
375	MS *m/z* $[M+H]^+$ 408.1; ^{1}H NMR (DMSO-*d*$_6$) δ: 8.91 (s, 1H), 8.29 (br s, 1H), 8.00 (br s, 1H), 7.88 (d, *J*= 8.8 Hz, 1H), 7.28 – 7.22 (m, 2H), 3.50 (m, 1H), 3.23 (s, 3H), 2.91 – 2.81 (m, 2H), 2.55 (m, 1H), 2.36 – 2.14 (m, 2H), 2.27 (s, 3H), 1.93 – 1.82 (m, 1H), NH and OH protons not observed.
382	MS *m/z* $[M+H]^+$ 426.0; ^{1}H NMR (DMSO-*d*$_6$) δ: 8.88 (s, 1H), 8.12 (s, 2H), 7.87 (d, *J*= 8.4 Hz, 1H), 7.51 (m, 1H), 7.35 – 7.19 (m, 2H), 5.53 – 5.30 (m, 1H), 3.56 (m, 1H), 3.21 (s, 3H), 3.04 (m, 1H), 2.98 – 2.73 (m, 2H), 2.64 (m, 1H), 2.29 (s, 3H), NH not observed.
383	MS *m/z* $[M+H]^+$ 448.0; ^{1}H NMR (DMSO-*d*$_6$) δ: 8.93 (s, 1H), 8.30 (s, 1H), 8.01 (s, 1H), 7.89 (d, *J*= 8.8 Hz, 1H), 7.28 – 7.23 (m, 2H), 3.50 (m, 1H), 3.25 – 2.90 (m, 5H), 2.45 – 2.22 (m, 1H), 2.10 – 1.60 (m, 6H), 1.00 – 0.20 (m, 4H), NH and OH protons not observed.
384	MS *m/z* $[M+H]^+$ 453.9; ^{1}H NMR (DMSO-*d*$_6$) δ: 8.91 (s, 1H), 8.29 (br s, 1H), 8.01 (br s, 1H), 7.88 (d, *J*= 8.8 Hz, 1H), 7.28 – 7.22 (m, 2H), 4.61 (d, *J*= 47.2 Hz, 2H), 3.35 – 2.65 (m, 8H), 2.44 – 2.15 (m, 2H), 2.06 – 1.72 (m, 4H), NH and OH protons not observed.
385	MS *m/z* $[M+H]^+$ 424.2; ^{1}H NMR (DMSO-*d*$_6$) δ: 8.91 (s, 1H), 8.34 (d, *J*= 2.4 Hz, 1H), 8.28 (d, *J*= 2.4 Hz, 1H), 7.91 (dd, *J*= 8.8, 6.4 Hz, 1H), 7.19 (d, *J*= 11.2 Hz, 2H), 4.37 (s, 4H), 3.56 (s, 4H), 2.21 (s, 3H), NH proton not observed.
388	MS *m/z* $[M+H]^+$ 420.3; ^{1}H NMR (methanol-*d*$_4$) δ: 8.75 (s, 1H), 8.01 (s, 2H), 7.82 (d, *J*= 8.2 Hz, 1H), 7.25 – 7.15 (m, 2H), 5.03 – 4.95 (m, 1H), 4.43 – 4.36 (m, 1H), 4.37 – 4.26 (m, 1H), 3.88 – 3.78 (m, 1H), 3.73 – 3.60 (m, 1H), 3.42 – 3.33 (m, 1H), 3.10 (d, *J*= 18.5 Hz, 1H), 3.02 (s, 3H), 2.97 (d, *J*= 16.4 Hz, 1H), 2.66 – 2.53 (m, 1H), 2.27 – 2.15 (m, 1H), NH and OH protons not observed.
390	MS *m/z* $[M+H]^+$ 420.3; ^{1}H NMR (methanol-*d*$_4$) δ: 8.67 (br s, 1H), 8.00 (s, 2H), 7.72 (d, *J*= 7.9 Hz, 1H), 7.16 – 7.09 (m, 2H), 5.03 – 4.93 (m, 1H), 4.43 – 4.26 (m, 2H), 3.82 (br s, 1H), 3.76 – 3.66 (m, 1H), 3.42 – 3.36 (m, 1H), 3.12 (br s, 1H), 3.04 (s, 3H), 3.00 (br s, 1H), 2.59 (br s, 1H), 2.28 – 2.17 (m, 1H), NH and OH protons not observed.

Cpd	Data
391	MS *m/z* $[M+H]^+$ 426.0; ^{1}H NMR (DMSO-d_6) δ: 8.82 (s, 1H), 8.25 – 8.19 (m, 2H), 7.90 (d, *J*= 8.4 Hz, 1H), 7.22 – 7.14 (m, 2H), 3.77 (m, 1H), 3.20 (s, 3H), 3.00 – 2.88 (m, 2H), 2.75 – 2.67 (m, 1H), 2.44 – 2.24 (m, 2H), 2.34 (s, 3H), 1.99 – 1.87 (m, 1H), NH proton not observed.
392	MS *m/z* $[M+H]^+$ 451.9; ^{1}H NMR (DMSO-d_6) δ: 8.96 (s, 1H), 8.26 (d, *J*= 2.0 Hz, 1H), 8.13 (s, 1H), 7.84 (d, *J*= 8.8 Hz, 1H), 7.26 – 7.20 (m, 2H), 4.14 (d, *J*= 30.8 Hz, 4H), 3.40 (d, *J*= 12.0 Hz, 2H), 3.00 (t, *J*= 12.0 Hz, 2H), 2.76 (s, 3H), 2.25 (d, *J*= 13.6 Hz, 2H), 1.92 (t, *J*= 12.0 Hz, 2H), NH or OH proton not observed.
393	MS *m/z* $[M+H]^+$ 450.0; ^{1}H NMR (DMSO-d_6) δ: 8.91 (s, 1H), 8.29 (s, 1H), 8.00 (s, 1H), 7.88 (d, *J*= 8.8 Hz, 1H), 7.28 – 7.23 (m, 2H), 3.48 (m, 1H), 3.15 (s, 3H), 2.98 (d, *J*= 12.0 Hz, 2H), 2.27 (t, *J*= 7.2 Hz, 2H), 2.04 (t, *J*= 11.2 Hz, 2H), 1.95 – 1.82 (m, 2H), 1.80 – 1.71 (m, 2H), 1.50 – 1.39 (m, 2H), 0.86 (t, *J*= 7.2 Hz, 3H), NH and OH protons not observed.
395	MS *m/z* $[M+H]^+$ 436.4; ^{1}H NMR (methanol-d_4) δ: 8.79 (s, 1H), 8.03 (s, 2H), 7.87 (d, *J*= 7.9 Hz, 1H), 7.27 – 7.22 (m, 2H), 4.80 (br s, 1H), 3.75 – 3.68 (m, 2H), 3.60 – 3.55 (m, 1H), 3.25 (s, 3H), 2.98 (s, 3H), 2.34 – 2.22 (m, 3H), 2.19 – 2.07 (m, 1H), 1.48 (d, *J*= 6.4 Hz, 3H), NH and OH protons not observed.
397	MS *m/z* $[M+H]^+$ 436.4; ^{1}H NMR (methanol-d_4) δ: 8.80 (s, 1H), 8.12 – 8.00 (m, 2H), 7.90 (d, *J*= 8.4 Hz, 1H), 7.33 – 7.23 (m, 2H), 4.03 – 3.94 (m, 1H), 3.57 – 3.46 (m, 2H), 3.25 (s, 3H), 3.23 – 3.12 (m, 1H), 2.92 (s, 3H), 2.52 – 2.43 (m, 1H), 2.30 (d, *J*= 8.8 Hz, 1H), 2.25 – 2.12 (m, 2H), 1.60 (d, *J*= 6.9 Hz, 3H), NH and OH protons not observed.
399	MS m/z $[M+H]^+$ 451.9; ^{1}H NMR (DMSO-d_6) δ: 14.50 – 13.45 (br s, 1H), 13.01 (s, 1H), 8.94 (s, 1H), 8.46 – 7.98 (br s, 2H), 7.88 (d, *J*= 8.8 Hz, 1H), 7.28 – 7.22 (m, 2H), 4.43 (s, 1H), 3.54 – 3.48 (m, 2H), 3.16 (s, 3H), 3.01 (d, *J*= 11.2 Hz, 2H), 2.43 (t, *J*= 6.4 Hz, 2H), 2.14 (t, *J*= 11.2 Hz, 2H), 1.96 – 1.83 (m, 2H), 1.79 – 1.70 (m, 2H), NH proton not observed.

Example 11

Preparation of Compound 12



Step 1: A mixture of 3,5-dibromopyridin-2-amine (2.5 g, 9.92 mmol, 1.00 eq.) and ethoxycarbothioylsulfanyl potassium (3.8 g, 24 mmol, 2.4 eq.) in DMF (12 mL) was stirred at 130 °C overnight. The reaction mixture was then cooled to room temperature, diluted with 1 N HCl (75 mL) and stirred at room temperature for 1 h. The resulting solid was filtered and washed with water and dried. The resulting material was suspended in dichloromethane (15 mL) and SO_2Cl_2 (14 g, 8.5 mL, 100 mmol, 10 eq.) was added slowly. After 2 h, water was added slowly at 0 °C to quench the reaction. The resulting precipitate was collected by filtration and dried to give 6-bromo-2-chloro-thiazolo[4,5-b]pyridine (1.7 g, 69%).

^{1}H NMR ($CDCl_3$) δ: 8.79 (br s, 1H), 8.33 (s, 1H).

Step 2: A mixture of 6-bromo-2-chloro-thiazolo[4,5-b]pyridine (250 mg, 1.0 mmol, 1.0 eq.), tert-butyl 4-(methylamino)piperidine-1-carboxylate (260 mg, 1.2 mmol, 1.2 eq.) and DIPEA (200 mg, 0.26 mL, 1.5 mmol, 1.5 eq.) in DMSO (2.0 mL) was stirred at 100 °C for 1 h. LC/MS indicated complete reaction. The mixture was cooled to room temperature, diluted with ethyl acetate and washed with water and brine, and then dried over sodium sulfate and concentrated. The residue was purified over silica gel with ethyl acetate in hexanes (5 to 15% gradient) to provide tert-butyl 4-[(6-bromothiazolo[4,5-b]pyridin-2-yl)-methyl-amino]piperidine-1-carboxylate (280 mg, 65%).

^{1}H NMR ($CDCl_3$) δ: 8.41 (d, *J*= 2.2 Hz, 1H), 7.96 (d, *J*= 2.2 Hz, 1H), 4.42 - 4.74 (m, 1H), 4.15 - 4.41 (m, 2H), 3.04 (s, 3H), 2.75 - 2.93 (m, 2H), 1.82 (d, *J*= 1.6 Hz, 2H), 1.63 - 1.77 (m, 2H), 1.48 (s, 9H).

Step 3: A mixture of tert-butyl 4-[(6-bromothiazolo[4,5-b]pyridin-2-yl)-methyl-amino]piperidine-1-carboxylate (75 mg, 0.18 mmol, 1.0 eq.), (2-methylindazol-5-yl)boronic acid (37 mg, 0.21 mmol, 1.2 eq.), $Pd_2(dba)_3$ (16 mg, 0.018 mmol, 0.10 eq.), $(t\text{-}Bu)_3P\ HBF_4$ (10 mg, 0.035 mmol, 0.20 eq.) and K_2CO_3 (2.0 M aq.) (0.26 mL, 0.53 mmol, 3.0 eq.) in dioxane (1.0 mL) was stirred at 90 °C for 1 h and then diluted with ethyl acetate and washed with brine, dried and concentrated. The residue was purified over silica gel with ethyl acetate in dichloromethane (0 to 20% gradient) to give tert-butyl 4-[methyl-[6-(2-methylindazol-5-yl)thiazolo[4,5-b]pyridin-2-yl]amino]piperidine-1-carboxylate. MS *m/z* 479.4 $[M+H]^+$.

Step 4: To a solution of tert-butyl 4-[methyl-[6-(2-methylindazol-5-yl)thiazolo[4,5-b]pyridin-2-yl]amino]piperidine-1-carboxylate (30 mg, 0.063 mmol, 1.0 eq.) in dioxane (0.25 mL) was added HCl (4 M in dioxane) (1.0 mL). The mixture was then stirred at room temperature for 1 h and then diluted with ether, filtered and dried to give *N*-methyl-6-(2-methylindazol-5-yl)-*N*-(4-piperidyl)thiazolo[4,5-b]pyridin-2-amine hydrochloride.

MS *m/z* 379.3 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.05 - 9.18 (m, 2H), 9.03 (br s, 1H), 8.72 (d, *J*= 1.9 Hz, 1H), 8.48 (s, 1H), 8.13 (d, *J*= 0.9 Hz, 1H), 7.75 (d, *J*= 9.1 Hz,1H), 7.65 (dd, *J*= 9.1, 1.9 Hz, 1H), 4.21 (s, 3H), 3.43 (d, *J*= 12.3 Hz, 2H), 3.19 (m, 6H), 2.17 - 2.28 (m, 2H), 1.97 (d, *J*= 12.6 Hz, 2H).

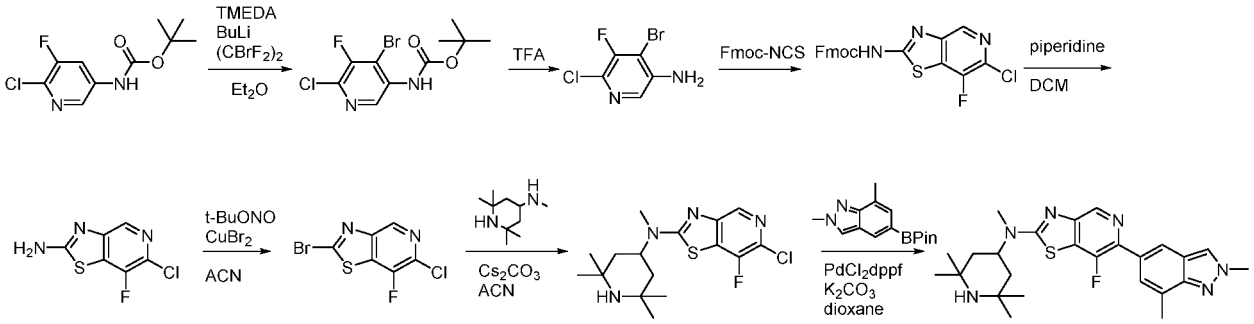
Using the procedure described for Example 11, above, additional compounds described herein were prepared by substituting the appropriate starting material, suitable reagents and reaction conditions, obtaining compounds such as those selected from:

Cpd	Data
13	MS *m/z* 393.3 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.12 - 9.28 (m, 2H), 9.08 (s, 1H), 8.70 (d, *J*= 1.9 Hz, 1H), 8.45 (s, 1H), 7.95 (d, *J*= 0.9 Hz, 1H), 7.46 (s, 1H), 4.21 (br s, 4H), 3.39 - 3.46 (m, 2H), 3.20 (s, 3H), 3.12 (d, *J*= 11.3 Hz, 2H), 2.59 (s, 3H), 2.15 - 2.30 (m, 2H), 1.90 - 2.00 (m, 2H).
14	MS *m/z* 379.3 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 10.34 - 10.44 (m, 1H), 9.06 - 9.22 (m, 2H), 9.01 (s, 1H), 8.63 (d, *J*= 1.9 Hz, 1H), 8.46 (s, 1H), 7.93 (d, *J*= 0.9 Hz, 1H), 7.43 (s, 1H), 4.21 (br s, 4H), 3.33 - 3.40 (m, 2H), 3.09 (d, *J*= 10.7 Hz, 2H), 2.58 (s, 3H), 2.14 - 2.24 (m, 2H), 1.84 - 1.95 (m, 2H).
15	MS *m/z* 365.3 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 10.47 (br s, 1H), 9.09 - 9.28 (m, 2H), 9.02 (br s, 1H), 8.63 (s, 1H), 8.49 (s, 1H), 8.12 (s, 1H), 7.74 (d, *J*= 8.8 Hz, 1H), 7.62 (d, *J*= 8.8 Hz, 1H), 4.20 (br s, 4H), 3.31 - 3.38 (m, 2H), 3.08 (d, *J*= 7.3 Hz, 2H), 2.18 (d, *J*= 11.0 Hz, 2H), 1.90 (d, *J*= 9.8 Hz, 2H).

Cpd	Data
16	MS *m/z* 435.4 $[M+H]^+$; ^1H NMR ($CDCl_3$) δ: 8.69 (d, *J*= 2.2 Hz, 1H), 8.12 (d, *J*= 2.2 Hz, 1H), 7.97 (s, 1H), 7.85 (dd, *J*= 1.6, 0.9 Hz, 1H), 7.79 - 7.83 (m, 1H), 7.56 (dd, *J*= 8.8, 1.6 Hz, 1H), 4.46 - 4.76 (m, 1H), 4.28 (s, 3H), 3.16 (s, 3H), 1.84 (dd, *J*= 12.3, 3.5 Hz, 2H), 1.46 - 1.56 (m, 2H), 1.41 (br s, 6H), 1.27 (br s, 6H).
17	MS *m/z* 449.4 $[M+H]^+$; ^1H NMR ($CDCl_3$) δ: 8.68 (*d*, *J*= 2.2 Hz, 1H), 8.12 (d, *J*= 2.2 Hz, 1H), 7.95 (s, 1H), 7.68 (d, *J*= 0.9 Hz, 1H), 7.31 - 7.35 (m, 1H), 4.42 -4.80 (m, 1H), 4.28 (s, 3H), 3.12 - 3.19 (m, 3H), 2.72 (s, 3H), 1.83 (dd, *J*= 12.6, 3.5 Hz, 2H), 1.47 (d, *J*= 18.6 Hz, 2H), 1.36 - 1.43 (br s, 6H), 1.26 (br s, 6H).

Example 12

Preparation of Compound 101



Step 1: To a solution of tert-butyl *N*-(6-chloro-5-fluoro-3-pyridyl)carbamate (500 mg, 2.0 mmol, 1.0 eq.) and TMEDA (710 mg, 0.93 mL, 6.1 mmol, 3.0 eq.) in Et_2O (10 mL) at -78°C was added dropwise BuLi (1.6 M in hexane) (3.8 mL, 6.1 mmol, 3.0 eq.) while maintaining the temperature below -60 °C. The solution became purple. Upon complete addition, the temperature was allowed to rise to -20 °C and the mixture was stirred at that temperature for 90 min and a turbid mixture was formed. The mixture was cooled to -78 °C again, to which $C_2Br_2F_4$ (1700 mg, 0.77 mL, 6.4 mmol, 3.1 eq.) was added dropwise and the temperature was allowed to rise to room temperature slowly over 1 h. The reaction was quenched by 1N HCl (5.0 mL) and ice water. The mixture was diluted with ether, washed with water, sodium bicarbonate and brine, dried over sodium sulfate and then concentrated to give a solid tert-butyl *N*-(4-bromo-6-chloro-5-fluoro-3-pyridyl)carbamate (660 mg, 100%), which was used in the next step without further purification.

Step 2: To a solution of tert-butyl *N*-(4-bromo-6-chloro-5-fluoro-3-pyridyl)carbamate (660 mg, 2.0 mmol, 1.0 eq.) in CH_2Cl_2 (10.0 mL) was added TFA (5.0 mL). The mixture was stirred at room temperature for 1 h and then concentrated and treated with ethyl acetate. The mixture was

washed with aqueous sodium bicarbonate and brine, and dried and concentrated to give 4-bromo-6-chloro-5-fluoro-pyridin-3-amine, which was used without further purification.

Step 3: A mixture of 4-bromo-6-chloro-5-fluoro-pyridin-3-amine (108 mg, 0.479 mmol, 1.00 eq.) and 2-(9*H*-fluoren-9-yloxy)acetyl isothiocyanate (148 mg, 0.527 mmol, 1.10 eq.) in acetone (1.0 mL) was stirred at 50 °C overnight and then cooled and treated with ether and filtered to give 9*H*-fluoren-9-ylmethyl *N*-(6-chloro-7-fluoro-thiazolo[4,5-c]pyridin-2-yl)carbamate as a solid. MS *m/z* 426.2, 428.3 $[M+H]^+$.

Step 4: To a suspension of 9*H*-fluoren-9-ylmethyl *N*-(6-chloro-7-fluoro-thiazolo[4,5-c]pyridin-2-yl)carbamate (210 mg, 0.49 mmol, 1.0 eq.) in CH_2Cl_2 (7.0 mL) was added piperidine (427 mg, 0.5 mL, 4.9 mmol, 10 eq.) and the mixture was stirred at room temperature for 2 h. LC/MS showed complete reaction. The mixture was diluted with ethyl acetate, washed with aq NH_4Cl and brine, dried and then concentrated. The residue was purified over silica gel with methanol in dichloromethane (0 to 10% gradient) to give 6-chloro-7-fluoro-thiazolo[4,5-c]pyridin-2-amine (100 mg, 100%)

^1H NMR (methanol-d_4) δ: 8.52 (s, 1H).

Step 5: To a suspension of 6-chloro-7-fluoro-thiazolo[4,5-c]pyridin-2-amine (100 mg, 0.49 mmol, 1.0 eq.) in acetonitrile (3.0 mL) was added tert-butyl nitrite (110 mg, 0.13 mL, 0.98 mmol, 2.0 eq.) followed by cupric bromide (120 mg, 0.54 mmol, 1.1 eq.). The solid was slowly dissolved and the mixture was stirred at 60 °C for 1 h. The mixture was diluted with ethyl acetate, washed with NH_4Cl and brine, and then dried and concentrated. The residue was purified with ethyl acetate in hexanes to give 2-bromo-6-chloro-7-fluoro-thiazolo[4,5-c]pyridine in almost quantitative yield.

^1H NMR ($CDCl_3$) δ: 8.82 (d, *J*= 0.9 Hz, 1H).

Step 6: A mixture of 2-bromo-6-chloro-7-fluoro-thiazolo[4,5-c]pyridine (32 mg, 0.12 mmol, 1.0 eq.), N,2,2,6,6-pentamethylpiperidin-4-amine;dihydrochloride (32 mg, 0.13 mmol, 1.1 eq.) and Cs_2CO_3 (160 mg, 0.48 mmol, 4.0 eq.) in acetonitrile (0.5 mL) was stirred at 80 °C overnight and then cooled to room temperature, diluted with ethyl acetate, filtered and evaporated to give 6-chloro-7-fluoro-*N*-methyl-*N*-(2,2,6,6-tetramethyl-4-piperidyl)thiazolo[4,5-c]pyridin-2-amine (45 mg, 110%) which was used in the next step without further purification.

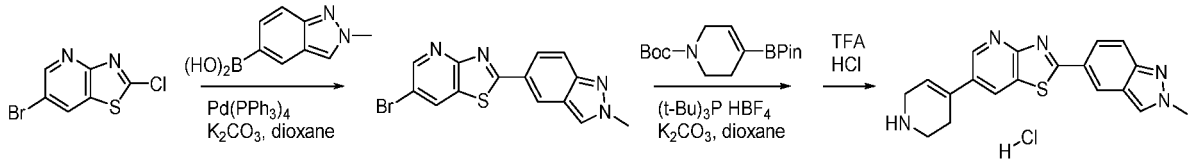
^{1}H NMR ($CDCl_3$) δ: 8.32 (d, *J*= 0.9 Hz, 1H), 4.21 - 4.46 (m, 1H), 3.03 (s, 3H), 1.71 (dd, *J*= 12.6, 3.5 Hz, 2H), 1.33 - 1.43 (m, 2H), 1.29 (s, 6H), 1.15 (s, 6H).

Step 7: A mixture of 6-chloro-7-fluoro-*N*-methyl-*N*-(2,2,6,6-tetramethyl-4-piperidyl)thiazolo[4,5-c]pyridin-2-amine (39 mg, 0.11 mmol, 1.0 eq.), 2,7-dimethyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indazole (45 mg, 0.16 mmol, 1.5 eq.), $PdCl_2$dppf DCM complex (9.0 mg, 0.011 mmol, 0.1 eq.) and aqueous K_2CO_3 (2.0 M, 0.16 mL, 3.0 eq.) in dioxane (1.0 mL) was heated at 100 °C overnight, then cooled, diluted with ethyl acetate, washed with water and brine, dried over sodium sulfate and concentrated. The residue was purified over basic alumina with ethyl acetate in hexanes (10 to 100% gradient) followed by methanol in dichloromethane (0 to 10% gradient) to provide 6-(2,7-dimethylindazol-5-yl)-7-fluoro-*N*-methyl-*N*-(2,2,6,6-tetramethyl-4-piperidyl)thiazolo[4,5-c]pyridin-2-amine (7.0 mg, 14%).

MS *m/z* 467.4 $[M+H]^+$; ^{1}H NMR ($CDCl_3$) δ: 8.76 (d, *J*= 2.2 Hz, 1H), 8.09 (s, 1H), 7.98 (s, 1H), 7.75 (d, *J*= 0.9 Hz, 1H), 4.29 (br. s., 4H), 3.16 (s, 3H), 2.73 (s, 3H), 1.89 (d, *J*= 11.7 Hz, 2H), 1.50 - 1.85 (m, 14H).

Example 13

Preparation of Compound 19



Step 1: A mixture of 6-bromo-2-chloro-thiazolo[4,5-b]pyridine (500 mg, 2.0 mmol, 1.0 eq.), (2-methylindazol-5-yl)boronic acid (390 mg, 2.2 mmol, 1.1 eq.), $Pd(PPh_3)_4$ (230 mg, 0.20 mmol, 0.10 eq.) and K_2CO_3 (2.0 M aq.) (3.0 mL, 6.0 mmol, 3.0 eq.) in dioxane (8.0 mL) was stirred at 100 °C overnight. The mixture was then treated with water, acidified with HCl and filtered. The filter cake was washed with acetonitrile and ether, and then dried to give 6-bromo-2-(2-methylindazol-5-yl)thiazolo[4,5-b]pyridine (100 mg, 14%), which was used in the next step without further purification.

Step 2: A mixture of 6-bromo-2-(2-methylindazol-5-yl)thiazolo[4,5-b]pyridine (100 mg, 0.29 mmol, 1.0 eq.), tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,6-dihydro-2*H*-pyridine-1-carboxylate (110 mg, 0.35 mmol, 1.2 eq.), $(t\text{-}Bu)_3P$ HBF_4 (8.5 mg, 0.029 mmol, 0.10 eq.) and K_2CO_3 (2.0 M aq.) (0.43 mL, 0.87 mmol, 3.0 eq.) in dioxane (1.0 mL) was stirred at 100 °C for 2 h then cooled, diluted with water and filtered. The filter cake was washed with

acetonitrile and ether. The solid was treated with TFA, concentrated and purified by C18 ISCO and further purified with prep-HPLC to give 2-(2-methylindazol-5-yl)-6-(1,2,3,6-tetrahydropyridin-4-yl)thiazolo[4,5-b]pyridine hydrochloride (22 mg, 20%) after treatment with HCl in ether.

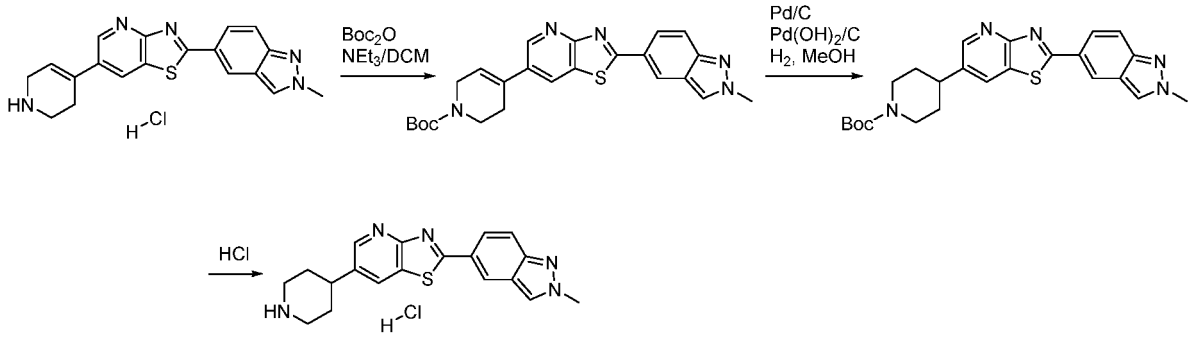
MS *m/z* 348.3 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.30 (br s, 2H), 8.79 (d, *J*= 1.9 Hz, 1H), 8.68 (d, *J*= 2.2 Hz, 1H), 8.55 (d, *J*= 11.7 Hz, 2H), 7.96 (dd, *J*= 9.0, 1.4 Hz, 1H), 7.71 (d, *J*= 8.8 Hz, 1H), 6.39 (br s, 1H), 4.17 (s, 3H), 3.74 (br s, 2H), 3.23 - 3.36 (m, 2H), 2.75 (br s, 2H).

Using the procedure described for Example 13, above, additional compounds described herein were prepared by substituting the appropriate starting material, suitable reagents and reaction conditions, obtaining compounds such as those selected from:

Cpd	Data
335	MS *m/z* $[M+H]^+$ 376.2; ^1H NMR (methanol-d_4) δ: 9.15-9.28 (m, 1H), 8.21-8.29 (m, 1H), 8.09-8.17 (m, 1H), 7.80-7.88 (m, 2H), 7.23-7.35 (m, 2H), 6.75-6.86 (m, 1H), 3.94 (br s, 2H), 3.51 (br s, 2H), 3.0 (br s, 2H), 2 NH and OH protons not observed.
337	MS *m/z* $[M+H]^+$ 432.3; ^1H NMR (methanol-d_4) δ: 9.22 (s, 1H), 8.33 (d, *J*=0.8 Hz, 1H), 8.09-8.20 (m, 1H), 7.96-8.06 (m, 2H), 7.27-7.35 (m, 2H), 6.71 (s, 1H), 2.92 (d, *J*=1.2 Hz, 2H), 1.68 (s, 6H), 1.58-1.63 (m, 6H), 2 NH and OH protons not observed.

Example 14

Preparation of Compound 43



Step 1: A mixture of 2-(2-methylindazol-5-yl)-6-(1,2,3,6-tetrahydropyridin-4-yl)thiazolo[4,5-b]pyridine hydrochloride (31 mg, 0.081 mmol, 1.0 eq., prepared in Example 13), Boc_2O (36 mg, 0.16 mmol, 2.0 eq.) and NEt_3 (25 mg, 0.034 mL, 0.24 mmol, 3.0 eq.) in CH_2Cl_2 (3.0 mL) was stirred at room temperature for three days. The mixture was then diluted with CH_2Cl_2, washed with water and brine, dried over sodium sulfate and concentrated to provide crude tert-butyl 4-[2-(2-methylindazol-5-yl)thiazolo[4,5-b]pyridin-6-yl]-3,6-dihydro-2*H*-pyridine-1-carboxylate (32

mg, 89%). MS m/z 448.4 $[M+H]^+$.

Step 2: A mixture of tert-butyl 4-[2-(2-methylindazol-5-yl)thiazolo[4,5-b]pyridin-6-yl]-3,6-dihydro-2*H*-pyridine-1-carboxylate (32 mg, 0.071 mmol, 1.0 eq.), 10% Pd/C (30 mg, 0.028 mmol, 0.39 eq.), 10% $Pd(OH)_2/C$ (30 mg, 0.021 mmol, 0.30 eq.) and 2 drops of 1 N HCl in MeOH (25 mL) was hydrogenated at room temperature for 16 h under a H_2 balloon. LC/MS indicated complete reaction. The reaction mixture was treated with Celite and then filtered. The filtrate was concentrated and the product was purified over silica gel with methanol in dichloromethane (0 to 6% gradient) to give tert-butyl 4-[2-(2-methylindazol-5-yl)thiazolo[4,5-b]pyridin-6-yl]piperidine-1-carboxylate (10 mg, 31%). MS m/z 450.4 $[M+H]^+$.

Step 3: To a solution of tert-butyl 4-[2-(2-methylindazol-5-yl)thiazolo[4,5-b]pyridin-6-yl]piperidine-1-carboxylate (10 mg, 0.022 mmol, 1.0 eq.) in dioxane (0.2 mL) was added HCl (4 M in dioxane) (1.0 mL). The mixture was then stirred at room temperature for 30 min, diluted with ether and filtered. The filter cake was collected and dried to give 2-(2-methylindazol-5-yl)-6-(4-piperidyl)thiazolo[4,5-b]pyridine hydrochloride (4.0 mg, 47%).

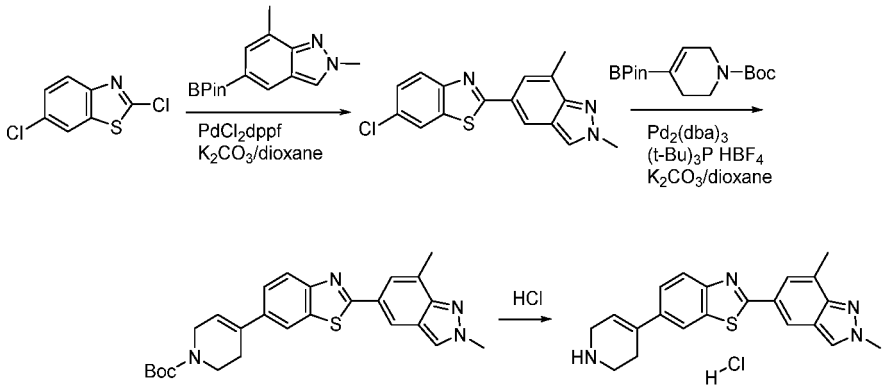
MS *m/z* 350.2 $[M+H]^+$; ^{1}H NMR (DMSO-d_6) δ: 9.38 (br s, 1H), 9.22 (br s, 1H), 8.98 - 9.08 (m, 3H), 8.93 (d, *J*= 1.9 Hz, 1H), 8.44 (dd, *J*= 9.1, 1.6 Hz, 1H), 8.21 (d, *J*= 9.1 Hz, 1H), 4.66 (s, 3H), 3.84 (d, *J*= 11.7 Hz, 2H), 3.41 - 3.57 (m, 3H), 2.48 (br s, 2H), 2.31 - 2.43 (m, 2H).

Using the procedure described for Example 14, above, additional compounds described herein were prepared by substituting the appropriate starting material, suitable reagents and reaction conditions, obtaining compounds such as those selected from:

Cpd	Data
61	MS *m/z* 365.3 $[M+H]^+$; ^{1}H NMR (DMSO-d_6) δ: 9.10 - 9.47 (m, 4H), 8.29 - 8.59 (m, 2H), 3.62 (br. s., 1H), 3.32 - 3.45 (m, 2H), 3.00 - 3.15 (m, 2H), 2.76 (br. s., 3H), 2.58 (br. s., 3H), 2.25 - 2.35 (m, 2H), 2.03 - 2.20 (m, 2H).

Example 15

Preparation of Compound 49



Step 1: A mixture of 2,6-dichloro-1,3-benzothiazole (200 mg, 0.98 mmol, 1.0 eq.), 2,7-dimethyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indazole (320 mg, 1.2 mmol, 1.2 eq.), $PdCl_2$dppf dichloromethane adduct (81 mg, 0.098 mmol, 0.10 eq.) and K_2CO_3 (2.0 M aq.) (1.5 mL, 2.9 mmol, 3.0 eq.) in dioxane (4.0 mL) was stirred at 90 °C for 12 h. After cooling, the reaction mixture was diluted with ethyl acetate, washed with brine, dried and then concentrated. The residue was purified over silica gel with ethyl acetate in dichloromethane (0 to 25% gradient) to give 6-chloro-2-(2,7-dimethylindazol-5-yl)-1,3-benzothiazole (200 mg, 65%).

^{1}H NMR ($CDCl_3$) δ: 8.28 (d, *J*= 0.6 Hz, 1H), 8.06 (s, 1H), 8.00 (d, *J*= 8.8 Hz, 1H), 7.90 (d, *J*= 1.9 Hz, 1H), 7.82 - 7.86 (m, 1H), 7.47 (dd, *J*= 8.7, 2.0 Hz, 1H), 4.31 (s, 3H), 2.74 (s, 3H).

Step 2: A mixture of 6-chloro-2-(2,7-dimethylindazol-5-yl)-1,3-benzothiazole (100 mg, 0.32 mmol, 1.0 eq.), tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,6-dihydro-2*H*-pyridine-1-carboxylate (120 mg, 0.38 mmol, 1.2 eq.), $Pd_2(dba)_3$ (15 mg, 0.016 mmol, 0.05 eq.), $(t\text{-}Bu)_3P$ HBF_4 (9.3 mg, 0.032 mmol, 0.10 eq.) and K_2CO_3 (2.0 M aq.) (0.48 mL, 0.96 mmol, 3.0 eq.) in dioxane (1.5 mL) was stirred at 100 °C for 12 h, then cooled, diluted with ethyl acetate and washed with water and brine, dried over sodium sulfate and evaporated. The residue was purified over silica gel with methanol in dichloromethane (0 to 5% gradient) to give tert-butyl 4-[2-(2,7-dimethylindazol-5-yl)-1,3-benzothiazol-6-yl]-3,6-dihydro-2*H*-pyridine-1-carboxylate (131 mg, 89%). MS m/z 461.4 $[M+H]^+$.

Step 3: To a suspension of tert-butyl 4-[2-(2,7-dimethylindazol-5-yl)-1,3-benzothiazol-6-yl]-3,6-dihydro-2*H*-pyridine-1-carboxylate (20 mg, 0.043 mmol, 1.0 eq.) in dioxane (0.25 mL) was added HCl (4 M in dioxane) (1.0 mL, 4.0 mmol, 92 eq.). The mixture was stirred at room temperature

for 30 min and then diluted with ether and filtered. The solid cake was washed with ether and dried to give 2-(2,7-dimethylindazol-5-yl)-6-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole hydrochloride (14 mg, 81%).

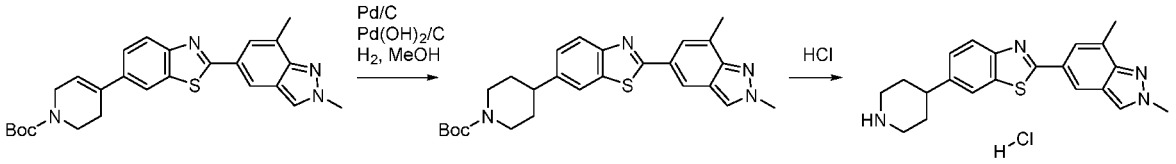
MS *m/z* 361.3 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.31 (br s, 2H), 8.46 (s, 1H), 8.26 (s, 1H), 8.17 (s, 1H), 7.93 (d, *J*= 8.5 Hz, 1H), 7.72 (s, 1H), 7.61 (d, *J*= 8.2 Hz, 1H), 6.27 (br s, 1H), 4.15 (s, 3H), 3.72 (br s, 2H), 3.27 (br s, 2H), 2.73 (br s, 2H), 2.53 (s, 3H).

Using the procedure described for Example 15, above, additional compounds described herein were prepared by substituting the appropriate starting material, suitable reagents and reaction conditions, obtaining compounds such as those selected from:

Cpd	Data
4	MS *m/z* 347.0 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.01 - 9.29 (m, 2H), 8.56 (s, 1H), 8.52 (s, 1H), 8.26 (s, 1H), 7.97 - 8.03 (m, 2H), 7.75 (d, *J*= 8.8 Hz, 1H), 7.68 (dd, *J*= 8.7, 1.4 Hz, 1H), 6.35 (br. s., 1H), 4.22 (s, 3H), 3.78 (br. s., 2H), 3.33 - 3.43 (m, 2H), 2.78 (br. s., 2H).

Example 16

Preparation of Compound 50



Step 1: A mixture of tert-butyl 4-[2-(2,7-dimethylindazol-5-yl)-1,3-benzothiazol-6-yl]-3,6-dihydro-2*H*-pyridine-1-carboxylate (65 mg, 0.14 mmol, 1.0 eq., prepared in Example 15 step 2), 10% Pd/C (50 mg, 0.047 mmol, 0.33 eq.) and 10% $Pd(OH)_2/C$ (50 mg, 0.036 mmol, 0.25 eq.) in MeOH (50 mL) and one drop of 1N HCl was shaken for 4 h at 60 psi using a Parr shaker. The mixture was filtered through Celite, concentrated and the residue was purified over silica gel with methanol in dichloromethane (0 to 10% gradient) to give tert-butyl 4-[2-(2,7-dimethylindazol-5-yl)-1,3-benzothiazol-6-yl]piperidine-1-carboxylate (22 mg, 34%). MS m/z 463.4 $[M+H]^+$.

Step 2: Applying the procedure of Example 15 step 3 to tert-butyl 4-[2-(2,7-dimethylindazol-5-yl)-1,3-benzothiazol-6-yl]piperidine-1-carboxylate (22 mg, 0.048 mmol, 1.0 eq.) provided 2-(2,7-dimethylindazol-5-yl)-6-(4-piperidyl)-1,3-benzothiazole hydrochloride (14 mg, 74%).

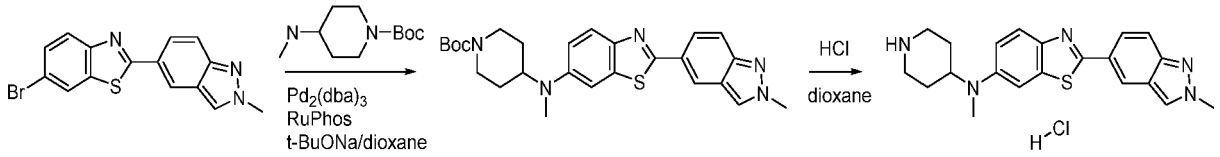
MS *m/z* 363.3 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.98 - 9.18 (m, 2H), 8.45 (s, 1H), 8.24 (d, *J*= 0.6 Hz, 1H), 7.84 - 7.96 (m, 2H), 7.71 (s, 1H), 7.34 (dd, *J*= 8.4, 1.4 Hz, 1H), 4.15 (s, 3H), 3.25 - 3.37 (m, 2H), 2.84 - 3.04 (m, 3H), 2.52 (s, 3H), 1.85 - 1.99 (m, 4H).

Using the procedure described for Example 16, above, additional compounds described herein were prepared by substituting the appropriate starting material, suitable reagents and reaction conditions, obtaining compounds such as those selected from:

Cpd	Data
5	MS *m/z* 349.1 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.86 - 9.44 (m, 2H), 8.56 (s, 1H), 8.49 (s, 1H), 7.95 - 8.02 (m, 3H), 7.75 (d, *J*= 8.8 Hz, 1H), 7.41 (d, *J*= 8.5 Hz, 1H), 4.23 (s, 3H), 3.40 - 3.55 (m, 2H), 2.96 - 3.09 (m, 3H), 1.93 - 2.06 (m, 4H).

Example 17

Preparation of Compound 11



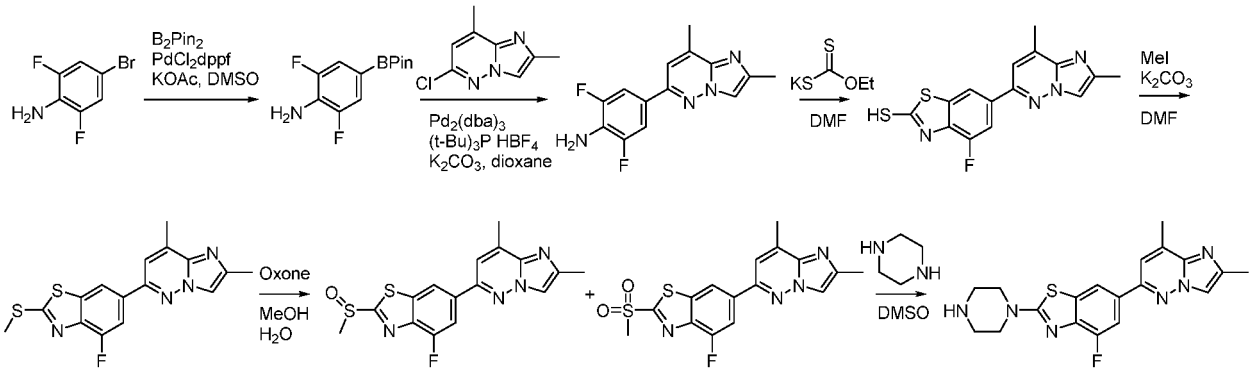
Step 1: A mixture of 6-bromo-2-(2-methyl-2*H*-indazol-5-yl)benzo[d]thiazole (160 mg, prepared according to Example 15 step 1), tert-butyl 4-(methylamino)piperidine-1-carboxylate (2.0 eq.), $Pd_2(dba)_3$ (0.1 eq.), RuPhos (0.2 eq.) and t-BuONa (2.5 eq.) in dioxane (1.0 mL) was stirred at 70 °C under nitrogen atmosphere for 16 h, then cooled, diluted with ethyl acetate, washed with water and brine, dried over sodium sulfate and concentrated. The residue was purified over silica gel with ethyl acetate and hexanes (10 to 100% gradient) to give tert-butyl 4-(methyl(2-(2-methyl-2*H*-indazol-5-yl)benzo[d]thiazol-6-yl)amino)piperidine-1-carboxylate (60 mg, 21.5%). MS *m/z* 478.1 $[M+H]^+$.

Step 2: Applying the procedure of Example 15 step 3 to tert-butyl 4-(methyl(2-(2-methyl-2*H*-indazol-5-yl)benzo[d]thiazol-6-yl)amino)piperidine-1-carboxylate (60 mg) provided *N*-methyl-2-(2-methyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)benzo[d]thiazol-6-amine hydrochloride (24 mg, 50%).

MS *m/z* 378.1 $[M+H]^+$. ^1H NMR (DMSO-d_6) δ: 8.89 - 9.01 (m, 1H), 8.67 - 8.80 (m, 1H), 8.52 (s, 1H), 8.40 (s, 1H), 7.94 - 7.98 (m, 1H), 7.87 - 7.93 (m, 1H), 7.64 - 7.75 (m, 2H), 7.23 - 7.35 (m, 1H), 4.22 (s, 3H), 4.04 - 4.15 (m, 1H), 3.37 (d, *J*= 12.6 Hz, 2H), 2.98 - 3.09 (m, 2H), 2.90 (s, 3H), 1.95 - 2.07 (m, 2H), 1.83 - 1.93 (m, 2H).

Example 18

Preparation of Compound 120



Step 1: A 100 mL round bottom flask was charged with 4-bromo-2,6-difluoro-aniline (2.5 g, 12 mmol), bis(pinacolato)diboron (3.40 g, 13 mmol), $Pd(dppf)Cl_2$ (300 mg, 0.364 mmol), and KOAc (3.50 g, 36 mmol). The reaction vessel was evacuated and purged with N_2 (3X). Anhydrous DMSO (15 mL) was added and the reaction was heated at 80 °C for 1.5 h, then cooled and diluted with EtOAc (100 mL) and $NaHCO_3$ (100 mL). The organic layer was separated and washed with brine, dried, and concentrated. The residue was purified by column chromatography on silica gel with ethyl acetate and hexanes (0-10% gradient) to afford a white solid (1.8 g, 59%). MS *m/z* 256.1 $[M+H]^+$.

Step 2: A 100 mL flask was charged with 6-chloro-2,8-dimethyl-imidazo[1,2-b]pyridazine (0.62 g, 3.41 mmol), boronate ester prepared as above (1.05 g, 4.12 mmol), $Pd_2(dba)_3$ (313 mg, 0.342 mmol), tBu_3PHBF_4 (200 mg, 0.682 mmol), and K_2CO_3 (1.42 g, 10.3 mmol). The reaction vessel was evacuated and purged with N_2 (3X). Dioxane (18 mL) and H_2O (6 mL) were added and the reaction was heated at 90 °C for 1.5 h, then cooled and diluted with CH_2Cl_2 (30 mL) and H_2O (15 mL). The organic layer was separated and the aqueous layer was further extracted with CH_2Cl_2 (2X). The combined organic extracts were washed with brine, dried and concentrated. The residue was purified by trituration with CH_3CN to give the desired intermediate as a tan solid (630 mg, 67%). MS *m/z* 275.3 $[M+H]^+$.

Step 3: A 20 mL vial was charged with 4-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2,6-difluoro-aniline (0.415 g, 1.51 mmol) and ethylxanthic acid potassium salt (0.606 g, 3.63 mmol) and 2.5 mL of anhydrous DMF was added. The resulting brown suspension was heated at 130 °C for 2 h, then cooled to ambient temperature and diluted with 9 mL of 1 N HCl. The resulting

suspension was stirred for 1 h and then filtered. The solid cake was washed with H_2O, collected and dried to give the desired intermediate as a brown solid (460 mg, 92%). MS *m/z* 331.1 $[M+H]^+$.

Step 4: To a mixture of 6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4-fluoro-1,3-benzothiazole-2-thiol (0.46 g, 1.39 mmol) in 5.5 mL of anhydrous DMF was added K_2CO_3 (0.462 g, 3.34 mmol) followed by MeI (0.166 mL, 2.65 mmol) dropwise via syringe. The brown mixture was stirred at ambient temperature for 2 h. The resulting precipitate was filtered, washed with H_2O, and dried to afford the desired as a tan solid (320 mg, 67%). MS *m/z* 345.0 $[M+H]^+$.

Step 5: To a suspension of the intermediate prepared above (0.317 g, 0.920 mmol) in MeOH (6.8 mL) was added Oxone (1.77 g, 2.85 mmol) in H_2O (6.8 mL) dropwise via syringe. The mixture was stirred overnight at ambient temperature and was then filtered through a phase separator followed by washing with H_2O. The solid was dried to afford a mixture of sulfone and sulfoxide at a ratio of 22:70 (330 mg, 95%). MS *m/z* 361.1, 377.1 $[M+H]^+$.

Step 6: A mixture of the sulfone and sulfoxide (50 mg, 0.13 mmol) and piperizine (17 mg, 0.20 mmol) in 0.17 mL of anhydrous DMSO was treated with DIPEA (0.046 mL, 0.26 mmol) and heated at 90 °C for 2 h. The reaction was then cooled to ambient temperature and diluted with EtOAc and H_2O. The phases were separated and the aqueous layer was further extracted with EtOAc (2X). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by column chromatography on silica gel with dichloromethane and methanol (0-15% gradient). The desired fractions were combined and concentrated and the residue was treated with HCl in Et_2O to give the desired product as a yellow solid (28 mg, 49%).

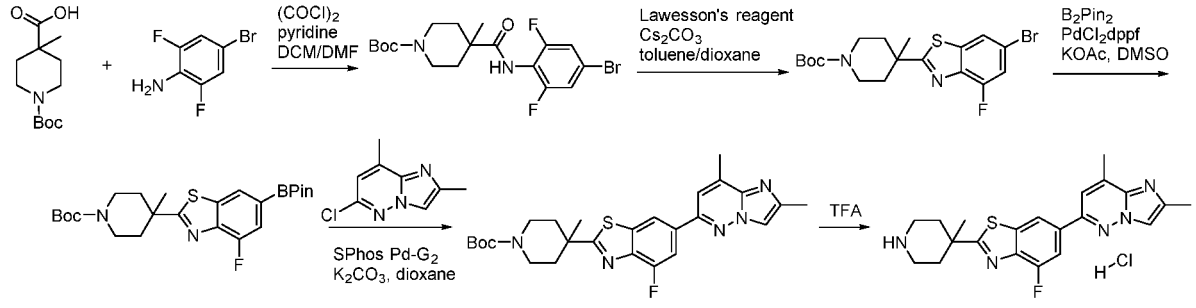
MS *m/z* 383.1 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.25 - 9.44 (m, 2H), 8.49 (d, *J*= 1.3 Hz, 1H), 8.21 - 8.34 (m, 1H), 7.99 - 8.15 (m, 1H), 7.88 - 7.97 (m, 1H), 3.85 - 3.95 (m, 4H), 3.30 (br s, 4H), 2.68 (s, 3H), 2.45 (s, 3H).

Using the procedure described for Example 18, above, additional compounds described herein were prepared by substituting the appropriate starting material, suitable reagents and reaction conditions, obtaining compounds such as those selected from:

Cpd	Data
121	MS *m/z* 397.4 $[M+H]^+$; ^1H NMR ($CDCl_3$) δ: 7.92 (d, *J*= 1.6 Hz, 1H), 7.67 (d, *J*= 0.6 Hz, 1H), 7.58 (dd, *J*= 11.8, 1.7 Hz, 1H), 7.15 (d, *J*= 1.3 Hz, 1H), 3.85 (br s, 2H), 3.78 (br s, 2H), 3.11 - 3.18 (m, 2H), 2.94 - 3.01 (m, 2H), 2.63 (d, *J*= 0.9 Hz, 3H), 2.46 (d, *J*= 0.6 Hz, 3H), 2.01 - 2.09 (m, 3H).
125	MS *m/z* 409.3 $[M+H]^+$; ^1H NMR ($CDCl_3$) δ: 7.92 (d, *J*= 1.6 Hz, 1H), 7.67 (d, *J*= 0.6 Hz, 1H), 7.59 (dd, *J*= 12.0, 1.6 Hz, 1H), 7.16 (d, *J*= 0.9 Hz, 1H), 3.66 (d, *J*= 5.0 Hz, 2H), 3.56 (s, 2H), 3.09 - 3.14 (m, 2H), 2.63 (d, *J*= 0.9 Hz, 3H), 2.46 (s, 3H), 0.76 (br s, 2H), 0.68 - 0.73 (m, 2H).
133	MS *m/z* 454.2 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.15 - 9.23 (m, 1H), 8.58 (d, *J*= 1.3 Hz, 1H), 8.50 - 8.56 (m, 1H), 8.28 - 8.36 (m, 1H), 8.08 - 8.16 (m, 1H), 8.01 - 8.06 (m, 1H), 5.63 - 5.72 (m, 1H), 2.69 (s, 3H), 2.50 (s, 3H), 2.40 (dd, *J*= 13.2, 4.1 Hz, 2H), 1.93 (d, *J*= 2.8 Hz, 2H), 1.52 (s, 12H).
135	^1H NMR (DMSO-d_6) δ: 9.06 - 9.17 (m, 1H), 8.73 - 8.85 (m, 1H), 8.57 (d, *J*= 1.6 Hz, 1H), 8.24 - 8.36 (m, 1H), 8.06 - 8.16 (m, 1H), 7.98 - 8.05 (m, 1H), 5.46 - 5.56 (m, 1H), 3.41 - 3.52 (m, 2H), 2.68 (s, 3H), 2.52 (s, 3H), 2.42 -2.47 (m, 2H), 1.66 - 1.77 (m, 2H), 1.34 (d, *J*= 6.6 Hz, 6H).
143	^1H NMR (DMSO-d_6) δ: 8.42 (d, *J*= 1.9 Hz, 1H), 8.33 - 8.39 (m, 1H), 8.16 - 8.25 (m, 1H), 7.84 - 7.96 (m, 1H), 3.87 - 3.95 (m, 2H), 3.78 - 3.86 (m, 1H), 3.41 - 3.52 (m, 2H), 2.68 (s, 3H), 2.54 (s, 3H), 1.84 - 1.93 (m, 2H), 1.46 - 1.57 (m, 2H).

Example 19

Preparation of Compound 210



Step 1: To a solution of 1-tert-butoxycarbonyl-4-methyl-piperidine-4-carboxylic acid (240 mg, 0.99 mmol, 1.0 eq.) in CH_2Cl_2 (8.0 mL) was added pyridine (320 mg, 0.32 mL, 3.9 mmol, 4.0 eq.), $(COCl)_2$ (130 mg, 0.088 mL, 0.99 mmol, 1.0 eq.) followed by 2 drops of DMF. After 1 h at

room temperature, 4-bromo-2,6-difluoro-aniline (210 mg, 0.99 mmol, 1.0 eq.) was added and the mixture was stirred at room temperature overnight, after which CH_2Cl_2 was added and washed with water and brine. The organic layers were dried, evaporated and purified over silica gel with ethyl acetate in hexanes (5 to 50% gradient) to give tert-butyl 4-[(4-bromo-2,6-difluoro-phenyl)carbamoyl]-4-methyl-piperidine-1-carboxylate (350 mg, 82%).

^{1}H NMR ($CDCl_3$) δ: 7.43 (s, 1H), 7.11 (d, *J*= 6.6 Hz, 2H), 3.65 - 3.81 (m, 2H), 3.14 - 3.22 (m, 2H), 2.09 (d, *J*= 13.9 Hz, 2H), 1.46 - 1.52 (m, 2H), 1.45 (s, 9H), 1.32 (s, 3H).

Step 2: A mixture of tert-butyl 4-[(4-bromo-2,6-difluoro-phenyl)carbamoyl]-4-methyl-piperidine-1-carboxylate (350 mg, 0.81 mmol, 1.0 eq.), Lawesson's reagent (200 mg, 0.48 mmol, 0.60 eq.), Cs_2CO_3 (660 mg, 2.0 mmol, 2.5 eq.) in toluene (4.0 mL) and dioxane (2.0 mL) was stirred at 100 °C overnight. After cooling the reaction mixture was treated with saturated aq. sodium bicarbonate and filtered. The filtrate was dried, concentrated and the residue was purified over silica gel with ethyl acetate in hexanes (5 to 35% gradient) to give tert-butyl 4-(6-bromo-4-fluoro-1,3-benzothiazol-2-yl)-4-methyl-piperidine-1-carboxylate (79 mg, 23%).

^{1}H NMR ($CDCl_3$) δ: 7.81 (dd, *J*= 1.6, 0.6 Hz, 1H), 7.35 (dd, *J*= 9.8, 1.6 Hz, 1H), 3.68 - 3.76 (m, 2H), 3.33 (s, 2H), 2.29 - 2.37 (m, 2H), 1.81 (s, 2H), 1.49 (s, 3H), 1.48 (s, 9H).

Step 3: A mixture of tert-butyl 4-(6-bromo-4-fluoro-1,3-benzothiazol-2-yl)-4-methyl-piperidine-1-carboxylate (79 mg, 0.18 mmol, 1.0 eq.), B_2Pin_2 (71 mg, 0.28 mmol, 1.5 eq.), $PdCl_2$dppf dichloromethane adduct (15 mg, 0.018 mmol, 0.10 eq.) and KOAc (55 mg, 0.55 mmol, 3.0 eq.) in dioxane (1.8 mL) was stirred at 100 °C for 2 h, then cooled, diluted with ethyl acetate and filtered through Celite. The filtrate was concentrated and purified over silica gel with ethyl acetate in hexanes (5 to 50% gradient) to give tert-butyl 4-[4-fluoro-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3-benzothiazol-2-yl]-4-methyl-piperidine-1-carboxylate (60 mg, 68%).

^{1}H NMR ($CDCl_3$) δ: 8.11 (d, *J*= 0.9 Hz, 1H), 7.57 (dd, *J*= 10.9, 0.8 Hz, 1H), 3.68 - 3.78 (m, 2H), 3.34 (s, 2H), 2.31 - 2.41 (m, 2H), 1.82 (s, 2H), 1.50 (s, 3H), 1.48 (s, 9H), 1.39 (s, 12H).

Step 4: A mixture of tert-butyl 4-[4-fluoro-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3-benzothiazol-2-yl]-4-methyl-piperidine-1-carboxylate (60 mg, 0.13 mmol, 1.0 eq.), 6-chloro-2,8-dimethyl-imidazo[1,2-b]pyridazine (23 mg, 0.13 mmol, 1.0 eq.), SPhos-Pd G2 (9.3 mg, 0.013 mmol, 0.10 eq.) and K_2CO_3 (2.0 M aq.) (0.19 mL, 0.38 mmol, 3.0 eq.) in dioxane (1.0 mL) was stirred at 100 °C for 2h, then cooled to room temperature, diluted with ethyl acetate and washed

with brine. The organic layer was dried and evaporated. The residue was purified over silica with ethyl acetate and dichloromethane (10 to 100% gradient) to give tert-butyl 4-[6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4-fluoro-1,3-benzothiazol-2-yl]-4-methyl-piperidine-1-carboxylate (35 mg, 56%). MS *m/z* 496.4 $[M+H]^+$.

Step 5: To tert-Butyl 4-[6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4-fluoro-1,3-benzothiazol-2-yl]-4-methyl-piperidine-1-carboxylate (35 mg, 0.071 mmol, 1.0 eq.) was added TFA (1.0 mL). The mixture was stirred for 15 min at room temperature after which the organic volatiles were removed by a stream of nitrogen. The residue was purified over a C18 column to give 6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4-fluoro-2-(4-methyl-4-piperidyl)-1,3-benzothiazole hydrochloride (28 mg, 92%) after treatment with HCl.

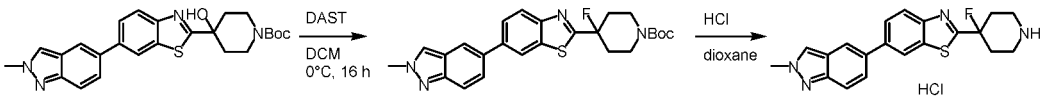
MS *m/z* 396.5 $[M+H]^+$; ^{1}H NMR (methanol-d_4) δ: 8.52 (d, *J*= 1.3 Hz, 1H), 8.14 - 8.22 (m, 2H), 7.93 (dd, *J*= 11.3, 1.3 Hz, 1H), 3.20 – 3.27 (m, 2H), 3.08 – 3.15 (m, 2H), 2.64 (s, 3H), 2.49 (d, *J*= 0.6 Hz, 3H), 2.42 - 2.48 (m, 2H), 1.92 – 1.98 (m, 2H), 1.44 (s, 3H).

Using the procedure described for Example 19, above, additional compounds described herein were prepared by substituting the appropriate starting material, suitable reagents and reaction conditions, obtaining compounds such as those selected from:

Cpd	Data
194	MS *m/z* 408.4 $[M+H]^+$; ^{1}H NMR (methanol-d_4) δ: 8.70 (d, *J*= 1.6 Hz, 1H), 8.35 (dd, *J*= 6.0, 0.9 Hz, 2H), 8.13 (dd, *J*= 11.5, 1.4 Hz, 1H), 3.58 - 3.66 (m, 6H), 2.82 (d, *J*= 1.3 Hz, 3H), 2.68 (d, *J*= 0.9 Hz, 3H), 2.49 - 2.56 (m, 6H).

Example 20

Preparation of Compound 41



Step 1: To a solution of tert-butyl 4-hydroxy-4-(6-(2-methyl-2*H*-indazol-5-yl)benzo[d]thiazol-2-yl)piperidine-1-carboxylate (500 mg, prepared according to the procedure in Example 8 step 2) in dichloromethane at 0 °C was added DAST (2.0 eq) and the temperature was allowed to rise to room temperature and stirred for 16 h. The reaction was quenched with saturated sodium bicarbonate. The mixture was extracted with ethyl acetate, dried over sodium sulfate and

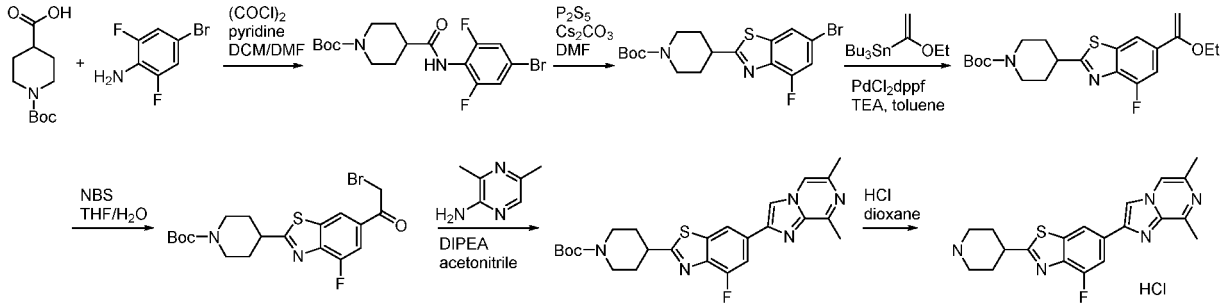
evaporated. The residue was purified by silica gel flash column chromatography to afford tert-butyl 4-fluoro-4-(6-(2-methyl-2*H*-indazol-5-yl)benzo[d]thiazol-2-yl)piperidine-1-carboxylate (450 mg, 89%). MS *m/z* 467.1 $[M+H]^+$.

Step 2: tert-Butyl 4-fluoro-4-(6-(2-methyl-2*H*-indazol-5-yl)benzo[d]thiazol-2-yl)piperidine-1-carboxylate (450 mg) was treated with 4.0 N HCl in dioxane. The mixture was stirred at room temperature for 16 h then diluted with large amount of ether and filtered. The solid was collected and dried to give 2-(4-fluoropiperidin-4-yl)-6-(2-methyl-2*H*-indazol-5-yl)benzo[d]thiazole hydrochloride (0.38 g, 98%).

MS *m/z* 367.1 $[M+H]^+$; ^{1}H NMR (DMSO-d_6) δ: 9.37 (br s, 2H), 8.53 (d, *J*= 1.6 Hz, 1H), 8.44 (s, 1H), 8.13 (d, *J*= 8.5 Hz, 1H), 8.08 (s, 1H), 7.92 (dd, *J*= 8.7, 1.7 Hz, 1H), 7.64 - 7.74 (m, 2H), 4.20 (s, 3H), 3.39 - 3.46 (m, 2H), 3.15 - 3.28 (m, 2H), 2.54 - 2.69 (m, 2H), 2.38 - 2.47 (m, 2H).

Example 21

Preparation of Compound 229



Step 1: To a solution of 1-tert-butoxycarbonyl-piperidine-4-carboxylic acid (2.29 g, 10.0 mmol, 1.00 eq.) in CH_2Cl_2 (100 mL) at room temperature was added pyridine (3.19 g, 3.26 mL, 40.0 mmol, 4.00 eq.) followed by $(COCl)_2$ (1360 mg, 0.934 mL, 10.5 mmol, 1.05 eq.) and DMF (73 mg, 0.078 mL, 3 mmol, 0.1 eq.). After 1 h, 4-bromo-2,6-difluoro-aniline (2.29 g, 11.0 mmol, 1.10 eq.) was added and the mixture was stirred at room temperature for 3 days. The mixture was then washed with water and brine, and dried and purified over silica gel with ethyl acetate in hexanes (5 to 50% gradient) to give tert-butyl 4-[(4-bromo-2,6-difluoro-phenyl)carbamoyl]piperidine-1-carboxylate (2.0 g, 48%). MS *m/z* 417.2, 419.2 $[M-H]^-$.

Step 2: A suspension of phosphorus pentasulfide (270 mg, 1.2 mmol, 1.0 eq.) in pyridine (4.0 mL) was stirred at 85 ° C for 30 min to give a clear solution, to which was added tert-butyl 4-[(4-bromo-2,6-difluoro-phenyl)carbamoyl]piperidine-1-carboxylate (500 mg, 1.2 mmol, 1.0 eq.). The mixture was stirred at 85° C overnight, and then cooled, poured into a mixture of saturated

sodium bicarbonate and water (1:1), stirred for 2 h and then filtered. The solid was collected and dried, followed by purification over silica gel with ethyl acetate and dichloromethane (0 to 10% gradient). The desired fractions were combined and evaporated. To the residue was added DMF (1.0 mL) and the mixture was heated with Cs_2CO_3 (390 mg, 1.2 mmol, 1.0 eq.) at 100 °C for 16 h. Aqueous work up followed by purification with ethyl acetate and dichloromethane (0 to 30% gradient) provided tert-butyl 4-(6-bromo-4-fluoro-1,3-benzothiazol-2-yl)piperidine-1-carboxylate (118 mg, 24%).

^{1}H NMR ($CDCl_3$) δ: 7.81 (dd, *J*= 1.7, 0.8 Hz, 1H), 7.36 (dd, *J*= 9.6, 1.7 Hz, 1H), 4.19 - 4.32 (m, 2H), 3.26 - 3.35 (m, 1H), 2.85 - 2.98 (m, 2H), 2.14 - 2.22 (m, 2H), 1.80 - 1.90 (m, 2H), 1.50 (s, 9H).

Step 3: A mixture of tert-butyl 4-(6-bromo-4-fluoro-1,3-benzothiazol-2-yl)piperidine-1-carboxylate (118 mg, 0.284 mmol, 1.00 eq.), tributyl(1-ethoxyvinyl)tin (212 mg, 0.198 mL, 0.568 mmol, 2.00 eq.), TEA (86.7 mg, 0.119 mL, 0.852 mmol, 3.00 eq.) and $PdCl_2$dppf dichloromethane adduct (23.4 mg, 0.0284 mmol, 0.100 eq.) in toluene (2.0 mL) was heated at 110 °C overnight, cooled and then purified over basic alumina with ethyl acetate and hexanes (0 to 25% gradient) to give tert-butyl 4-[6-(1-ethoxyvinyl)-4-fluoro-1,3-benzothiazol-2-yl]piperidine-1-carboxylate (57 mg, 49%).

^{1}H NMR (acetone-d_6) δ: 8.15 (d, *J*= 1.6 Hz, 1H), 7.55 (dd, *J*= 12.3, 1.3 Hz, 1H), 4.90 (d, *J*= 3.2 Hz, 1H), 4.41 (d, *J*= 2.8 Hz, 1H), 4.15 - 4.28 (m, 2H), 4.00 (q, *J*= 6.9 Hz, 2H), 3.35 - 3.46 (m, 1H), 2.90 - 3.11 (m, 2H), 2.15 - 2.23 (m, 2H), 1.75 - 1.87 (m, 2H), 1.48 (s, 9H), 1.45 (t, *J*= 7.1 Hz, 3H).

Step 4: To a solution of tert-butyl 4-[6-(1-ethoxyvinyl)-4-fluoro-1,3-benzothiazol-2-yl]piperidine-1-carboxylate (57 mg, 0.14 mmol, 1.0 eq.) in THF (1.0 mL) and water (0.3 mL) was added NBS (25 mg, 0.14 mmol, 1.0 eq.). The mixture was stirred at room temperature for 1 h then diluted with ethyl acetate, washed with water, $NaHCO_3$ and brine. The organic layer was dried and concentrated, and then purified over silica gel with ethyl acetate and dichloromethane (0 to 20% gradient) to give tert-butyl 4-[6-(2-bromoacetyl)-4-fluoro-1,3-benzothiazol-2-yl]piperidine-1-carboxylate (62 mg, 97%).

^{1}H NMR ($CDCl_3$) δ: 8.35 (d, *J*= 1.6 Hz, 1H), 7.81 (dd, *J*= 10.7, 1.6 Hz, 1H), 4.49 (s, 2H), 4.21 - 4.35 (m, 2H), 3.30 - 3.43 (m, 1H), 2.87 - 3.01 (m, 2H), 2.16 - 2.28 (m, 2H), 1.82 - 1.95 (m, 2H), 1.50 (s, 9H).

Step 5: A mixture of tert-butyl 4-[6-(2-bromoacetyl)-4-fluoro-1,3-benzothiazol-2-yl]piperidine-1-

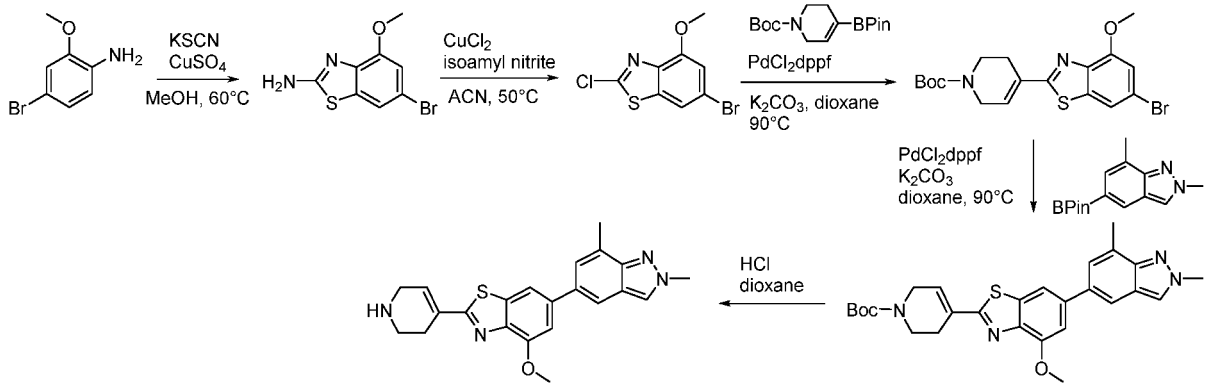
carboxylate (62 mg, 0.14 mmol, 1.0 eq.), 3,5-dimethylpyrazin-2-amine (20 mg, 0.16 mmol, 1.2 eq.) and DIPEA (18 mg, 0.024 mL, 0.14 mmol, 1.0 eq.) in acetonitrile (0.5 mL) was heated at 90 °C for 2 h. Aqueous work up followed by purification with ethyl acetate in dichloromethane (0 to 100% gradient) provided tert-butyl 4-[6-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-4-fluoro-1,3-benzothiazol-2-yl]piperidine-1-carboxylate (38 mg, 58%). MS *m/z* 482.3 $[M+H]^+$.

Step 6: tert-Butyl 4-[6-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-4-fluoro-1,3-benzothiazol-2-yl]piperidine-1-carboxylate (38 mg, 0.079 mmol, 1.0 eq.) was treated with TFA (0.5 mL) then concentrated and purified using a C18 column to give 6-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-4-fluoro-2-(4-piperidyl)-1,3-benzothiazole hydrochloride (26 mg, 79%) after treatment with HCl.

MS *m/z* 382.3 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.76 (s, 1H), 8.52 (s, 1H), 8.44 (d, *J*= 1.6 Hz, 1H), 7.85 - 7.91 (m, 1H), 3.36 - 3.49 (m, 3H), 3.04 - 3.11 (m,2H), 2.97 (s, 3H), 2.46 (s, 3H), 2.25 - 2.33 (m, 2H), 1.98 - 2.09 (m, 2H).

Example 22

Preparation of Compound 98



Step 1: A mixture of 4-bromo-2-methoxy-aniline (1 g, 4.94 mmol), KSCN (1.46 g, 14.85 mmol) and $CuSO_4$ (1.19 g, 7.42 mmol) in 50 mL of MeOH was heated to 60 °C for 16 h. The reaction was cooled to room temperature, filtered through Celite, concentrated, and then purified on an ISCO eluting with EtOAc/hexanes (10-70% gradient) to afford 6-bromo-4-methoxy-1,3-benzothiazol-2-amine (1.1 g, 86%) as a dark brown solid, which was used directly in the next step (~ 85% pure).

Step 2: To a solution of 6-bromo-4-methoxy-1,3-benzothiazol-2-amine (1.1 g, 4.2 mmol) in 200 mL of acetonitrile was added $CuCl_2$ (1.1 g, 8.5 mmol) and isoamyl nitrite (1.2 mL, 8.5 mmol).

The reaction mixture was stirred at room temperature for 1 h, and then heated to 50 °C for 3 h. The reaction was cooled to room temperature, filtered through Celite, diluted with water and extracted with EtOAc. The combined organic extracts were dried over Na_2SO_4, concentrated, and purified on an ISCO eluting with an EtOAc/hexanes (0-40% gradient) to afford 6-bromo-2-chloro-4-methoxy-1,3-benzothiazole (675 mg, 57%) as a white solid.

MS *m/z* 279.9 $[M+H]^+$; ^1H NMR (acetone-d_6) δ: 7.84 (d, *J*= 1.9 Hz, 1H), 7.27 (d, *J*= 1.9 Hz, 1H), 4.07 (s, 3H).

Step 3: To a round bottom flask was added 6-bromo-2-chloro-4-methoxy-1,3-benzothiazole (298 mg, 1.07 mmol), tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,6-dihydro-2*H*-pyridine-1-carboxylate (331 mg, 1.07 mmol), $Pd(dppf)Cl_2$ (80 mg, 0.1 mmol) and, K_2CO_3 (448 mg, 3.2 mmol). The reaction was degassed with N_2 for 15 min and dioxane (10 mL) and water (2.5 mL) were added. The reaction was heated to 90 °C for 3 h. UPLC showed 90% of the desired product. The reaction was cooled down to room temperature, and partitioned between EtOAc and water. The organic phase was dried over Na_2SO_4, concentrated under reduced pressure and then purified on an ISCO through silica gel eluting with EtOAc/hexanes (0% to 20% gradient) to provide tert-butyl 4-(6-bromo-4-methoxy-1,3-benzothiazol-2-yl)-3,6-dihydro-2*H*-pyridine-1-carboxylate (388 mg, 85.3%).

MS *m/z* 425.2, 427.2 $[M+H]^+$; ^1H NMR (acetone-d_6) δ: 7.79 (d, *J*= 1.9 Hz, 1H), 7.19 (d, *J*= 1.9 Hz, 1H), 6.72-6.82 (m, 1H), 4.12-4.24 (m, 2H), 3.67 (s, 3H), 2.80-2.84 (m, 2H), 2.75-2.79 (m, 2H), 1.50 (s, 9H).

Step 4: To a round bottom flask was added tert-butyl 4-(6-bromo-4-methoxy-1,3-benzothiazol-2-yl)-3,6-dihydro-2*H*-pyridine-1-carboxylate (70 mg, 0.16 mmol), 2,7-dimethyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indazole (54 mg, 0.19 mmol), $PddppfCl_2$ (12 mg, 0.016 mmol) and K_2CO_3 (69 mg, 0.49 mmol). The reaction was degassed with N_2 for 15 min and dioxane (10 mL) and water (2.5 mL) were added and the reaction was heated to 90 °C for 16 h. The reaction was cooled to room temperature, and then partitioned between EtOAc and water. The organic phase was dried over Na_2SO_4, concentrated under reduced pressure and purified on an ISCO through silica gel eluting with EtOAc/hexanes (0% to 100%), providing tert-butyl 4-[6-(2,7-dimethylindazol-5-yl)-4-methoxy-1,3-benzothiazol-2-yl]-3,6-dihydro-2*H*-pyridine-1-carboxylate (80 mg, 99%). MS *m/z* 491.3 $[M+H]^+$.

Step 5: tert-Butyl 4-[6-(2,7-dimethylindazol-5-yl)-4-methoxy-1,3-benzothiazol-2-yl]-3,6-dihydro-

2*H*-pyridine-1-carboxylate (12 mg, 0.025 mmol) was dissolved in 0.5 mL of MeOH and HCl (4 M) in 1,4-dioxane (0.012 mL) was added. The reaction mixture was stirred at room temperature for 1h until UPLC showed complete consumption of the starting material. The reaction was concentrated, triturated in Et_2O, and the resultant precipitate was filtered to yield 6-(2,7-dimethyl-2*H*-indazol-5-yl)-4-methoxy-2-(1,2,3,6-tetrahydropyridin-4-yl)benzo[d]thiazole hydrochloride (8 mg, 76.6%) as a yellow solid.

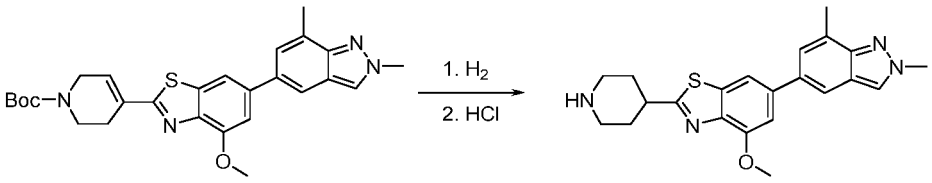
MS *m/z* 391.5 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.94-9.14 (m, 1H), 8.40 (s, 1H), 7.96 (d, *J*= 1.9 Hz, 1H), 7.93 (d, *J*= 1.9 Hz, 1H), 7.42-7.55 (m, 1H), 7.31-7.39 (m, 1H), 6.67-6.80 (m, 1H), 4.21 (s, 3H), 4.08 (s, 3H), 3.83-3.91 (m, 2H), 3.33-3.42 (m, 2H), 2.86-3.00 (m, 2H), 2.59 (s, 3H).

Using the procedure described for Example 22, above, additional compounds described herein were prepared by substituting the appropriate starting material, suitable reagents and reaction conditions, obtaining compounds such as those selected from:

Cpd	Data
153	MS *m/z* 399.8 $[M+H]^+$; ^1H NMR (DMSO-d_6): δ: 9.11-9.32 (m, 1H), 8.58 (d, *J*= 2.5 Hz, 1H), 8.49 (d, *J*= 1.6 Hz, 1H), 8.03 (d, *J*= 1.6 Hz, 1H), 8.03 (d, *J*= 1.3 Hz, 1H), 7.56 (dd, *J*= 13.1, 1.4 Hz, 1H), 6.72-6.95 (m, 1H), 4.24 (s, 3H), 3.77-3.86 (m, 2H), 3.28-3.43 (m, 2H), 2.89-3.02 (m, 2H).
154	MS *m/z* 406.9 $[M+H]^+$; ^1H NMR (DMSO-d_6): δ: 9.16-9.27 (m, 1H), 8.73 (s, 1H), 8.57 (d, *J*= 1.9 Hz, 1H), 8.55 (d, *J*= 1.6 Hz, 1H), 8.39 (d, *J*= 1.6 Hz, 1H), 8.11 (d, *J*= 1.9 Hz, 1H), 6.81-6.94 (m, 1H), 4.29 (s, 3H), 3.88-4.00 (m, 2H), 3.34-3.47 (m, 2H), 2.83-3.01 (m, 2H).

Example 23

Preparation of Compound 99



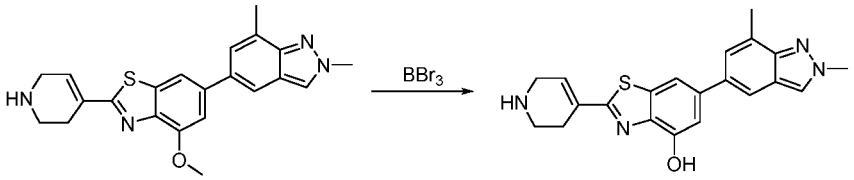
tert-Butyl 4-[6-(2,7-dimethylindazol-5-yl)-4-methoxy-1,3-benzothiazol-2-yl]-3,6-dihydro-2*H*-pyridine-1-carboxylate (46 mg, 0.09 mmol, prepared in Example 23, step 4) was dissolved in 5 mL of MeOH. 10 mg of Pd/C was added and the reaction was subjected to 70 psi H_2 in a Parr shaker for 48 h, then filtered and concentrated to yield crude tert-butyl 4-[6-(2,7-dimethylindazol-5-yl)-4-methoxy-1,3-benzothiazol-2-yl]piperidine-1-carboxylate (30 mg). This

was dissolved in 0.5 mL of MeOH and 4M HCl in 1,4-dioxane (30 µL) was added. The reaction mixture was stirred at room temperature for 1 h until UPLC showed complete consumption of the starting material. The reaction mixture was then concentrated, triturated in Et_2O, and the precipitate was filtered to yield 6-(2,7-dimethyl-2*H*-indazol-5-yl)-4-methoxy-2-(piperidin-4-yl)benzo[d]thiazole hydrochloride (11 mg, 46.0%) as a yellow solid.

MS *m/z* 393.5 $[M+H]^+$; ^1H NMR (DMSO-d_6): δ 8.88-8.99 (m, 1H), 8.43 (s, 1H), 7.77-7.89 (m, 1H), 7.42-7.55 (m, 1H), 7.31-7.39 (m, 1H), 6.67-6.80 (m, 1H), 4.27 (s, 3H), 4.18 (s, 3H), 3.45-3.52 (m, 2H), 3.25-3.34 (m, 2H), 3.15-3.20 (m, 1H), 2.53 (s, 3H), 2.41 – 2. 48 (m, 2H), 2.18 -2.24 (m, 2H).

Example 24

Preparation of Compound 100

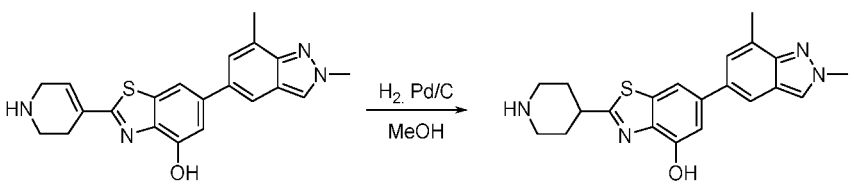


6-(2,7-dimethylindazol-5-yl)-4-methoxy-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole (40 mg, 0.10 mmol) was dissolved in 2 mL of CH_2Cl_2 and BBr_3 (1.0 M) in CH_2Cl_2 (0.51 mL) was added dropwise. The reaction mixture was stirred at room temperature for 2 h until UPLC (quenched with MeOH) showed complete consumption of the starting material. The reaction was quenched with MeOH, concentrated to dryness, triturated in CH_2Cl_2, and the precipitate was filtered and dried to yield 6-(2,7-dimethyl-2*H*-indazol-5-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)benzo[d]thiazol-4-ol hydrobromide (41 mg, 87.5%) as an orange solid.

MS *m/z* 377.5 $[M+H]^+$; ^1H NMR (DMSO-d_6): δ 8.84-9.00 (m, 1H), 8.29-8.46 (m, 1H), 7.80 (d, *J*= 1.6 Hz, 1H), 7.78 (d, *J*= 1.6 Hz, 1H), 7.36 (s, 1H), 7.14-7.26 (m, 1H), 6.64-6.78 (m, 1H), 4.20 (s, 3H), 3.85-3.94 (m, 2H), 3.36-3.46 (m, 2H), 2.83-3.00 (m, 2H), 2.57 (s, 3H).

Example 25

Preparation of Compound 134



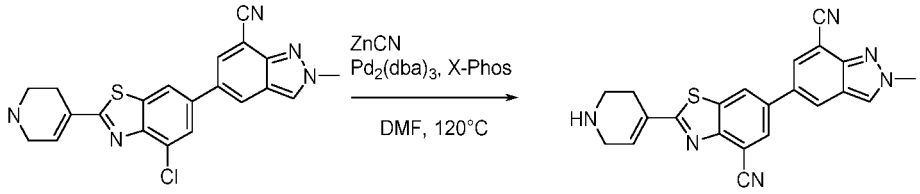
6-(2,7-Dimethyl-2*H*-indazol-5-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)benzo[d]thiazol-4-ol (30 mg,

0.07 mmol) was dissolved in 5 mL of MeOH. Approximately 10 mg of Pd/C was added and the reaction was subjected to 70 psi H_2 in a Parr shaker for 48 h. The reaction mixture was then filtered and concentrated to yield the desired product (~30 mg, ~ 80% purity by ^{1}H NMR). The product was purified on an ISCO through silica gel, eluting CH_2Cl_2/MeOH (0% to 30% gradient) containing NH_4OH (2.5%) to provide 6-(2,7-dimethyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)benzo[d]thiazol-4-ol (14 mg, 56.4%) as a tan solid.

MS *m/z* 379.5 $[M+H]^+$; ^{1}H NMR (methanol-d_4) δ: 8.42 (br s, 1H), 8.24 (s, 1H), 7.74-7.78 (m, 1H), 7.68 (d, *J*= 1.9 Hz, 1H), 7.40 (d, *J*= 1.9 Hz, 1H), 7.38-7.39 (m, 1H), 7.20 (d, *J*= 1.6 Hz, 1H), 4.26 (s, 3H), 3.52-3.60 (m, 3H), 3.27 (td, *J*= 12.5, 3.0 Hz, 2H), 2.64 (s, 3H), 2.45 (dd, *J*= 14.8, 3.8 Hz, 2H), 2.22 (tdd, *J*= 14.8, 12.5, 3.0 Hz, 2H).

Example 26

Preparation of Compound 172

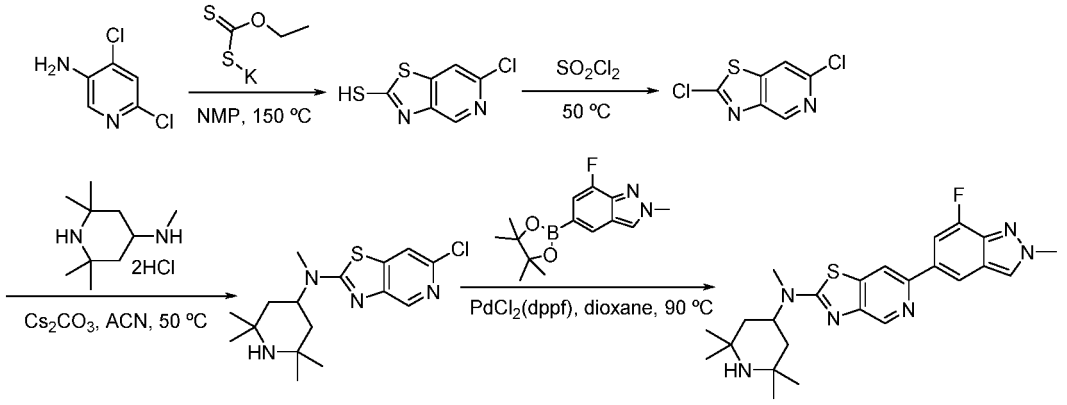


tert-Butyl 4-[4-chloro-6-(7-cyano-2-methyl-indazol-5-yl)-1,3-benzothiazol-2-yl]-3,6-dihydro-2*H*-pyridine-1-carboxylate (40 mg, 0.08 mmol, prepared as in Example 23), ZnCN (9.5 mg, 0.08 mmol), Pd_2dba_3 (4 mg, 0.004 mmol) and X-Phos (3.8 mg, 0.008 mmol) were mixed together in dry DMF (1.2 mL) in a microwave tube and heated for 30 min to 120 °C in the microwave. The mixture was poured onto aqueous $NaHCO_3$, and the precipitate was filtered and dried, to provide tert-butyl 4-[4-cyano-6-(7-cyano-2-methyl-indazol-5-yl)-1,3-benzothiazol-2-yl]-3,6-dihydro-2*H*-pyridine-1-carboxylate (33 mg, 84.1%) as dark greenish-grey solid. The solid was dissolved in 0.5 ml of CH_2Cl_2 and was treated with a solution of 4M HCl 1,4-dioxane (6 µL) and the reaction was stirred for 2 h. The reaction mixture was concentrated under reduced pressure and dried to provide 6-(7-cyano-2-methyl-indazol-5-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole-4-carbonitrile hydrochloride (3.7 mg, 71%) as a yellow solid.

MS *m/z* 397.5 $[M+H]^+$; ^{1}H NMR (methanol-d_4) δ: 8.64 (d, *J*= 1.9 Hz, 1H), 8.56 (s, 1H), 8.43 (d, *J*= 1.9 Hz, 1H), 8.29 (d, *J*= 1.9 Hz, 1H), 8.23 (d, *J*= 1.9 Hz, 1H), 8.01 (br s, 1H), 6.96-6.99 (m, 1H), 4.34 (s, 3H), 4.05 (dd, *J*= 6.3, 2.5 Hz, 2H), 3.55-3.61 (m, 2H), 3.13-3.18 (m, 2H).

Example 27

Preparation of Compound 86



Step 1: A mixture of 4,6-dichloropyridin-3-amine (10 g, 61.35 mmol), potassium *O*-ethyl carbonodithioate (14.8 g, 92.3 mmol), and NMP (60 mL) was stirred at 150 °C for 6 h. LC/MS showed the disappearance of starting dichloride. The reaction mixture was cooled to room temperature and acetic acid (10 mL) was added and then water (500 mL). The precipitate formed was collected by filtration, washed with water, dried and used directly in the next step. LC-MS *m/z* 203.2, 205.2 $[M+H]^+$, RT 1.10 min.

Step 2: The above material was treated with sulfuryl dichloride (50 mL) at 50 °C overnight and then added to a stirred mixture of ice-$NaHCO_3$ / CH_2Cl_2 (~1L). The precipitate was removed by filtration and the filtrate was concentrated. The residue was chromatographed (silica gel, ethyl acetate in hexanes, 0-40%) to provide 2,6-dichlorothiazolo[4,5-c]pyridine (3.62 g, 28.8% for 2 steps). LC-MS *m/z* 205.1, 207.1, 209.1 $[M+H]^+$, RT 1.27 min.

Step 3: A mixture of 2,6-dichlorothiazolo[4,5-c]pyridine (3.62 g, 17.7 mmol), N,2,2,6,6-pentamethylpiperidin-4-amine dihydrochloride (4.51 g, 18.5 mmol), Cs_2CO_3 (25.9 g, 79.5 mmol) and acetonitrile (35 mL) was stirred at 50 °C for 24 h. The reaction mixture was then diluted with ethyl acetate and filtered. The filtrate was concentrated and the residue was chromatographed (silica gel, MeOH in CH_2Cl_2 0-20%) to provide 6-chloro-*N*-methyl-*N*-(2,2,6,6-tetramethyl-4-piperidyl)thiazolo[4,5-c]pyridin-2-amine (4.92 g, 82.2%) as an off white powder.

LC-MS *m/z* 339.2, 341.3 $[M+H]^+$, RT 0.99 min; ^1H NMR ($CDCl_3$) δ: 8.54 (d, *J*= 0.6 Hz, 1H), 7.54 (d, *J*= 0.6 Hz, 1H), 4.42 (br s, 1H), 3.09 (s, 3H), 1.79 (dd, *J*= 12.6, 3.5 Hz, 2H), 1.43-1.56 (m, 2H), 1.38 (s, 6H), 1.26 (br s, 6H).

Step 4: To a mixture of 6-chloro-*N*-methyl-*N*-(2,2,6,6-tetramethyl-4-piperidyl)thiazolo[4,5-c]pyridin-2-amine (0.169 g, 0.50 mmol), 7-fluoro-2-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indazole (0.166 g, 0.60 mmol), $PdCl_2$(dppf) (0.042 g, 0.050 mmol) in 1,4-dioxane (2.0 mL) under an argon atmosphere, was added K_2CO_3 (0.63 mL, 1.3 mmol, 2.0 M). The mixture was stirred at 90 °C for 2 h and then cooled and diluted with ethyl acetate. The precipitate was removed by filtration and the filtrate was concentrated. The residue was chromatographed (silica gel, MeOH in CH_2Cl_2, 0-20%) to provide, after trituration with ethyl ether, 6-(7-fluoro-2-methyl-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethyl-4-piperidyl)thiazolo[4,5-c]pyridin-2-amine (180 mg, 79.8%).

LC-MS *m/z* 453.4 $[M+H]^+$, RT 0.88 min; ^1H NMR ($CDCl_3$) δ: 8.87 (d, *J*= 0.9 Hz, 1H), 8.07 (d, *J*= 1.3 Hz, 1H), 8.01 (d, *J*= 1.0 Hz, 1H), 7.98 (d, *J*= 0.9 Hz, 1H), 7.66 (dd, *J*= 12.8, 1.4 Hz, 1H), 4.55 (br s, 1H), 4.27 (s, 3H), 3.14 (s, 3H), 1.02-1.89 (m, 16H).

Using the procedure described for Example 27, above, additional compounds described herein were prepared by substituting the appropriate starting material, suitable reagents and reaction conditions, obtaining compounds such as those selected from:

Cpd	Data
27	MS *m/z* 378.9 $[M+H]^+$; ^1H NMR (methanol-*d4*): δ: 8.78 (s, 1H), 8.77 (s, 1H), 8.65 (s, 1H), 8.42 (s, 1H), 7.92 (d, *J*= 9 Hz, 1H), 7.88 (dd, *J*= 9 Hz, 1.5 Hz, 1H), 4.10-4.30 (br s, 1H), 4.36 (s, 3H), 3.61-3.68 (m, 2H), 3.24-3.30 (m, 5H), 2.24-2.33 (m, 2H), 2.17-2.21 (m, 2H).
30	MS *m/z* 393.0 $[M+H]^+$; ^1H NMR (methanol-*d4*): δ: 8.76 (s, 1H), 8.74 (s, 1H), 8.55 (s, 1H), 8.20 (s, 1H), 7.61 (s, 1H), 4.60-4.80 (br s, 1H), 4.34 (s, 3H), 3.61-3.68 (m, 2H), 3.23-3.33 (m, 5H), 2.72 (s, 3H), 2.17-2.31 (m, 4H).
31	MS *m/z* 449.0 $[M+H]^+$; ^1H NMR (methanol-*d4*): δ: 8.72 (s, 1H), 8.28 (s, 1H), 8.26 (s, 1H), 8.08 (s, 1H), 7.71 (s, 1H), 4.60 (br s, 1H), 4.27 (s, 3H), 3.18 (s, 3H), 2.66 (s, 3H), 2.01-2.06 (m, 2H), 1.90-2.00 (m, 2H), 1.69 (s, 6H), 1.48 (s, 6H).
32	MS *m/z* 435.0 $[M+H]^+$; ^1H NMR (methanol-*d4*): δ: 8.71 (s, 1H), 8.30 (s, 1H), 8.26 (s, 1H), 8.25 (s, 1H), 7.94 (dd, *J*= 9 Hz, 1.5 Hz, 1H), 7.70 (d, *J*= 9 Hz, 1H), 4.58 (br s, 1H), 4.26 (s, 3H), 3.18 (s, 3H), 1.80-1.84 (m, 2H), 1.60-1.65 (m, 2H), 1.41 (s, 6H), 1.28 (s, 6H).
87	LC-MS *m/z* 435.4 $[M+H]^+$, RT 0.75 min.; ^1H NMR ($CDCl_3$) δ: 8.78-8.87 (m, 2H), 7.92 (d, *J*= 0.6 Hz, 1H), 7.67 (dd, *J*= 9.5, 1.6 Hz, 1H), 7.56 (d, *J*= 9.1 Hz, 1H), 7.40 (s, 1H), 4.43 (br s, 1H), 3.13 (s, 3H), 2.48 (s, 3H), 1.81 (dd, *J*= 12.6, 3.5 Hz, 2H), 1.14-1.64 (m, 14H).

Cpd	Data
88	LC-MS *m/z* 449.5 $[M+H]^+$, RT 0.80 min.; ^{1}H NMR ($CDCl_3$) δ: 8.85 (d, *J*= 0.6 Hz, 1H), 8.67 (s, 1H), 7.94 (s, 1H), 7.52 (t, *J*= 1.0 Hz, 1H), 7.40 (d, *J*= 0.9 Hz, 1H), 4.40-4.92 (m, 1H), 3.14 (s, 3H), 2.68 (s, 3H), 2.50 (d, *J*= 0.6 Hz, 3H), 1.80-1.92 (m, 2H), 1.28-1.78 (m, 14H).
89	LC-MS *m/z* 436.4 $[M+H]^+$, RT 0.84 min.; ^{1}H NMR ($CDCl_3$) δ: 8.86 (d, *J*= 0.6 Hz, 1H), 8.60 (d, *J*= 0.6 Hz, 1H), 8.16 (d, *J*= 9.5 Hz, 1H), 7.89 (dd, *J*= 9.5, 0.6 Hz, 1H), 7.76 (s, 1H), 4.53 (br s, 1H), 3.14 (s, 3H), 2.53 (d, *J*= 0.6 Hz, 3H), 1.83 (dd, *J*= 12.5, 3.3 Hz, 2H), 1.27-1.71 (m, 14H).
90	LC-MS *m/z* 450.4 $[M+H]^+$, RT 0.85 min.; ^{1}H NMR ($CDCl_3$) δ: 8.87 (d, *J*= 0.6 Hz, 1H), 8.61 (d, *J*= 0.6 Hz, 1H), 7.99 (d, *J*= 1.3 Hz, 1H), 7.74 (d, *J*= 0.6 Hz, 1H), 4.78 (br s, 1H), 3.15 (s, 3H), 2.72 (d, *J*= 0.9 Hz, 3H), 2.54 (d, *J*= 0.6 Hz, 3H), 1.83-1.91 (m, 2H), 1.41-1.81 (m, 14H).
105	LC-MS *m/z* 436.4 $[M+H]^+$, RT 0.76 min.; ^{1}H NMR ($CDCl_3$) δ: 9.11 (d, *J*= 2.2 Hz, 1H), 9.02 (d, *J*= 2.2 Hz, 1H), 8.85 (d, *J*= 0.6 Hz, 1H), 8.01 (d, *J*= 0.6 Hz, 1H), 7.36 (d, *J*= 0.9 Hz, 1H), 4.52 (br s, 1H), 3.12-3.16 (m, 3H), 2.53 (d, *J*= 0.9 Hz, 3H), 1.83 (br dd, *J*= 12.5, 3.3 Hz, 2H), 1.23-1.76 (m, 14H).
116	LC-MS *m/z* 503.3 $[M+H]^+$, RT 0.96 min.; ^{1}H NMR ($CDCl_3$) δ: 8.89 (d, *J*= 0.6 Hz, 1H), 8.48 (d, *J*= 0.6 Hz, 1H), 8.32 (s, 1H), 8.07 (s, 1H), 8.03 (d, *J*= 0.9 Hz, 1H), 4.47 (br s, 1H), 4.31 (s, 3H), 3.14 (s, 3H), 1.83 (dd, *J*= 12.5, 3.3 Hz, 2H), 1.21-1.69 (m, 14H).
117	LC-MS *m/z* 460.4 $[M+H]^+$, RT 0.93 min.; ^{1}H NMR ($CDCl_3$) δ: 8.88 (d, *J*= 0.6 Hz, 1H), 8.54 (d, *J*= 1.6 Hz, 1H), 8.43 (d, *J*= 1.6 Hz, 1H), 8.10 (s, 1H), 8.00 (d, *J*= 0.6 Hz, 2H), 4.48 (br s, 1H), 4.32 (s, 3H), 3.12-3.16 (s, 3H), 1.83 (br dd, *J*= 12.1, 3.0 Hz, 2H), 1.18-1.73 (m, 14H).
136	LC-MS *m/z* 436.3 [M+H]+, RT 0.92 min.; ^{1}H NMR ($CDCl_3$) δ: 9.09-9.11 (m, 1H), 8.84 (d, *J*= 0.6 Hz, 1H), 8.11 (dd, *J*= 9.3, 1.7 Hz, 1H), 7.91-7.93 (m, 1H), 7.66 (d, *J*= 9.1 Hz, 1H), 4.41 (br s, 1H), 3.12 (s, 3H), 2.61 (s, 3H), 1.79 (dd, *J*= 12.5, 3.3 Hz, 2H), 1.19-1.52 (m, 14H).
147	LC-MS *m/z* 453.2 $[M+H]^+$, RT 0.85 min.; ^{1}H NMR (DMSO-d_6) δ: 9.08 (d, *J*= 1.6 Hz, 1H), 8.73 (s, 1H), 8.45 (s, 1H), 7.89 (d, *J*= 2.2 Hz, 1H), 7.75 (dd, *J*= 12.8, 1.4 Hz, 1H), 4.37 (br s, 1H), 3.07 (s, 3H), 2.37 (s, 3H), 1.41-1.80 (m, 4H), 1.01-1.38 (m, 12H).
179	LC-MS *m/z* 460.2 $[M+H]^+$, RT 0.94 min.; ^{1}H NMR (DMSO-d_6) δ: 9.48 (d, *J*= 1.6 Hz, 1H), 8.72 (s, 1H), 8.48-8.53 (m, 2H), 7.96 (s, 1H), 4.39 (br s, 1H), 3.06 (s, 3H), 2.33-2.46 (m, 3H), 0.90-1.80 (m, 16H).
198	LC-MS *m/z* 404.2 $[M+H]^+$, RT 0.84 min.; ^{1}H NMR (DMSO-d_6) δ: 9.69 (s, 1H), 9.00 (br s, 2H), 8.84 (br s, 1H), 8.80 (s, 1H), 8.65 (s, 1H), 8.13 (s, 1H), 4.48 (br s, 1H), 3.33-3.46 (m, 2H), 3.09 (s, 3H), 2.47 (s, 3H), 2.09-2.24 (m, 2H), 1.86-1.99 (m, 2H), 1.34-1.70 (m, 2H).

Cpd	Data
199	LC-MS *m/z* 416.2 $[M+H]^+$, RT 0.84 min.; ^{1}H NMR (DMSO-d_6) δ: 9.68 (d, *J*= 1.3 Hz, 1H), 9.16-9.33 (m, 2H), 8.96 (br d, *J*= 6.6 Hz, 1H), 8.81 (s, 1H), 8.76 (s, 1H), 8.55 (s, 1H), 8.14 (s, 1H), 4.18-4.34 (m, 1H), 4.05 (br s, 2H), 2.47 (s, 3H), 2.21 (br d, *J*= 13.6 Hz, 2H), 1.94-2.08 (m, 4H), 1.89 (br t, *J*= 1.0 Hz, 2H).
203	LC-MS *m/z* 430.2 $[M+H]^+$, RT 0.89 min.; ^{1}H NMR (DMSO-d_6) δ: 9.60-9.73 (m, 2H), 9.11 (br s, 1H), 8.73-8.86 (m, 2H), 8.61 (s, 1H), 8.10 (s, 1H), 4.65 (br s, 1H), 4.11 (br s, 2H), 3.12 (s, 3H), 2.46 (s, 3H), 2.37 (br t, *J*= 11.5 Hz, 2H), 1.93-2.16 (m, 4H), 1.81-1.92 (m, 2H).
204	LC-MS *m/z* 423.2 $[M+H]^+$, RT 0.80 min.; ^{1}H NMR (DMSO-d_6) δ: 9.52 (br d, *J*= 9.8 Hz, 1H), 9.34-9.47 (m, 1H), 9.01 (br d, *J*= 10.7 Hz, 1H), 8.83 (s, 1H), 8.61 (s, 1H), 8.37 (br d, *J*= 11.0 Hz, 1H), 8.19 (s, 1H), 4.65 (br s, 1H), 4.11 (br s, 2H), 3.12 (s, 3H), 2.47-2.53 (s, 3H, obscured by DMSO-d_6), 2.34 (br t, *J*= 11.5 Hz, 2H), 1.94-2.12 (m, 4H), 1.80-1.91 (m, 2H).
205	LC-MS *m/z* 423.2 $[M+H]^+$, RT 0.87 min.; ^{1}H NMR (DMSO-d$_6$) δ: 9.82 (br d, *J*= 8.8 Hz, 1H), 9.19 (br s, 1H), 8.80-8.91 (m, 2H), 8.73 (d, *J*= 2.8 Hz, 1H), 8.29 (d, *J*= 0.9 Hz, 1H), 7.74 (dd, *J*= 12.9, 1.3 Hz, 1H), 4.57-4.84 (m, 1H), 4.25 (s, 3H), 4.02-4.20 (m, 2H), 3.19 (s, 3H), 2.43 (br t, *J*= 11.7 Hz, 2H), 1.78-2.13 (m, 6H).
206	LC-MS *m/z* 430.2 $[M+H]^+$, RT 0.90 min.; ^{1}H NMR (DMSO-d_6) δ: 9.63 (br d, *J*= 8.8 Hz, 1H), 9.08 (br d, *J*= 8.8 Hz, 1H), 8.84 (s, 1H), 8.78 (s, 2H), 8.71 (s, 1H), 8.56 (d, *J*= 1.6 Hz, 1H), 4.66 (br s, 1H), 4.28 (s, 3H), 4.12 (br s, 2H), 3.14 (s, 3H), 2.37 (br t, *J*= 11.5 Hz, 2H), 1.93-2.14 (m, 4H), 1.80-1.94 (m, 2H).
211	LC-MS *m/z* 409.2 $[M+H]^+$, RT 0.83 min.; ^{1}H NMR (DMSO-d_6) δ: 8.87-9.23 (m, 2H), 8.70-8.87 (m, 2H), 8.63-8.69 (m, 1H), 8.61 (br s, 1H), 8.24 (d, *J*= 0.9 Hz, 1H), 7.73 (d, *J*= 12.9 Hz, 1H), 4.19-4.32 (m, 4H), 4.06 (br s, 2H), 2.16-2.28 (m, 2H), 1.79-2.10 (m, 6H).
212	LC-MS *m/z* 409.3 $[M+H]^+$, RT 0.78 min.; ^{1}H NMR (DMSO-d_6) δ: 9.44 (s, 1H), 9.13-9.31 (m, 2H), 8.90 (br d, *J*= 6.6 Hz, 1H), 8.75 (s, 1H), 8.54 (s, 1H), 8.41 (d, *J*= 1.0 Hz, 1H), 8.23 (s, 1H), 4.16-4.31 (m, 1H), 3.95-4.16 (m, 2H), 2.47-2.53 (s, 3H, obscured by DMSO-d_6), 2.13-2.29 (m, 2H), 1.77-2.09 (m, 6H).
213	LC-MS *m/z* 416.2 $[M+H]^+$, RT 0.87 min.; ^{1}H NMR (DMSO-d_6) δ: 9.01-9.21 (m, 2H), 8.94 (br s, 1H), 8.69-8.85 (m, 3H), 8.62 (s, 1H), 8.54 (d, *J*= 1.3 Hz, 1H), 4.19-4.38 (m, 4H), 4.06 (br s, 2H), 2.15-2.29 (m, 2H), 1.79-2.09 (m, 6H).
214	LC-MS *m/z* 404.2 $[M+H]^+$, RT 0.88 min.; ^{1}H NMR (DMSO-d_6) δ: 8.99 (br s, 2H), 8.79-8.82 (m, 2H), 8.77 (s, 1H), 8.71 (s, 1H), 8.58 (d, *J*= 1.0 Hz, 1H), 4.48 (br s, 1H), 4.28 (s, 3H), 3.33-3.45 (m, 2H), 3.02-3.18 (m, 5H), 2.08-2.24 (m, 2H), 1.87-1.99 (m, 2H).
215	LC-MS *m/z* 397.3 $[M+H]^+$, RT 0.77 min.; ^{1}H NMR (DMSO-d_6) δ: 9.46 (s, 1H), 9.24-9.35 (m, 1H), 9.13-9.22 (m, 1H), 8.80 (s, 1H), 8.65 (s, 1H), 8.45 (br d, *J*= 12.0 Hz, 1H), 8.24 (s, 1H), 4.47 (br s, 1H), 3.32-3.43 (m, 2H), 3.09 (s, 5H), 2.52 (s, 3H), 2.13-2.32 (m, 2H), 1.84-2.00 (m, 2H).

Cpd	Data
216	LC-MS *m/z* 397.3 $[M+H]^+$, RT 0.84 min.; ^{1}H NMR (DMSO-d_6) δ: 8.98-9.20 (m, *J*= 12.9 Hz, 2H), 8.79 (s, 1H), 8.76 (s, 1H), 8.67 (d, *J*= 2.5 Hz, 1H), 8.28 (d, *J*= 0.9 Hz, 1H), 7.77 (dd, *J*= 13.2, 0.9 Hz, 1H), 4.45 (br s, 1H), 4.24 (s, 3H), 3.33-3.49 (m, 2H), 3.01-3.21 (m, 5H), 2.08-2.28 (m, 2H), 1.85-2.02 (m, 2H).
222	LC-MS 446.4 *m/z* $[M+H]^+$, RT 0.91 min.; ^{1}H NMR (DMSO-d_6) δ: 9.50 (d, *J*= 1.6 Hz, 1H), 8.67 (s, 1H), 8.52 (d, *J*= 1.6 Hz, 1H), 8.42-8.46 (m, 1H), 8.44 (s, 1H), 8.35-8.41 (m, 1H), 8.40 (br s, 1H), 7.96 (d, *J*= 0.9 Hz, 1H), 4.22 (br s, 1H), 2.40 (s, 3H), 1.95 (br s, 2H), 0.97-1.41 (m, 14H).
223	LC-MS *m/z* 417.3 $[M+H]^+$, RT 0.90 min.; ^{1}H NMR (DMSO-d_6) δ: 9.70 (s, 1H), 9.51 (br d, *J*= 9.8 Hz, 1H), 9.23-9.45 (m, 1H), 9.03 (s, 1H), 8.77 (s, 1H), 8.71 (s, 1H), 8.12 (s, 1H), 5.44-5.61 (m, 1H), 4.13 (br s, 2H), 2.42-2.48 (m, 5H), 1.95-2.18 (m, 6H).
232	LC-MS *m/z* 439.3 $[M+H]^+$, RT 0.87 min.; ^{1}H NMR (DMSO-d_6) δ: 9.12 (br d, *J*= 11.7 Hz, 1H), 8.81 (br s, 1H), 8.72 (s, 1H), 8.62 (br d, *J*= 2.2 Hz, 1H), 8.55 (s, 1H), 8.23 (d, *J*= 0.6 Hz, 1H), 8.15 (br d, *J*= 13.9 Hz, 1H), 7.75 (d, *J*= 13.6 Hz, 1H), 4.35 (br s, 1H), 4.23 (s, 3H), 2.18 (br dd, *J*= 13.2, 3.2 Hz, 2H), 1.59 (br t, *J*= 12.6 Hz, 2H), 1.39-1.53 (m, 12H).
233	LC-MS *m/z* 446.3 $[M+H]^+$, RT 0.89 min.; ^{1}H NMR (DMSO-d_6) δ: 8.93 (br s, 1H), 8.77 (d, *J*= 1.3 Hz, 1H), 8.65-8.74 (m, 2H), 8.48-8.63 (m, 3H), 7.99 (br s, 1H), 4.23-4.43 (m, 4H), 2.07-2.30 (m, 2H), 1.22-1.79 (m, 14H).
234	LC-MS *m/z* 439.3 $[M+H]^+$, RT 0.81 min.; ^{1}H NMR (DMSO-d_6) δ: 9.09 (s, 2H), 8.67 (s, 1H), 8.51-8.64 (m, 1H), 8.40 (s, 1H), 7.97-8.23 (m, 1H), 7.84-7.96 (m, 1H), 7.74 (br d, *J*= 12.9 Hz, 1H), 4.32 (br s, 1H), 2.37 (s, 3H), 2.07-2.23 (m, 2H), 1.23-1.73 (m, 14H).
238	LC-MS *m/z* 444.4 $[M+H]^+$, RT 0.91 min.; ^{1}H NMR ($CDCl_3$) δ: 8.86 (d, *J*= 0.6 Hz, 1H), 8.53 (d, *J*= 1.6 Hz, 1H), 8.43 (d, *J*= 1.6 Hz, 1H), 8.10 (s, 1H), 7.99 (d, *J*= 1.0 Hz, 1H), 4.64 (br s, 1H), 4.31 (s, 3H), 3.49 (br s, 2H), 3.16 (s, 3H), 2.48 (br s, 3H), 2.17-2.33 (m, 2H), 1.42-2.11 (m, 6H).
239	LC-MS *m/z* 437.4 $[M+H]^+$, RT 0.89 min.; ^{1}H NMR ($CDCl_3$) δ: 8.82 (d, *J*= 0.9 Hz, 1H), 8.65 (d, *J*= 1.3 Hz, 1H), 7.89 (d, *J*= 0.9 Hz, 1H), 7.41-7.50 (m, 2H), 4.83 (br s, 1H), 3.61 (br s, 2H), 3.21 (s, 3H), 2.59 (br s, 3H), 2.52 (s, 3H), 2.32(br s, 2H), 1.43-2.21 (m, 6H).
240	LC-MS *m/z* 444.5 $[M+H]^+$, RT 0.91 min.; ^{1}H NMR ($CDCl_3$) δ: 9.02 (d, *J*= 1.6 Hz, 1H), 8.81 (d, *J*= 0.6 Hz, 1H), 8.16 (d, *J*= 1.6 Hz, 1H), 7.91 (d, *J*= 0.6 Hz, 1H), 7.52 (d, *J*= 0.9 Hz, 1H), 4.59 (br s, 1H), 3.45 (br s, 2H), 3.15 (s, 3H), 2.54 (s, 3H), 2.45 (br s, 3H), 2.14-2.35 (m, 2H), 1.66-2.03 (m, 6H).
241	LC-MS *m/z* 437.5 $[M+H]^+$, RT 0.88 min.; ^{1}H NMR ($CDCl_3$) δ: 8.85 (d, *J*= 0.9 Hz, 1H), 8.06 (d, *J*= 1.3 Hz, 1H), 8.00 (d, *J*= 2.5 Hz, 1H), 7.97 (d, *J*= 0.9 Hz, 1H), 7.66 (dd, *J*= 12.6, 1.3 Hz, 1H), 4.63 (br s, 1H), 4.27 (s, 3H), 3.49 (br s, 2H), 3.15 (s, 3H), 2.48 (br s, 3H), 2.10-2.30 (m, 2H), 1.53-2.08 (m, 6H).

Cpd	Data
244	LC-MS *m/z* 430.5 $[M+H]^+$, RT 0.90 min.; ^{1}H NMR (DMSO-d_6) δ: 8.76 (d, *J*= 1.6 Hz, 1H), 8.70 (s, 1H), 8.68 (d, *J*= 0.6 Hz, 1H), 8.58 (d, *J*= 1.6 Hz, 1H), 8.48 (s, 1H), 8.38 (br d, *J*= 1.0 Hz, 1H), 4.26 (s, 3H), 4.03-4.24 (m, 1H), 3.23-3.61 (m, 5H), 2.30-2.45 (m, 2H), 1.94-2.19 (m, 3H), 1.64-1.89 (m, 3H).
245	LC-MS *m/z* 430.4 $[M+H]^+$, RT 0.90 min.; ^{1}H NMR (DMSO-d_6) δ: 9.50 (d, *J*= 1.9 Hz, 1H), 8.70 (s, 1H), 8.60 (br d, *J*= 5.4 Hz, 1H), 8.52 (d, *J*= 1.6 Hz, 1H), 8.46 (s, 1H), 7.97 (d, *J*= 0.6 Hz, 1H), 4.14-4.33 (m, 1H), 3.83 (br s, 2H), 3.32 (s, 3H), 2.58-2.71 (m, 2H), 2.36-2.45 (m, 3H), 2.13-2.28 (m, 3H), 1.84-2.07 (m, 3H).
246	LC-MS *m/z* 421.0 $[M-H]^-$, RT 0.86 min.; ^{1}H NMR (DMSO-d_6) δ: 8.67 (d, *J*= 0.6 Hz, 1H), 8.55 (d, *J*= 2.8 Hz, 1H), 8.39-8.50 (m, 2H), 8.22 (d, *J*= 0.9 Hz, 1H), 7.78 (dd, *J*= 13.6, 1.3 Hz, 1H), 4.21 (s, 3H), 3.78 (br s, 1H), 3.27-3.36 (m, 5H), 2.53-2.72 (m, 2H), 2.08-2.34 (m, 3H), 1.75-2.06 (m, 3H).
247	LC-MS *m/z* 421.3 $[M-H]^-$, RT 0.82 min.; ^{1}H NMR (DMSO-d_6) δ: 9.08 (d, *J*= 1.6 Hz, 1H), 8.68 (d, *J*= 0.6 Hz, 1H), 8.59 (br d, *J*= 5.7 Hz, 1H), 8.39 (d, *J*= 0.6 Hz, 1H), 7.88-7.90 (m, 1H), 7.74 (dd, *J*= 12.8, 1.4 Hz, 1H), 4.15-4.33 (m, 1H), 3.85 (br s, 2H), 3.32 (s, 3H), 2.64 (br s, 2H), 2.31-2.43 (m, 3H), 2.12-2.31 (m, 3H), 1.87-2.10 (m, 3H).
251	LC-MS *m/z* 444.4 $[M+H]^+$, RT 0.86 min.; ^{1}H NMR (DMSO-d_6) δ: 9.71 (br d, *J*= 11.0 Hz, 1H), 9.65 (d, *J*= 1.6 Hz, 1H), 9.01 (br d, *J*= 10.7 Hz, 1H), 8.81 (d, *J*= 0.9 Hz, 1H), 8.76 (s, 1H), 8.61 (d, *J*= 0.6 Hz, 1H), 8.10 (s, 1H), 5.30 (br s, 1H), 3.75 (br s, 2H), 3.11 (s, 3H), 2.47-2.53 (m, 2H, obscured by DMSO-d_6), 2.46 (d, *J*= 0.6 Hz, 3H), 1.72-2.15 (m, 8H).
252	LC-MS *m/z* 444.4 $[M+H]^+$, RT 0.87 min.; ^{1}H NMR (DMSO-d_6) δ: 9.58 (br d, *J*= 11.0 Hz, 1H), 8.90-9.00 (m, 1H), 8.82 (s, 1H), 8.78 (d, *J*= 1.9 Hz, 1H), 8.76 (s, 1H), 8.68 (s, 1H), 8.58 (d, *J*= 1.6 Hz, 1H), 5.27 (br s, 1H), 4.28 (s, 3H), 3.76 (br s, 2H), 3.11 (s, 3H), 2.40-2.48 (m, 2H), 1.72-2.14 (m, 8H).
253	LC-MS *m/z* 437.4 $[M+H]^+$, RT 0.83 min.; ^{1}H NMR (DMSO-d_6) δ: 9.82 (br d, *J*= 10.4 Hz, 1H), 9.08 (br d, *J*= 10.4 Hz, 1H), 8.84 (s, 1H), 8.75 (s, 1H), 8.68 (d, *J*= 2.8 Hz, 1H), 8.27 (d, *J*= 1.3 Hz, 1H), 7.75 (dd, *J*= 13.2, 1.3 Hz, 1H), 5.29 (br s, 1H), 4.24 (s, 3H), 3.75 (br s, 2H), 3.15 (s, 3H), 2.51-2.58 (m, 2H), 1.68-2.19 (m, 8H).
260	LC-MS *m/z* 419.4 $[M+H]^+$, RT 0.73 min.; ^{1}H NMR (DMSO-d_6) δ: 9.76 (br d, *J*= 11.3 Hz, 1H), 9.59 (dd, *J*= 1.6, 0.9 Hz, 1H), 9.04 (br s, 1H), 8.84 (d, *J*= 0.9 Hz, 1H), 8.64 (d, *J*= 0.6 Hz, 1H), 8.55 (dd, *J*= 9.6, 1.7 Hz, 1H), 8.17 (s, 1H), 8.00 (d, *J*= 9.5 Hz, 1H), 4.92 (br s, 1H), 3.75 (br s, 2H), 3.12 (s, 3H), 2.52 (d, *J*= 1.3 Hz, 3H), 2.44-2.48 (m, 2H), 1.75-2.15 (m, 8H).
261	LC-MS *m/z* 433.5 $[M+H]^+$, RT 0.75 min.; ^{1}H NMR (DMSO-d_6) δ: 9.85 (br d, *J*= 11.3 Hz, 1H), 9.43 (s, 1H), 9.09 (br d, *J*= 9.5 Hz, 1H), 8.82 (d, *J*= 0.6 Hz, 1H), 8.61 (s, 1H), 8.41 (s, 1H), 8.16 (d, *J*= 0.9 Hz, 1H), 5.32 (br s, 1H), 3.74 (br s, 2H), 3.12 (s, 3H), 2.67 (s, 3H), 2.51-2.57 (m, *J*= 0.9 Hz, 5H), 1.74-2.15 (m, 8H).

Cpd	Data
262	LC-MS *m/z* 419.5 $[M+H]^+$, RT 0.76 min.; ^{1}H NMR (DMSO-d_6) δ: 9.71 (br d, *J*= 10.7 Hz, 1H), 9.00 (br d, *J*= 8.2 Hz, 1H), 8.86 (s, 1H), 8.76 (br s, 1H), 8.57 (s, 1H), 8.37-8.45 (m, 1H), 7.87 (dd, *J*= 9.1, 1.3 Hz, 1H), 7.77 (d, *J*= 9.1 Hz, 1H), 5.27 (br s, 1H), 4.22 (s, 3H), 3.76 (br s, 2H), 3.15 (s, 3H), 2.47-2.53 (m, 2H, obscured by DMSO-d_6), 1.68-2.16 (m, 8H).
263	LC-MS *m/z* 433.5 $[M+H]^+$, RT 0.79 min.; ^{1}H NMR (DMSO-d_6) δ: 10.10 (br d, *J*= 10.7 Hz, 1H), 9.29 (br d, *J*= 10.7 Hz, 1H), 8.91 (s, 1H), 8.83 (s, 1H), 8.61 (s, 1H), 8.27 (d, *J*= 0.9 Hz, 1H), 7.61 (s, 1H), 5.37 (br s, 1H), 4.23 (s, 3H), 3.74 (br s, 2H), 3.19 (s, 3H), 2.54-2.66 (m, 5H), 1.75-2.19 (m, 8H).
264	LC-MS *m/z* 449.5 $[M+H]^+$, RT 0.77 min.; ^{1}H NMR (DMSO-d_6) δ: 9.66 (br d, *J*= 12.0 Hz, 1H), 8.97 (br d, *J*= 11.7 Hz, 1H), 8.85 (s, 1H), 8.82 (br s, 1H), 8.51 (s, 1H), 7.95 (d, *J*= 1.3 Hz, 1H), 7.27 (s, 1H), 5.30 (br s, 1H), 4.18 (s, 3H), 3.95-4.11 (m, 3H), 3.77 (br s, 2H), 3.15 (s, 3H), 2.47-2.53 (m, 2H, obscured by DMSO-d_6), 1.76-2.16 (m, 8H).
266	LC-MS *m/z* 460.5 $[M+H]^+$, RT 0.81 min.; ^{1}H NMR (DMSO-d_6) δ: 10.29 (br d, *J*= 5.0 Hz, 1H), 9.68 (d, *J*= 1.6 Hz, 1H), 8.99 (br d, *J*= 6.9 Hz, 1H), 8.81 (s, 1H), 8.69-8.77 (m, 1H), 8.56 (s, 1H), 8.13 (d, *J*= 0.9 Hz, 1H), 4.26-4.45 (m, 1H), 2.69 (d, *J*= 5.4 Hz, 3H), 2.47 (d, *J*= 0.9 Hz, 3H), 2.22 (dd, *J*= 13.2, 3.5 Hz, 2H), 2.06 (br t, *J*= 12.8 Hz, 2H), 1.55 (s, 6H), 1.43 (s, 6H).
267	LC-MS *m/z* 453.5 $[M+H]^+$, RT 0.70 min.; ^{1}H NMR (DMSO-d_6) δ: 10.42 (br d, *J*= 5.0 Hz, 1H), 9.48 (d, *J*= 1.3 Hz, 1H), 9.09 (br d, *J*= 6.9 Hz, 1H), 8.74 (d, *J*= 0.6 Hz, 1H), 8.53-8.63 (m, 1H), 8.43-8.51 (m, 1H), 8.17-8.37 (m, 1H), 4.26-4.47 (m, 1H), 2.68 (d, *J*= 5.0 Hz, 3H), 2.53 (d, *J*= 0.9 Hz, 3H), 2.22 (dd, *J*= 13.6, 3.5 Hz, 2H), 2.03-2.15 (m, 2H), 1.55 (s, 6H), 1.43 (s, 6H).
268	LC-MS *m/z* 460.6 $[M+H]^+$, RT 0.82 min.; ^{1}H NMR (DMSO-d_6) δ: 10.21 (br d, *J*= 5.0 Hz, 1H), 9.18 (br s, 1H), 8.82 (s, 1H), 8.75-8.79 (m, 2H), 8.68 (s, 1H), 8.53 (d, *J*= 1.3 Hz, 1H), 4.37 (br s, 1H), 4.24-4.33 (m, 3H), 2.70 (d, *J*= 5.0 Hz, 3H), 2.24 (br dd, *J*= 13.4, 3.3 Hz, 2H), 2.00-2.12 (m, 2H), 1.54 (s, 6H), 1.43 (s, 6H).
269	LC-MS *m/z* 453.5; $[M+H]^+$, RT 0.78 min.; ^{1}H NMR (DMSO-d_6) δ: 10.31 (br d, *J*= 4.7 Hz, 1H), 9.40 (br s, 1H), 8.71-8.79 (m, 3H), 8.28 (d, *J*= 1.3 Hz, 1H), 7.71 (dd, *J*= 12.9, 1.6 Hz, 1H), 4.39 (br s, 1H), 4.25 (s, 3H), 2.70 (d, *J*= 5.0 Hz, 3H), 2.24 (dd, *J*= 13.6, 3.5 Hz, 2H), 2.00-2.19 (m, 2H), 1.55 (s, 6H), 1.43 (s, 6H).
270	LC-MS *m/z* 458.5 $[M+H]^+$, RT 0.82 min.; ^{1}H NMR (DMSO-d_6) δ: 9.49 (d, *J*= 1.9 Hz, 1H), 8.74 (s, 1H), 8.46-8.55 (m, 2H), 7.96 (d, *J*= 0.9 Hz, 1H), 5.04 (br s, 1H), 3.32 (br s, 5H), 3.08 (s, 3H), 2.95 (br s, 2H), 2.40 (d, *J*= 0.6 Hz, 3H), 1.44-2.32 (m, 8H).
271	LC-MS *m/z* 451.5 $[M+H]^+$, RT 0.71 min.; ^{1}H NMR ($CDCl_3$) δ: 8.82 (d, *J*= 0.6 Hz, 1H), 8.65 (d, *J*= 1.3 Hz, 1H), 7.88 (d, *J*= 0.6 Hz, 1H), 7.40-7.50 (m, 2H), 5.31 (br s, 1H), 3.27 (br s, 2H), 3.13-3.22 (m, 3H), 2.75 (br s, 3H), 2.50 (d, *J*= 0.6 Hz, 3H), 2.03-2.33 (m, 4H), 1.45-1.97 (m, 6H).

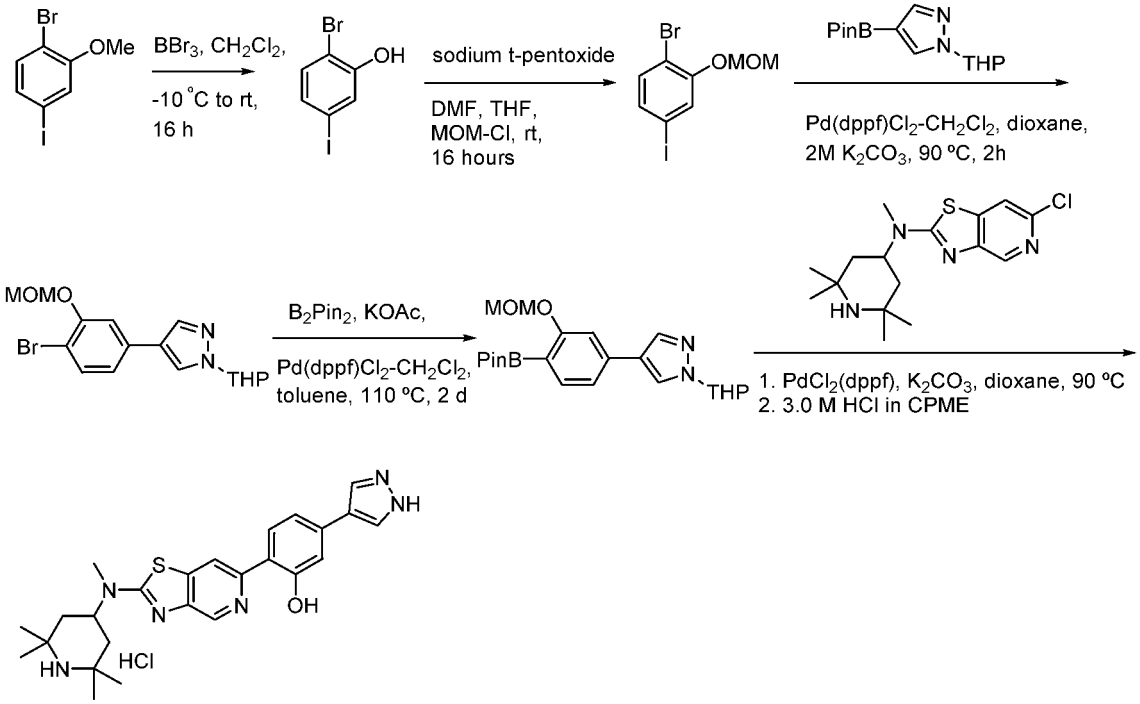
Cpd	Data
272	LC-MS *m/z* 458.5 $[M+H]^+$, RT 0.83 min.; ^{1}H NMR ($CDCl_3$) δ: 8.87 (d, *J*= 0.6 Hz, 1H), 8.53 (d, *J*= 1.6 Hz, 1H), 8.36-8.49 (m, 1H), 8.10 (s, 1H), 8.00 (d, *J*= 0.6 Hz, 1H), 5.26 (br s, 1H), 4.32 (s, 3H), 3.26 (br s, 2H), 3.19 (s, 3H), 2.74 (br s, 3H), 2.03-2.34 (m, 4H), 1.46-1.97 (m, 6H).
273	LC-MS *m/z* 451.5 $[M+H]^+$, RT 0.80 min.; ^{1}H NMR ($CDCl_3$) δ: 8.86 (d, *J*= 0.6 Hz, 1H), 8.06 (d, *J*= 1.3 Hz, 1H), 8.00 (d, *J*= 2.5 Hz, 1H), 7.98 (d, *J*= 0.6 Hz, 1H), 7.66 (dd, *J*= 12.9, 1.3 Hz, 1H), 5.19 (br s, 1H), 4.27 (s, 3H), 3.09-3.26 (m, 5H), 2.70 (br s, 3H), 2.02-2.28 (m, 4H), 1.62-1.95 (m, 6H).
285	MS *m/z* $[M+H]^+$ 458.4; ^{1}H NMR (DMSO-d_6) δ: 9.49 (d, *J*=1.6 Hz, 1H), 8.73 (d, *J*=0.6 Hz, 1H), 8.52 (d, *J*=1.6 Hz, 1H), 8.49 (d, *J*=0.6 Hz, 1H), 7.96 (d, *J*=0.9 Hz, 1H), 4.41 (br s, 1H), 3.25-3.39 (m, 1H), 2.97-3.11 (m, 3H), 2.37-2.45 (m, 3H), 1.46-1.87 (m, 8H), 1.21 (s, 6H).
286	MS *m/z* $[M+H]^+$ 451.5; ^{1}H NMR (DMSO-d_6) δ: 10.05-10.14 (m, 1H), 9.44-9.50 (m, 1H), 9.15-9.24 (m, 1H), 8.81-8.87 (m, 1H), 8.63 (s, 1H), 8.45 (br d, *J*=12.0 Hz, 1H), 8.24 (s, 1H), 4.57-4.85 (m, 1H), 3.12-3.19 (m, 3H), 2.51-2.53 (m, 3H), 2.27-2.36 (m, 2H), 2.03-2.14 (m, 2H), 1.83-1.97 (m, 4H), 1.48 (s, 6H).
287	MS *m/z* $[M+H]^+$ 458.4; ^{1}H NMR (DMSO-d_6) δ: 8.77 (d, *J*=1.58 Hz, 1H), 8.74 (d, *J*=0.63 Hz, 1H), 8.70 (s, 1H), 8.59 (d, *J*=1.58 Hz, 1H), 8.55 (d, *J*=0.63 Hz, 1H), 4.31-4.52 (m, 1H), 4.24-4.28 (m, 3H), 2.95-3.10 (m, 3H), 1.48-1.86 (m, 8H), 1.20 (s, 6H), NH proton not observed.
296	MS *m/z* $[M+H]^+$ 450.5; ^{1}H NMR (DMSO-d_6) δ: 9.43-9.58 (m, 1H), 8.80 (d, *J*=0.63 Hz, 3H), 8.54-8.61 (m, 1H), 8.41-8.49 (m, 1H), 4.61-4.88 (m, 1H), 3.03-3.19 (m, 3H), 2.81-2.99 (m, 3H), 2.48 (s, 3H), 2.06-2.18 (m, 2H), 1.82-1.92 (m, 2H), 1.44-1.60 (m, 12H).
297	MS *m/z* $[M+H]^+$ 449.5; ^{1}H NMR (DMSO-d_6) δ: 9.38-9.53 (m, 1H), 8.71-8.87 (m, 2H), 8.57 (s, 1H), 8.34-8.48 (m, 2H), 8.22 (s, 1H), 4.61-4.81 (m, 1H), 3.10 (s, 3H), 2.93 (s, 3H), 2.44 (d, *J*=0.95 Hz, 3H), 2.03-2.16 (m, 2H), 1.83-1.95 (m, 2H), 1.48-1.57 (m, 12H).
298	MS *m/z* $[M+H]^+$ 451.4; ^{1}H NMR (DMSO-d_6) δ: 8.72 (d, *J*=0.95 Hz, 1H), 8.55 (d, *J*=2.84 Hz, 1H), 8.49 (d, *J*=0.63 Hz, 1H), 8.24 (d, *J*=0.95 Hz, 1H), 7.80 (dd, *J*=13.87, 1.26 Hz, 1H), 4.32-4.54 (m, 1H), 4.21 (s, 3H), 3.04 (s, 3H), 1.50-1.88 (m, 8H), 1.22 (s, 6H), NH proton not observed.
299	MS *m/z* $[M+H]^+$ 447.5; ^{1}H NMR (DMSO-d_6) δ: 8.98-9.03 (m, 1H), 8.72 (d, *J*=0.63 Hz, 1H), 8.40 (s, 1H), 7.70-7.75 (m, 2H), 4.41 (br s, 1H), 2.52 (s, 3H), 3.03 (s, 3H),2.34 (d, *J*=1.00 Hz, 3H), 1.47-1.82 (m, 8H), 1.18 (s, 6H), NH proton not observed.
300	MS *m/z* $[M+H]^+$ 433.5; ^{1}H NMR (MHz, DMSO-d_6) δ: 9.17 (dd, *J*=1.89, 0.95 Hz, 1H), 8.73 (d, *J*=0.63 Hz, 1H), 8.42 (d, *J*=0.63 Hz, 1H), 7.85 (dd, *J*=9.46, 1.89 Hz, 1H), 7.76 (s, 1H), 7.50 (d, *J*=9.46 Hz, 1H), 4.37 (br s, 1H), 3.04 (s, 3H), 2.27-2.41 (m, 3H), 1.44-1.85 (m, 8H),1.18 (s, 6H), NH proton not observed.

Cpd	Data
301	MS *m/z* $[M+H]^+$ 459.4; ^{1}H NMR (methanol-d_4) δ: 8.77 (s, 1H), 8.48 (d, *J*=1.00 Hz, 1H), 8.41 (s, 1H), 8.29-8.38 (m, 1H), 4.90-5.04 (m, 1H), 3.16 (s, 3H), 2.75 (s, 3H), 2.01-2.41 (m, 8H), 1.57 (s, 6H), NH proton not observed.
302	MS *m/z* $[M+H]^+$ 441.4; ^{1}H NMR (DMSO-d_6) δ: 9.36 (br d, *J*=12.30 Hz, 1H), 8.62-8.81 (m, 2H), 8.48 (br s, 1H), 8.32 (br d, *J*=11.98 Hz, 1H), 7.88 (s, 1H), 4.55-4.83 (m, 1H), 3.13 (s, 3H), 2.45 (br d, *J*=1.26 Hz, 3H), 2.01-2.15 (m, 2H), 1.81-1.95 (m, 2H), 1.51 (d, *J*=10.40 Hz, 12H).
305	MS *m/z* $[M+H]^+$ 441.4; ^{1}H NMR (DMSO-d_6) δ: 8.63 (d, *J*=0.63 Hz, 1H), 8.35 (d, *J*=0.95 Hz, 1H), 8.18 (s, 1H), 6.90 (d, *J*=1.26 Hz, 1H), 4.23-4.51 (m, 1H), 3.05 (s, 3H), 2.44 (d, *J*=1.26 Hz, 3H), 1.40-1.72 (m, 4H), 1.27 (br s, 6H), 1.12 (br s, 6H), NH proton not observed.
308	MS *m/z* $[M+H]^+$ 442.5; ^{1}H NMR (DMSO-d_6) δ: 9.45 (br d, *J*=12.30 Hz, 1H), 8.79-8.98 (m, 1H), 8.73 (s, 2H), 8.40 (br d, *J*=11.35 Hz, 1H), 4.60-4.80 (m, 1H), 3.12 (s, 3H), 2.77 (s, 3H), 2.01-2.19 (m, 2H), 1.81-1.94 (m, 2H), 1.52 (br d, *J*=6.62 Hz, 12H).
322	MS *m/z* $[M+H]^+$ 448.5; ^{1}H NMR (DMSO-d_6) δ: 8.69 (s, 1H), 8.56 (s, 1H), 8.41 (s, 1H), 8.28 (s, 1H), 4.27-4.50 (m, 1H), 3.03 (s, 3H), 2.75 (s, 3H), 2.37 (s, 3H), 1.43-1.80 (m, 8H), 1.18 (s, 6H), NH proton not observed.
325	MS *m/z* $[M+H]^+$ 478.2; ^{1}H NMR (methanol-d_4) δ: 9.70 (d, *J*=1.5 Hz, 1H), 9.10 (d, *J*=1.5 Hz, 1H), 8.94 (s, 1H), 8.64 (s, 1H), 8.26 (d, *J*=1.2 Hz, 1H), 5.37-5.51 (m, 1H), 5.05 (d, *J*=48.5 Hz, 1H), 3.33 (s, 3H), 2.66 (s, 3H), 2.49 (t, *J*=13.4 Hz, 1H), 2.10 (dd, *J*=13.4, 3.7 Hz, 1H), 1.75 (d, *J*=0.9 Hz, 3H), 1.71 (s, 3H), 1.63 (s, 3H), 1.59 (d, *J*=2.1 Hz, 3H); 1 NH not observed.
326	MS *m/z* $[M+H]^+$ 469.2; ^{1}H NMR (methanol-d_4) δ: 9.30 (d, *J*=0.9 Hz, 1H), 8.92 (s, 1H), 8.57 (s, 1H), 8.49 (dd, *J*=11.3, 0.9 Hz, 1H), 8.19 (d, *J*=0.6 Hz, 1H), 5.17-5.30 (m, 1H), 5.02-5.14 (m, 1H), 3.31 (d, *J*=1.5 Hz, 3H), 2.64 (d, *J*=0.6 Hz, 3H), 2.50 (br t, *J*=13.3 Hz, 1H), 2.33-2.42 (m, 2H), 2.15 (br dd, *J*=13.6, 5.6 Hz, 2H), 2.05 (s, 1H), 1.65 (s, 3H), 1.63 (s, 3H); 1NH not observed.
377	MS *m/z* $[M+H]^+$ 432.4; ^{1}H NMR (DMSO-d_6) δ: 8.77 (s, 1H), 8.74 (s, 1H), 8.69 (s, 1H), 8.60 (s, 1H), 8.55 (s, 1H), 4.26 (s, 3H), 4.00-4.16 (m, 1H), 3.07 (s, 3H), 2.84-2.95 (m, 1H), 1.97-2.27 (m, 5H), 1.79-1.95 (m, 1H), 1.65-1.79 (m, 2H), 1.49-1.63 (m, 1H), 1.06 (d, *J*=6.1 Hz, 3H).
378	MS *m/z* $[M+H]^+$ 425.4; ^{1}H NMR (DMSO-d_6) δ: 8.72 (s, 1H), 8.54 (d, *J*=1.8 Hz, 1H), 8.47 (s, 1H), 8.23 (s, 1H), 7.80 (d, *J*=13.7 Hz, 1H), 4.21 (s, 3H), 3.96-4.14 (m, 1H), 3.05 (s, 3H), 2.84-2.93 (m, 1H), 2.09-2.24 (m, 4H), 1.97-2.08 (m, 1H), 1.80-1.93 (m, 1H), 1.65-1.76 (m, 2H), 1.48-1.62 (m, 1H), 1.05 (d, *J*=6.1 Hz, 3H).
379	MS *m/z* $[M+H]^+$ 432.4; ^{1}H NMR (DMSO-d_6) δ: 9.50 (d, *J*=1.5 Hz, 1H), 8.74 (s, 1H), 8.53 (d, *J*=1.5 Hz, 1H), 8.50 (s, 1H), 7.96 (s, 1H), 3.98-4.21 (m, 1H), 3.07 (s, 3H), 2.84-2.99 (m, 1H), 2.40 (s, 3H), 1.47-2.31 (m, 9H), 1.08 (br d, *J*=5.2 Hz, 3H).

Cpd	Data
380	MS *m/z* $[M+H]^+$ 425.4; ^{1}H NMR (methanol-d_4) δ: 9.21 (s, 1H), 8.78 (s, 1H), 8.37-8.45 (m, 2H), 8.10 (br s, 1H), 4.63-4.74 (m, 1H), 3.66-3.75 (m, 1H), 3.23-3.61 (m, 2H), 3.14-3.22 (m, 3H), 2.96 (s, 3H), 2.59 (s, 3H), 2.00-2.37 (m, 4H), 1.48 (d, *J*=6.1 Hz, 3H).

Example 28

Preparation of Compound 137



Step 1: 1-Bromo-4-iodo-2-methoxybenzene (50 g, 160 mmol) was suspended in dichloromethane (75 mL) at −10 °C. Boron tribromide (250 mL, 250 mmol, 1M in CH_2Cl_2,) was cannulated in over 30 minutes, with the internal temperature remaining below 0 °C throughout the addition. After the addition, the mixture was stirred at 0 °C for 1 h, and then at room temperature for 16 h. The mixture was cooled in an ice bath and 10% aqueous Na_2CO_3 (250 mL) was added in portions. The mixture was then partitioned between H_2O and dichloromethane. The dichloromethane layer was dried over $MgSO_4$ and then filtered. 2-Bromo-5-iodophenol (46 g, 96%) was obtained from the filtrate as a pinkish-white solid.

^{1}H NMR (acetone-d_6) δ: 9.24 (br s, 1H), 7.38 (d, *J*= 2 Hz, 1H), 7.31 (d, *J*= 8.5 Hz, 1H), 7.17 (dd, *J*= 8.5 Hz, 2 Hz, 1H).

Step 2: 2-Bromo-5-iodophenol (54.9 g, 184 mmol), was dissolved in DMF (240 mL) at 0 °C. Sodium *tert*-pentoxide (2.5 M in THF, 90 mL, 230 mmol) was then added dropwise. The reaction was stirred at 0 °C for 15 min after the addition was complete. Chloromethyl methyl ether (18 mL, 225 mmol) was added dropwise over 30 min. The mixture was warmed to ambient temperature and was stirred for 16 h. The mixture was diluted with 1.5 L of H_2O and was extracted into EtOAc (2 x 400 mL). The combined organic layers were washed with H_2O (300 mL), and then with brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude product was flushed through a silica plug using CH_2Cl_2 in hexanes (0–10%) to yield 1-bromo-4-iodo-2-(methoxymethoxy)benzene (61 g, 97%) as a clear liquid.

^{1}H NMR (acetone-d_6) δ: 7.56 (d, *J*= 2 Hz, 1H), 7.38 (d, *J*= 8Hz, 1H), 7.33 (dd, *J*= 8 Hz, 2 Hz, 1H), 5.35 (s, 2H), 3.50 (s, 3H).

Step 3: 1-Bromo-4-iodo-2-(methoxymethoxy)benzene (49 g, 143 mmol), 1-(tetrahydro-2*H*-pyran-2-yl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrazole (48.4 g, 174 mmol), $PdCl_2$(dppf)-dichloromethane adduct (3.1 g, 3.6 mmol), dioxane (500 mL), and aqueous K_2CO_3 (350 mL, 350 mmol, 1M) were heated at 90 °C for 2 h. The reaction mixture was then partitioned between H_2O and EtOAc. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. Purification by silica gel chromatography (EtOAc in hexanes, 20–50%), followed by trituration with hexanes, yielded 4-(4-bromo-3-(methoxymethoxy)phenyl)-1-(tetrahydro-2*H*-pyran-2-yl)-1*H*-pyrazole (40.4 g, 77%) as an off-white solid.

^{1}H NMR (acetone-d_6) δ: 8.22 (s, 1H), 7.88 (s, 1H), 7.55 (d, *J*= 8.5 Hz, 1H), 7.47 (d, *J*= 2 Hz, 1H), 7.23 (dd, *J*= 8.5 Hz, 2 Hz, 1H), 5.44 (dd, *J*= 9.5 Hz, 2.5 Hz, 1H), 5.38 (S, 2H), 4.01 (m, 1H), 3.72 (m, 1H), 3.51 (s, 3H), 2.1-2.23 (m, 1H), 2.0-2.1 (m, 2H), 1.7-1.8 (m, 1H), 1.6-1.7 (m, 2H).

Step 4: Potassium acetate (22 g, 224 mmol) was pumped dry at 180 °C for 2 h, and then the flask was filled with argon. 4-(4-bromo-3-(methoxymethoxy)phenyl)-1-(tetrahydro-2*H*-pyran-2-yl)-1*H*-pyrazole (20 g, 54.5 mmol), Pd Cl_2(dppf)-dichloromethane adduct (1.22 g, 1.47 mmol), bis(pinacolato)diboron (20.8 g, 81.9 mmol), and dry toluene (200 mL) was added. This mixture was heated at 110 °C for 2 days. The mixture was filtered through Celite, eluting with ether. The filtrate was concentrated under vacuum, re-dissolved in ether, and was filtered again through Celite to remove solid impurities. Purification by silica gel chromatography (EtOAc in hexanes, 20–50%) yielded crude product (12 g) that mostly free of protodeboronated by-product. This was dissolved in ether (100 mL) and washed with aqueous $NaHCO_3$ (2x1.5 L), brine, dried over

$MgSO_4$, and then filtered. The filtrate was concentrated to provide pure product (7.05 g, 32%) as a glassy semi-solid.

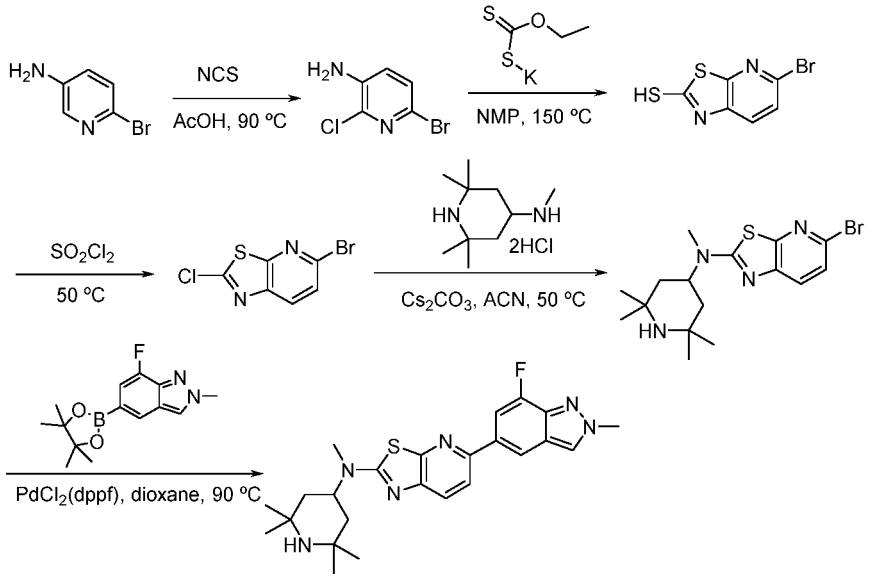
^{1}H NMR (acetone-d_6): δ: 8.24 (s, 1H), 7.90 (s, 1H), 7.65 (d, *J*= 8 Hz, 1H), 7.33 (d, *J*= 1.5 Hz, 1H), 7.29 (dd, *J*= 8 Hz, 1.5 Hz, 1H), 5.45 (dd, *J*= 10 Hz, 2.5 Hz, 1H), 5.25 (s, 2H), 4.01 (m, 1H), 3.69-3.74 (m, 1H), 3.52 (s, 3H), 2.15-2.2 (m, 1H), 2.0-2.1 (m, 2H), 1.7-1.8 (m, 1H), 1.6-1.68 (m, 2H), 1.35 (s, 12H).

Step 5: To a mixture of 6-chloro-*N*-methyl-*N*-(2,2,6,6-tetramethyl-4-piperidyl)thiazolo[4,5-c]pyridin-2-amine (169 mg, 0.50 mmol), 3-[3-(methoxymethoxy)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]-1-tetrahydropyran-2-yl-pyrazole (249 mg, 0.60 mmol), $PdCl_2$(dppf) (50 mg, 0.06 mmol) in 1,4-dioxane (2.0 mL), under argon was added K_2CO_3 (0.63 mL, 1.3 mmol, 2.0 M). The mixture was stirred at 90 ºC for 2 h, cooled, and then diluted with EtOAc. The precipitate was removed by filtration. The filtrate was concentrated and chromatographed (MeOH in CH_2Cl_2, 0-20%) to provide the coupling product, which was treated with HCl (5 mL, 3 M in CPME) at room temperature overnight. The precipitate was collected by filtration and dried to provide 2-[2-[methyl-(2,2,6,6-tetramethyl-4-piperidyl)amino]thiazolo[4,5-c]pyridin-6-yl]-5-(1*H*-pyrazol-3-yl)phenol hydrochloride (102 mg, 41%).

LC-MS 463.2 *m/z* $[M+H]^+$, RT 0.95 min; ^{1}H NMR (DMSO-d_6) δ: 9.50 (br d, *J*= 11.3 Hz, 1H), 8.73-8.88 (m, 2H), 8.44 (br d, *J*= 12.0 Hz, 1H), 8.13 (s, 2H), 7.78 (br d, *J*= 8.5 Hz, 1H), 7.21-7.31 (m, 2H), 4.65 (br s, 1H), 3.13 (s, 3H), 2.12 (br t, *J*= 12.8 Hz, 2H), 1.83-1.94 (m, 2H), 1.42-1.60 (m, 12H).

Example 29

Preparation of Compound 128



Step 1: A mixture of 6-bromopyridin-3-amine (11.7 g, 67.6 mmol), 1-chloropyrrolidine-2,5-dione (9.93 g, 74.4 mmol) and acetic acid (70 mL) was stirred at 90 °C for 2 h. The solvent was removed on a rotovap and the residue was washed with water and dried to provide 6-bromo-2-chloro-pyridin-3-amine (13.1 g, 93.4%). LC-MS *m/z* 207.1, 209.1 $[M+H]^+$, RT: 1.12 min.

Step 2: A mixture of 6-bromo-2-chloro-pyridin-3-amine (13.1 g, 63.1 mmol), ethylxanthic acid potassium salt (15.2 g, 94.8 mmol), and NMP (60 mL) was stirred at 150 °C for 6 h. LC/MS showed the disappearance of the starting pyridine. The reaction was then cooled to room temperature and acetic acid (10 mL) was added and then diluted with water (500 mL). The precipitate was collected by filtration, washed with water, dried and used directly in the next step.

Step 3: The above material was treated with sulfuryl chloride (20 mL, 247.9 mmol) and heated at 50 °C overnight and the mixture was then added to an ice and $NaHCO_3/CH_2Cl_2$ (~0.5 L). The precipitate was removed by filtration and the filtrate was concentrated. The residue was chromatographed (silica gel, ethyl acetate in hexanes, 0-40%) to provide 5-bromo-2-chlorothiazolo[5,4-b]pyridine (3.94 g, 63.5%). LC-MS *m/z* 251.0 $[M+H]^+$, RT: 1.44 min.

Step 4: A mixture of 6-bromo-2-chloro-thiazolo[4,5-c]pyridine (3.94 g, 15.8 mmol), N,2,2,6,6-pentamethylpiperidin-4-amine (2.82 g, 16.6 mmol), Cs_2CO_3(12.9 g, 39.6 mmol) and acetonitrile (32 mL) was heated at 50 °C for 24 h. The reaction mixture was then diluted with ethyl acetate

and filtered. The filtrate was concentrated and the residue was chromatographed (silica gel, MeOH in CH_2Cl_2 0-20%) to provide 5-bromo-*N*-methyl-*N*-(2,2,6,6-tetramethyl-4-piperidyl)thiazolo[5,4-b]pyridin-2-amine (5.41 g, 89.4%) as an off white powder. LC-MS *m/z* 383.2, 385.1 $[M+H]^+$, RT: 1.02 min.

Step 5: To a mixture of 5-bromo-*N*-methyl-*N*-(2,2,6,6-tetramethyl-4-piperidyl)thiazolo[5,4-b]pyridin-2-amine (95.8 mg, 0.25 mmol), 7-fluoro-2-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indazole (82.8 mg, 0.30 mmol), and $PdCl_2$(dppf) (21 mg, 0.025 mmol) in 1,4-dioxane (1.0 mL), under an argon atmosphere, was added K_2CO_3 (0.31 mL, 0.62 mmol, 2.0 M). The mixture was heated at 90 °C for 2 h and then cooled and diluted with ethyl acetate. The precipitate was removed by filtration and the filtrate was concentrated and chromatographed (silica gel, MeOH in CH_2Cl_2, 0-20%) to provide, after trituration with ethyl ether, 5-(7-fluoro-2-methyl-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethyl-4-piperidyl)thiazolo[5,4-b]pyridin-2-amine (65 mg, 57.5%).

LC-MS *m/z* 453.3 $[M+H]^+$, RT 1.04 min.; ^{1}H NMR ($CDCl_3$) δ: 8.04 (d, *J*= 0.9 Hz, 1H), 7.99 (d, *J*= 2.5 Hz, 1H), 7.64-7.77 (m, 2H), 7.27 (s, 1H), 4.46 (br s, 1H), 4.26 (s, 3H), 3.12 (s, 3H), 1.82 (dd, *J*= 12.5, 3.3 Hz, 2H), 1.16-1.60 (m, 14H).

Using the procedure described for Example 29, above, additional compounds described herein were prepared by substituting the appropriate starting material, suitable reagents and reaction conditions, obtaining compounds such as those selected from:

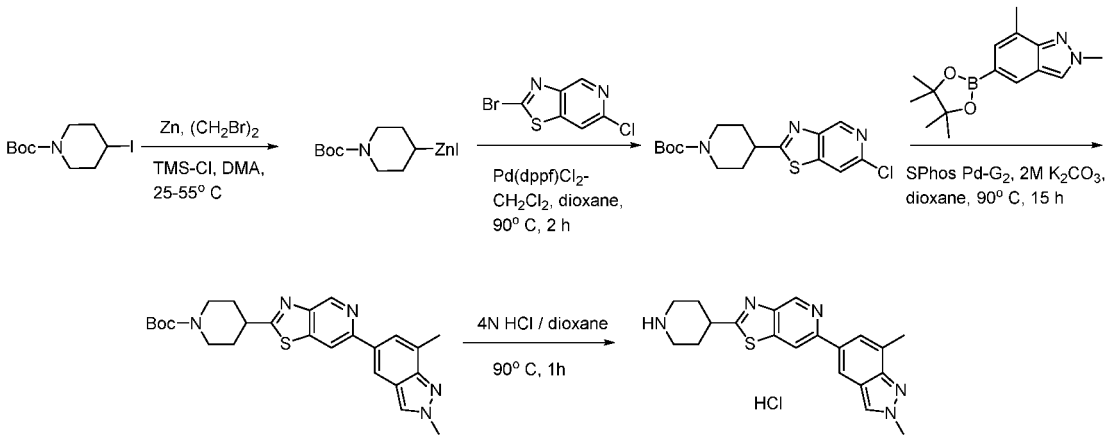
Cpd	Data
25	MS *m/z* 435.0 $[M+H]^+$; ^{1}H NMR (DMSO-d_6): δ: 8.42 (s, 1H), 8.39 (s, 1H), 7.99 (dd, *J*= 9 Hz, 1.5 Hz, 1H), 7.91 (d, *J*= 9 Hz, 1H), 7.79 (d, *J*= 8 Hz, 1H), 7.65 (d, *J*= 9 Hz, 1H), 4.37 (br s, 1H), 4.19 (s, 3H), 3.04 (s, 3H), 1.61-1.96 (m, 2H), 1.47-1.53 (m, 2H), 1.25 (s, 6H), 1.11 (s, 6H).
26	MS *m/z* 378.9 $[M+H]^+$; ^{1}H NMR (DMSO-d_6): δ: 8.85-9.00 (m, 2H), 8.44 (s, 1H), 8.40 (s, 1H), 7.99 (dd, *J*= 9 Hz, 1.5 Hz, 1H), 7.93 (d, *J*= 8.5 Hz, 1H), 7.81 (d, *J*= 8.5 Hz, 1H), 7.67 (d, *J*= 8 Hz, 1H), 4.40-4.48 (m, 1H), 4.19 (s, 3H), 3.37-3.42 (m, 2H), 3.10-3.18 (m, 2H), 3.07 (s, 3H), 2.08-2.20 (m, 2H), 1.90-1.95 (m, 2H).
36	MS *m/z* 393.3 $[M+H]^+$; ^{1}H NMR (DMSO-d_6): δ: 8.97-9.12 (m, 2), 8.40 (s, 1H), 8.20 (s, 1H), 7.92 (d, *J*= 9 Hz, 1H), 7.80 (d, *J*= 8.5 Hz, 1H), 7.78 (s, 1H), 4.44-4.53 (m, 1H), 4.20 (s, 3H), 3.35-3.45 (m, 2H), 3.10-3.18 (m, 2H), 3.08 (s, 3H), 2.64 (s, 3H), 2.12-2.21 (m, 2H), 1.90-1.95 (m, 2H).

Cpd	Data
129	LC-MS *m/z* 435.3 $[M+H]^+$, RT 0.82 min.; ^{1}H NMR ($CDCl_3$) δ: 8.73-8.83 (m, 1H), 7.75 (d, *J*= 8.5 Hz, 1H), 7.71 (dd, *J*= 9.5, 1.6 Hz, 1H), 7.60 (d, *J*= 8.5 Hz, 1H), 7.56 (d, *J*= 9.1 Hz, 1H), 7.39 (s, 1H), 4.52 (br s, 1H), 3.12 (s, 3H), 2.47 (d, *J*= 0.6 Hz, 3H), 1.82 (dd, *J*= 12.5, 3.3 Hz, 2H), 1.28-1.73 (m, 14H).
148	LC-MS *m/z* 460.3 $[M+H]^+$, RT 1.04 min.; ^{1}H NMR (DMSO-d_6) δ: 8.79 (d, *J*= 1.3 Hz, 1H), 8.69 (s, 1H), 8.59 (d, *J*= 1.6 Hz, 1H), 8.02 (d, *J*= 8.5 Hz, 1H), 7.82 (d, *J*= 8.5 Hz, 1H), 4.43 (br s, 1H), 4.26 (s, 3H), 3.07 (s, 3H), 0.99-1.80 (m, 16H).
149	LC-MS *m/z* 463.3 $[M+H]^+$, RT 1.02 min.; ^{1}H NMR (DMSO-d_6) δ: 9.59 (br d, *J*= 11.3 Hz, 1H), 8.47 (br d, *J*= 11.7 Hz, 1H), 8.20 (s, 2H), 8.11 (d, *J*= 8.8 Hz, 1H), 7.93 (d, *J*= 8.8 Hz, 2H), 7.13-7.27 (m, 2H), 4.61 (br s, 1H), 3.08 (s, 3H), 2.12 (br t, *J*= 12.9 Hz, 2H), 1.85 (br dd, *J*= 12.8, 3.0 Hz, 2H), 1.42-1.65 (m, 12H).
177	LC-MS *m/z* 453.2 $[M+H]^+$, RT 0.87 min.; ^{1}H NMR (DMSO-d_6) δ: 9.09 (d, *J*= 1.6 Hz, 1H), 7.85-7.92 (m, 2H), 7.81 (d, *J*= 8.5 Hz, 1H), 7.76 (dd, *J*= 12.9, 1.3 Hz, 1H), 4.36 (br s, 1H), 3.05 (s, 3H), 2.36 (d, *J*= 0.6 Hz, 3H), 1.62 (br dd, *J*= 11.8, 3.0 Hz, 2H), 1.47 (br t, *J*= 12.1 Hz, 2H), 1.23 (s, 6H), 1.09 (s, 6H).
178	LC-MS *m/z* 460.2 $[M+H]^+$, RT 0.98 min.; ^{1}H NMR (DMSO-d_6) δ: 9.48 (d, *J*= 1.6 Hz, 1H), 8.53 (d, *J*= 1.9 Hz, 1H), 7.91-7.97 (m, 2H), 7.82 (d, *J*= 8.5 Hz, 1H), 4.12-4.65 (m, 1H), 3.05 (s, 3H), 2.36-2.42 (m, 3H), 0.95-1.78 (m, 16H).
276	LC-MS *m/z* 430.4 $[M+H]^+$, RT 0.84 min.; ^{1}H NMR (DMSO-d_6) δ: 9.61 (d, *J*= 1.6 Hz, 1H), 9.42 (br d, *J*= 10.4 Hz, 1H), 8.93-9.02 (m, 1H), 8.74 (s, 1H), 8.06 (s, 1H), 8.03 (d, *J*= 8.5 Hz, 1H), 7.91 (d, *J*= 8.5 Hz, 1H), 4.67 (br s, 1H), 4.12 (br s, 2H), 3.10 (s, 3H), 2.45 (d, *J*= 0.9 Hz, 3H), 2.28-2.37 (m, 2H), 1.94-2.14 (m, 4H), 1.82-1.91 (m, 2H).
277	LC-MS *m/z* 423.4 $[M+H]^+$, RT 0.74 min.; ^{1}H NMR (DMSO-d_6) δ: 9.68 (br d, *J*= 10.1 Hz, 1H), 9.46 (s, 1H), 9.11 (br d, *J*= 8.8 Hz, 1H), 8.46 (br d, *J*= 12.0 Hz, 1H), 8.22 (s, 1H), 8.05 (d, *J*= 8.5 Hz, 1H), 7.94 (d, *J*= 8.5 Hz, 1H), 4.68 (br s, 1H), 4.11 (br s, 2H), 3.13 (s, 3H), 2.51 (d, *J*= 0.9 Hz, 3H), 2.34-2.43 (m, 2H), 2.04-2.13 (m, 2H), 1.92-2.01 (m, 2H), 1.80-1.90 (m, 2H).
278	LC-MS *m/z* 430.4 $[M+H]^+$, RT 0.89 min.; ^{1}H NMR (DMSO-d_6) δ: 9.28 (br d, *J*= 10.4 Hz, 1H), 8.91 (br d, *J*= 12.3 Hz, 1H), 8.80 (d, *J*= 1.6 Hz, 1H), 8.70 (s, 1H), 8.59 (d, *J*= 1.6 Hz, 1H), 8.04 (d, *J*= 8.5 Hz, 1H), 7.86 (d, *J*= 8.5 Hz, 1H), 4.65 (br s, 1H), 4.21-4.33 (m, 3H), 4.12 (br s, 2H), 3.09 (s, 3H), 2.22-2.34 (m, 2H), 1.94-2.13 (m, 4H), 1.79-1.92 (m, 2H).
279	LC-MS *m/z* 444.4 $[M+H]^+$, RT 0.87 min.; ^{1}H NMR (DMSO-d_6) δ: 9.57-9.70 (m, 2H), 8.97 (br d, *J*= 11.0 Hz, 1H), 8.79 (s, 1H), 8.08 (d, *J*= 0.6 Hz, 1H), 8.03 (d, *J*= 8.5 Hz, 1H), 7.92 (d, *J*= 8.5 Hz, 1H), 5.33 (br s, 1H), 3.75 (br s, 2H), 3.09 (s, 3H), 2.39-2.48 (m, 5H), 1.72-2.13 (m, 8H).
280	LC-MS *m/z* 437.5 $[M+H]^+$, RT 0.76 min.; ^{1}H NMR (DMSO-d_6) δ: 9.87 (br d, *J*= 10.1 Hz, 1H), 9.48 (d, *J*= 0.9 Hz, 1H), 9.11 (br d, *J*= 10.7 Hz, 1H), 8.49 (br d, *J*= 12.0 Hz, 1H), 8.23 (d, *J*= 0.9 Hz, 1H), 8.05 (d, *J*= 8.5 Hz, 1H), 7.94 (d, *J*= 8.5 Hz, 1H), 5.34 (br s, 1H), 3.74 (br s, 2H), 3.11 (s, 3H), 2.51-2.58 (m, 5H), 1.72-2.18 (m, 8H).

Cpd	Data
281	LC-MS *m/z* 444.5 $[M+H]^+$, RT 0.92 min.; ^{1}H NMR (DMSO-d_6) δ: 9.26 (br d, *J*= 11.0 Hz, 1H), 8.77-8.88 (m, 2H), 8.70 (s, 1H), 8.60 (d, *J*= 1.6 Hz, 1H), 8.04 (d, *J*= 8.5 Hz, 1H), 7.86 (d, *J*= 8.5 Hz, 1H), 5.29 (br s, 1H), 4.27 (s, 3H), 3.77 (br s, 2H), 3.07 (s, 3H), 2.33-2.45 (m, 2H), 1.72-2.11 (m, 8H).
291	MS *m/z* $[M+H]^+$ 458.4; ^{1}H NMR (DMSO-d_6) δ: 9.47 (d, *J*=1.58 Hz, 1H), 8.53 (d, *J*=1.58 Hz, 1H), 7.89-8.00 (m, 2H), 7.83 (d, *J*=8.51 Hz, 1H), 4.26-4.60 (m, 1H), 3.03 (s, 3H), 2.40 (d, *J*=0.63 Hz, 3H), 1.47-1.87 (m, 8H), 1.20 (s, 6H), NH proton not observed.
292	MS *m/z* $[M+H]^+$ 451.6; ^{1}H NMR (DMSO-d_6) δ: 9.10 (d, *J*=1.58 Hz, 1H), 7.90-7.95 (m, 1H), 7.89 (dd, *J*=3.15, 0.95 Hz, 1H), 7.86 (d, *J*=8.51 Hz, 1H), 7.77 (dd, *J*=12.77, 1.42 Hz, 1H), 4.58-4.76 (m, 1H), 3.09 (s, 3H), 2.37 (d, *J*=1.00 Hz, 3H), 1.78-2.21 (m, 8H), 1.43 (br s, 6H), NH proton not observed.
293	MS *m/z* $[M+H]^+$ 458.5; ^{1}H NMR (DMSO-d_6) δ: 8.78 (d, *J*=1.00 Hz, 1H), 8.69 (s, 1H), 8.59 (d, *J*=1.58 Hz, 1H), 8.01 (d, *J*=8.51 Hz, 1H), 7.77-7.87 (m, *J*=8.51 Hz, 1H), 4.34-4.59 (m, 1H), 4.26 (s, 3H), 3.04 (s, 3H), 1.45-1.96 (m, 8H), 1.22 (br s, 6H), NH proton not observed.
294	MS *m/z* $[M+H]^+$ 451.4; ^{1}H NMR (DMSO-d_6) δ: 8.55 (d, *J*=2.52 Hz, 1H), 8.25 (s, 1H), 7.95 (d, *J*=8.51 Hz, 1H), 7.73-7.82 (m, 2H), 4.50 (br s, 1H), 4.21 (s, 3H), 3.05 (s, 3H), 1.55-2.06 (m, 8H), 1.17-1.44 (m, 6H), NH proton not observed.
295	MS *m/z* $[M+H]^+$ 437.5; ^{1}H NMR (DMSO-d_6) δ: 9.47 (br d, *J*=11.03 Hz, 1H), 8.91 (br d, *J*=11.67 Hz, 1H), 8.55 (d, *J*=2.52 Hz, 1H), 8.26 (d, *J*=0.95 Hz, 1H), 7.97 (d, *J*=8.51 Hz, 1H), 7.83 (d, *J*=8.51 Hz, 1H), 7.78 (dd, *J*=13.56, 1.26 Hz, 1H), 5.27 (br s, 1H), 4.22 (s, 3H), 3.76 (br s, 2H), 3.08 (s, 3H), 2.39-2.47 (m, 2H), 1.73-2.13 (m, 8H).

Example 30

Preparation of Compound 59



Step 1: Zinc powder (2.11 g, 32.3 mmol) was suspended in dimethylacetamide (5.2 mL) at room temperature under argon. A mixture of 1,2-dibromoethane (260 µL, 3 mmol) and TMSCl (365 µL, 8.22 mmol) was added dropwise to the zinc suspension at such a rate as to keep the internal temperature below 45 °C. Once addition was complete, the reaction mixture was stirred for another 15 min, by which time the internal temperature dropped to 30 °C. A solution of tert-butyl 4-iodopiperidine-1-carboxylate (8.25 g, 26 mmol) in DMA (13 mL) was added to this mixture at such a rate that the internal temperature did not rise above 55 °C. Upon completion of the addition, the mixture was allowed to cool to ambient temperature. The mixture was filtered under an inert argon atmosphere through glass wool to yield 20 mL of ~ 1M of (1-(tert-butoxycarbonyl)piperidin-4-yl)zinc(II) iodide in DMA.

Step 2: A mixture of 2-bromo-6-chlorothiazolo[4,5-c]pyridine (300 mg, 1.2 mmol), Pd(dppf)Cl_2-CH_2Cl_2 (50 mg, 0.06 mmol), and dioxane (2.5 mL) was stirred under argon, while 1.8 mL of the zinc iodide solution prepared in step 1 was added. The mixture was heated at 90° C for 2 h. The reaction mixture was then quenched with aqueous NH_4Cl, and the mixture was partitioned between EtOAc and H_2O. The organic layer was dried over $MgSO_4$, filtered, and then concentrated under vacuum. Purification by silica gel chromatography (20% EtOAc in CH_2Cl_2), followed by trituration with 1:4 ether/hexane, yielded tert-butyl 4-(6-chlorothiazolo[4,5-c]pyridin-2-yl)piperidine-1-carboxylate (196 mg, 46%) as an off-white solid. ^{1}H NMR showed 20 mol% of the des-bromo byproduct 6-chlorothiazolo[4,5-c]pyridine, along with the desired intermediate.

^{1}H NMR (acetone-d_6): δ: 8.98 (s, 1H), 8.19 (s, 1H), 4.20 (m, 2H), 3.46 (m, 1H), 3.0 (br s, 2H), 2.18-2.23 (m, 2H), 1.78-1.86 (m, 2H), 1.48 (s, 9H).

Step 3: Crude tert-butyl 4-(6-chlorothiazolo[4,5-c]pyridin-2-yl)piperidine-1-carboxylate (60 mg, 80% purity, 0.17 mmol), 2,7-dimethyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2*H*-indazole (60 mg, 0.22 mmol), SPhos Pd G2 (10 mg, 0.014 mmol), 2M K_2CO_3 (0.2 mL, 0.4 mmol), and dioxane (0.6 mL) were heated at 90 °C for 15 h. The mixture was then partitioned between EtOAc and H_2O. The organic layer was dried over $MgSO_4$, filtered, and then concentrated under vacuum. Purification by silica gel chromatography (20-50% acetone in CH_2Cl_2), followed by ether trituration, yielded tert-butyl 4-(6-(2,7-dimethyl-2*H*-indazol-5-yl)thiazolo[4,5-c]pyridin-2-yl)piperidine-1-carboxylate (58 mg, 73%) as a tan solid. UPLC showed 80% purity, with 20% 6-(2,7-dimethyl-2*H*-indazol-5-yl)thiazolo[4,5-c]pyridine present. MS *m/z* 464.4 $[M+H]^+$.

Step 4: Crude tert-butyl 4-(6-(2,7-dimethyl-2*H*-indazol-5-yl)thiazolo[4,5-c]pyridin-2-yl)piperidine-1-carboxylate (58 mg, 80% purity, 0.12 mmol) was heated with 4N HCl in dioxane (1.0 mL, 1 mmol) at 90 °C for 1 h. The mixture was diluted in ether and was filtered. The solids were purified by C18 preparatory HPLC. Treatment of the collected fractions with concentrated HCl, followed by concentration under vacuum, yielded the title compound (29 mg, 60%) as a pure yellow solid.

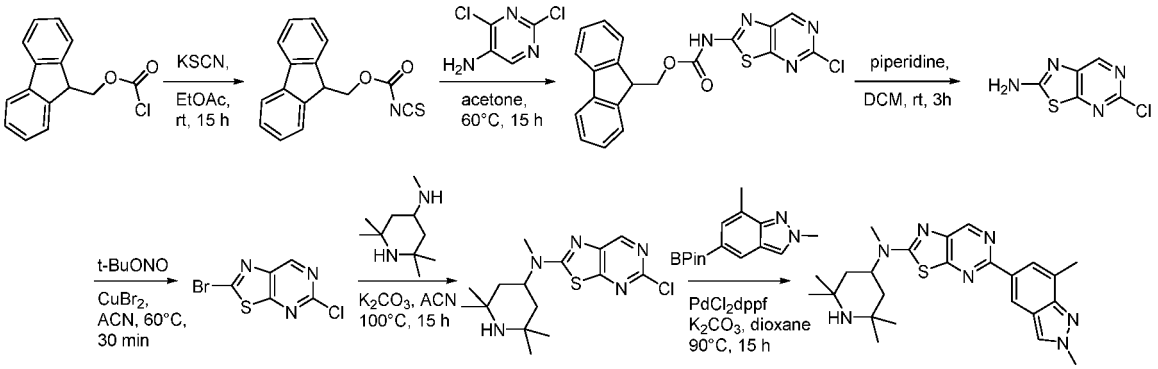
MS *m/z* 364.3 $[M+H]^+$; ^1H NMR (DMSO-d_6): δ: 9.31 (s, 1H), 8.80 (s, 1H), 8.47 (s, 1H), 8.33 (s, 1H), 7.84 (s, 1H), 4.20 (s, 3H), 3.57-3.63 (m, 1H), 3.39-3.43 (m, 2H), 3.05-3.13 (m, 2H), 2.59 (s, 3H), 2.30-2.36 (m, 2H), 2.00-2.11 (m, 2H).

Using the procedure described for Example 30, above, additional compounds described herein were prepared by substituting the appropriate starting material, suitable reagents and reaction conditions, obtaining compounds such as those selected from:

Cpd	Data
60	MS *m/z* 418.3 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 9.52 (s, 1H), 9.03 (s, 1H), 8.70 (s, 1H), 8.69 (s, 1H), 8.28 (s, 1H), 4.37 (s, 3H), 3.75-3.83 (m, 1H), 3.59-3.64 (m, 2H), 3.25-3.30 (m, 2H), 2.52-2.58 (m, 2H), 2.20-2.35 (m, 2H).
74	MS *m/z* 375.3 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.32 (s, 1H), 8.91 (d, *J*= 1.5 Hz, 1H), 8.89 (s, 1H), 8.77 (s, 1H), 8.67 (d, *J*= 1.5 Hz, 1H), 3.57- 3.64 (m, 1H), 3.40-3.45 (m, 2H), 3.05-3.12 (m, 2H), 2.30-2.35 (m, 2H), 2.03-2.08 (m, 2H).
75	MS *m/z* 378.3 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 9.51 (s, 1H), 9.08 (s, 1H), 8.55 (s, 1H), 8.29 (d, *J*= 2 Hz, 1H), 7.66 (s, 1H), 4.34 (s, 3H), 3.76 - 3.85 (m, 1H), 3.57 - 3.66 (m, 2H), 3.25 - 3.32 (m, 2H), 3.18 (q, *J*= 7.5 Hz, 2H), 2.53 - 2.60 (m, 2H), 2.23 - 2.35 (m, 2H), 1.49 (t, *J*= 7.5 Hz, 3H).
76	MS *m/z* 368.1 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.31 (s, 1H), 8.83 (s, 1H), 8.62 (d, *J*= 3 Hz, 1H), 8.38 (s, 1H), 7.85 (d, *J*= 13.5 Hz, 1H), 4.23 (s, 3H), 3.55-3.65 (m, 1H), 3.38-3.43 (m, 2H), 3.06-3.14 (m, 2H), 2.30-2.36 (m, 2H), 2.00-2.12 (m, 2H).
77	MS *m/z* 350.1 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 9.54 (s, 1H), 9.35 (s, 1H), 8.76 (s, 1H), 8.70 (dd, *J*= 9.5 Hz, 1.5 Hz, 1H), 8.10 (s, 1H), 7.98 (d, *J*= 9.5 Hz, 1H), 3.64-3.73 (m, 1H), 3.57-3.62 (m, 2H), 3.23-3.32 (m, 2H), 2.62 (s, 3H), 2.46-2.55 (m, 2H), 2.18-2.30 (m, 2H).
109	MS *m/z* 376.1 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 9.34 (s, 1H), 9.23 (d, *J*= 1.5 Hz, 1H), 8.91 (d, *J*= 1.5 Hz, 1H), 8.62 (s, 1H), 4.33 (s, 3H), 3.63-3.72 (m, 1H), 3.60 (dt, *J*= 13 Hz, 3.5 Hz, 2H), 3.28 (td, *J*= 12.5 Hz, 3 Hz, 2H), 2.48-2.55 (m, 2H), 2.29-2.40 (m, 2H).
110	MS *m/z* 365.1 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 9.40 (s, 1H), 8.97 (s, 1H), 8.86 (s, 1H), 8.62 (m, 1H), 4.43 (s, 3H), 3.65-3.72 (m, 1H), 3.60 (dt, *J*= 13 Hz, 3.5 Hz, 2H), 3.28 (td, *J*= 12.5 Hz, 3 Hz, 2H), 2.73 (s, 3H), 2.48-2.55 (m, 2H), 2.29-2.40 (m, 2H).

Example 31

Preparation of Compound 122



Step 1: (9*H*-Fluoren-9-yl)methyl carbonochloridate (2.0 g, 7.77 mmol), potassium thiocyanate (826 mg, 8.51 mmol) and EtOAc (15 mL) were stirred under argon at room temperature for 15 h. The reaction mixture was then flushed through silica with EtOAc to remove inorganics. The filtrate was then concentrated under vacuum. Purification by silica gel chromatography (1:1 hexanes/CH_2Cl_2), yielded *O*-((9*H*-fluoren-9-yl)methyl) carbonisothiocyanatidate (1.71 g, 78%) as a white solid.

^{1}H NMR ($CDCl_3$): δ: 7.81 (d, *J*= 7.5 Hz, 2H), 7.62 (d, *J*= 7.5 Hz, 2H), 7.47 (t, *J*= 7.5 Hz, 2H), 7.37 (t, *J*= 7.5 Hz, 2H), 4.50 (d, *J*= 7.5 Hz, 2H), 4.30 (t, *J*= 7.5 Hz, 1H).

Step 2: *O*-((9*H*-Fluoren-9-yl)methyl) carbonisothiocyanatidate (562 mg, 2 mmol), 2,4-dichloropyrimidin-5-amine (328 mg, 2 mmol) and acetone (5 mL) were heated at 60 °C for 15 h. The reaction mixture was filtered and the solids were washed with acetone to yield (9*H*-fluoren-9-yl)methyl (5-chlorothiazolo[5,4-d]pyrimidin-2-yl)carbamate (716 mg, 88%) as a yellow solid.

^{1}H NMR (DMSO-d_6): δ: 12.9 (s,1H), 9.07 (s, 1H), 7.93 (d, *J*= 7.5 Hz, 2H), 7.81 (d, *J*= 7.5 Hz, 2H), 7.45 (t, *J*= 7.5 Hz, 2H), 7.37 (t, *J*= 7.5 Hz, 2H), 4.62 (d, *J*= 7 Hz, 2H), 4.38 (t, *J*= 7 Hz, 1H).

Step 3: (9*H*-Fluoren-9-yl)methyl (5-chlorothiazolo[5,4-d]pyrimidin-2-yl)carbamate (650 m, 1.56 mmol) was stirred in CH_2Cl_2 (25 mL) and piperidine (2.5 mL, 25 mmol) at room temperature for 3 h. After this time, the precipitated solid was filtered and was washed with CH_2Cl_2 to yield 5-chlorothiazolo[5,4-d]pyrimidin-2-amine (211 mg, 72%) as an off-white solid.

^{1}H NMR (DMSO-d_6): δ: 8.55 (s, 1H), 8.30 (br s, 2H).

Step 4: 5-Chlorothiazolo[5,4-d]pyrimidin-2-amine (180 mg, 0.96 mmol), acetonitrile (6.6 mL), t-butyl nitrite (0.25 mL, 2.1 mmol), and $CuBr_2$ (252 mg, 1.14 mmol) were heated at 60 °C for 30 min. The reaction mixture was partitioned between EtOAc and H_2O. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. Purification by silica gel chromatography (0-2% EtOAc in CH_2Cl_2) yielded 2-bromo-5-chlorothiazolo[5,4-d]pyrimidine (211 mg, 87%) as a white solid.

^{1}H NMR (acetone-d_6): δ: 9.29 (s, 1H).

Step 5: 2-Bromo-5-chlorothiazolo[5,4-d]pyrimidine (180 mg, 0.72 mmol), N,2,2,6,6-pentamethylpiperidin-4-amine (204 mg, 0.84 mmol), K_2CO_3 (490 mg, 3.54 mmol), and acetonitrile (3 mL) were heated at 100 °C for 15 h. The reaction mixture was diluted with ether and was filtered. The filtrate was concentrated under vacuum, re-dissolved in ether and was then filtered to remove orange particulate matter. The filtrate was concentrated under vacuum. Hexane trituration yielded 5-chloro-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)thiazolo[5,4-d]pyrimidin-2-amine (193 mg, 79%) as a white solid.

^{1}H NMR (acetone-d_6): δ: 8.55 (s, 1H), 4.40-4.70 (br s, 1H), 3.18 (s, 3H), 1.75 (dd, *J*= 12.5 Hz, 3.5 Hz, 2H), 1.58 (t, *J*= 12.5 Hz, 2H), 1.31 (s, 6H), 1.16 (s, 6H).

Step 6: 5-Chloro-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)thiazolo[5,4-d]pyrimidin-2-amine (40 mg, 0.12 mmol), 2,7-dimethyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2*H*-indazole (44 mg, 0.16 mmol), $Pd(dppf)Cl_2$-CH_2Cl_2 (10 mg, 0.012 mmol), dioxane (0.45 mL), and 2M K_2CO_3 (0.15 mL, 0.3 mmol) were heated at 90 °C for 15 h. The reaction mixture was partitioned between H_2O and EtOAc. The organic layer was dried over $MgSO_4$, filtered, and then concentrated under vacuum. Purification by silica gel chromatography (20% MeOH in CH_2Cl_2, followed by 9/1/0.1 H_2Cl_2/MeOH/NH_4OH), followed by ether trituration yielded the title product (34 mg, 64%) as a white solid.

MS *m/z* 450.5 $[M+H]^+$; ^{1}H NMR (DMSO-d_6): δ: 8.82 (s, 1H), 8.58 (s, 1H), 8.45 (s, 1H), 8.06 (s, 1H), 4.30-4.70 (br s, 1H), 4.20 (s, 3H), 3.10 (s, 3H), 2.58 (s, 3H), 1.45-1.75 (m, 4H), 1.29 (br s, 6H), 1.17 (br s, 6H).

Using the procedure described for Example 31, above, additional compounds described herein were prepared by substituting the indicated intermediate in Step 5, if any, the appropriate

starting material, the suitable reagents and reaction conditions, obtaining compounds such as those selected from:

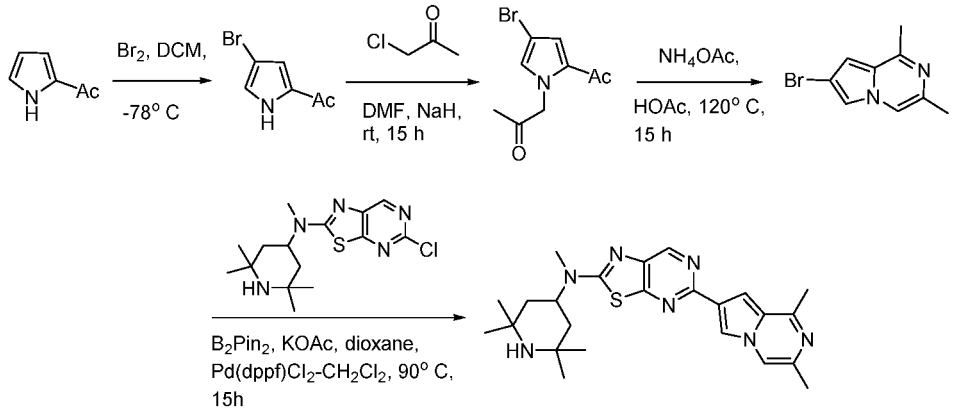
Cpd	Intermediate and Data
123	MS *m/z* 461.3 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.09 (d, *J*= 1.5 Hz, 1H), 8.86 (s, 1H), 8.76 (s, 1H), 8.75 (d, *J*= 1.5 Hz, 1H), 4.3-4.7 (br s, 1H),4.28 (s, 3H), 3.11 (s, 3H), 1.4-1.8 (m, 4H), 1.28 (br s, 6H), 1.15 (br s, 6H).
124	MS *m/z* 454.2 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.83 (s, 1H), 8.62 (d, *J*= 3 Hz, 1H), 8.60 (d, *J*= 1 Hz, 1H), 7.94 (dd, *J*= 8.5 Hz, 1Hz, 1H), 4.3-4.7 (br s, 1H), 4.20 (s, 3H), 3.10 (s, 3H), 1.65 (m, 2H), 1.47-1.53 (m, 2H), 1.25 (br s, 6H), 1.11 (br s, 6H).
142	MS *m/z* 464.3 $[M+H]^+$; ^1H NMR (methanol-d_4,) δ: 8.81 (s, 1H), 8.57-8.65 (m, 2H), 8.44-8.54 (m, 1H), 7.36 (s, 2H), 4.98-5.17 (m, 1H), 3.26 (s, 3H), 2.05-2.17 (m, 4H), 1.67 (s, 6H), 1.58 ppm (s, 6H).
170	MS *m/z* 461.4 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.69 (d, *J*= 1.5 Hz, 1H), 8.83 (s, 1H), 8.57 (d, *J*= 1.5 Hz, 1H), 8.03 (s, 1H), 4.1-4.7 (br s, 1H), 3.09 (s, 3H), 2.41 (s, 3H), 1.63-1.67 (m, 2H), 1.45-1.55 (m, 2H), 1.25 (br s, 6H), 1.11 (br s, 6H).
171	MS *m/z* 454.2 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.33 (d, *J*= 1.5 Hz, 1H), 8.84 (s, 1H), 7.98 (d, *J*= 2.5 Hz, 1H), 7.82 (dd, *J*= 12 Hz, 1.5 Hz, 1H), 4.3-4.7 (br s, 1H), 3.1 (s, 3H), 2.38 (s, 3H), 1.63-1.67 (m, 2H), 1.45-1.55 (m, 2H), 1.25 (br s, 6H), 1.11 (br s, 6H).
183	MS *m/z* 450.2 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.28 (s, 1H), 8.83 (s, 1H), 7.91 (s, 1H), 7.83 (s, 1H), 4.3-4.7 (br s, 1H), 3.10 (s, 3H), 2.53 (s, 3H), 2.40 (s, 3H), 1.0-1.8 (m, 16 H).
184	MS *m/z* 451.2 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.91 (s, 1H), 8.12 (s, 1H), 7.97 (s, 1H), 4.4-4.9 (br s, 1H), 3.13 (s, 3H), 2.64 (s, 3H), 2.43 (s, 3H), 1.0-1.8 (m, 16H).
193	MS *m/z* 405.2 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.09 (d, *J*= 1.5 Hz, 1H), 8.87-8.95 (m, 2H), 8.86 (s, 1H), 8.77 (s, 1H), 8.75 (d, *J*= 2 Hz, 1H), 4.51 (br s, 1H), 4.28 (s, 3H), 3.38-3.42 (m, 2H), 3.08-3.17 (m, 5H), 2.10-2.20 (m, 2H), 1.95-1.99 (m, 2H).
196	MS *m/z* 405.4 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.76 (d, *J*= 1.5 Hz, 1H), 8.88-9.02 (m, 2H), 8.87 (s, 1H), 8.69(d, *J*=1.5 Hz, 1H), 8.11 (1H), 4.51 (br s, 1H), 3.39-3.43 (m, 2H), 3.10-3.18 (m, 5H), 3.27 (s, 3H), 2.14-2.21 (m, 2H), 1.94-1.98 (m, 2H).
197	MS *m/z* 466.3 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.84 (s, 1H), 8.43 (s, 1H), 8.35 (d, *J*= 1.5 Hz, 1H), 7.63 (d, *J*= 1.5 Hz, 1H), 4.3-4.7 (br s, 1H), 4.17 (s, 3H), 4.00 (s, 3H), 3.11 (s, 3H), 1.0-1.8 (m, 16H).
207	Intermediate 3 MS *m/z* 431.2 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.81 (d, *J*= 1.5 Hz, 1H), 9.62 (m, 1H), 9.08, (m, 1H), 8.92 (s, 1H), 8.76 (s, 1H), 8.14 (s, 1H), 4.68 (br s, 1H), 4.13 (br s, 2H), 3.16 (s, 3H), 2.46 (s, 3H), 2.31-2.39 (m, 2H), 1.80-2.15 (m, 6H).

Cpd	Intermediate and Data
208	Intermediate 3 MS *m/z* 431.2 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.40 (m, 1H), 9.10 (d, *J*= 1.5 Hz, 1H), 8.96 (m, 1H), 8.78 (s, 1H), 8.75 (d, *J*= 1.5 Hz, 1H), 4.70 (br s, 1H), 4.33 (s, 3H), 4.13 (br s, 2H), 3.17 (s, 3H), 2.30-2.36 (m, 2H), 1.95-2.14 (m, 4H), 1.83-1.92 (m, 2H).
217	Intermediate 3 MS *m/z* 424.4 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 9.59 (s, 1H), 8.88 (s, 1H), 8.71 (d, *J*= 11 Hz, 1H), 8.21 (s, 1H), 5.01 (br s, 1H), 4.25 (br s, 2H), 3.22 (s, 3H), 2.63 (s, 3H), 2.32-2.39 (m, 2H), 2.20-2.28 (m, 4H), 2.07-2.11 (m, 2H).
218	Intermediate 3 MS *m/z* 424.4 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.86 (s, 1H), 8.61 (d, *J*= 1.5 Hz, 1H), 8.59 (d, *J*= 2.5 Hz, 1H), 7.94 (dd, *J*= 13 Hz, 1 Hz, 1H), 4.97 (br s, 1H), 4.32 (s, 3H), 4.26 (br s, 2H), 3.19 (s, 3H), 2.32-2.41(m, 2H), 2.20-2.28 (m, 4H), 2.07-2.11 (m, 2H).
227	Intermediate 1 MS *m/z* 424.3$[M+H]^+$; ^1H NMR (methanol-d_4) δ: 9.59 (s, 1H), 8.90 (s, 1H), 8.71 (d, *J*= 11.5 Hz, 1H), 8.21 (s, 1H), 4.39 (s, 1H), 3.49 (d, *J*= 13 Hz, 2H), 3.40 (dd, *J*= 13 Hz, 3 Hz, 2H), 3.30 (s, 3H), 3.01 (br s, 2H), 2.63 (s, 3H), 2.16-2.22 (m, 2H), 1.94-2.04 (m, 2H).
228	Intermediate 1 MS *m/z* 431.3 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 9.96 (d, *J*= 1.5 Hz, 1H), 9.37 (d, *J*= 1.5 Hz, 1H), 8.92 (s, 1H), 8.27 (d, *J*= 1 Hz, 1H), 4.41 (s, 1H), 3.47-3.52 (m, 2H), 3.38-3.43 (m, 2H), 3.32 (s, 3H), 3.02 (br s, 2H), 2.65 (s, 3H), 2.18-2.24 (m, 2H), 1.95-2.03 (m, 2H).
242	Intermediate 2 MS *m/z* 475.5 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 9.56 (d, *J*= 1.5 Hz, 1H), 8.72 (s, 1H), 8.69 (d, *J*= 1.5 Hz, 1H), 7.87 (s, 1H), 4.5-4.7 (br s, 1H), 3.66 (q, *J*= 7 Hz, 2H), 2.49 (s, 3H), 1.93-1.98 (m, 2H), 1.75-1.85 (m, 2H), 1.47 (s, 6H), 1.25-1.40 (m, 9H).
243	Intermediate 2 MS *m/z* 468.4 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 9.20 (d, *J*= 1.5 Hz, 1H), 8.73 (s, 1H), 7.97 (dd, *J*= 12 Hz, 1.5 Hz, 1H), 7.81 (d, *J*= 2 Hz, 1H), 4.5-4.7 (br s, 1H), 3.66 (q, *J*= 7 Hz, 2H), 2.46 (s, 3H), 1.89-1.93 (m, 2H), 1.69-1.79 (m, 2H), 1.38 (s, 6H), 1.36 (t, *J*= 7 Hz, 3H), 1.31 (s, 6H).
254	MS *m/z* 460.4 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.07 (d, *J*= 1.5 Hz, 1H), 8.84 (s, 1H), 8.75 (s, 1H), 8.74 (d, *J*= 1.5 Hz, 1H), 4.3-4.6 (br s, 1H), 4.27 (s, 3H), 3.07 (s, 3H), 1.74-1.77 (m, 2H), 1.50-1.66 (m, 6H), 1.18 (s, 6H).
255	MS *m/z* 459.6 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 9.48 (d, *J*= 1.5 Hz, 1H), 8.66 (s, 1H), 8.61 (d, *J*= 1.5 Hz, 1H), 7.84 (d, *J*= 1 Hz, 1H), 4.5-4.7 (br s, 1H), 3.12 (s, 3H), 2.48 (s, 3H), 1.95-2.00 (m, 2H), 1.70-1.81 (m, 6H), 1.33 (s, 6H).

Cpd	Intermediate and Data
256	Intermediate 3 MS *m/z* 445.1 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 9.95 (d, *J*= 1.5 Hz, 1H), 9.37 (d, *J*= 1.5 Hz, 1H), 8.90 (s, 1H), 8.26 (s, 1H), 5.63 (s, 1H), 3.91 (br s, 2H), 3.25 (s, 3H), 2.65 (s, 3H), 2.45-2.52 (m, 2H), 2.05-2.25 (m, 7H), 1.97 (m, 1H).
257	MS *m/z* 438.0 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 9.59 (s, 1H), 8.88 (s, 1H), 8.71 (d, *J*= 11 Hz, 1H), 8.21 (s, 1H), 5.64 (br s, 1H), 3.91 (br s, 2H), 3.21 (s, 3H), 2.63 (s, 3H), 2.45-2.53 (m, 2H), 2.05-2.25 (m, 7H), 1.97 (m, 1H).
275	MS *m/z* 462.5 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.87 (s, 1H), 8.80 (d, *J*= 1.5 Hz, 1H), 8.70 (d, *J*= 1.5 Hz, 1H), 4.2-4.7 (br s, 1H), 3.11 (s, 3H), 2.75 (s, 3H), 1.64-1.68 (m, 2H), 1.47-1.54 (m, 2H), 1.26 (s, 6H), 1.12 (s, 6H).
284	MS *m/z* 452.4 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 9.18 (d, *J*= 1 Hz, 1H), 8.71 (s, 1H), 7.94 (dd, *J*= 12, 1 Hz, 1H), 7.80 (d, *J*= 1 Hz, 1H), 4.55-4.75 (br s, 1H), 3.14 (s, 3H), 2.46 (s, 3H), 2.02 (m, 2H), 1.75-1.85 (m, 6H), 1.37 (s, 6H), NH proton not observed.
289	MS *m/z* 452.3 $[M+H]^+$. ^1H NMR (methanol-d_4) δ: 8.73 (s,1H), 8.59 (d, *J*= 1.5 Hz, 1H), 8.43 (d, *J*= 3 Hz, 1H), 8.02 (dd, *J*= 13, 1.5 Hz, 1H), 4.55-4.75 (br s, 1H), 4.27 (s, 3H), 3.14 (s, 3H), 2.05 (m, 2H), 1.79-1.87 (m, 6H), 1.38 (s, 6H), NH proton not observed.
290	MS *m/z* 460.2 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.88 (s,1H), 8.81 (d, *J*= 1.5 Hz, 1H), 8.70 (d, *J*= 1.5 Hz, 1H), 4.3-4.7 (br s, 1H), 3.09 (s, 3H), 2.76 (s, 3H), 1.91 (br s, 2H), 1.53-1.70 (m, 6H), 1.22 (s, 6H), NH proton not observed.
303	Intermediate 3a MS *m/z* 487.2 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 9.52 (d, *J*= 1.5 Hz, 1H), 8.69 (s, 1H), 8.64 (d, *J*= 2 Hz, 1H), 7.86 (s, 1H), 4.5-4.7 (br s, 1H), 3.15 (s, 3H), 2.49 (s, 3H), 1.8-2.1 (m, 4H), 1.6-1.8 (m, 8H), 1.02 (t, *J*= 7.5 Hz, 6H), NH proton not observed.
304	Intermediate 3a MS *m/z* 480.3 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 9.21 (d, *J*= 1.5 Hz, 1H), 8.75 (s, 1H), 7.97 (dd, *J*= 12, 1.5 Hz, 1H), 7.82 (s, 1H), 3.19 (s, 3H), 2.46 (s, 3H), 2.12 (m, 2H), 1.99 (m, 2H), 1.7-1.9 (m, 8H), 1.04 (t, *J*= 7.5 Hz, 6H), CH methyne proton (broad) and NH proton not observed.
324	Intermediate 7 MS *m/z* 479.6 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 9.98 (s, 1H), 9.38 (s, 1H), 8.92 (s, 1H), 8.27 (s, 1H), 5.47 (dd, *J*=32.7, 12.8 Hz, 1H), 5.03 (d, *J*=48.5 Hz, 1H), 3.34 (s, 3H), 2.66 (s, 3H), 2.47 (t, *J*=13.7 Hz, 1H), 2.09 (d, *J*=13.1 Hz, 1H), 1.74 (s, 3H), 1.74 (s, 3H), 1.64 (s, 3H), 1.59 (d, *J*=1.8 Hz, 3H), NH proton not observed.

Example 32

Preparation of Compound 265



Step 1: 1-(1*H*-pyrrol-2-yl)ethan-1-one (1.09 g, 10 mmol) was dissolved in CH_2Cl_2 (50 mL) at -78 °C. A solution of Br_2 (0.62 mL, 12.1 mmol) in CH_2Cl_2 (12 mL) was added by syringe. After the addition was complete, the mixture was poured onto ice. The bilayer was separated, and then the organic layer was washed with aqueous 1N NaOH to remove the dibrominated byproduct. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum to yield 1-(4-bromo-1*H*-pyrrol-2-yl)ethan-1-one (1.42 g, 76%) as a grayish solid.

^{1}H NMR (acetone-d_6) δ: 11.08 (br s, 1H), 7.19 (t, *J*= 1.5 Hz, 1H), 7.02 (t, *J*= 1.5 Hz, 1H), 2.36 (s, 3H).

Step 2: 1-(4-Bromo-1*H*-pyrrol-2-yl)ethan-1-one (1.36 g, 7.23 mmol) was dissolved in DMF (15 mL) at 0 °C. NaH (60%, 316 mg, 7.9 mmol) was added. The reaction mixture was then stirred at room temperature for 30 minutes. Chloroacetone (0.6 mL, 7 mmol) was then added dropwise. The mixture was stirred at room temperature for 15 h then partitioned between EtOAc and H_2O. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. Purification by silica gel chromatography (30% EtOAc in hexanes) yielded 1-(2-acetyl-4-bromo-1*H*-pyrrol-1-yl)propan-2-one (1.2 g, 68%) as a white solid.

^{1}H NMR (acetone-d_6) δ: 7.13 (d, *J*= 2Hz, 1H), 7.10 (d, *J*= 2Hz, 1H), 5.17 (s, 2H), 2.36 (s, 3H), 2.18 (s, 3H).

Step 3: 1-(2-Acetyl-4-bromo-1*H*-pyrrol-1-yl)propan-2-one (1.15 g, 4.71 mmol), NH_4OAc (7.2 g, 93 mmol), and HOAc (40 mL) were heated at 120 °C for 15 h. The solvent was then removed under vacuum and the concentrate was treated with aqueous NaOH, and then extracted into EtOAc. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum.

Purification by silica gel chromatography (10-50% EtOAc in CH_2Cl_2) yielded 7-bromo-1,3-dimethylpyrrolo[1,2-a]pyrazine (975 mg, 92%) as a light tan solid.

^{1}H NMR (acetone-d_6) δ: 7.86 (s, 1H), 7.63 (d, J= 1.5 Hz, 1H), 6.84 (t, J= 1 Hz, 1H), 2.56 (s, 3H), 2.31 (s, 3H).

Step 4: 7-Bromo-1,3-dimethylpyrrolo[1,2-a]pyrazine (32 mg, 0.14 mmol), KOAc (46 mg, 0.47 mmol), bis(pinacolato)diboron (46 mg, 0.18 mmol), Pd(dppf)Cl_2-CH_2Cl_2 (8 mg, 0.016 mmol), and dioxane (0.6 mL) were heated at 90 °C for 1 h, then cooled. 5-Chloro-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)thiazolo[5,4-d]pyrimidin-2-amine (40 mg, 0.12 mmol, prepared as in Example 32, Pd(dppf)Cl_2-CH_2Cl_2 (8 mg, 0.016 mmol), and 2M K_2CO_3 (0.2 mL, 0.4 mmol) were added. The mixture was heated at 90 °C for 15 h. The mixture was partitioned between CH_2Cl_2 and H_2O. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. Purification by silica gel chromatography (5% MeOH in CH_2Cl_2, followed by 9/1/0.1 CH_2Cl_2 / MeOH / NH_4OH), followed by ether trituration, yielded the title compound (16 mg, 30%) as a white solid.

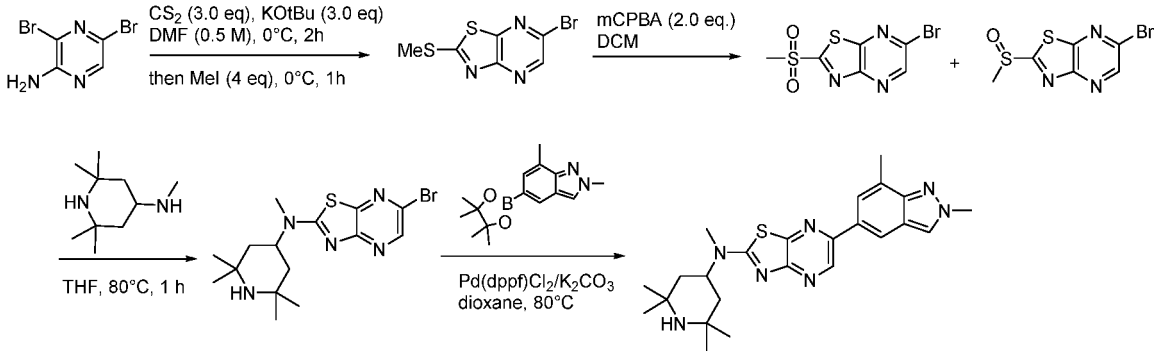
MS *m/z* 450.5 $[M+H]^+$; ^{1}H NMR (methanol-d_4) δ: 8.68 (s, 1H), 8.15 (d, J= 1.5 Hz, 1H), 7.88 (s, 1H), 7.47 (s, 1H), 4.2-4.4 (br s, 1H), 3.19 (s, 3H), 2.67 (s, 3H), 2.36 (s, 3H), 1.87-1.93 (m, 2H), 1.68-1.78 (m, 2H), 1.47 (br s, 6H), 1.35 (s, 6H).

Using the procedure described for Example 32, above, additional compounds described herein were prepared by substituting the appropriate starting material, suitable reagents and reaction conditions, obtaining compounds such as those selected from:

Cpd	Data
323	MS *m/z* 448.5 $[M+H]^+$; ^{1}H NMR (methanol-d$_4$) δ: 8.67 (s, 1H), 8.15 (s, 1H), 7.87 (s, 1H), 7.46 (s, 1H), 4.55-4.75 (br s, 1H), 3.14 (s, 3H), 2.67 (s, 3H), 2.36 (s, 3H), 2.02 (m, 2H), 1.75-1.85 (m, 6H), 1.37 (s, 6H), NH proton not observed.

Example 33

Preparation of Compound 131



Step 1: 3,5-Dibromopyrazin-2-amine (1.0 g, 4 mmol) was dissolved in DMF (8.0 mL) and CS_2 (0.5 mL, 8 mmol, 2 eq.) was added. The solution was cooled and stirred at 0 °C and to the cold solution was added t-BuOK (1M solution, 8 mL, 2 eq) in THF. The resulting solution was stirred for 1 h at 0 °C and added additional CS_2 (0.25 mL, 4 mmole, 1 eq) and tBuOK (4 mL, 1 eq) in THF. The solution was stirred for an additional hour and the disappearance of SM was observed by UPLC. MeI (1 mL, 4 eq) was added and the reaction was stirred for 1 h. The reaction was then quenched with ice-cold water. The resulting precipitate was filtered, washed with hexanes and dried to give 6-bromo-2-(methylthio)thiazolo[4,5-b]pyrazine (0.84 g, 81%). MS *m/z* 262.1, 264.1 $[M+H]^+$.

Step 2: 6-Bromo-2-(methylthio)thiazolo[4,5-b]pyrazine (0.5 g, 1.9 mmol) was dissolved in CH_2Cl_2 and the solution was cooled to 0 °C. To the solution was added mCPBA (0.95 g, 3.8 mmol, 70% purity, 2 eq.). The solution was then stirred at 0 °C for 1 h and then slowly warmed to room temperature. The reaction was then quenched with $NaHCO_3$ and the mixture was extracted with CH_2Cl_2. The organic layer was dried and evaporated to give a mixture of 6-bromo-2-(methylsulfonyl)thiazolo[4,5-]pyrazine and 6-bromo-2-(methylsulfinyl)thiazolo[4,5-b]pyrazine (600 mg), which was utilized in the next step without any further purification.

Step 3: The mixture of 6-bromo-2-(methylsulfonyl)thiazolo[4,5-]pyrazine and 6-bromo-2-(methylsulfinyl)thiazolo[4,5-b]pyrazine prepared above (0.375 g, 1.28 mmol) was dissolved in THF (4 mL). To the solution was added *N*-2,2,6,6-pentamethylpiperidin-4-amine (0.45 mL, 2.56 mmol) and the mixture was heated at 80 °C for 1 h. The reaction was complete and the mixture was purified on silica gel, eluting with 0-30% MeOH in dichloromethane to give 6-bromo-*N*-

methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)thiazolo[4,5-b]pyrazin-2-amine (0.34 g, 70%). MS *m/z* 384.1, 386.1 $[M+H]^+$.

Step 4: 6-Bromo-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)thiazolo[4,5-b]pyrazin-2-amine was combined with 2,7-dimethyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indazole (50 mg, 0.13 mmol), [1,1′-bis(diphenylphosphino) ferrocene]dichloropalladium(II) dichloromethane complex (10 mg, 0.013 mmol), 1,4-dioxane (2 mL) and aqueous 1 M K_2CO_3 (0.4 mL). The mixture was heated at 80 °C for 8 h under an Ar atmosphere, then cooled and partitioned between EtOAc and H_2O. The organic layer was washed with brine, dried over Na_2SO_4, filtered and then concentrated. The residue was chromatographed on silica gel, eluting with 10-100% EtOAc in hexanes to afford 6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)thiazolo[4,5-b]pyrazin-2-amine (35 mg, 60%).

MS *m/z* 450.4 $[M+H]^+$; ^1H NMR (methanol-*d*4, 500MHz): δ: 8.86 (s, 1H), 8.30 (s, 1H), 8.22 (d, *J*= 0.6 Hz, 1H), 7.80 (s, 1H), 5.04-5.15 (m, 1H), 4.27 (s, 3H), 3.23 (s, 3H), 2.66 (s, 3H), 2.01-2.16 (m, 4H), 1.67 (s, 6H), 1.56 ppm (s, 6H).

Using the procedure described for Example 33, above, additional compounds described herein were prepared by substituting the appropriate starting material, suitable reagents and reaction conditions, obtaining compounds such as those selected from:

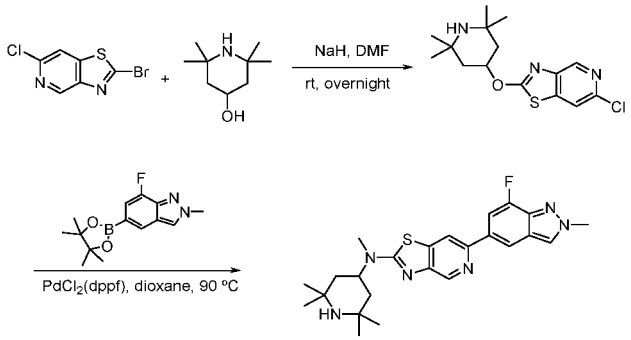
Cpd	Data
130	MS *m/z* 464.2 $[M+H]^+$; ^1H NMR (methanol-*d*4): δ: 9.09 (s, 1H), 8.36 (br s, 2H), 8.02 (d, *J*= 8.2 Hz, 1H), 7.28 (dd, *J*= 8.2, 1.9 Hz, 1H), 7.25 (d, *J*= 1.6 Hz, 1H), 4.99-5.19 (m, 1H), 3.24 (s, 3H), 2.00-2.15 (m, 4H), 1.65 (s, 6H), 1.55 (s, 6H).
140	MS *m/z* 461.2 $[M+H]^+$; ^1H NMR (methanol-*d*4, 500MHz) δ: 8.84 (s, 1H), 8.67 (d, *J*= 1.6 Hz, 1H), 8.45-8.53 (m, 2H), 4.89-4.97 (m, 1H), 4.29 (s, 3H), 3.19 (s, 3H), 1.72-1.93 (m, 4H), 1.45 (br s, 6H), 1.34 (br s, 6H).
141	MS *m/z* 437.2 $[M+H]^+$; ^1H NMR (methanol-*d*4, 500MHz): δ: 9.25 (s, 1H), 8.12 (d, *J*= 9.8 Hz, 1H), 7.94-8.02 (m, 2H), 5.10-5.37 (m, 1H), 3.23 (s, 3H), 2.50 (s, 3H), 2.06 (d, *J*= 7.3 Hz, 4H), 1.63 (s, 6H), 1.52 (s, 6H).
150	MS *m/z* 454.3 $[M+H]^+$; ^1H NMR (methanol-*d*4) δ: 8.87 (s, 1H), 8.40 (d, *J*= 2.8 Hz, 1H), 8.22 (d, *J*= 1.3 Hz, 1H), 7.75 (dd, *J*= 12.9, 1.3 Hz, 1H), 4.94-5.29 (m, 1H), 4.26 (s, 3H), 3.21 (s, 3H), 2.07 (d, *J*= 3.5 Hz, 4H), 1.64 (s, 6H), 1.52 (s, 6H).
161	MS *m/z* 484.3 $[M+H]^+$; ^1H NMR (methanol-*d*4) δ: 8.80 (d, *J*= 1.3 Hz, 1H), 8.34 (s, 2H), 7.87 (dd, *J*= 8.5, 1.6 Hz, 1H), 7.68 (dd, *J*= 8.2, 1.6 Hz, 1H), 5.01-5.29 (m, 1H), 3.25 (s, 3H), 2.11 (m, 4H), 1.66 (s, 6H), 1.56 (s, 6H).

Cpd	Data
162	MS *m/z* 451.2 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 9.24 (s, 1H), 7.95 (dd, *J*= 2.7, 1.1 Hz, 2H), 5.01-5.41 (m, 1H), 3.23 (s, 3H), 2.68 (d, *J*= 0.9 Hz, 3H), 2.50 (s, 3H), 2.02-2.11 (m, 4H), 1.65 (s, 6H), 1.53 (s, 6H).
163	MS *m/z* 461.4 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.55 (d, *J*= 1.6 Hz, 1H), 9.02 (s, 1H), 8.61 (d, *J*= 1.6 Hz, 1H), 7.97 (d, *J*= 0.9 Hz, 1H), 4.69-5.20 (m, 1H), 3.14 (s, 3H), 2.41 (s, 3H), 1.80-2.01 (m, 4H), 1.47 (br s, 12H).
173	MS *m/z* 377.1 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 9.39 (d, *J*= 1.6 Hz, 1H), 8.89 (s, 1H), 8.52 (d, *J*= 1.6 Hz, 1H), 7.87 (s, 1H), 3.95 (br s, 4H), 3.22-3.27 (m, 4H), 2.50 (s, 3H).
174	MS *m/z* 370.3 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 9.41 (d, *J*= 0.9 Hz, 1H), 9.03 (s, 1H), 8.55 (dd, *J*= 11.3, 1.3 Hz, 1H), 8.10-8.25 (m, 1H), 4.07-4.24 (m, 4H), 3.40-3.56 (m, 4H), 2.64 (d, *J*= 0.9 Hz, 3H).
180	MS *m/z* 441.4 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 9.10 (d, *J*= 8.8 Hz, 2H), 7.84 (s, 2H), 5.85-5.95 (m, 1H), 2.54-2.62 (m, 2H), 2.48 (s, 3H), 1.87-2.01 (m, 2H), 1.63 (s, 6H), 1.56 (s, 6H).
181	MS *m/z* 448.4 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 9.48 (br. s., 1H), 9.11 (s, 1H), 8.58 (s, 1H), 7.88 (s, 1H), 5.83-5.95 (m, 1H), 2.53-2.62 (m, 2H), 2.49 (s, 3H), 1.84-2.00 (m, 2H), 1.62 (s, 6H), 1.56 (s, 6H).
182	MS *m/z* 353.1 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 9.41 (s, 1H), 8.75 (d, *J*= 9.5 Hz, 1H), 8.49 (d, *J*= 9.8 Hz, 1H), 8.42 (s, 1H), 4.16 (br. s., 4H), 3.47-3.55 (m, 4H), 2.68 (d, *J*= 0.9 Hz, 3H).
274	MS *m/z* 408.4 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.95 (s, 1H), 7.93-8.06 (m, 2H), 7.89 (d, *J*= 7.9 Hz, 1H), 7.20 (d, *J*= 7.9 Hz, 1H), 7.16 (s, 1H), 3.91-4.09 (m, 1H), 3.00 (br s, 2H), 2.41 (br s, 5H), 2.18 (d, *J*= 12.3 Hz, 2H), 1.74 (d, *J*= 10.1 Hz, 2H).
282	MS m/z 408.4 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 9.07 (s, 1H), 8.18 (s, 2H), 7.73-7.77 (m, 1H), 7.35-7.39 (m, 1H), 7.29 (d, *J*= 1.3 Hz, 1H), 4.97-5.06 (m, 1H), 3.57-3.63 (m, 2H), 3.34 (s, 3H), 2.14-2.37 (m, 6H).
283	MS m/z 422.4 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.67 (s, 1H), 7.94-8.09 (m, 2H), 7.83 (d, *J*= 9.1 Hz, 1H), 7.20 (m, 2H), 4.88-4.92 (m, 1H), 3.21 (br s, 3H), 3.07-3.15 (m, 2H), 2.42 (s, 3H), 2.30-2.39 (m, 2H), 2.01-2.12 (m, 2H), 1.85-1.96 (m, 2H).
118	MS *m/z* 450.3 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.53 (s, 1H), 8.33 (s, 1H), 8.18 (s, 1H), 7.82 (d, *J*= 1.3 Hz, 1H), 5.29-5.43 (m, 1H), 4.28 (s, 3H), 3.24 (s, 3H), 2.68 (s, 3H), 2.05 (d, *J*= 3.5 Hz, 4H), 1.61 (s, 6H), 1.49 (s, 6H).
119	MS *m/z* 464.5 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 9.09 (s, 1H), 8.32 (s, 2H), 7.73-7.81 (m, 1H), 7.36-7.42 (m, 1H), 7.25-7.34 (m, 1H), 5.28-5.41 (m, 1H), 3.33 (br. s., 3H), 2.07-2.18 (m, 4H), 1.65 (s, 6H), 1.58 (s, 6H).
157	MS *m/z* 454.4 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.96 (s, 1H), 8.49 (s, 1H), 7.76-7.86 (m, 2H), 5.08-5.44 (m, 1H), 3.19-3.26 (m, 3H), 2.47 (d, *J*= 0.6 Hz, 3H), 1.79-1.90 (m, 2H), 1.62-1.74 (m, 2H), 1.41 (br s, 6H), 1.28 (br s, 6H).

Cpd	Data
158	MS *m/z* 461.4 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.68 (d, *J*= 1.6 Hz, 1H), 8.57 (s, 1H), 8.56 (s, 1H), 8.55 (d, *J*= 1.6 Hz, 1H), 5.03-5.31 (m, 1H), 4.32 (s, 3H), 3.23 (s, 3H), 2.09 (br s, 4H), 1.64 (s, 6H), 1.52 (s, 6H).
288	MS *m/z* 394.4 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 9.31 (s, 1H), 8.97 (s, 1H), 8.45 (s, 1H), 8.04 (s, 1H), 3.61 (d, *J*=15.3 Hz, 2H), 3.27 (m, 6H), 2.74 (s, 3H), 2.62 (s, 3H), 2.27 (td, *J*=13.3, 11.1 Hz, 2H), 2.17 (d, *J*=15.1 Hz, 2H) , NH proton not observed.

Example 34

Preparation of Compound 312



Step 1: To a solution of 2,2,6,6-tetramethylpiperidin-4-ol (472 mg, 3.00 mmol) in DMF (8.5 mL) was added NaH (150 mg, 3.75 mmol, 60 mass% in oil). The mixture was stirred at room temperature for 5 min followed by the addition of 2-bromo-6-chloro-thiazolo[4,5-c]pyridine (624 mg, 2.50 mmol), and then stirred at room temperature overnight. The mixture was diluted with ice water and extracted with EtOAc. The organic phase was washed with water, brine and dried over Na_2SO_4. The solvent was removed and the residue was chromatographed (MeOH in dichloromethane 0-20%) to provide 6-chloro-2-[(2,2,6,6-tetramethyl-4-piperidyl)oxy]thiazolo[4,5-c]pyridine (487 mg, 59.8%) as a white solid.

MS *m/z* 326.3, 328.2 $[M+H]^+$, RT 0.94 min; ^1H NMR ($CDCl_3$) δ: 8.67-8.72 (m, 1H), 7.61-7.65 (m, 1H), 5.58-5.68 (m, 1H), 2.20-2.44 (m, 2H), 1.08-1.82 (m, 14H), NH proton not observed.

Step 2: The procedure for Example 28 step 4 was followed to give 6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)thiazolo[4,5-c]pyridin-2-amine.

MS *m/z* $[M+H]^+$ 440.2; ^1H NMR (500 MHz, DMSO-d_6) δ: 8.94 (s, 1H), 8.63 (s, 1H), 8.60 (d, *J*=1.00 Hz, 1H), 8.30 (d, *J*=1.26 Hz, 1H), 7.81 (dd, *J*=13.56, 1.26 Hz, 1H), 5.54-5.68 (m, 1H), 4.22 (s, 3H), 2.15-2.35 (m, 2H), 1.02-1.70 (m, 14H), NH proton not observed.

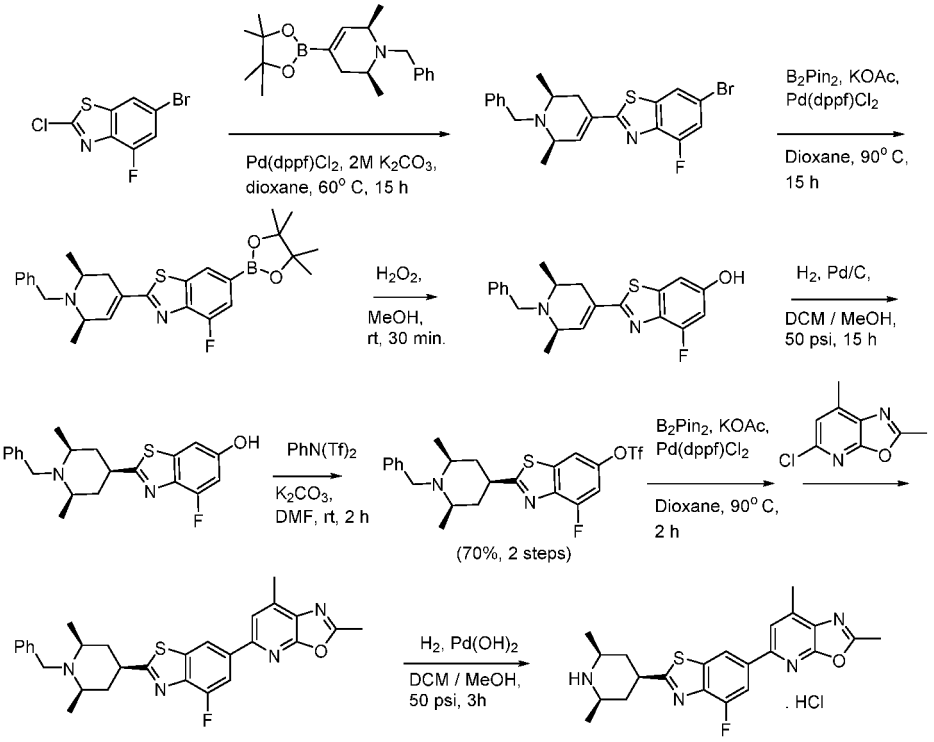
Using the procedure described for Example 34, above, additional compounds described herein were prepared by substituting the appropriate starting material, suitable reagents and reaction conditions, obtaining compounds such as those selected from:

Cpd	Data
306	MS *m/z* $[M+H]^+$ 398.4; ^{1}H NMR (DMSO-d_6) δ: 8.95 (br d, *J*=1.00 Hz, 2H), 8.57 (d, *J*=1.58 Hz, 1H), 8.32 (br s, 1H), 8.13 (br s, 1H), 8.02 (dd, *J*=11.98, 1.58 Hz, 1H), 5.44-5.57 (m, 1H), 3.08-3.39 (m, 4H), 2.69 (s, 3H), 2.24-2.34 (m, 2H), 2.52 (s, 3H), 2.03-2.16 (m, 2H).
307	MS *m/z* $[M+H]^+$ 401.3; ^{1}H NMR (DMSO-d$_6$) δ: 8.76 (br s, 2H), 8.55 (d, *J*=2.84 Hz, 1H), 8.16 (d, *J*=1.58 Hz, 1H), 7.92 (d, *J*=1.26 Hz, 1H), 7.70 (dd, *J*=12.45, 1.73 Hz, 1H), 7.47 (dd, *J*=13.24, 1.26 Hz, 1H), 5.43-5.51 (m, 1H), 4.22 (s, 3H), 3.13-3.34 (m, 4H), 2.23-2.35 (m, 2H), 2.00-2.12 (m, 2H).
309	MS *m/z* $[M+H]^+$ 447.4; ^{1}H NMR (DMSO-d_6) δ: 9.56 (d, *J*=1.89 Hz, 1H), 8.97 (d, *J*=0.63 Hz, 1H), 8.64 (s, 1H), 8.54 (d, *J*=1.58 Hz, 1H), 8.00 (d, *J*=0.95 Hz, 1H), 5.56-5.68 (m, 1H), 2.41 (s, 3H), 2.06-2.36 (m, 2H), 0.83-1.80 (m, 14H), NH proton not observed.
310	MS *m/z* $[M+H]^+$ 440.5; ^{1}H NMR (DMSO-d_6) δ: 9.15 (d, *J*=1.26 Hz, 1H), 8.96 (d, *J*=0.63 Hz, 1H), 8.58 (s, 1H), 7.91-7.96 (m, 1H), 7.76 (dd, *J*=12.77, 1.42 Hz, 1H), 5.54-5.70 (m, 1H), 2.36-2.40 (m, 3H), 2.15-2.34 (m, 2H), 1.04-1.70 (m, 14H), NH proton not observed.
311	MS *m/z* $[M+H]^+$ 447.5; ^{1}H NMR (DMSO-d_6) δ: 8.96 (d, *J*=0.63 Hz, 1H), 8.82 (d, *J*=1.00 Hz, 1H), 8.68 (s, 1H), 8.74 (s, 1H), 8.60 (d, *J*=1.58 Hz, 1H), 5.54-5.67 (m, 1H), 4.27 (s, 3H),2.14-2.34 (m, 2H), 1.02-1.70 (m, 14H), NH proton not observed.
313	MS *m/z* $[M+H]^+$ 391.3; ^{1}H NMR (DMSO-d_6) δ: 9.66 (d, *J*=1.58 Hz, 1H), 9.10 (br s, 2H), 9.02 (d, *J*=0.95 Hz, 1H), 8.68-8.75 (m, 2H), 8.10 (d, *J*=1.00 Hz, 1H), 5.43-5.53 (m, 1H), 3.09-3.36 (m, 4H), 2.45 (d, *J*=0.63 Hz, 3H), 2.24-2.35 (m, 2H), 2.04-2.19 (m, 2H).
314	MS *m/z* $[M+H]^+$ 384.3; ^{1}H NMR (DMSO-d_6) δ: 9.45 (s, 1H), 9.20 (d, *J*=1.00 Hz, 2H), 9.04 (d, *J*=0.95 Hz, 1H), 8.73 (d, *J*=1.00 Hz, 1H), 8.35 (br d, *J*=11.66 Hz, 1H), 8.22 (s, 1H), 5.43-5.52 (m, 1H), 3.09-3.34 (m, 4H), 2.50 (3H, obscured by DMSO-d$_6$ signal), 2.26-2.36 (m, 2H), 2.03-2.18 (m, 2H).
315	MS *m/z* $[M+H]^+$ 391.4; ^{1}H NMR (DMSO-d_6) δ: 9.00 (d, *J*=0.95 Hz, 1H), 8.95 (br s, 2H), 8.83 (d, *J*=1.58 Hz, 1H), 8.76 (s, 1H), 8.73 (d, *J*=0.63 Hz, 1H), 8.61 (d, *J*=1.58 Hz, 1H), 5.44-5.51 (m, 1H), 4.27 (s, 3H), 3.12-3.34 (m, 4H), 2.23-2.34 (m, 2H), 2.02-2.15 (m, 2H).
316	MS *m/z* $[M+H]^+$ 384.4; ^{1}H NMR (DMSO-d_6) δ: 9.09 (br s, 2H), 8.99 (d, *J*=0.63 Hz, 1H), 8.70 (d, *J*=0.63 Hz, 1H), 8.63 (d, *J*=2.84 Hz, 1H), 8.30 (d, *J*=1.26 Hz, 1H), 7.80 (dd, *J*=13.56, 1.26 Hz, 1H), 5.43-5.52 (m, 1H), 4.23 (s, 3H), 3.23-3.34 (m, 2H), 3.11-3.22 (m, 2H), 2.24-2.35 (m, 2H), 2.04-2.16 (m, 2H).

Cpd	Data
317	MS *m/z* $[M+H]^+$ 408.3; 1H NMR (DMSO-d_6) δ: 9.32 (s, 1H), 8.83-9.02 (m, 2H), 8.44 (s, 1H), 8.20 (d, *J*=1.2 Hz, 1H), 7.93 (s, 1H), 7.78 (dd, *J*=12.1, 1.4 Hz, 1H), 5.43-5.53 (m, 1H), 3.11-3.34 (m, 4H), 2.43 (s, 3H), 2.22-2.34 (m, 2H), 2.00-2.15 (m, 2H).
318	MS *m/z* $[M+H]^+$ 408.4; 1H NMR (DMSO-d_6) δ: 8.93 (br d, *J*=18.92 Hz, 2H), 8.70 (s, 1H), 8.46 (s, 1H), 8.30 (s, 1H), 8.21 (s, 1H), 7.77 (br d, *J*=12.21 Hz, 1H), 5.39-5.55 (m, 1H), 4.27 (s, 3H), 3.10-3.33 (m, 4H), 2.22-2.35 (m, 2H), 2.00-2.15 (m, *J*=9.20 Hz, 2H).
319	MS *m/z* $[M+H]^+$ 397.4; 1H NMR (DMSO-d_6) δ: 9.01-9.24 (m, 3H), 8.23 (s, 1H), 8.16 (s, 1H), 8.06 (s, 1H), 7.78 (br d, *J*=11.9 Hz, 1H), 5.44-5.52 (m, 1H), 3.09-3.33 (m, 4H), 2.65 (s, 3H), 2.53 (s, 3H), 2.22-2.35 (m, 2H), 2.01-2.15 (m, 2H).
320	MS *m/z* $[M+H]^+$ 412.2; ^{1}H NMR (DMSO-d_6) δ: 8.43 (d, *J*=1.22 Hz, 1H), 8.02 (s, 1H), 7.92 (dd, *J*=12.21, 1.22 Hz, 1H), 7.67 (s, 1H), 5.18-5.29 (m, 1H), 2.56-2.62 (m, 3H), 2.62-2.76 (m, 2H), 2.31-2.44 (m, 5H), 2.26 (s, 3H), 2.06-2.17 (m, 2H), 1.82-1.95 (m, 2H).
321	MS *m/z* $[M+H]^+$ 426.2; ^{1}H NMR (DMSO-d_6) δ: 8.43 (d, *J*=1.22 Hz, 1H), 8.02 (s, 1H), 7.92 (dd, *J*=12.21, 1.22 Hz, 1H), 7.67 (s, 1H), 5.18-5.29 (m, 1H), 3.31 (m, 2H, obscured by H_2O signal), 2.62-2.76 (m, 2H), 2.59 (s, 3H), 2.31-2.44 (m, 5H), 2.26 (s, 3H), 2.06-2.17 (m, 2H), 1.82-1.95 (m, 2H).

Example 35

Preparation of Compound 359



Step 1: 6-Bromo-2-chloro-4-fluorobenzo[d]thiazole (800 mg, 3.0 mmol), (2*S*,6*R*)-1-benzyl-2,6-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,2,3,6-tetrahydropyridine (1.0 g, 2.75 mmol, 90% purity), $Pd(dppf)Cl_2$-CH_2Cl_2 (100 mg, 0.12 mmol), dioxane (12 mL), and 2M aqueous K_2CO_3 (6 mL, 12 mmol) were heated at 60 °C for 15 h. After cooling, the reaction mixture was partitioned between H_2O and CH_2Cl_2. The organic layer was dried over $MgSO_4$, filtered, and then concentrated under vacuum. Purification by silica chromatography (10% EtOAc in hexanes) yielded 2-((2*S*,6*R*)-1-benzyl-2,6-dimethyl-1,2,3,6-tetrahydropyridin-4-yl)-6-bromo-4-fluorobenzo[d]thiazole (833 mg, 70%) as a white solid.

^{1}H NMR (methanol-d_4) δ: 7.97 (s, 1H), 7.40-7.47 (m, 3H), 7.30-7.35 (m, 2H), 7.20-7.26 (m, 1H), 6.69 (s, 1H), 4.00 (d, *J*= 15.5 Hz, 1H), 3.90 (d, *J*= 15.5 Hz, 1H), 3.50-3.54 (m, 1H), 3.05-3.11 (m, 1H), 2.80-2.86 (m, 1H), 2.48-2.55 (m, 1H), 1.33 (d, *J*= 7 Hz, 3H), 1.26 (d, *J*= 7 Hz, 3H).

Step 2: Potassium acetate (1.25 g, 12.7 mmol) was dried under sweeping argon at 180 °C for 15 minutes and then cooled to room temperature. 2-((2*S*,6*R*)-1-benzyl-2,6-dimethyl-1,2,3,6-tetrahydropyridin-4-yl)-6-bromo-4-fluorobenzo[d]thiazole (900 mg, 2.09 mmol), $Pd(dppf)Cl_2$-CH_2Cl_2 (100 mg, 0.12 mmol), bis(pinacolatodiboron) (800 mg, 3.15 mmol), and dioxane (7 mL)

were added. The reaction mixture was heated at 90 °C for 15 h, cooled and then diluted in EtOAc and filtered through Celite. The filtrate was concentrated under vacuum. The crude product was purified by silica chromatography (10-20% EtOAc in CH_2Cl_2) and then the product was dissolved in ether and filtered to remove red solid impurities. The filtrate was concentrated to provide 2-((2*S*,6*R*)-1-benzyl-2,6-dimethyl-1,2,3,6-tetrahydropyridin-4-yl)-4-fluoro-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzo[d]thiazole (970 mg, 90% purity, 87% yield) as a tan oil.

^{1}H NMR (methanol-d_4) δ: 8.10 (s, 1H), 7.49 (d, *J*= 11 Hz, 1H), 7.42-7.46 (m, 2H), 7.31-7.35 (m, 2H), 7.22-7.27 (m, 1H), 6.73 (s, 1H), 4.03 (d, *J*= 15.5 Hz, 1H), 3.91 (d, *J*= 15.5 Hz, 1H), 3.46-3.53 (m, 1H), 3.10 (m, 1H), 2.83-2.89 (m, 1H), 2.52-2.57 (m, 1H), 1.39 (s, 12H), 1.35 (d, *J*= 7 Hz, 3H), 1.27 (d, *J*= 7 Hz, 3H).

Step 3: 2-((2*S*,6*R*)-1-Benzyl-2,6-dimethyl-1,2,3,6-tetrahydropyridin-4-yl)-4-fluoro-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzo[d]thiazole (970 mg, 90% purity, 1.82 mmol) was suspended in MeOH (10 mL) at 0 °C. Hydrogen peroxide (0.22 mL, 35%, 2.5 mmol) was added dropwise. The mixture was then stirred at room temperature for 30 min. MeOH was removed under vacuum. Purification by silica chromatography (20-30% EtOAc in CH_2Cl_2) yielded 2-((2*S*,6*R*)-1-benzyl-2,6-dimethyl-1,2,3,6-tetrahydropyridin-4-yl)-4-fluorobenzo[d]thiazol-6-ol (492 mg, 70%) as a light tan solid.

^{1}H NMR (methanol-d_4) δ:7.41-7.45 (m, 2H), 7.31-7.35 (m, 2H), 7.21-7.26 (m, 1H), 7.07 (s, 1H), 6.72 (d, *J*= 12 Hz, 1H), 6.52 (s, 1H), 4.01 (d, *J*= 15.5 Hz, 1H), 3.90 (d, *J*= 15.5 Hz, 1H), 3.45-3.51 (m, 1H), 3.04-3.09 (m, 1H), 2.79-2.84 (m, 1H), 2.45-2.53 (m, 1H), 1.32 (d, *J*= 7 Hz, 3H), 1.27 (d, *J*= 7 Hz, 3H), OH not observed.

Step 4: 2-((2*S*,6*R*)-1-Benzyl-2,6-dimethyl-1,2,3,6-tetrahydropyridin-4-yl)-4-fluorobenzo[d]thiazol-6-ol (490 mg, 1.26 mmol), CH_2Cl_2 (5 mL), MeOH (5 mL), and 10% palladium on carbon (240 mg) were combined and hydrogenated at 50 psi for 15 h. The mixture was filtered through Celite, using MeOH / CH_2Cl_2 to wash the filter pad. The filtrate was concentrated under vacuum. Purification by silica chromatography (95:5:0.5 CH_2Cl_2 / MeOH / NH_4OH) yielded crude 2-((2*S*,4r,6*R*)-1-benzyl-2,6-dimethylpiperidin-4-yl)-4-fluorobenzo[d]thiazol-6-ol (425 mg, ca. 5:1 cis- / trans-).

Step 5: Crude 2-((2*S*,4r,6*R*)-1-benzyl-2,6-dimethylpiperidin-4-yl)-4-fluorobenzo[d]thiazol-6-ol (420 mg), K_2CO_3 (291 mg, 2.1 mmoL), *N*,*N*-bis(trifluoromethylsulfonyl)aniline (593 mg, 1.66 mmol), and DMF (3.8 mL) were stirred at room temperature for 2 h. This was partitioned between

H_2O and EtOAc. Purification by silica (10-20% EtOAc in CH_2Cl_2) yielded 2-((2S,4r,6R)-1-benzyl-2,6-dimethylpiperidin-4-yl)-4-fluorobenzo[d]thiazol-6-yl trifluoromethanesulfonate (439 mg, 70% over 2 steps) as a brown oil.

^{1}H NMR (acetone-d_6) δ: 8.14 (s, 1H), 7.56 (d, J= 13 Hz, 1H), 7.42-7.46 (m, 2H), 7.29-7.33 (m, 2H), 7.17-7.21 (m, 1H), 3.87 (s, 2H), 3.35-3.42 (m, 1H), 2.79-2.83 (m, 2H), 2.15-2.19 (m, 2H), 1.74 (q, J= 12 Hz, 2H), 1.13 (d, J= 7 Hz, 6H).

Step 6: 2-((2*S*,4r,6*R*)-1-Benzyl-2,6-dimethylpiperidin-4-yl)-4-fluorobenzo[d]thiazol-6-yl trifluoromethanesulfonate (100 mg, 0.2 mmol), potassium acetate (70 mg, 0.71 mmol), bis(pinacolatodiboron) (61 mg, 0.24 mmol), Pd(dppf)Cl_2-CH_2Cl_2 (15 mg, 0.018 mmol), and dioxane (0.8 mL) were heated at 90 °C for 2 h. The reaction mixture was then diluted with EtOAc and was filtered through Celite. The filtrate was then concentrated under vacuum. The product was re-dissolved in CH_2Cl_2 and was filtered though celite to remove black insoluble materials. The filtrate was concentrated to afford 160 mg of crude boronic acid. To this boronic acid was added 5-chloro-2,7-dimethyl-oxazolo[5,4-b]pyridine (87 mg, 0.2 mmol), Pd(dppf)Cl_2-CH_2Cl_2 (10 mg, 0.012 mmol), dioxane (0.7 mL) and 2M aqueous K_2CO_3 (0.35 mL, 0.7 mmol). This mixture was heated at 90 °C for 1 h. The reaction mixture was then partitioned between $CH_2Cl_2$and H_2O. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. Purification by silica chromatography (20-30% EtOAc in CH_2Cl_2), followed by trituration with ether / hexanes, yielded 5-(2-((2*S*,4*r*,6*R*)-1-benzyl-2,6-dimethylpiperidin-4-yl)-4-fluorobenzo[d]thiazol-6-yl)-2,7-dimethyloxazolo[5,4-b]pyridine (63 mg, 60%).

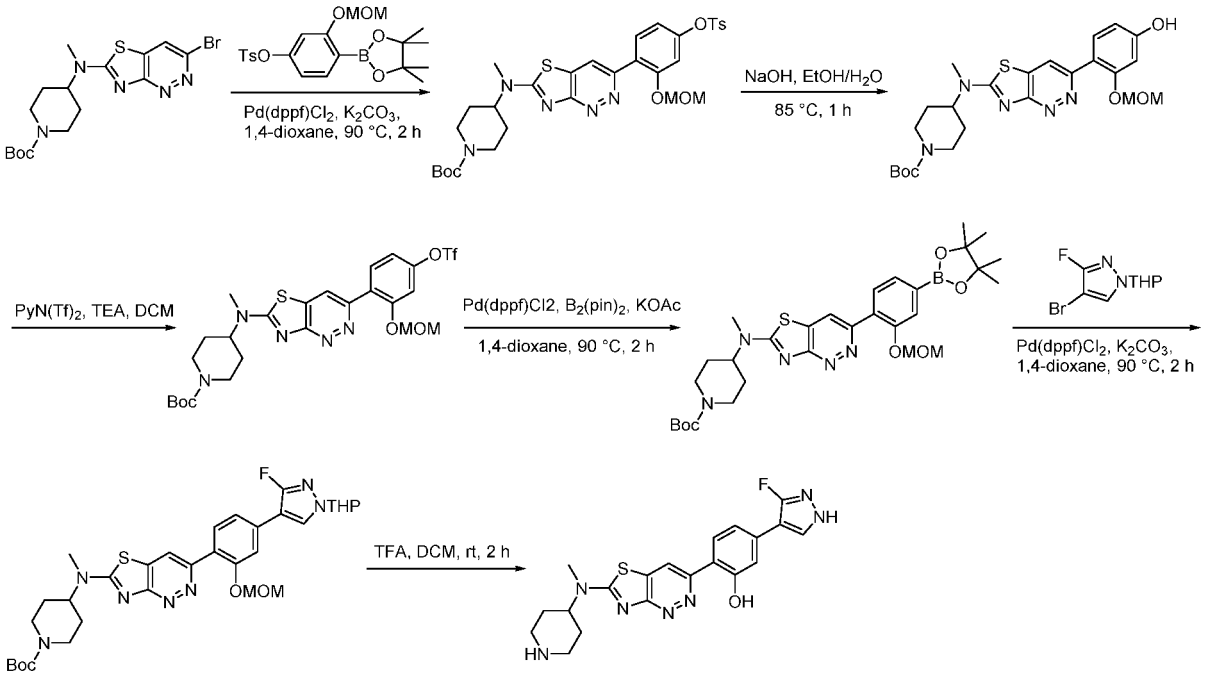
^{1}H NMR (acetone-d_6) δ: 8.63 (s, 1H), 8.06 (d, J= 12.5 Hz, 1H), 7.98 (s, 1H), 7.48 (m, 2H), 7.31 (m, 2H), 7.19 (m, 1H), 3.87 (s, 2H), 3.32-3.40 (m, 1H), 2.80 (m, 2H, obscured by HDO peak), 2.69 (s, 3H), 2.67 (s, 3H), 2.16-2.20 (m, 2H), 1.75 (q, J= 12 Hz, 2H), 1.14 (d, J= 6 Hz, 6H).

Step 7: 5-(2-((2*S*,4r,6*R*)-1-Benzyl-2,6-dimethylpiperidin-4-yl)-4-fluorobenzo[d]thiazol-6-yl)-2,7-dimethyloxazolo[5,4-b]pyridine (61 mg, 0.12 mmol) was dissolved in CH_2Cl_2 (1 mL) and methanol (1 mL). $Pd(OH)_2$ (20% on C, 200 mg) was added. This was hydrogenated at 50 psi for 3 h, during which time HCl is generated from catalytic reduction of dichloromethane. The mixture was filtered through Celite and rinsed with CH_2Cl_2/ MeOH. The filtrate was concentrated under vacuum and purified by silica chromatography (5-10% MeOH in CH_2Cl_2). Trituration with 9:1 CH_2Cl_2/ MeOH yielded title product (28 mg, 49% yield) as an off-white solid.

MS m/z 411.3 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.52 (s, 1H), 8.01 (d, *J*= 12 Hz, 1H), 7.88 (s, 1H), 3.65 (m, 1H), 3.45 (m, 2H), 2.71 (s, 3H), 2.68 (s, 3H), 2.50 (m, 2H), 1.85 (q, *J*= 13 Hz, 2H), 1.45 (d, *J*= 6.5 Hz, 6H).

Example 36

Preparation of Compound 329



Step 1: A mixture of *tert*-butyl 4-((3-bromothiazolo[4,5-c]pyridazin-6-yl)(methyl)amino)piperidine-1-carboxylate (427 mg, 1 mmol), prepared according to the procedure starting from 2-amino-6-bromopyridazine described in Example 34, 3-(methoxymethoxy)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl 4-methylbenzenesulfonate (434 mg, 1 mmol), Pd (dppf)Cl_2 (73 mg, 0.1 mmol) and K_2CO_3 (345 mg, 2.5 mmol) in a mixture of 1,4-dioxane (4 mL) and water (1 mL) was stirred at 90 °C under N_2 for 2 h. The solution was concentrated and the residue was purifed by flash column chromatography eluting with 5% MeOH in CH_2Cl_2 to afford the desired compound *tert*-butyl 4-((3-(2-(methoxymethoxy)-4-(tosyloxy)phenyl)thiazolo[4,5-c]pyridazin-6-yl)(methyl)amino)piperidine-1-carboxylate (393 mg, 60% yield). MS *m/z*: 656 $[M+H]^+$.

Step 2: A mixture of *tert*-butyl 4-((3-(2-(methoxymethoxy)-4-(tosyloxy)phenyl)thiazolo[4,5-c]pyridazin-6-yl)(methyl)amino)piperidine-1-carboxylate (400 mg, 0.61 mmol) and NaOH (122 mg, 3.05 mmol) in EtOH (3 mL) and water (1 mL) was stirred at 85 °C for 1 h. The solution was

concentrated and the residue was purified by flash column chromatography eluting with 5%-10% MeOH in CH_2Cl_2 to afford the desired compound *tert*-butyl 4-((3-(4-hydroxy-2-(methoxymethoxy)phenyl)thiazolo[4,5-c]pyridazin-6-yl)(methyl)amino)piperidine-1-carboxylate (269 mg, 88% yield) as a white solid. MS *m/z*: 502 $[M+H]^+$.

Step 3: To a mixture of *tert*-butyl 4-((3-(4-hydroxy-2-(methoxymethoxy)phenyl)thiazolo[4,5-c]pyridazin-6-yl)(methyl)amino)piperidine-1-carboxylate (269 mg, 0.54 mmol) and Et_3N (227 μL, 1.63 mmol) in CH_2Cl_2 (2 mL) was added $PhNTf_2$ (289 mg, 0.81 mmol). The resulting mixture was stirred at room temperature for 16 h. The solution was concentrated and the residue was purified by flash column chromatography eluting with 5% MeOH in CH_2Cl_2 to afford the desired compound *tert*-butyl 4-((3-(2-(methoxymethoxy)-4-(((trifluoromethyl)sulfonyl)oxy)phenyl)thiazolo[4,5-c]pyridazin-6-yl)(methyl)amino)piperidine-1-carboxylate (214 mg, 65% yield) as a white solid. MS *m/z:* 634 $[M+H]^+$.

Step 4: A mixture of *tert*-butyl 4-((3-(2-(methoxymethoxy)-4-(((trifluoromethyl)sulfonyl)oxy)phenyl)thiazolo[4,5-c]pyridazin-6-yl)(methyl)amino)piperidine-1-carboxylate (214 mg, 0.34 mmol), $B_2(pin)_2$ (104 mg, 0.41 mmol), Pd (dppf)Cl_2 (25 mg, 0.034 mmol) and KOAc (100 mg, 1.02 mmol) in dioxane (3 mL) was stirred at 95 °C under N_2 for 2 h to afford a mixture containing *tert*-butyl 4-((3-(2-(methoxymethoxy)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)thiazolo[4,5-c]pyridazin-6-yl)(methyl)amino)piperidine-1-carboxylate, which was used in next step without any work-up. MS *m/z:* 612 [M+H]+.

Step 5: A mixture of *tert*-butyl 4-((3-(2-(methoxymethoxy)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)thiazolo[4,5-c]pyridazin-6-yl)(methyl)amino)piperidine-1-carboxylate obtained in step 4 (1.3 mL mixture from step 4, 0.15 mmol theoretically), 4-bromo-3-fluoro-1-(tetrahydro-2*H*-pyran-2-yl)-1*H*-pyrazole (37 mg, 0.15 mmol), Pd (dppf)Cl_2 (11 mg, 0.015 mmol) and K_2CO_3 (62 mg, 0.45 mmol) in a mixture of 1,4-dioxane (0.8 mL) and water (0.2 mL) was stirred at 95 °C under N_2 for 2 h. The solution was concentrated and the residue was purified by prep-HPLC to afford *tert*-butyl 4-((3-(4-(3-fluoro-1-(tetrahydro-2*H*-pyran-2-yl)-1*H*-pyrazol-4-yl)-2-(methoxymethoxy)phenyl)thiazolo[4,5-c]pyridazin-6-yl)(methyl)amino)piperidine-1-carboxylate (58 mg, 70% yield). MS *m/z*: 654 $[M+H]^+$.

Step 6: To a solution of *tert*-butyl 4-((3-(4-(3-fluoro-1-(tetrahydro-2*H*-pyran-2-yl)-1*H*-pyrazol-4-yl)-2-(methoxymethoxy)phenyl)thiazolo[4,5-c]pyridazin-6-yl)(methyl)amino)piperidine-1-carboxylate (58 mg, 0.09 mmol) in CH_2Cl_2 (1 mL) was added TFA (1 mL). The mixture was stirred at room temperature for 2 h. The solution was concentrated, and the residue was basified by excess NH_3 in MeOH. The volatiles were removed again, and the residue was purified by prep-HPLC to afford 5-(3-fluoro-1*H*-pyrazol-4-yl)-2-(6-(methyl(piperidin-4-yl)amino)thiazolo[4,5-c]pyridazin-3-yl)phenol (17 mg, 46% yield).

MS *m/z*: 426 $[M+H]^+$; ^{1}H NMR (DMSO-d_6) δ 8.94 (s, 1H), 8.30 (d, *J*= 2.1 Hz, 1H), 7.94 (d, *J*= 8.5 Hz, 1H), 7.20 (d, *J*= 7.6 Hz, 2H), 3.16 (s, 3H), 3.06 (d, *J*= 13.4 Hz, 2H), 2.95 – 2.86 (m, 1H), 2.69 – 2.55 (m, 2H), 1.82 – 1.64 (m, 4H), 2NH and OH protons not observed.

Using the procedure described for Example 36, above, additional compounds described herein were prepared by substituting the appropriate starting material, suitable reagents and reaction conditions, obtaining compounds such as those selected from:

Cpd	Data
331	MS *m/z* 446.1 $[M+H]^+$; ^{1}H NMR (methanol-d_4) δ: 8.50 (br s, 1H), 8.33 - 8.31 (m, 1H), 7.97 – 7.92 (m, 2H), 7.58 (dd, *J*= 12.1, 6.2 Hz, 1H), 7.45 (s, 1H), 3.47 (d, *J*= 13.1 Hz, 2H), 3.32 (s, 1H), 3.29 – 3.15 (m, 3H), 3.05 (t, *J*= 12.3 Hz, 2H), 2.26 – 2.13 (m, 2H), 2.10 – 1.99 (m, 2H).
333	MS *m/z* 408.0 $[M+H]^+$; ^{1}H NMR (DMSO-d_6) δ: 13.90 (s, 1H), 13.02 (s, 1H), 8.95 (s, 1H), 8.31 (s, 1H), 8.01 (s, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.26 – 7.22 (m, 2H), 4.90 – 4.05 (br s, 2H), 2.89 – 2.72 (m, 4H), 1.07 (d, *J* = 5.6 Hz, 6H), 1 NH proton not observed.
334	MS *m/z* 380.1; $[M+H]^+$; ^{1}H NMR (DMSO-d_6) δ: 13.85 (s, 1H), 13.02 (s, 1H), 8.96 (s, 1H), 8.31 (br s, 1H), 8.01 (br s, 1H), 7.89 (d, *J*= 9.0 Hz, 1H), 7.32 – 7.21 (m, 2H), 5.30 – 4.30 (br s, 1H), 3.74 (s, 4H), 3.02 – 2.88 (m, 4H).
338	MS *m/z* 420.4; $[M+H]^+$; ^{1}H NMR (DMSO-d_6) δ: 9.41 (s, 2H), 9.07 (s, 1H), 8.14 (s, 2H), 7.76 (d, *J*= 8.2 Hz, 1H), 7.31 (s, 1H), 7.29 (d, *J*= 8.2 Hz, 1H), 4.35 (d, *J*= 8.4 Hz, 2H), 4.10 (d, *J*= 9.4 Hz, 2H), 3.42 – 3.29 (m, 2H), 3.03 – 2.90 (m, 2H), 2.01 – 1.88 (m, 2H), 1.82 – 1.71 (m, 2H), 1 NH proton not observed.
341	MS *m/z* 438.2 $[M+H]^+$; ^{1}H NMR (DMSO-d_6) δ: 13.75 (br s, 1H), 12.74 (br s, 1H), 8.95 (s, 1H), 8.39 (s, 1H), 8.29 (d, *J*= 1.2 Hz, 1H), 7.91 (d, *J*= 8.4 Hz, 1H), 7.26 – 7.17 (m, 2H), 4.04 (s, 4H), 2.83 (s, 4H), 1.84 (s, 4H).
344	MS *m/z* 420.4 $[M+H]^+$; ^{1}H NMR (DMSO-d_6) δ: 9.16 (br s, 1H), 9.03 (s, 1H), 8.92 (br s, 1H), 8.14 (s, 2H), 7.82 (d, *J*= 8.5 Hz, 1H), 7.31 – 7.24 (m, 2H), 4.46 (br s, 1H), 3.79 (br s, 1H), 3.64 (br s, 1H), 3.39 – 3.19 (m, 3H), 3.07 – 2.96 (m, 1H), 2.77 – 2.68 (m, 1H), 2.53 – 2.35 (m, 2H), 2.18 – 2.07 (m, 1H), 1.92 (br s, 1H), 1 NH not observed.

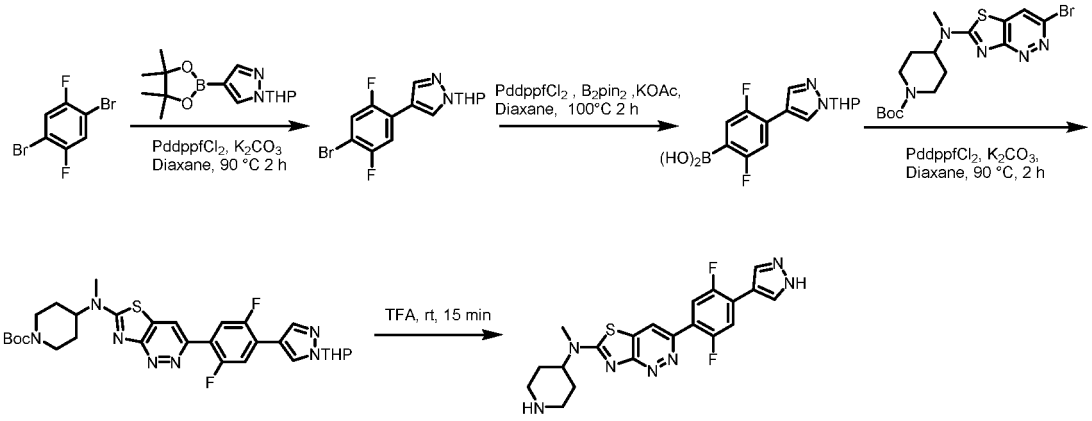
Cpd	Data
345	MS *m/z* 436.3 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.11 (br s, 2H), 9.05 (s, 1H), 8.14 (s, 2H), 7.77 (d, *J*= 8.1 Hz, 1H), 7.31 – 7.26 (m, 2H), 4.56 (br s, 1H), 3.20 (br s, 3H), 3.05 – 2.93 (m, 1H), 2.54 (t, *J*= 5.4 Hz, 3H), 2.21 (d, *J*= 11.3 Hz, 2H), 1.96 – 1.87 (m, 2H), 1.82 (q, *J*= 11.2, 10.4 Hz, 2H), 1.68 – 1.55 (m, 2H), 1 NH not observed.
346	MS *m/z* 412.1 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.83 (s, 1H), 8.23 (s, 1H), 8.10 (br s, 2H), 7.87 (d, *J*= 8.4 Hz, 1H), 7.28 – 7.19 (m, 2H), 5.56 – 5.35 (m, 1H), 5.00 (br s, 1H), 3.50 – 3.24 (m, 4H), 3.22 (s, 3H), 2 NH protons not observed.
348	MS *m/z* 408.3 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.78 (br s, 1H), 9.31 (br s, 1H), 9.11 (s, 1H), 8.15 (s, 2H), 7.78 (d, *J*= 8.2 Hz, 1H), 7.32 (s, 1H), 7.29 (dd, *J*= 8.2, 1.7 Hz, 1H), 4.97 (br s, 1H), 3.42 – 3.12 (m, 6H), 2.86 (q, *J*= 12.5, 12.1 Hz, 1H), 2.14 – 1.78 (m, 4H), 1 NH proton not observed.
349	MS *m/z* 408.3 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.77 (s, 1H), 9.12 (s, 1H), 8.16 (s, 2H), 7.78 (d, *J*= 8.2 Hz, 1H), 7.32 (s, 1H), 7.29 (d, *J*= 8.2 Hz, 1H), 4.97 (br s, 1H), 3.41 – 3.17 (m, 6H), 2.86 (q, *J*= 13.5, 13.0 Hz, 1H), 2.07 – 1.80 (m, 4H), NH and OH protons not observed.
350	MS *m/z* 408.3; $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 2:1 mixture of diastereomers δ: 13.78 (br s, 0.7H), 13.11 (br s, 0.3H), 9.04 (br s, 2H), 8.96 (s, 1H), 8.15 (s, 2H), 7.88 (d, *J*= 7.9 Hz, 1H), 7.29 – 7.19 (m, 2H), 5.24 (br s, 0.7H), 4.71 (br s, 0.3H), 3.70 (s, 0.7H), 3.56 – 3.45 (m, 0.3H), 3.28 (s, 2H), 3.26 (s, 1H), 2.89 – 2.75 (m, 1.7H), 2.69 – 2.61 (m, 0.3H), 2.61 – 2.51 (m, 5H).
353	MS *m/z* 380.3; $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 2:1 mixture of rotamers δ: 9.28 – 8.97 (m, 2H), 8.28 (br s, 1H), 8.15 (s, 2H), 7.86 (d, *J*= 6.5 Hz, 1H), 7.28 (s, 1H), 5.37 (br s, 0.7H), 5.21 (br s, 0.3H), 4.40 (br s, 2H), 4.26 (br s, 2H), 3.38 (s, 2H), 3.22 (s, 1H), 1 NH and OH protons not observed.
354	MS *m/z* 420.4 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.36 (br s, 1H), 9.05 (s, 1H), 8.67 (br s, 1H), 8.15 (s, 2H), 7.80 (d, *J*= 8.2 Hz, 1H), 7.34 – 7.26 (m, 2H), 4.22 (s, 2H), 3.41 (d, *J*= 12.6 Hz, 2H), 2.94 (q, *J*= 11.6, 11.2 Hz, 2H), 2.68 (br s, 2H), 2.50 – 2.44 (m, 2H), 2.19 (d, *J*= 13.1 Hz, 2H), 1 NH proton not observed.
355	MS *m/z* 436.4 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.51 (br s, 1H), 9.10 (s, 1H), 8.78 (br s, 1H), 8.16 (s, 2H), 7.80 (d, *J*= 8.1 Hz, 1H), 7.35 – 7.26 (m, 2H), 4.97 (br s, 1H), 3.39 – 3.30 (m, 1H), 3.31 – 3.12 (m, 4H), 3.06 (s, 2H), 2.45 – 2.28 (m, 1H), 1.93 (d, *J*= 13.9 Hz, 1H), 1.26 (s, 3H), 1.03 (s, 3H), 1 NH proton not observed.
356	MS *m/z* 420.4 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.05 (s, 1H), 8.27 (br s, 2H), 8.14 (s, 2H), 7.89 – 7.77 (m, 1H), 7.33 – 7.23 (m, 2H), 4.72 (br s, 1H), 4.14 – 3.89 (m, 2H), 3.43 – 3.06 (m, 5H), 2.68 – 2.55 (m, 2H), 2.49 – 2.27 (m, 2H), 1 NH proton not observed.
357	MS *m/z* 394.1 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.82 (s, 1H), 8.39 (s, 1H), 8.14 (br s, 2H), 7.86 (d, *J*= 8.8 Hz, 1H), 7.28 – 7.21 (m, 2H), 4.14 (br s, 1H), 3.28 – 3.14 (m, 2H), 3.00 – 2.84 (m, 2H), 2.20 – 2.15 (m, 2H), 1.75 – 1.56 (m, 2H), 2 NH protons not observed.

Cpd	Data
358	MS *m/z* 426.0; $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.97 (s, 1H), 8.26 (s, 1H), 8.15 (s, 2H), 7.89 (d, *J*= 8.8 Hz, 1H), 7.29 – 7.23 (m, 2H), 4.96 (d, *J*= 50.4 Hz, 1H), 4.95 – 4.57 (br s, 1H), 3.35-3.30 (m, 1H), 3.22 (s, 3H), 3.20 – 3.05 (m, 2H), 2.98 – 2.68 (m, 2H), 2.21 – 2.07 (m, 1H), 1.76 – 1.65 (m, 1H), 1NH proton not observed.
361	MS *m/z* 408.5 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.67 (br s, 2H), 9.09 (s, 1H), 8.15 (s, 2H), 7.77 (d, *J*= 8.1 Hz, 1H), 7.31 (s, 1H), 7.29 (d, *J*= 8.4 Hz, 1H), 5.07 – 4.23 (m, 1H), 3.54 – 3.45 (m, 1H), 3.41 (s, 3H), 2.74 (q, *J*= 9.7, 9.2 Hz, 2H), 2.69 – 2.59 (m, 2H), 2.49 – 2.40 (m, 3H), 1 NH proton not observed.
362	MS *m/z* 420.3 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.16 (br s, 1H), 9.08 (br s, 1H), 9.05 (s, 1H), 8.15 (s, 2H), 7.83 (d, *J*= 8.7 Hz, 1H), 7.30 – 7.26 (m, 2H), 4.52 (br s, 1H), 3.75 (br s, 1H), 3.61 (br s, 1H), 3.53 (br s, 2H), 3.15 – 3.04 (m, 2H), 2.68 (br s, 1H), 2.21 (br s, 1H), 2.16 – 2.03 (m, 2H), 1.85 (d, *J*= 13.5 Hz, 1H), 1 NH not observed.
363	MS *m/z* 420.4 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.79 (s, 1H), 9.42 (d, *J*= 9.8 Hz, 1H), 9.06 (s, 1H), 8.15 (s, 2H), 7.78 (d, *J*= 8.2 Hz, 1H), 7.30 (d, *J*= 1.4 Hz, 1H), 7.28 (dd, *J*= 8.2, 1.6 Hz, 1H), 4.24 (dd, *J*= 7.7 Hz, 2H), 3.75 – 3.67 (m, 1H), 3.61 – 3.52 (m, 1H), 3.21 – 3.15 (m, 1H), 2.96 (q, *J*= 11.7 Hz, 1H), 2.76 (dt, *J*= 11.2, 7.7 Hz, 1H), 2.48 – 2.40 (m, 1H), 2.37 (dt, *J*= 11.3, 7.8 Hz, 1H), 2.16 (d, *J*= 12.8 Hz, 1H), 2.01 – 1.90 (m, 1H), 1.82 – 1.70 (m, 1H), 1 NH proton not observed.
365	MS *m/z* 426.0; $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.90 (s, 1H), 8.29 – 8.04 (br s, 2H), 8.19 (s, 1H), 7.89 (d, *J*= 8.8 Hz, 1H), 7.28 – 7.22 (m, 2H), 4.80 (m, 2H), 3.36 – 3.15 (m, 4H), 3.00 – 2.91 (m, 1H), 2.65 – 2.55 (m, 2H), 1.91 – 1.79 (m, 2H), NH protons not observed.
367	MS *m/z* 380.1 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.87 (s,1H), 8.35 (s, 1H), 8.15 (br s, 2H), 7.87 (d, *J*= 8.4 Hz, 1H), 7.29 – 7.24 (m, 2H), 4.63 (s, 1H), 3.41 – 3.31 (m, 2H), 3.20 – 3.07 (m, 3H), 2.25 (m, 1H), 1.99 (m, 1H), NH and OH protons not observed.
368	MS *m/z* 410.3 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.85 (s, 1H), 8.39 (s, 2H), 8.23 (s, 1H), 7.92 (d, *J*= 8 Hz, 1H), 7.21 (s, 1H), 4.48 - 4.44 (m, 4H), 4.22-3.95 (m, 4H), 2 NH protons not observed.
371	MS *m/z* 438.4 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.83 (br s, 1H), 9.10 (s, 1H), 8.78 (br d, *J*= 10.1 Hz, 1H), 8.16 (s, 2H), 7.78 (d, *J*= 8.2 Hz, 1H), 7.32 (d, *J*= 1.5 Hz, 1H), 7.31 – 7.26 (m, 1H), 4.74 (br s, 1H), 3.94 (dd, *J*= 11.6, 8.3 Hz, 1H), 3.77 (dd, *J*= 11.6, 5.1 Hz, 1H), 3.67 – 3.60 (m, 1H), 3.41 – 3.30 (m, 1H), 3.30 – 3.18 (m, 4H), 2.42 – 2.24 (m, 2H), 1.97 (d, *J*= 12.6 Hz, 2H), NH proton not observed.
374	MS *m/z* 394.1; $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.98 (s, 1H), 8.15 (s, 2H), 7.88 (d, *J*= 8.8 Hz, 1H), 7.29 – 7.24 (m, 2H), 5.23 (br s, 1H), 3.55 (m, 1H), 3.40 – 3.22 (m, 3H), 3.21 (s, 3H), 2.40 – 2.28 (m, 1H), 2.25 – 2.12 (m, 1H), 2 NH and OH protons not observed.
376	MS *m/z* 408.5 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 9.05 (s, 1H), 8.15 (s, 2H), 7.74 (d, *J*= 8.1 Hz, 1H), 7.35 (d, *J*= 8.3 Hz, 1H), 7.27 (s, 1H), 5.41 (br s, 1H), 3.98 – 3.84 (m, 1H), 3.46 (br s, 3H), 3.04 (dt, *J*= 16.0, 8.2 Hz, 2H), 2.82 – 2.74 (m, 2H), 2.72 (s, 3H), 2 NH and OH protons not observed.

Cpd	Data
381	MS *m/z* 411.9 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.92 (s, 1H), 8.13 (s, 2H), 7.88 (d, *J*= 8.8 Hz, 1H), 7.29 – 7.20 (m, 2H), 5.33 (d, *J*= 52.0 Hz, 1H), 5.12 – 4.80 (br s, 1H), 3.58 – 3.25 (m, 5H), 3.15 (s, 3H), NH and OH protons not observed.
386	MS *m/z* 406.3 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.77 (br s, 1H), 8.01 (s, 2H), 7.83 (d, *J*= 7.2 Hz, 1H), 7.29 – 7.12 (m, 2H), 5.03 – 4.96 (m, 1H), 4.51 – 4.33 (m, 1H), 4.11 – 3.92 (m, 2H), 3.65 – 3.54 (m, 1H), 3.47 (d, *J*= 16.4 Hz, 1H), 3.18 – 3.03 (m, 2H), 2.44 – 2.31 (m, 1H), 2.14 – 2.01 (m, 1H), 2NH and OH protons not observed.
387	MS *m/z* 411.9; $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.94 (s, 1H), 8.32 (s, 1H), 8.28 (s, 1H), 7.93 (d, *J*= 8.4 Hz, 1H), 7.24 – 7.16 (m, 2H), 5.50 – 4.80 (br s, 1H), 3.35 – 2.95 (m, 5H), 3.19 (s, 3H), 2.27 – 2.14 (m, 1H), 2.07 – 1.92 (m, 1H), 1 NH proton not observed.
389	MS *m/z* 406.2 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: 8.82 (s, 1H), 8.02 (s, 2H), 7.82 (d, *J*= 9.2 Hz, 1H), 7.27 – 7.18 (m, 2H), 5.02 – 4.97 (m, 1H), 4.47 – 4.39 (m, 1H), 4.09 – 3.97 (m, 2H), 3.63 – 3.55 (m, 1H), 3.48 (d, *J*= 13.3 Hz, 1H), 3.27 – 3.23 (m, 1H), 3.16 – 3.07 (m, 1H), 2.45 – 2.34 (m, 1H), 2.15 – 2.03 (m, 1H), 2NH and OH protons not observed.
394	MS *m/z* 422.4 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: δ: 8.79 (s, 1H), 8.03 (s, 2H), 7.81 (d, *J*= 8.2 Hz, 1H), 7.24 (d, *J*= 9.4 Hz, 1H), 7.22 (s, 1H), 4.81 (br s, 1H), 3.63 – 3.55 (m, 1H), 3.53 – 3.43 (m, 1H), 3.32 – 3.27 (m, 1H), 3.25 (s, 3H), 2.27 – 2.12 (m, 3H), 1.99 (q, *J*= 12.3 Hz, 1H), 1.42 (d, *J*= 6.5 Hz, 3H), 2NH and OH protons not observed.
396	MS *m/z* 422.4 $[M+H]^+$; ^1H NMR (methanol-d_4) δ: δ: 8.83 (s, 1H), 8.03 (s, 2H), 7.81 (d, *J*= 8.2 Hz, 1H), 7.26 (d, *J*= 8.2 Hz, 1H), 7.23 (s, 1H), 4.91 (br s, 1H), 4.05 – 3.95 (m, 1H), 3.52 – 3.39 (m, 2H), 3.26 (s, 3H), 2.37 (td, *J*= 12.9, 5.2 Hz, 1H), 2.26 – 2.12 (m, 2H), 2.03 (d, *J*= 14.0 Hz, 1H), 1.57 (d, *J*= 7.1 Hz, 3H), NH and OH protons not observed.
398	MS *m/z* 439.2; $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.92 (s, 1H), 8.27 (d, *J*= 2.0 Hz, 1H), 7.93 (d, *J*= 8.8 Hz, 1H), 7.24 – 7.16 (m, 2H), 4.83 (br s, 1H), 3.35 – 3.03 (m, 7H), 2.24 – 1.76 (m, 6H), 2NH and OH protons not observed.

Example 37

Preparation of 328



Step 1: A mixture of 4-(4-bromo-2,5-difluorophenyl)-1-(tetrahydro-2*H*-pyran-2-yl)-1*H*-pyrazole (1.0 g, 3.7 mmol), 1-(tetrahydro-2*H*-pyran-2-yl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrazole (1.24 g, 4.4 mmol), $Pd(dppf)Cl_2$ (267 mg, 0.37 mmol) and K_2CO_3 (1.02 mg, 7.4 mmol) in dioxane-H_2O (12 mL, 9/3, v/v) was stirred at 90 °C under N_2 for 2 h. The solution was concentrated, and the residue was purified by silica gel chromatography, eluting with 10%-20% EtOAc in petroleum ether to give 4-(4-bromo-2,5-difluorophenyl)-1-(tetrahydro-2*H*-pyran-2-yl)-1*H*-pyrazole as light-yellow solid (470 mg, 37% yield). MS *m/z*: 343, 345 $[M+H]^+$.

Step 2: A mixture of 4-(4-bromo-2,5-difluorophenyl)-1-(tetrahydro-2*H*-pyran-2-yl)-1*H*-pyrazole (100 mg, 0.29 mmol), $B_2(Pin)_2$ (89 mg, 0.35 mmol), Pd (dppf)Cl_2 (22 mg, 0.03 mmol) and KOAc (57 mg, 0.58 mmol) in dioxane (5 mL) was stirred at 90 °C under N_2 for 2 h. The resulting solution was used in the next step without purification. MS *m/z*: 309 $[M+H]^+$.

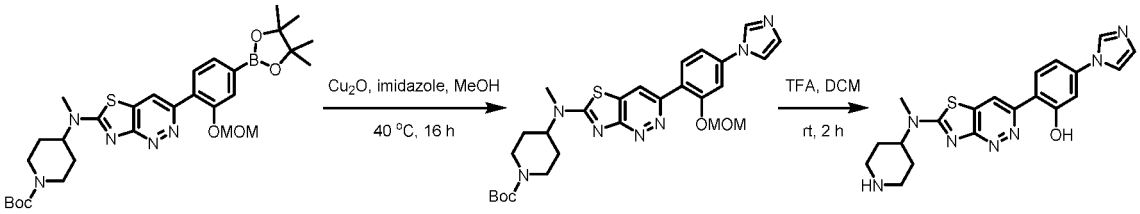
Step 3: The reaction mixture from step 2 and *tert*-butyl 4-((3-bromothiazolo[4,5-c]pyridazin-6-yl)(methyl)amino)piperidine-1-carboxylate (139 mg, 0.32mmol), Pd (dppf)Cl_2 (24 mg, 0.03 mmol) and K_2CO_3 (88 mg, 0.64 mmol) in dioxane-H_2O (5 mL, 9/3, v/v) was stirred at 90 °C under N_2 for 2 h. The solution was concentrated, and the residue was purified by silica gel chromatography eluting with 20%-30% EtOAc in petroleum ether to give *tert*-butyl 4-((3-(2,5-difluoro-4-(1-(tetrahydro-2*H*-pyran-2-yl)-1*H*-pyrazol-4-yl)phenyl)thiazolo[4,5-c]pyridazin-6-yl)(methyl)amino)piperidine-1-carboxylate as light-yellow solid (50 mg, 35% yield). MS *m/z*: 612 $[M+H]^+$.

Step 4: *tert*-Butyl 4-((3-(2,5-difluoro-4-(1-(tetrahydro-2*H*-pyran-2-yl)-1*H*-pyrazol-4-yl)phenyl)thiazolo[4,5-c]pyridazin-6-yl)(methyl)amino)piperidine-1-carboxylate (80 mg, 0.13 mmol) was dissolved in TFA (1 mL). After 15 min, the volatiles were removed. To the above residue was added NH_3-MeOH (15 ml) and the resultant mixture was stirred at room temperature for 1 h. The volatiles were then removed again under reduced pressure. The residue was purified by Prep-HPLC to afford 3-(2,5-difluoro-4-(1*H*-pyrazol-4-yl)phenyl)-*N*-methyl-*N*-(piperidin-4-yl)thiazolo[4,5-c]pyridazin-6-amine as a white solid (22 mg, 39% yield).

MS *m/z*: 428 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 8.55 (s, 1H), 8.32 (s, 2H), 7.92 - 7.83 (m, 2H), 3.20 - 3.14 (m, 6H), 2.77 - 2.72 (m, 2H), 1.86 - 1.76 (m, 4H), 2NH protons not observed.

Example 38

Preparation of 327



Step 1: A mixture of *tert*-butyl 4-((3-(2-(methoxymethoxy)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)thiazolo[4,5-c]pyridazin-6-yl)(methyl)amino)piperidine-1-carboxylate (90 mg, 0.15 mmol), prepared according to the procedure described in Example 37, imidazole (20 mg, 0.3 mmol) and Cu_2O (4 mg, 0.03 mmol) in MeOH (2 mL) was stirred at 40 °C under air for 16 h. The solution was concentrated and the residue was purified by prep-TLC eluting with 7% MeOH in CH_2Cl_2 to afford *tert*-butyl 4-((3-(4-(1*H*-imidazol-1-yl)-2-(methoxymethoxy)phenyl)thiazolo[4,5-c]pyridazin-6-yl)(methyl)amino)piperidine-1-carboxylate (49 mg, 60% yield). MS *m/z:* 552 $[M+H]^+$.

Step 2: To a solution *tert*-butyl 4-((3-(4-(1*H*-imidazol-1-yl)-2-(methoxymethoxy)phenyl)thiazolo[4,5-c]pyridazin-6-yl)(methyl)amino)piperidine-1-carboxylate (49 mg, 0.09 mmol) in CH_2Cl_2 (1 mL) was added TFA (1 mL). The mixture was stirred at room temperature for 2 h. The solution was concentrated, and the residue was basified by excess of NH_3 in MeOH. The volatiles were removed and the residue was purified by prep-HPLC to afford 5-(1*H*-imidazol-1-yl)-2-(6-(methyl(piperidin-4-yl)amino)thiazolo[4,5-c]pyridazin-3-yl)phenol (15 mg, 42% yield).

MS *m/z*: 408.2 $[M+H]^+$; ^1H NMR (DMSO-d_6) δ: 9.02 (s, 1H), 8.41 (s, 1H), 8.29 (s, 1H), 8.06 (d, *J*= 8.6 Hz, 1H), 7.88 (s, 1H), 7.42 – 7.26 (m, 2H), 7.13 (s, 1H), 3.27 (d, *J*= 11.3 Hz, 3H), 3.16 (s, 3H), 2.99 – 2.87 (m, 2H), 2.03 – 1.79 (m, 4H), 1NH proton not observed.

BIOLOGICAL EXAMPLES

The following *in vitro* biological examples demonstrate the usefulness of the compounds of the present description for treating Huntington's disease.

To describe in more detail and assist in understanding the present description, the following non-limiting biological examples are offered to more fully illustrate the scope of the description and are not to be construed as specifically limiting the scope thereof. Such variations of the present description that may be now known or later developed, which would be within the purview of one skilled in the art to ascertain, are considered to fall within the scope of the present description and as hereinafter claimed.

Compounds of Formula (I) or Formula (II) were tested using the Meso Scale Discovery (MSD) Assay provided in International Application No. PCT/US2016/066042, filed on December 11, 2016 and claiming priority to United States Provisional Application U.S. 62/265,652 filed on December 10, 2015, the entire contents of which are incorporated herein by reference.

The Endogenous Huntingtin Protein assay used in Example 1 was developed using the ELISA-based MSD electrochemiluminescence assay platform.

Example 1

Endogenous Huntingtin Protein Assay

Meso Scale Discovery (MSD) 96-well or 384-well plates were coated overnight at 4°C with MW1 (expanded polyglutamine) or MAB2166 monoclonal antibody (for capture) at a concentration of 1 µg/mL in PBS (30 µL per well). Plates were then washed three times with 300 µL wash buffer (0.05% Tween-20 in PBS) and blocked (100 µL blocking buffer; 5% BSA in PBS) for 4-5 hours at room temperature with rotational shaking and then washed three times with wash buffer.

Samples (25 µL) were transferred to the antibody-coated MSD plate and incubated overnight at 4°C. After removal of the lysates, the plate was washed three times with wash buffer, and 25 µL of #5656S (Cell signaling; rabbit monoclonal) secondary antibody (diluted to 0.25 µg/mL in 0.05% Tween-20 in blocking buffer) was added to each well and incubated with

shaking for 1Hour at room temperature. Following incubation with the secondary antibody, the wells were rinsed with wash buffer after which 25 µL of goat anti-rabbit SULFO TAG secondary detection antibody (required aspect of the MSD system) (diluted to 0.25 µg/mL in 0.05% Tween-20 in blocking buffer) was added to each well and incubated with shaking for 1 hour at room temperature. After rinsing three times with wash buffer, 150 µL of read buffer T with surfactant (MSD) were added to each empty well, and the plate was imaged on a SI 6000 imager (MSD) according to manufacturers' instructions provided for 96- or 384-well plates. The resulting IC_{50} values (µM) for compounds tested are shown in Table 1.

As shown in Table 1, test compounds described herein had the following IC_{50} values, an IC_{50} value between > 3 µM and ≤ 9 µM is indicated by a single star (*), an IC_{50} value between > 1 µM and ≤ 3 µM is indicated by two stars (**), an IC_{50} value between > 0.5 µM and ≤ 1 µM is indicated by three stars (***), an IC_{50} value between > 0.1 µM and ≤ 0.5 µM is indicated by four stars (****) and an IC_{50} value of ≤ 0.1 µM is indicated by five stars (*****).

Table 1

Cpd	IC_{50}	Cpd	IC_{50}	Cpd	IC_{50}
1	****	133	*****	266	****
2	****	134	****	267	****
3	***	135	*****	268	****
4	****	136	****	269	****
5	***	137	*	270	*****
6	**	138	*****	271	****
7	**	139	*****	272	****
8	****	140	*****	273	***
9	**	141	*****	274	*****
10	**	142	****	275	*****
11	**	143	****	276	*****
12	**	144	*****	277	****
13	***	145	*****	278	*****
14	**	146	****	279	*****
15	**	147	*****	280	*****
16	***	148	*****	281	*****
17	****	149	****	282	*****
18	****	150	*****	283	***
19	****	151	*****	284	*****

Cpd	IC_{50}	Cpd	IC_{50}	Cpd	IC_{50}
20	*****	152	*****	285	*****
21	****	153	**	286	*****
22	*****	154	**	287	*****
23	*****	155	****	288	****
24	*****	156	**	289	*****
25	****	157	*****	290	*****
26	***	158	****	291	*****
27	***	161	**	292	*****
28	**	162	*****	293	*****
29	**	163	*****	294	****
30	****	164	*****	295	****
31	*****	165	*****	296	*****
32	*****	166	*****	297	*****
33	*****	167	*****	298	*****
34	****	168	*****	299	*****
35	****	169	****	300	*****
36	****	170	*****	301	*****
37	*****	171	*****	303	*****
38	**	172	**	304	****
39	*****	173	**	305	***
40	*****	174	**	306	*****
41	**	175	*****	307	*****
42	****	176	*****	308	**
43	****	177	*****	309	*****
44	*****	178	*****	310	*****
45	*****	179	*****	311	*****
46	*****	180	****	312	****
47	*****	181	****	313	****
48	****	182	***	314	****
49	****	183	*****	315	****
50	****	184	**	316	****
51	****	185	*****	317	*****
52	**	186	*****	318	*****
53	****	187	*****	319	*****
54	****	188	*****	320	*****

Cpd	IC_{50}	Cpd	IC_{50}	Cpd	IC_{50}
55	*****	189	****	321	*****
56	***	190	**	322	*****
57	*****	191	**	323	*****
58	***	192	*****	324	*****
59	****	193	*****	325	*****
60	****	194	*****	326	*****
61	*****	195	*****	327	****
62	*****	196	*****	328	****
63	****	197	****	329	*****
64	**	198	*****	332	*****
65	****	199	*****	334	****
66	*****	200	*****	335	**
67	**	201	****	336	**
68	**	202	*****	337	***
70	*****	203	*****	338	***
71	****	204	*****	339	*****
72	****	205	*****	340	**
73	*****	206	*****	341	***
74	*****	207	*****	342	****
75	****	208	*****	343	****
76	****	209	*****	344	*****
77	****	210	***	345	****
78	***	211	*****	346	****
79	*****	212	*****	347	**
80	**	213	*****	348	****
81	****	214	*****	349	*****
82	****	215	*****	350	****
83	*****	216	****	351	**
84	*****	217	*****	352	*****
85	****	218	****	353	****
86	*****	219	**	354	*****
87	*****	220	*****	355	*****
88	*****	221	*****	356	****
89	***	222	*****	357	****
90	****	223	****	358	***

Cpd	IC50	Cpd	IC50	Cpd	IC50
91	*****	224	*****	359	*****
92	*****	225	*****	361	****
93	****	226	*****	362	*****
94	*****	227	**	363	*****
95	****	228	***	364	**
96	****	229	*****	365	****
97	*****	230	*****	366	*****
98	****	231	*****	367	****
99	**	232	*****	368	****
100	***	233	*****	369	****
101	****	234	*****	370	*****
102	*****	235	*****	371	*****
103	*****	236	*****	372	*****
104	*****	237	****	373	*****
105	****	238	*****	374	*****
106	*****	239	****	375	*****
107	*****	240	****	376	****
108	***	241	****	377	****
109	****	242	****	378	****
110	****	243	****	379	*****
111	*****	244	**	380	****
112	****	245	**	381	****
113	*****	246	**	382	****
114	*****	247	****	383	*****
115	***	248	****	384	*****
116	****	249	*****	385	*****
117	*****	250	****	386	*****
118	****	251	*****	387	*****
119	*****	252	*****	388	****
120	*****	253	*****	389	*****
121	*****	254	*****	390	*****
122	****	255	*****	391	*****
123	*****	256	*****	392	**
124	*****	257	*****	393	**
125	****	258	*****	394	*****

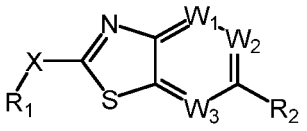
Cpd	IC_{50}	Cpd	IC_{50}	Cpd	IC_{50}
126	*****	259	*****	395	*****
127	*****	260	*****	396	*****
128	****	261	*****	397	*****
129	***	262	*****	398	*****
130	*****	263	*****	399	*****
131	*****	264	*****		
132	*****	265	*****		

Without regard to whether a document cited herein was specifically and individually indicated as being incorporated by reference, all documents referred to herein are incorporated by reference into the present application for any and all purposes to the same extent as if each individual reference was fully set forth herein.

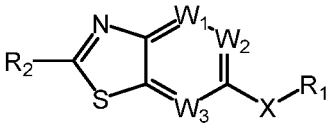
Having now fully described the subject matter of the claims, it will be understood by those having ordinary skill in the art that the same can be performed within a wide range of equivalents without affecting the scope of the subject matter or particular aspects described herein. It is intended that the appended claims be interpreted to include all such equivalents.

What is claimed is:

1. A compound comprising a compound of Formula (I) or Formula (II):



(I)



(II)

or a form thereof, wherein:

W_1, W_2 and W_3 are independently C-R_a or N;

R_a is, in each instance, independently selected from hydrogen, cyano, halogen, hydroxy, C_{1-6}alkyl, halo-C_{1-6}alkyl, C_{1-6}alkyl-carbonyl, C_{1-6}alkoxy, halo-C_{1-6}alkoxy, C_{1-6}alkoxy-C_{1-6}alkyl, C_{1-6}alkoxy-carbonyl, amino, C_{1-6}alkyl-amino, (C_{1-6}alkyl)$_2$-amino, amino-C_{1-6}alkyl, and hydroxy-C_{1-6}alkyl;

X is selected from N-R_b, O, or a bond;

R_b is selected from hydrogen and C_{1-6}alkyl;

R_1 is selected from C_{3-10}cycloalkyl and heterocyclyl,

wherein heterocyclyl is a saturated or partially unsaturated 3-7 membered monocyclic, 6-10 membered bicyclic or 13-16 membered polycyclic ring system having 1, 2, or 3 heteroatom ring members independently selected from N, O, or S, and

wherein, each instance of C_{3-10}cycloalkyl and heterocyclyl is optionally substituted with one, two three, or four R_3 substituents and optionally, with one additional R_4 substituent, or,

wherein, alternatively, each instance of C_{3-10}cycloalkyl and heterocyclyl is optionally substituted with one, two, three, four, or five R_3 substituents;

R_3 is, in each instance, independently selected from cyano, halogen, hydroxy, C_{1-6}alkyl, halo-C_{1-6}alkyl, C_{1-6}alkyl-carbonyl, C_{1-6}alkoxy, halo-C_{1-6}alkoxy, C_{1-6}alkoxy-C_{1-6}alkyl, C_{1-6}alkoxy-carbonyl, amino, C_{1-6}alkyl-amino, (C_{1-6}alkyl)$_2$-amino, amino-C_{1-6}alkyl, and hydroxy-C_{1-6}alkyl;

R_4 is selected from C_{3-10}cycloalkyl, phenyl, heterocyclyl, and heteroaryl;

wherein heterocyclyl is a saturated or partially unsaturated 3-7 membered monocyclic, 6-10 membered bicyclic or 13-16 membered polycyclic ring system having 1, 2, or 3 heteroatom ring members independently selected from N, O, or S,

wherein heteroaryl is a 3-7 membered monocyclic or 6-10 membered bicyclic ring system having 1, 2, 3, or 4 heteroatom ring members independently selected from N, O, or S, and

wherein, each instance of C_{3-10}cycloalkyl, phenyl, heterocyclyl, and heteroaryl is optionally substituted with one, two or three R_7 substituents;

R_2 is selected from phenyl and heteroaryl,

wherein heteroaryl is a 3-7 membered monocyclic or 6-10 membered bicyclic ring system having 1, 2, 3, or 4 heteroatom ring members independently selected from N, O, or S,

wherein, each instance of phenyl and heteroaryl is optionally substituted with one, two or three R_5 substituents and optionally, with one additional R_6 substituent, or,

wherein, alternatively, each instance of phenyl and heteroaryl is optionally substituted with one, two, three or four R_5 substituents;

R_5 is, in each instance, independently selected from cyano, halogen, hydroxy, C_{1-6}alkyl, halo-C_{1-6}alkyl, C_{1-6}alkyl-carbonyl, C_{1-6}alkoxy, halo-C_{1-6}alkoxy, C_{1-6}alkoxy-C_{1-6}alkyl, C_{1-6}alkoxy-carbonyl, C_{1-6}alkoxy-carbonyl-C_{1-6}alkyl, carboxyl, C_{1-6}alkyl-carboxyl, amino, C_{1-6}alkyl-amino, $(C_{1-6}alkyl)_2$-amino, amino-C_{1-6}alkyl, amino-carbonyl, and hydroxy-C_{1-6}alkyl;

R_6 is selected from C_{3-10}cycloalkyl, phenyl, phenyl-C_{1-6}alkoxy, phenyl-oxy, heterocyclyl, and heteroaryl;

wherein heterocyclyl is a saturated or partially unsaturated 3-7 membered monocyclic, 6-10 membered bicyclic or 13-16 membered polycyclic ring system having 1, 2, or 3 heteroatom ring members independently selected from N, O, or S,

wherein heteroaryl is a 3-7 membered monocyclic or 6-10 membered bicyclic ring system having 1, 2, 3, or 4 heteroatom ring members independently selected from N, O, or S, and

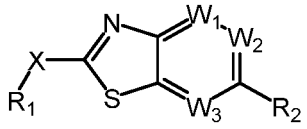
wherein, each instance of C_{3-10}cycloalkyl, phenyl, heterocyclyl, and heteroaryl is optionally substituted with one, two or three R_7 substituents; and

R_7 is, in each instance, independently selected from cyano, halogen, hydroxy, C_{1-6}alkyl, halo-C_{1-6}alkyl, C_{1-6}alkyl-carbonyl, C_{1-6}alkoxy, halo-C_{1-6}alkoxy,

C_{1-6}alkoxy-C_{1-6}alkyl, C_{1-6}alkoxy-carbonyl, amino, C_{1-6}alkyl-amino, $(C_{1-6}alkyl)_2$-amino, amino-C_{1-6}alkyl, and hydroxy-C_{1-6}alkyl;

wherein a form of the compound is selected from the group consisting of a salt, hydrate, solvate, racemate, enantiomer, diastereomer, stereoisomer, and tautomer form thereof.

2. The compound of claim 1, wherein the compound is a compound of Formula (I):



(I)

or a form thereof.

3. The compound of claim 1, wherein R_1 is heterocyclyl selected from azetidinyl, tetrahydrofuranyl, pyrrolidinyl, piperidinyl, piperazinyl, 1*H*-azepinyl, 2,3,6,7-tetrahydro-1*H*-azepinyl, azepanyl, 1,4-diazepanyl, 1,2,5,6-tetrahydropyridinyl, 1,2,3,6-tetrahydropyridinyl, octahydroindolizinyl, octahydro-1*H*-pyrrolo[3,2-*c*]pyridinyl, (3a*S*,7a*R*)-octahydro-1*H*-pyrrolo[3,2-*c*]pyridinyl, 1-azabicyclo[2.2.2]octyl, 3-azabicyclo[3.1.0]hexyl, (1*R*,5*S*)-3-azabicyclo[3.1.0]hexyl, 3-azabicyclo[3.2.1]octyl, 8-azabicyclo[3.2.1]octyl, (1*R*,5*S*)-8-azabicyclo[3.2.1]octyl, 8-azabicyclo[3.2.1]oct-2-en-yl, (1*R*,5*S*)-8-azabicyclo[3.2.1]oct-2-en-yl, 9-azabicyclo[3.3.1]nonyl, (1*R*,5*S*)-9-azabicyclo[3.3.1]nonyl, 2,5-diazabicyclo[2.2.1]heptyl, (1*S*,4*S*)-2,5-diazabicyclo[2.2.1]heptyl, 1,4-diazabicyclo[3.1.1]heptyl, 3,6-diazabicyclo[3.2.0]heptyl, 2,5-diazabicyclo[2.2.2]octyl, 1,4-diazabicyclo[3.2.1]octyl, 3,8-diazabicyclo[3.2.1]octyl, (1*R*,5*S*)-3,8-diazabicyclo[3.2.1]octyl, 1,4-diazabicyclo[3.2.2]nonyl, 3,8-diazabicyclo[4.2.0]octyl, (1*S*,6*R*)-3,8-diazabicyclo[4.2.0]octyl, (1*R*,6*S*)-3,8-diazabicyclo[4.2.0]octyl, 2-azaspiro[3.3]heptyl, 4,7-diazaspiro[2.5]octyl, 2,6-diazaspiro[3.3]heptyl, 2,6-diazaspiro[3.4]octyl, 1,6-diazaspiro[3.5]nonyl, 1,7-diazaspiro[3.5]nonyl, 2,6-diazaspiro[3.5]nonyl, 2,7-diazaspiro[3.5]nonyl, 5,8-diazaspiro[3.5]nonyl, 1,7-diazaspiro[4.4]nonyl, 2,7-diazaspiro[4.4]nonyl, 2,7-diazaspiro[4.5]decyl, and 6,9-diazaspiro[4.5]decyl, optionally substituted with one, two three, or four R_3 substituents and optionally, with one

additional R_4 substituent, or, alternatively, optionally substituted with one, two, three, four, or five R_3 substituents.

4. The compound of claim 1, wherein R_2 is heteroaryl selected from furanyl, 1*H*-pyrazolyl, 1*H*-imidazolyl, 1*H*-1,2,3-triazolyl, 4*H*-1,2,4-triazolyl, 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, 1*H*-indolyl, 2*H*-indolyl, 1*H*-indazolyl, 2*H*-indazolyl, indolizinyl, benzofuranyl, 1*H*-benzimidazolyl, 1,3-benzoxazolyl, furo[2,3-*b*]pyridinyl, furo[2,3-*c*]pyridinyl, furo[3,2-*b*]pyridinyl, furo[3,2-*c*]pyridinyl, 1*H*-pyrrolo[2,3-*b*]pyridinyl, 1*H*-pyrrolo[2,3-*c*]pyridinyl, pyrrolo[1,2-*a*]pyrimidinyl, pyrrolo[1,2-*a*]pyrazinyl, pyrrolo[1,2-*b*]pyridazinyl, pyrazolo[1,5-*a*]pyridinyl, 1*H*-pyrazolo[4,3-b]pyridinyl, 2*H*-pyrazolo[4,3-*b*]pyridinyl, 2*H*-pyrazolo[4,3-*c*]pyridinyl, pyrazolo[1,5-*a*]pyrazinyl, pyrazolo[1,5-a]pyrimidinyl, imidazo[1,2-*a*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*a*]pyrazinyl, imidazo[1,2-*b*]pyridazinyl, imidazo[1,2-*c*]pyrimidinyl, imidazo[1,5-*a*]pyridinyl, imidazo[2,1-*b*][1,3]thiazolyl, imidazo[2,1-*b*][1,3,4]thiadiazolyl, [1,3]oxazolo[4,5-*b*]pyridinyl, [1,2,4]triazolo[1,5-a]pyridnyl, [1,2,4]triazolo[1,5-b]pyridazinyl, and quinolinyl, optionally substituted with one, two or three R_5 substituents and optionally, with one additional R_6 substituent, or, alternatively, optionally substituted with one, two, three or four R_5 substituents.

5. The compound of claim 1, wherein the form of the compound is a compound salt selected from hydrochloride, hydrobromide, trifluoroacetate, formate, or dihydrochloride.

6. A compound selected from the group consisting of:

6-(2-methyl-2*H*-indazol-5-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole;
6-(2-methyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)-1,3-benzothiazole;
6-(2-methyl-2*H*-indazol-5-yl)-2-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)- 1,3-benzothiazole;
2-(2-methyl-2*H*-indazol-5-yl)-6-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole;
2-(2-methyl-2*H*-indazol-5-yl)-6-(piperidin-4-yl)-1,3-benzothiazole;
2-(2-methyl-2*H*-indazol-5-yl)-6-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)- 1,3-benzothiazole;
6-(2-methyl-2*H*-indazol-5-yl)-2-(piperazin-1-yl)-1,3-benzothiazole;

N-methyl-6-(2-methyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)-1,3-benzothiazol-2-amine;

6-(2-methyl-2*H*-indazol-5-yl)-2-(1-methylpiperidin-4-yl)-1,3-benzothiazole;

2-(2-methyl-2*H*-indazol-5-yl)-6-(1-methylpiperidin-4-yl)-1,3-benzothiazole;

N-methyl-2-(2-methyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)-1,3-benzothiazol-6-amine;

N-methyl-6-(2-methyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-b]pyridin-2-amine;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-b]pyridin-2-amine;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-b]pyridin-2-amine;

6-(2-methyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-b]pyridin-2-amine;

N-methyl-6-(2-methyl-2*H*-indazol-5-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-b]pyridin-2-amine;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-b]pyridin-2-amine;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole;

2-(2-methyl-2*H*-indazol-5-yl)-6-(1,2,3,6-tetrahydropyridin-4-yl)[1,3]thiazolo[4,5-b]pyridine;

N-methyl-6-(2-methyl-2*H*-indazol-5-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)- 1,3-benzothiazol-2-amine;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)-1,3-benzothiazole

4-fluoro-*N*-methyl-6-(2-methyl-2*H*-indazol-5-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-4-fluoro-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine;

N-methyl-5-(2-methyl-2*H*-indazol-5-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[5,4-b]pyridin-2-amine;

N-methyl-5-(2-methyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)[1,3]thiazolo[5,4-b]pyridin-2-amine;

N-methyl-6-(2-methyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

N,*N*-dimethyl-1-[6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazol-2-yl]piperidin-4-amine;

1-[6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazol-2-yl]piperidin-4-amine;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

N-methyl-6-(2-methyl-2*H*-indazol-5-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

6-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine;

6-(1*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine;

6-(2-methyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)-1,3-benzothiazol-2-amine;

5-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[5,4-b]pyridin-2-amine;

4-fluoro-*N*-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)- *N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine;

N-methyl-6-(2-methyl-2*H*-indazol-5-yl)-*N*-(pyrrolidin-3-yl)-1,3-benzothiazol-2-amine;

6-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-4-fluoro-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine;

N-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine;

2-(4-fluoropiperidin-4-yl)-6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazole;

2-(azepan-4-yl)-6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazole;

2-(2-methyl-2*H*-indazol-5-yl)-6-(piperidin-4-yl)[1,3]thiazolo[4,5-b]pyridine;

6-[4-fluoro-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazol-6-yl]- 2-methylimidazo[1,2-b]pyridazine;

6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]- 2-methylimidazo[1,2-b]pyridazine;

6-[4-fluoro-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazol-6-yl]- 2,8-dimethylimidazo[1,2-b]pyridazine;

6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]- 2,8-dimethylimidazo[1,2-b]pyridazine;

N-methyl-6-(2-methyl[1,2,4]triazolo[1,5-b]pyridazin-6-yl)- *N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine;

2-(2,7-dimethyl-2*H*-indazol-5-yl)-6-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole;

2-(2,7-dimethyl-2*H*-indazol-5-yl)-6-(piperidin-4-yl)-1,3-benzothiazole;

N-methyl-6-[2-methyl-7-(trifluoromethyl)-2*H*-indazol-5-yl]- *N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine;

6-(2-methyl-2*H*-indazol-5-yl)-2-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazole;

6-[4-fluoro-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazol-6-yl]- 2,8-dimethylimidazo[1,2-a]pyrazine;

6-(7-ethyl-2-methyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine;

6-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine;

6-(2-methyl-2*H*-indazol-5-yl)-2-(2,3,6,7-tetrahydro-1*H*-azepin-4-yl)-1,3-benzothiazole;

6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine;

6-(2-methyl-2*H*-indazol-5-yl)-2-(2-methylpiperidin-4-yl)-1,3-benzothiazole;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridine;

6-[2-methyl-7-(trifluoromethyl)-2*H*-indazol-5-yl]-2-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridine;

6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-(piperidin-4-yl)[1,3]thiazolo[4,5-b]pyridine;

2-methyl-5-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino]-1,3-benzothiazol-6-yl}-2*H*-indazole-7-carbonitrile;

N-methyl-6-(2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine;

6-(2-methyl-2*H*-indazol-5-yl)-2-[(2,2,6,6-tetramethylpiperidin-4-yl)oxy]- 1,3-benzothiazole;

6-(2-methyl-2*H*-indazol-5-yl)-2-(2-methyl-1,2,3,6-tetrahydropyridin-4-yl)- 1,3-benzothiazole;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2-methylpiperidin-4-yl)- 1,3-benzothiazol-2-amine;

6-(2-methyl-2*H*-indazol-5-yl)-2-(6-methyl-1,2,3,6-tetrahydropyridin-4-yl)- 1,3-benzothiazole;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-2-[(2,2,6,6-tetramethylpiperidin-4-yl)oxy]- 1,3-benzothiazole;

6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methyl-1,3-benzoxazole;

6-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-4-fluoro-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole;

4-fluoro-6-(2-methyl-2*H*-indazol-5-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)- 1,3-benzothiazole;

4-fluoro-6-(2-methyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)-1,3-benzothiazole;

2-methyl-5-[2-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-6-yl]-2*H*-indazole-7-carbonitrile;

6-(7-ethyl-2-methyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridine;

6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridine;

6-(2-methylimidazo[1,2-a]pyridin-6-yl)-2-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridine

5-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-1*H*-pyrazolo[4,3-b]pyridine

5-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methyl-2*H*-pyrazolo[4,3-b]pyridine;

6-(7-cyclopropyl-2-methyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine;

N-methyl-6-(2-methyl-2*H*-indazol-5-yl)-*N*-(2-methylpiperidin-4-yl)- 1,3-benzothiazol-2-amine;

6-(2-methylimidazo[1,2-a]pyridin-6-yl)-2-(piperidin-4-yl)-1,3-benzothiazole;

6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)-1,3-benzothiazole;

2-methyl-5-[2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2*H*-indazole-7-carbonitrile;

6-(7-ethyl-2-methyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)-1,3-benzothiazole;

6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

N-methyl-6-(2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

6-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

N-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

5-{4-fluoro-2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino]-1,3-benzothiazol-6-yl}-2-methyl-2*H*-indazole-7-carbonitrile;

6-[4-fluoro-2-(1-methylpiperidin-4-yl)-1,3-benzothiazol-6-yl]- 2-methylimidazo[1,2-b]pyridazine;

6-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine;

6-(2,4-dimethyl-1*H*-benzimidazol-6-yl)-2-(piperidin-4-yl)-1,3-benzothiazole;

6-(2-methyl-1*H*-benzimidazol-6-yl)-2-(piperidin-4-yl)-1,3-benzothiazole;

N-methyl-6-[2-methyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-6-yl]- *N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine;

2-methyl-6-[2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]imidazo[1,2-b]pyridazine;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-4-methoxy-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole

6-(2,7-dimethyl-2*H*-indazol-5-yl)-4-methoxy-2-(piperidin-4-yl)-1,3-benzothiazole;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazol-4-ol;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-7-fluoro-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

5-[4-fluoro-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazol-6-yl]-2-methyl-2*H*-indazole-7-carbonitrile;

1-{5-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methyl-2*H*-indazol-7-yl}methanamine;

5-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methyl-2*H*-indazole-7-carbonitrile;

N-methyl-6-(2-methylimidazo[1,2-a]pyrimidin-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

6-[2-(1-ethylpiperidin-4-yl)-4-fluoro-1,3-benzothiazol-6-yl]- 2-methylimidazo[1,2-b]pyridazine;

6-[4-fluoro-2-(1-methylpiperidin-4-yl)-1,3-benzothiazol-6-yl]- 2,8-dimethylimidazo[1,2-b]pyridazine;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-(1,2-dimethylpiperidin-4-yl)- *N*-methyl-1,3-benzothiazol-2-amine;

2-methyl-5-[2-(piperidin-4-yl)[1,3]thiazolo[5,4-d]pyrimidin-5-yl]- 2*H*-indazole-7-carbonitrile;

5-(2,7-dimethyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)[1,3]thiazolo[5,4-d]pyrimidine;

6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine;

2-methyl-6-[2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-1,3-benzoxazole;

6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-(piperidin-4-yl)-1,3-benzothiazole;

6-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-2-(piperidin-4-yl)-1,3-benzothiazole;

2-(2,2-dimethylpiperidin-4-yl)-6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazole;

N-methyl-6-[2-methyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-6-yl]- *N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

2-methyl-5-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2*H*-indazole-7-carbonitrile;

3-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridazin-6-amine;

2-{6-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol;

6-[4-fluoro-2-(piperazin-1-yl)-1,3-benzothiazol-6-yl]- 2,8-dimethylimidazo[1,2-b]pyridazine;

6-[2-(1,4-diazepan-1-yl)-4-fluoro-1,3-benzothiazol-6-yl]- 2,8-dimethylimidazo[1,2-b]pyridazine;

5-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[5,4-d]pyrimidin-2-amine;

2-methyl-5-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-2*H*-indazole-7-carbonitrile;

5-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[5,4-d]pyrimidin-2-amine;

6-[2-(4,7-diazaspiro[2.5]oct-7-yl)-4-fluoro-1,3-benzothiazol-6-yl]- 2,8-dimethylimidazo[1,2-b]pyridazine;

4-fluoro-6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)-1,3-benzothiazole;

6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4-fluoro-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine;

5-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[5,4-b]pyridin-2-amine;

N-methyl-5-(2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[5,4-b]pyridin-2-amine;

2-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-b]pyrazin-6-yl}-5-(1*H*-pyrazol-4-yl)phenol;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-b]pyrazin-2-amine;

6-[2-(3,5-dimethylpiperazin-1-yl)-4-fluoro-1,3-benzothiazol-6-yl]- 2,8-dimethylimidazo[1,2-b]pyridazine;

6-{4-fluoro-2-[(2,2,6,6-tetramethylpiperidin-4-yl)oxy]-1,3-benzothiazol-6-yl}-2,8-dimethylimidazo[1,2-b]pyridazine;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)-1,3-benzothiazol-4-ol;

6-{2-[(2,6-dimethylpiperidin-4-yl)oxy]-4-fluoro-1,3-benzothiazol-6-yl}-2,8-dimethylimidazo[1,2-b]pyridazine;

N-methyl-6-(2-methyl[1,2,4]triazolo[1,5-a]pyridin-6-yl)- *N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

2-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-5-(1*H*-pyrazol-4-yl)phenol;

2-methyl-6-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino]-1,3-benzothiazol-6-yl}imidazo[1,2-a]pyridine-8-carbonitrile;

2,8-dimethyl-6-[2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]imidazo[1,2-b]pyridazine;

2-methyl-5-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-b]pyrazin-6-yl}-2*H*-indazole-7-carbonitrile;

N-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-b]pyrazin-2-amine;

2-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-5-(1*H*-pyrazol-4-yl)phenol;

1-[6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4-fluoro-1,3-benzothiazol-2-yl]piperidin-4-ol;

6-{4-fluoro-2-[(2R)-2-methylpiperidin-4-yl]-1,3-benzothiazol-6-yl}-2-methylimidazo[1,2-b]pyridazine;

6-[4-fluoro-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazol-6-yl]-8-methoxy-2-methylimidazo[1,2-b]pyridazine;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-(2,2-dimethylpiperidin-4-yl)-*N*-methyl-1,3-benzothiazol-2-amine;

6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

2-methyl-5-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[5,4-b]pyridin-5-yl}-2*H*-indazole-7-carbonitrile;

2-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[5,4-b]pyridin-5-yl}-5-(1*H*-pyrazol-4-yl)phenol;

6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-b]pyrazin-2-amine;

6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-8-methoxy-2-methylimidazo[1,2-b]pyridazine;

4-fluoro-6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-(piperidin-4-yl)- 1,3-benzothiazole;

4-chloro-6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole;

5-[4-chloro-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazol-6-yl]-2-methyl-2*H*-indazole-7-carbonitrile;

N-(2,2-dimethylpiperidin-4-yl)-*N*-methyl-6-(2-methyl-2*H*-indazol-5-yl)- 1,3-benzothiazol-2-amine;

2-methyl-6-[2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]imidazo[1,2-a]pyrimidine;

3-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridazin-6-amine;

2-methyl-5-{6-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-2*H*-indazole-7-carbonitrile;

6-[2,3-difluoro-4-(1*H*-pyrazol-4-yl)phenyl]-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-b]pyrazin-2-amine;

6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-b]pyrazin-2-amine;

2-methyl-6-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-b]pyrazin-6-yl}imidazo[1,2-a]pyridine-8-carbonitrile;

4-fluoro-*N*-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-[(2*S*)-2-methylpiperidin-4-yl]-1,3-benzothiazol-2-amine;

6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4-fluoro-*N*-methyl-*N*-[(2*S*)-2-methylpiperidin-4-yl]-1,3-benzothiazol-2-amine;

6-[4-fluoro-2-(octahydroindolizin-7-yl)-1,3-benzothiazol-6-yl]- 2-methylimidazo[1,2-b]pyridazine;

6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-*N*,2-dimethylimidazo[1,2-b]pyridazin-8-amine;

6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-*N*,*N*,2-trimethylimidazo[1,2-b]pyridazin-8-amine;

2-methyl-6-[2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]imidazo[1,2-a]pyrazine;

2-methyl-6-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}imidazo[1,2-a]pyridine-8-carbonitrile;

5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[5,4-d]pyrimidin-2-amine;

6-(7-cyano-2-methyl-2*H*-indazol-5-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole-4-carbonitrile;

2-methyl-6-[2-(piperazin-1-yl)[1,3]thiazolo[4,5-b]pyrazin-6-yl]imidazo[1,2-a]pyridine-8-carbonitrile;

6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-(piperazin-1-yl)[1,3]thiazolo[4,5-b]pyrazine;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-(2,6-dimethylpiperidin-4-yl)-*N*-methyl-1,3-benzothiazol-2-amine;

N-(2,6-dimethylpiperidin-4-yl)-*N*-methyl-6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazol-2-amine;

5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[5,4-b]pyridin-2-amine;

2-methyl-6-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[5,4-b]pyridin-5-yl}imidazo[1,2-a]pyridine-8-carbonitrile;

2-methyl-6-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}imidazo[1,2-a]pyridine-8-carbonitrile;

6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)- 2-[(2,2,6,6-tetramethylpiperidin-4-yl)oxy][1,3]thiazolo[4,5-b]pyrazine;

2-methyl-6-{2-[(2,2,6,6-tetramethylpiperidin-4-yl)oxy][1,3]thiazolo[4,5-b]pyrazin-6-yl}imidazo[1,2-a]pyridine-8-carbonitrile;

6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-2-(piperazin-1-yl)[1,3]thiazolo[4,5-b]pyrazine;

5-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[5,4-d]pyrimidin-2-amine;

5-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[5,4-d]pyrimidin-2-amine;

4-fluoro-*N*-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-(piperidin-4-yl)-1,3-benzothiazol-2-amine;

6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4-fluoro-*N*-methyl-*N*-(piperidin-4-yl)-1,3-benzothiazol-2-amine;

8-(benzyloxy)-6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazine;

6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazin-8-amine;

6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazin-8-ol;

2-(2,6-dimethylpiperidin-4-yl)-6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazole;

4-fluoro-6-(4-fluoro-3-methoxyphenyl)-2-(piperidin-4-yl)-1,3-benzothiazole;

N-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4-fluoro-*N*-methyl-1,3-benzothiazol-2-amine;

2-methyl-5-{2-[methyl(piperidin-4-yl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-2*H*-indazole-7-carbonitrile;

6-[2-(1-azabicyclo[2.2.2]oct-4-yl)-4-fluoro-1,3-benzothiazol-6-yl]-2,8-dimethylimidazo[1,2-b]pyridazine;

6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methyl-8-phenoxyimidazo[1,2-b]pyridazine;

2-methyl-6-{2-[methyl(piperidin-4-yl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}imidazo[1,2-a]pyridine-8-carbonitrile;

5-(7-methoxy-2-methyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[5,4-d]pyrimidin-2-amine;

2-methyl-6-{2-[methyl(piperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}imidazo[1,2-a]pyridine-8-carbonitrile;

6-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-ylamino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile;

4-fluoro-6-(8-methoxy-2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine;

6-{4-fluoro-2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino]-1,3-benzothiazol-6-yl}-2-methylimidazo[1,2-b]pyridazin-8-amine;

4-fluoro-6-(8-methoxy-2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-methyl-*N*-(piperidin-4-yl)-1,3-benzothiazol-2-amine;

6-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile;

N-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine;

N-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine;

5-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methyl-2*H*-indazole-7-carbonitrile;

6-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile;

5-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-2-methyl-2*H*-indazole-7-carbonitrile;

N-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-4-fluoro-*N*-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-1,3-benzothiazol-2-amine;

6-[4-fluoro-2-(4-methylpiperidin-4-yl)-1,3-benzothiazol-6-yl]-2,8-dimethylimidazo[1,2-b]pyridazine;

N-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

N-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

5-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-ylamino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methyl-2*H*-indazole-7-carbonitrile;

2-methyl-5-{2-[methyl(piperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2*H*-indazole-7-carbonitrile;

6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

N-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[5,4-d]pyrimidin-2-amine;

N-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-5-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[5,4-d]pyrimidin-2-amine;

6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazine-8-carboxylic acid;

methyl {6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazin-8-yl}acetate;

{6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazin-8-yl}acetic acid;

2-methyl-6-{2-[(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}imidazo[1,2-a]pyridine-8-carbonitrile;

6-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yloxy][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile;

6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazine-8-carboxamide;

6-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-4-fluoro-*N*-methyl-*N*-(piperidin-4-yl)-1,3-benzothiazol-2-amine;

6-{4-fluoro-2-[methyl(piperidin-4-yl)amino]-1,3-benzothiazol-6-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile;

N-[(8-anti)-3-azabicyclo[3.2.1]oct-8-yl]-5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[5,4-d]pyrimidin-2-amine;

6-{2-[(8-anti)-3-azabicyclo[3.2.1]oct-8-yl(methyl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile;

2-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-6,8-dimethylimidazo[1,2-a]pyrazine;

6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazine-8-carbonitrile;

6-{4-fluoro-2-[methyl(piperidin-4-yl)amino]-1,3-benzothiazol-6-yl}-2-methylimidazo[1,2-b]pyridazine-8-carbonitrile;

6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

2-methyl-5-{2-[(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2*H*-indazole-7-carbonitrile;

6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

6-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino]-4-fluoro-1,3-benzothiazol-6-yl}-2-methylimidazo[1,2-b]pyridazine-8-carbonitrile;

6-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino]-4-fluoro-1,3-benzothiazol-6-yl}-2-methylimidazo[1,2-b]pyridazine-8-carboxamide;

N-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-4-fluoro-*N*-methyl-6-(2-methyl-2*H*-pyrazolo[4,3-b]pyridin-5-yl)-1,3-benzothiazol-2-amine;

2-methyl-5-(2-{methyl[(3-exo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]amino}[1,3]thiazolo[4,5-c]pyridin-6-yl)-2*H*-indazole-7-carbonitrile;

6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-[(3-exo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl][1,3]thiazolo[4,5-c]pyridin-2-amine;

2-methyl-6-(2-{methyl[(3-exo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]amino}[1,3]thiazolo[4,5-c]pyridin-6-yl)imidazo[1,2-a]pyridine-8-carbonitrile;

6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-[(3-exo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl][1,3]thiazolo[4,5-c]pyridin-2-amine;

6-{2-[ethyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile;

N-ethyl-5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[5,4-d]pyrimidin-2-amine;

2-methyl-5-(2-{[(3-exo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]amino}[1,3]thiazolo[4,5-c]pyridin-6-yl)-2*H*-indazole-7-carbonitrile;

2-methyl-6-(2-{[(3-exo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]amino}[1,3]thiazolo[4,5-c]pyridin-6-yl)imidazo[1,2-a]pyridine-8-carbonitrile;

6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-[(3-exo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl][1,3]thiazolo[4,5-c]pyridin-2-amine;

6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-[(3-exo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl][1,3]thiazolo[4,5-c]pyridin-2-amine;

N-(azetidin-3-yl)-6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4-fluoro-*N*-methyl-1,3-benzothiazol-2-amine;

5-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylpyrazolo[1,5-a]pyrimidine;

4-fluoro-*N*-methyl-6-(2-methylpyrazolo[1,5-a]pyrimidin-5-yl)-*N*-(piperidin-4-yl)-1,3-benzothiazol-2-amine;

6-{2-[9-azabicyclo[3.3.1]non-3-yl(methyl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile;

5-{2-[9-azabicyclo[3.3.1]non-3-yl(methyl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methyl-2*H*-indazole-7-carbonitrile;

N-(9-azabicyclo[3.3.1]non-3-yl)-6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine;

5-{2-[(1,5-dimethyl-8-azabicyclo[3.2.1]oct-3-yl)(methyl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-2-methyl-2*H*-indazole-7-carbonitrile;

6-(2-{[(1*R*)-1,5-dimethyl-8-azabicyclo[3.2.1]oct-3-yl](methyl)amino}[1,3]thiazolo[5,4-d]pyrimidin-5-yl)-2-methylimidazo[1,2-a]pyridine-8-carbonitrile;

6-{2-[(1*R*,5*S*)-9-azabicyclo[3.3.1]non-3-yl(methyl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile;

N-[(1*R*,5*S*)-9-azabicyclo[3.3.1]non-3-yl]-5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[5,4-d]pyrimidin-2-amine;

4-fluoro-*N*-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-[(2*S*,4*S*)-2-methylpiperidin-4-yl]-1,3-benzothiazol-2-amine;

4-fluoro-*N*-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-[(2*S*,4*R*)-2-methylpiperidin-4-yl]-1,3-benzothiazol-2-amine;

N-(9-azabicyclo[3.3.1]non-3-yl)-*N*-methyl-6-(2-methylimidazo[1,2-a]pyridine-6-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

N-(9-azabicyclo[3.3.1]non-3-yl)-6-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine;

N-(9-azabicyclo[3.3.1]non-3-yl)-*N*-methyl-6-(2-methyl-2*H*-indazol-5-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

N-(9-azabicyclo[3.3.1]non-3-yl)-6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine;

N-(9-azabicyclo[3.3.1]non-3-yl)-6-(7-methoxy-2-methyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine;

5-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[5,4-d]pyrimidin-2-amine;

2-methyl-6-{2-[(1,2,2,6,6-pentamethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}imidazo[1,2-a]pyridine-8-carbonitrile;

6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-(1,2,2,6,6-pentamethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

2-methyl-5-{2-[(1,2,2,6,6-pentamethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2*H*-indazole-7-carbonitrile;

6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-(1,2,2,6,6-pentamethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

2-methyl-6-{2-[methyl(9-methyl-9-azabicyclo[3.3.1]non-3-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}imidazo[1,2-a]pyridine-8-carbonitrile;

6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(9-methyl-9-azabicyclo[3.3.1]non-3-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

2-methyl-5-{2-[methyl(9-methyl-9-azabicyclo[3.3.1]non-3-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2*H*-indazole-7-carbonitrile;

6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(9-methyl-9-azabicyclo[3.3.1]non-3-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

2-{2-[methyl(piperidin-4-yl)amino][1,3]thiazolo[4,5-b]pyrazin-6-yl}-5-(1*H*-pyrazol-4-yl)phenol;

2-methyl-6-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-1,3-benzoxazole-4-carbonitrile;

6-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino][1,3]thiazolo[5,4-b]pyridin-5-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile;

N-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[5,4-b]pyridin-2-amine;

5-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino][1,3]thiazolo[5,4-b]pyridin-5-yl}-2-methyl-2*H*-indazole-7-carbonitrile

6-{2-[(3-exo)-9-azabicyclo[3.3.1]non-3-yl(methyl)amino][1,3]thiazolo[5,4-b]pyridin-5-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile;

N-[(3-exo)-9-azabicyclo[3.3.1]non-3-yl]-5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[5,4-b]pyridin-2-amine;

5-{2-[(3-exo)-9-azabicyclo[3.3.1]non-3-yl(methyl)amino][1,3]thiazolo[5,4-b]pyridin-5-yl}-2-methyl-2*H*-indazole-7-carbonitrile;

2-{6-[methyl(piperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol;

2-{6-[methyl(1-methylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol;

N-[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl]-5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[5,4-d]pyrimidin-2-amine;

6-(2-{[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridin-6-yl)-2-methylimidazo[1,2-a]pyridine-8-carbonitrile;

N-[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl]-6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine;

5-(2-{[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridin-6-yl)-2-methyl-2*H*-indazole-7-carbonitrile;

6-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-b]pyrazin-2-amine;

N-[(1*R*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl]-5-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[5,4-d]pyrimidin-2-amine;

6-(2-{[(1*R*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl](methyl)amino}[1,3]thiazolo[5,4-d]pyrimidin-5-yl)-2-methyl-1,3-benzoxazole-4-carbonitrile;

6-(2-{[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl](methyl)amino}[1,3]thiazolo[5,4-b]pyridin-5-yl)-2-methylimidazo[1,2-a]pyridine-8-carbonitrile;

N-[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl]-5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[5,4-b]pyridin-2-amine;

5-(2-{[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl](methyl)amino}[1,3]thiazolo[5,4-b]pyridin-5-yl)-2-methyl-2*H*-indazole-7-carbonitrile;

N-[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl]-5-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[5,4-b]pyridin-2-amine;

N-(9-azabicyclo[3.3.1]nonan-3-yl)-5-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[5,4-b]pyridin-2-amine;

6-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

6-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

N-[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl]-6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine;

N-[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl]-6-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine;

N-[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl]-*N*-methyl-6-(2-methylimidazo[1,2-a]pyridin-6-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

6-(2-{[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridin-6-yl)-2-methyl-1,3-benzoxazole-4-carbonitrile;

N-methyl-6-(2-methylimidazo[2,1-b][1,3]thiazol-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

6-(2-{[(1*R*,3*r*,5*S*)-1,5-diethyl-8-azabicyclo[3.2.1]octan-3-yl](methyl)amino}[1,3]thiazolo[5,4-d]pyrimidin-5-yl)-2-methylimidazo[1,2-a]pyridine-8-carbonitrile;

N-[(1*R*,3*r*,5*S*)-1,5-diethyl-8-azabicyclo[3.2.1]octan-3-yl]-5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[5,4-d]pyrimidin-2-amine;

N-methyl-6-(3-methylimidazo[2,1-b][1,3]thiazol-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

6-{4-fluoro-2-[(piperidin-4-yl)oxy]-1,3-benzothiazol-6-yl}-2,8-dimethylimidazo[1,2-b]pyridazine;

4-fluoro-6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-2-[(piperidin-4-yl)oxy]-1,3-benzothiazole;

N-methyl-6-(2-methylimidazo[2,1-b][1,3,4]thiadiazol-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine;

2-methyl-6-{2-[(2,2,6,6-tetramethylpiperidin-4-yl)oxy][1,3]thiazolo[4,5-c]pyridin-6-yl}imidazo[1,2-a]pyridine-8-carbonitrile;

6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-[(2,2,6,6-tetramethylpiperidin-4-yl)oxy][1,3]thiazolo[4,5-c]pyridine;

2-methyl-5-{2-[(2,2,6,6-tetramethylpiperidin-4-yl)oxy][1,3]thiazolo[4,5-c]pyridin-6-yl}-2*H*-indazole-7-carbonitrile;

6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-2-[(2,2,6,6-tetramethylpiperidin-4-yl)oxy][1,3]thiazolo[4,5-c]pyridine;

2-methyl-6-{2-[(piperidin-4-yl)oxy][1,3]thiazolo[4,5-c]pyridin-6-yl}imidazo[1,2-a]pyridine-8-carbonitrile;

6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-[(piperidin-4-yl)oxy][1,3]thiazolo[4,5-c]pyridine;

2-methyl-5-{2-[(piperidin-4-yl)oxy][1,3]thiazolo[4,5-c]pyridin-6-yl}-2*H*-indazole-7-carbonitrile;

6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-2-[(piperidin-4-yl)oxy][1,3]thiazolo[4,5-c]pyridine;

6-{4-fluoro-2-[(piperidin-4-yl)oxy]-1,3-benzothiazol-6-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile;

5-{4-fluoro-2-[(piperidin-4-yl)oxy]-1,3-benzothiazol-6-yl}-2-methyl-2*H*-indazole-7-carbonitrile;

6-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-4-fluoro-2-[(piperidin-4-yl)oxy]-1,3-benzothiazole;

6-{4-fluoro-2-[(1-methylpiperidin-4-yl)oxy]-1,3-benzothiazol-6-yl}-2,8-dimethylimidazo[1,2-b]pyridazine;

6-{2-[(1-ethylpiperidin-4-yl)oxy]-4-fluoro-1,3-benzothiazol-6-yl}-2,8-dimethylimidazo[1,2-b]pyridazine;

N-[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl]-6-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine;

N-[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl]-5-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-*N*-methyl[1,3]thiazolo[5,4-d]pyrimidin-2-amine;

6-(2-{[(3*R*,4*R*)-3-fluoro-2,2,6,6-tetramethylpiperidin-4-yl](methyl)amino}[1,3]thiazolo[5,4-d]pyrimidin-5-yl)-2-methylimidazo[1,2-a]pyridine-8-carbonitrile;

6-(2-{[(3*R*,4*R*)-3-fluoro-2,2,6,6-tetramethylpiperidin-4-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridin-6-yl)-2-methylimidazo[1,2-a]pyridine-8-carbonitrile;

N-[(1*R*,2*S*,3*S*,5*S*)-2-fluoro-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl]-6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine;

5-(1*H*-imidazol-1-yl)-2-{6-[methyl(piperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}phenol;

3-[2,5-difluoro-4-(1*H*-pyrazol-4-yl)phenyl]-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridazin-6-amine;

5-(3-fluoro-1*H*-pyrazol-4-yl)-2-{6-[methyl(piperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}phenol;

5-(1*H*-imidazol-1-yl)-2-{6-[methyl(1-methylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}phenol;

3-[2,5-difluoro-4-(3-fluoro-1*H*-pyrazol-4-yl)phenyl]-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridazin-6-amine;

5-(3-fluoro-1*H*-pyrazol-4-yl)-2-{6-[methyl(1-methylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}phenol;

2-{6-[(3*R*,5*S*)-3,5-dimethylpiperazin-1-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol;

2-[6-(piperazin-1-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(1*H*-pyrazol-4-yl)phenol;

5-(1*H*-pyrazol-4-yl)-2-[6-(1,2,3,6-tetrahydropyridin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-yl]phenol;

2-(6-{[(3*R*,4*S*)-4-fluoro-1-methylpyrrolidin-3-yl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol;

5-(1*H*-pyrazol-4-yl)-2-[6-(2,2,6,6-tetramethyl-1,2,3,6-tetrahydropyridin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-yl]phenol;

2-[6-(2,6-diazaspiro[3.5]nonan-2-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(1*H*-pyrazol-4-yl)phenol;

2-[6-(7-methyl-1,7-diazaspiro[3.5]nonan-1-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(1*H*-pyrazol-4-yl)phenol;

2-[6-(7-methyl-2,7-diazaspiro[4.4]nonan-2-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(1*H*-pyrazol-4-yl)phenol;

2-[6-(2,7-diazaspiro[3.5]nonan-2-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(3-fluoro-1*H*-pyrazol-4-yl)phenol;

2-(6-{[(3*S*,4*S*)-4-fluoro-1-methylpyrrolidin-3-yl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol;

2-{6-[methyl(1-methylazetidin-3-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol;

2-{6-[(3a*S*,7a*R*)-octahydro-1*H*-pyrrolo[3,2-c]pyridin-1-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol;

2-(6-{methyl[(1*s*,4*s*)-4-(methylamino)cyclohexyl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol;

2-(6-{[(3*R*,4*S*)-4-fluoropyrrolidin-3-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol;

2-{6-[(3a*S*,7a*R*)-5-methyloctahydro-1*H*-pyrrolo[3,2-c]pyridin-1-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol;

2-(6-{methyl[(3*R*)-piperidin-3-yl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol;

2-(6-{methyl[(3*S*)-piperidin-3-yl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol;

2-(6-{methyl[3-(methylamino)cyclobutyl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol;

2-(6-{[(1*r*,4*r*)-4-(dimethylamino)cyclohexyl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol;

2-(6-{methyl[(3*S*)-1-methylpiperidin-3-yl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol;

2-{6-[(azetidin-3-yl)(methyl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol;

2-[6-(1,7-diazaspiro[3.5]nonan-1-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(1*H*-pyrazol-4-yl)phenol;

2-{6-[(3,3-dimethylpiperidin-4-yl)(methyl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol;

2-{6-[(2-azaspiro[3.3]heptan-6-yl)(methyl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol;

2-{6-[(piperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol;

2-(6-{[(3*R*,4*S*)-3-fluoropiperidin-4-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol;

5-{2-[(2*R*,4*r*,6*S*)-2,6-dimethylpiperidin-4-yl]-4-fluoro-1,3-benzothiazol-6-yl}-2,7-dimethyl[1,3]oxazolo[5,4-b]pyridine;

2-{6-[methyl(1,3,3-trimethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol;

2-(6-{methyl[(1*s*,3*s*)-3-(methylamino)cyclobutyl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol;

2-{6-[(3a*R*,7a*S*)-octahydro-1*H*-pyrrolo[2,3-c]pyridin-1-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol;

2-[6-(1,6-diazaspiro[3.5]nonan-1-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(1*H*-pyrazol-4-yl)phenol;

2-(6-{[(1*s*,3*s*)-3-(dimethylamino)cyclobutyl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol;

2-(6-{[(3*R*,4*R*)-3-fluoropiperidin-4-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol;

2-{6-[(1-methylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol;

5-(1*H*-pyrazol-4-yl)-2-{6-[(pyrrolidin-3-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}phenol;

2-[6-(2,6-diazaspiro[3.3]heptan-2-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(3-fluoro-1*H*-pyrazol-4-yl)phenol;

2-{6-[(3a*R*,7a*S*)-6-methyloctahydro-1*H*-pyrrolo[2,3-c]pyridin-1-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol;

2-[6-(6-methyl-1,6-diazaspiro[3.5]nonan-1-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(1*H*-pyrazol-4-yl)phenol;

2-(6-{[(2*S*,4*S*)-2-(hydroxymethyl)piperidin-4-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol;

2-(6-{[(2*S*,4*S*)-2-(hydroxymethyl)-1-methylpiperidin-4-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol;

2-{6-[(1-methylpyrrolidin-3-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol;

2-{6-[methyl(pyrrolidin-3-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol;

2-{6-[methyl(1-methylpyrrolidin-3-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol;

2-(6-{methyl[(1*r*,3*r*)-3-(methylamino)cyclobutyl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol;

5-{2-[(1,2-dimethylpiperidin-4-yl)(methyl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methyl-2*H*-indazole-7-carbonitrile;

N-(1,2-dimethylpiperidin-4-yl)-6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine;

6-{2-[(1,2-dimethylpiperidin-4-yl)(methyl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile;

N-(1,2-dimethylpiperidin-4-yl)-6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine;

2-(6-{[(3*S*,4*S*)-4-fluoropyrrolidin-3-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol;

2-(6-{[(3*S*,4*S*)-4-fluoro-1-methylpyrrolidin-3-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol;

2-{6-[(1-cyclopropylpiperidin-4-yl)(methyl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol;

2-(6-{[1-(2-fluoroethyl)piperidin-4-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol;

5-(3-fluoro-1*H*-pyrazol-4-yl)-2-[6-(6-methyl-2,6-diazaspiro[3.3]heptan-2-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]phenol;

2-{6-[(1*S*,6*R*)-3,8-diazabicyclo[4.2.0]octan-8-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol;

5-(3-fluoro-1*H*-pyrazol-4-yl)-2-{6-[methyl(pyrrolidin-3-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}phenol;

2-{6-[(1*S*,6*R*)-3-methyl-3,8-diazabicyclo[4.2.0]octan-8-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol;

2-{6-[(1*R*,6*S*)-3,8-diazabicyclo[4.2.0]octan-8-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol;

2-{6-[(1*R*,6*S*)-3-methyl-3,8-diazabicyclo[4.2.0]octan-8-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol;

5-(3-fluoro-1*H*-pyrazol-4-yl)-2-{6-[methyl(1-methylpyrrolidin-3-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}phenol;

5-(3-fluoro-1*H*-pyrazol-4-yl)-2-[6-(7-methyl-2,7-diazaspiro[3.5]nonan-2-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]phenol;

2-{6-[methyl(1-propylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol;

2-(6-{methyl[(2*S*,4*S*)-2-methylpiperidin-4-yl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol;

2-(6-{[(2*S*,4*S*)-1,2-dimethylpiperidin-4-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol;

2-(6-{methyl[(2*R*,4*S*)-2-methylpiperidin-4-yl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol;

2-(6-{[(2*R*,4*S*)-1,2-dimethylpiperidin-4-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol;

2-{6-[(azepan-4-yl)(methyl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(3-fluoro-1*H*-pyrazol-4-yl)phenol; and

2-(6-{[1-(2-hydroxyethyl)piperidin-4-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol;

or a form thereof.

7. The compound of claim 6, wherein the form of the compound is a compound salt or a form thereof selected from the group consisting of:

2-(2-methyl-2*H*-indazol-5-yl)-6-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole hydrochloride;

2-(2-methyl-2*H*-indazol-5-yl)-6-(piperidin-4-yl)-1,3-benzothiazole hydrochloride;

2-(2-methyl-2*H*-indazol-5-yl)-6-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole hydrochloride;

N-methyl-6-(2-methyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride;

2-(2-methyl-2*H*-indazol-5-yl)-6-(1-methylpiperidin-4-yl)-1,3-benzothiazole hydrochloride;

N-methyl-2-(2-methyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)-1,3-benzothiazol-6-amine hydrochloride;

N-methyl-6-(2-methyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-b]pyridin-2-amine hydrochloride;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-b]pyridin-2-amine hydrochloride;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-b]pyridin-2-amine hydrochloride;

6-(2-methyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-b]pyridin-2-amine hydrochloride;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole hydrochloride;

2-(2-methyl-2*H*-indazol-5-yl)-6-(1,2,3,6-tetrahydropyridin-4-yl)[1,3]thiazolo[4,5-b]pyridine hydrochloride;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)-1,3-benzothiazole hydrochloride;

N-methyl-5-(2-methyl-2*H*-indazol-5-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[5,4-b]pyridin-2-amine hydrochloride;

N-methyl-5-(2-methyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)[1,3]thiazolo[5,4-b]pyridin-2-amine hydrochloride;

N-methyl-6-(2-methyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride;

N,*N*-dimethyl-1-[6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazol-2-yl]piperidin-4-amine hydrochloride;

1-[6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazol-2-yl]piperidin-4-amine hydrochloride;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride;

6-(1*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride;

6-(2-methyl-2*H*-indazol-5-yl)-*N*-(piperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride;

5-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[5,4-b]pyridin-2-amine hydrochloride;

N-methyl-6-(2-methyl-2*H*-indazol-5-yl)-*N*-(pyrrolidin-3-yl)-1,3-benzothiazol-2-amine hydrochloride;

N-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride;

2-(4-fluoropiperidin-4-yl)-6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazole hydrochloride;

2-(azepan-4-yl)-6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazole hydrochloride;

2-(2-methyl-2*H*-indazol-5-yl)-6-(piperidin-4-yl)[1,3]thiazolo[4,5-b]pyridine hydrochloride;

6-[4-fluoro-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazine hydrochloride;

6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazine hydrochloride;

6-[4-fluoro-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazol-6-yl]-2,8-dimethylimidazo[1,2-b]pyridazine hydrochloride;

6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2,8-dimethylimidazo[1,2-b]pyridazine hydrochloride;

2-(2,7-dimethyl-2*H*-indazol-5-yl)-6-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole hydrochloride;

2-(2,7-dimethyl-2*H*-indazol-5-yl)-6-(piperidin-4-yl)-1,3-benzothiazole hydrochloride;

N-methyl-6-[2-methyl-7-(trifluoromethyl)-2*H*-indazol-5-yl]-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride;

6-[4-fluoro-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazol-6-yl]-2,8-dimethylimidazo[1,2-a]pyrazine hydrochloride;

6-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride;

6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride;

6-(2-methyl-2*H*-indazol-5-yl)-2-(2-methylpiperidin-4-yl)-1,3-benzothiazole hydrochloride;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridine hydrochloride;

6-[2-methyl-7-(trifluoromethyl)-2*H*-indazol-5-yl]-2-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridine hydrochloride;

6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-2-(piperidin-4-yl)[1,3]thiazolo[4,5-b]pyridine hydrochloride;

2-methyl-5-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino]-1,3-benzothiazol-6-yl}-2*H*-indazole-7-carbonitrile hydrochloride;

N-methyl-6-(2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride;

6-(2-methyl-2*H*-indazol-5-yl)-2-(2-methyl-1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole hydrochloride;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2-methylpiperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride;

6-(2-methyl-2*H*-indazol-5-yl)-2-(6-methyl-1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole hydrochloride;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-2-[(2,2,6,6-tetramethylpiperidin-4-yl)oxy]-1,3-benzothiazole hydrochloride;

6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methyl-1,3-benzoxazole hydrochloride;

6-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-4-fluoro-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole hydrochloride;

4-fluoro-6-(2-methyl-2*H*-indazol-5-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole hydrochloride;

4-fluoro-6-(2-methyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)-1,3-benzothiazole hydrochloride;

2-methyl-5-[2-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-6-yl]-2*H*-indazole-7-carbonitrile hydrochloride;

6-(7-ethyl-2-methyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridine hydrochloride;

6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridine hydrochloride;

6-(2-methylimidazo[1,2-a]pyridin-6-yl)-2-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridine hydrochloride;

5-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-1*H*-pyrazolo[4,3-b]pyridine hydrochloride;

5-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methyl-2*H*-pyrazolo[4,3-b]pyridine hydrochloride;

6-(7-cyclopropyl-2-methyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride;

N-methyl-6-(2-methyl-2*H*-indazol-5-yl)-*N*-(2-methylpiperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride;

2-methyl-5-[2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2*H*-indazole-7-carbonitrile hydrochloride;

6-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride;

6-(2,4-dimethyl-1*H*-benzimidazol-6-yl)-2-(piperidin-4-yl)-1,3-benzothiazole hydrochloride;

6-(2-methyl-1*H*-benzimidazol-6-yl)-2-(piperidin-4-yl)-1,3-benzothiazole dihydrochloride;

2-methyl-6-[2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]imidazo[1,2-b]pyridazine hydrochloride;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-4-methoxy-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole hydrochloride;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-4-methoxy-2-(piperidin-4-yl)-1,3-benzothiazole hydrochloride;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazol-4-ol hydrobromide

5-[4-fluoro-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazol-6-yl]-2-methyl-2*H*-indazole-7-carbonitrile hydrochloride;

1-{5-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methyl-2*H*-indazol-7-yl}methanamine dihydrochloride;

5-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methyl-2*H*-indazole-7-carbonitrile hydrochloride;

2-methyl-5-[2-(piperidin-4-yl)[1,3]thiazolo[5,4-d]pyrimidin-5-yl]-2*H*-indazole-7-carbonitrile hydrochloride;

5-(2,7-dimethyl-2*H*-indazol-5-yl)-2-(piperidin-4-yl)[1,3]thiazolo[5,4-d]pyrimidine hydrochloride;

6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride;

6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-(piperidin-4-yl)-1,3-benzothiazole hydrochloride;

6-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-2-(piperidin-4-yl)-1,3-benzothiazole hydrochloride;

2-(2,2-dimethylpiperidin-4-yl)-6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazole hydrochloride;

2-{6-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol hydrochloride;

2-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-b]pyrazin-6-yl}-5-(1*H*-pyrazol-4-yl)phenol hydrochloride;

6-[2-(3,5-dimethylpiperazin-1-yl)-4-fluoro-1,3-benzothiazol-6-yl]-2,8-dimethylimidazo[1,2-b]pyridazine hydrochloride;

6-{4-fluoro-2-[(2,2,6,6-tetramethylpiperidin-4-yl)oxy]-1,3-benzothiazol-6-yl}-2,8-dimethylimidazo[1,2-b]pyridazine hydrochloride;

6-{2-[(2,6-dimethylpiperidin-4-yl)oxy]-4-fluoro-1,3-benzothiazol-6-yl}-2,8-dimethylimidazo[1,2-b]pyridazine hydrochloride;

2-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-5-(1*H*-pyrazol-4-yl)phenol hydrochloride;

2-methyl-6-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino]-1,3-benzothiazol-6-yl}imidazo[1,2-a]pyridine-8-carbonitrile hydrochloride;

2,8-dimethyl-6-[2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]imidazo[1,2-b]pyridazine hydrochloride;

2-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-5-(1*H*-pyrazol-4-yl)phenol hydrochloride;

6-{4-fluoro-2-[(2*R*)-2-methylpiperidin-4-yl]-1,3-benzothiazol-6-yl}-2-methylimidazo[1,2-b]pyridazine hydrochloride;

6-[4-fluoro-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazol-6-yl]-8-methoxy-2-methylimidazo[1,2-b]pyridazine hydrochloride;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-(2,2-dimethylpiperidin-4-yl)-*N*-methyl-1,3-benzothiazol-2-amine hydrochloride;

2-{2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino][1,3]thiazolo[5,4-b]pyridin-5-yl}-5-(1*H*-pyrazol-4-yl)phenol hydrochloride;

6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-8-methoxy-2-methylimidazo[1,2-b]pyridazine hydrochloride;

4-fluoro-6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-(piperidin-4-yl)-1,3-benzothiazole hydrochloride;

4-chloro-6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole hydrochloride;

5-[4-chloro-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazol-6-yl]-2-methyl-2*H*-indazole-7-carbonitrile hydrochloride;

N-(2,2-dimethylpiperidin-4-yl)-*N*-methyl-6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazol-2-amine hydrochloride;

6-[2,3-difluoro-4-(1*H*-pyrazol-4-yl)phenyl]-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-b]pyrazin-2-amine hydrochloride;

4-fluoro-*N*-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-[(2*S*)-2-methylpiperidin-4-yl]-1,3-benzothiazol-2-amine hydrochloride;

6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4-fluoro-*N*-methyl-*N*-[(2*S*)-2-methylpiperidin-4-yl]-1,3-benzothiazol-2-amine hydrochloride;

6-[4-fluoro-2-(octahydroindolizin-7-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazine hydrochloride;

6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-*N*,2-dimethylimidazo[1,2-b]pyridazin-8-amine hydrochloride;

6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-*N*,*N*,2-trimethylimidazo[1,2-b]pyridazin-8-amine hydrochloride;

6-(7-cyano-2-methyl-2*H*-indazol-5-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-1,3-benzothiazole-4-carbonitrile hydrochloride;

2-methyl-6-[2-(piperazin-1-yl)[1,3]thiazolo[4,5-b]pyrazin-6-yl]imidazo[1,2-a]pyridine-8-carbonitrile hydrochloride;

6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-(piperazin-1-yl)[1,3]thiazolo[4,5-b]pyrazine hydrochloride;

6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-(2,6-dimethylpiperidin-4-yl)-*N*-methyl-1,3-benzothiazol-2-amine hydrochloride;

N-(2,6-dimethylpiperidin-4-yl)-*N*-methyl-6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazol-2-amine hydrochloride;

6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-2-(piperazin-1-yl)[1,3]thiazolo[4,5-b]pyrazine hydrochloride;

4-fluoro-*N*-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-(piperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride;

6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4-fluoro-*N*-methyl-*N*-(piperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride;

8-(benzyloxy)-6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazine hydrochloride;

6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazin-8-amine hydrochloride;

6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazin-8-ol hydrochloride;

2-(2,6-dimethylpiperidin-4-yl)-6-(2-methyl-2*H*-indazol-5-yl)-1,3-benzothiazole hydrochloride;

4-fluoro-6-(4-fluoro-3-methoxyphenyl)-2-(piperidin-4-yl)-1,3-benzothiazole hydrochloride;

N-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4-fluoro-*N*-methyl-1,3-benzothiazol-2-amine hydrochloride;

2-methyl-5-{2-[methyl(piperidin-4-yl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-2*H*-indazole-7-carbonitrile hydrochloride;

6-[2-(1-azabicyclo[2.2.2]oct-4-yl)-4-fluoro-1,3-benzothiazol-6-yl]-2,8-dimethylimidazo[1,2-b]pyridazine hydrochloride;

6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methyl-8-phenoxyimidazo[1,2-b]pyridazine hydrochloride;

2-methyl-6-{2-[methyl(piperidin-4-yl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}imidazo[1,2-a]pyridine-8-carbonitrile hydrochloride;

2-methyl-6-{2-[methyl(piperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}imidazo[1,2-a]pyridine-8-carbonitrile hydrochloride;

6-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-ylamino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile hydrochloride;

6-{4-fluoro-2-[methyl(2,2,6,6-tetramethylpiperidin-4-yl)amino]-1,3-benzothiazol-6-yl}-2-methylimidazo[1,2-b]pyridazin-8-amine hydrochloride;

4-fluoro-6-(8-methoxy-2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-methyl-*N*-(piperidin-4-yl)-1,3-benzothiazol-2-amine hydrochloride;

6-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile hydrochloride;

N-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride;

N-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride;

5-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methyl-2*H*-indazole-7-carbonitrile hydrochloride;

6-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile hydrochloride;

5-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-2-methyl-2*H*-indazole-7-carbonitrile hydrochloride;

N-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-4-fluoro-*N*-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-1,3-benzothiazol-2-amine hydrochloride;

6-[4-fluoro-2-(4-methylpiperidin-4-yl)-1,3-benzothiazol-6-yl]-2,8-dimethylimidazo[1,2-b]pyridazine hydrochloride;

N-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride;

N-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride;

5-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-ylamino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methyl-2*H*-indazole-7-carbonitrile hydrochloride;

2-methyl-5-{2-[methyl(piperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2*H*-indazole-7-carbonitrile hydrochloride;

6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride;

6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride;

N-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[5,4-d]pyrimidin-2-amine hydrochloride;

N-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-5-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[5,4-d]pyrimidin-2-amine hydrochloride;

6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazine-8-carboxylic acid hydrochloride;

methyl {6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazin-8-yl}acetate hydrochloride;

{6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazin-8-yl}acetic acid hydrochloride;

6-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yloxy][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile hydrochloride;

6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazine-8-carboxamide trifluoroacetate;

6-{4-fluoro-2-[methyl(piperidin-4-yl)amino]-1,3-benzothiazol-6-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile hydrochloride;

N-[(8-anti)-3-azabicyclo[3.2.1]oct-8-yl]-5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[5,4-d]pyrimidin-2-amine hydrochloride;

6-{2-[(8-anti)-3-azabicyclo[3.2.1]oct-8-yl(methyl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile hydrochloride;

2-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-6,8-dimethylimidazo[1,2-a]pyrazine hydrochloride;

6-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylimidazo[1,2-b]pyridazine-8-carbonitrile hydrochloride;

6-{4-fluoro-2-[methyl(piperidin-4-yl)amino]-1,3-benzothiazol-6-yl}-2-methylimidazo[1,2-b]pyridazine-8-carbonitrile hydrochloride;

6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride;

6-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino]-4-fluoro-1,3-benzothiazol-6-yl}-2-methylimidazo[1,2-b]pyridazine-8-carbonitrile hydrochloride;

6-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino]-4-fluoro-1,3-benzothiazol-6-yl}-2-methylimidazo[1,2-b]pyridazine-8-carboxamide hydrochloride;

N-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-4-fluoro-*N*-methyl-6-(2-methyl-2*H*-pyrazolo[4,3-b]pyridin-5-yl)-1,3-benzothiazol-2-amine hydrochloride;

N-(azetidin-3-yl)-6-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4-fluoro-*N*-methyl-1,3-benzothiazol-2-amine hydrochloride;

5-[4-fluoro-2-(piperidin-4-yl)-1,3-benzothiazol-6-yl]-2-methylpyrazolo[1,5-a]pyrimidine hydrochloride;

4-fluoro-*N*-methyl-6-(2-methylpyrazolo[1,5-a]pyrimidin-5-yl)-*N*-(piperidin-4-yl)-,3-benzothiazol-2-amine hydrochloride;

6-{2-[9-azabicyclo[3.3.1]non-3-yl(methyl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile hydrochloride;

5-{2-[9-azabicyclo[3.3.1]non-3-yl(methyl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2-methyl-2*H*-indazole-7-carbonitrile hydrochloride;

N-(9-azabicyclo[3.3.1]non-3-yl)-6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride;

6-{2-[(1*R*,5*S*)-9-azabicyclo[3.3.1]non-3-yl(methyl)amino][1,3]thiazolo[5,4-d]pyrimidin-5-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile hydrochloride;

N-[(1*R*,5*S*)-9-azabicyclo[3.3.1]non-3-yl]-5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[5,4-d]pyrimidin-2-amine hydrochloride;

4-fluoro-*N*-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-[(2*S*,4*S*)-2-methylpiperidin-4-yl]-1,3-benzothiazol-2-amine hydrochloride;

4-fluoro-*N*-methyl-6-(2-methylimidazo[1,2-b]pyridazin-6-yl)-*N*-[(2*S*,4*R*)-2-methylpiperidin-4-yl]-1,3-benzothiazol-2-amine hydrochloride;

N-(9-azabicyclo[3.3.1]non-3-yl)-*N*-methyl-6-(2-methylimidazo[1,2-a]pyridin-6-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride;

N-(9-azabicyclo[3.3.1]non-3-yl)-6-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride;

N-(9-azabicyclo[3.3.1]non-3-yl)-*N*-methyl-6-(2-methyl-2*H*-indazol-5-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride;

N-(9-azabicyclo[3.3.1]non-3-yl)-6-(2,7-dimethyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride;

N-(9-azabicyclo[3.3.1]non-3-yl)-6-(7-methoxy-2-methyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride;

2-methyl-6-{2-[(1,2,2,6,6-pentamethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}imidazo[1,2-a]pyridine-8-carbonitrile hydrochloride;

6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-(1,2,2,6,6-pentamethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride;

2-methyl-5-{2-[(1,2,2,6,6-pentamethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridin-6-yl}-2*H*-indazole-7-carbonitrile hydrochloride;

6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-(1,2,2,6,6-pentamethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride;

2-{2-[methyl(piperidin-4-yl)amino][1,3]thiazolo[4,5-b]pyrazin-6-yl}-5-(1*H*-pyrazol-4-yl)phenol hydrochloride;

6-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino][1,3]thiazolo[5,4-b]pyridin-5-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile hydrochloride;

N-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[5,4-b]pyridin-2-amine hydrochloride;

5-{2-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl(methyl)amino][1,3]thiazolo[5,4-b]pyridin-5-yl}-2-methyl-2*H*-indazole-7-carbonitrile hydrochloride;

6-{2-[(3-exo)-9-azabicyclo[3.3.1]non-3-yl(methyl)amino][1,3]thiazolo[5,4-b]pyridin-5-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile hydrochloride;

N-[(3-exo)-9-azabicyclo[3.3.1]non-3-yl]-5-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[5,4-b]pyridin-2-amine hydrochloride;

5-{2-[(3-exo)-9-azabicyclo[3.3.1]non-3-yl(methyl)amino][1,3]thiazolo[5,4-b]pyridin-5-yl}-2-methyl-2*H*-indazole-7-carbonitrile hydrochloride;

2-{6-[methyl(piperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol hydrochloride;

2-{6-[methyl(1-methylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol hydrochloride;

N-[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl]-6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride;

6-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-b]pyrazin-2-amine hydrochloride;

N-(9-azabicyclo[3.3.1]nonan-3-yl)-5-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-*N*-methyl[1,3]thiazolo[5,4-b]pyridin-2-amine hydrochloride;

6-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride;

6-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-*N*-methyl-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride;

6-(2-{[(1*R*,3*s*,5*S*)-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridin-6-yl)-2-methyl-1,3-benzoxazole-4-carbonitrile trifluoroacetate;

N-methyl-6-(2-methylimidazo[2,1-b][1,3]thiazol-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride;

6-{4-fluoro-2-[(piperidin-4-yl)oxy]-1,3-benzothiazol-6-yl}-2,8-dimethylimidazo[1,2-b]pyridazine hydrochloride;

4-fluoro-6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-2-[(piperidin-4-yl)oxy]-1,3-benzothiazole hydrochloride;

N-methyl-6-(2-methylimidazo[2,1-b][1,3,4]thiadiazol-6-yl)-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-amine hydrochloride;

2-methyl-6-{2-[(piperidin-4-yl)oxy][1,3]thiazolo[4,5-c]pyridin-6-yl}imidazo[1,2-a]pyridine-8-carbonitrile hydrochloride;

6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-[(piperidin-4-yl)oxy][1,3]thiazolo[4,5-c]pyridine hydrochloride;

2-methyl-5-{2-[(piperidin-4-yl)oxy][1,3]thiazolo[4,5-c]pyridin-6-yl}-2*H*-indazole-7-carbonitrile hydrochloride;

6-(7-fluoro-2-methyl-2*H*-indazol-5-yl)-2-[(piperidin-4-yl)oxy][1,3]thiazolo[4,5-c]pyridine hydrochloride;

6-{4-fluoro-2-[(piperidin-4-yl)oxy]-1,3-benzothiazol-6-yl}-2-methylimidazo[1,2-a]pyridine-8-carbonitrile hydrochloride;

5-{4-fluoro-2-[(piperidin-4-yl)oxy]-1,3-benzothiazol-6-yl}-2-methyl-2*H*-indazole-7-carbonitrile hydrochloride;

6-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-4-fluoro-2-[(piperidin-4-yl)oxy]-1,3-benzothiazole hydrochloride;

6-(2-{[(3*R*,4*R*)-3-fluoro-2,2,6,6-tetramethylpiperidin-4-yl](methyl)amino}[1,3]thiazolo[5,4-d]pyrimidin-5-yl)-2-methylimidazo[1,2-a]pyridine-8-carbonitrile dihydrochloride;

6-(2-{[(3*R*,4*R*)-3-fluoro-2,2,6,6-tetramethylpiperidin-4-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridin-6-yl)-2-methylimidazo[1,2-a]pyridine-8-carbonitrile dihydrochloride;

N-[(1*R*,2*S*,3*S*,5*S*)-2-fluoro-1,5-dimethyl-8-azabicyclo[3.2.1]octan-3-yl]-6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine dihydrochloride;

5-(1*H*-imidazol-1-yl)-2-{6-[methyl(piperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}phenol formate;

3-[2,5-difluoro-4-(1*H*-pyrazol-4-yl)phenyl]-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridazin-6-amine formate;

3-[2,5-difluoro-4-(3-fluoro-1*H*-pyrazol-4-yl)phenyl]-*N*-methyl-*N*-(piperidin-4-yl)[1,3]thiazolo[4,5-c]pyridazin-6-amine formate;

2-[6-(piperazin-1-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(1*H*-pyrazol-4-yl)phenol formate;

5-(1*H*-pyrazol-4-yl)-2-[6-(1,2,3,6-tetrahydropyridin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-yl]phenol hydrochloride;

2-(6-{[(3*R*,4*S*)-4-fluoro-1-methylpyrrolidin-3-yl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol formate;

5-(1*H*-pyrazol-4-yl)-2-[6-(2,2,6,6-tetramethyl-1,2,3,6-tetrahydropyridin-4-yl)[1,3]thiazolo[4,5-c]pyridin-2-yl]phenol hydrochloride;

2-[6-(2,6-diazaspiro[3.5]nonan-2-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride;

2-[6-(7-methyl-1,7-diazaspiro[3.5]nonan-1-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride;

2-[6-(7-methyl-2,7-diazaspiro[4.4]nonan-2-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride;

2-[6-(2,7-diazaspiro[3.5]nonan-2-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(3-fluoro-1*H*-pyrazol-4-yl)phenol formate;

2-(6-{[(3*S*,4*S*)-4-fluoro-1-methylpyrrolidin-3-yl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol formate;

2-{6-[(3a*S*,7a*R*)-octahydro-1*H*-pyrrolo[3,2-c]pyridin-1-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride;

2-(6-{methyl[(1*s*,4*s*)-4-(methylamino)cyclohexyl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride;

2-(6-{[(3*R*,4*S*)-4-fluoropyrrolidin-3-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol formate;

2-{6-[(3a*S*,7a*R*)-5-methyloctahydro-1*H*-pyrrolo[3,2-c]pyridin-1-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride;

2-(6-{methyl[(3*R*)-piperidin-3-yl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride;

2-(6-{methyl[(3*S*)-piperidin-3-yl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride;

2-(6-{methyl[3-(methylamino)cyclobutyl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol ditrifluoroacetate;

2-(6-{[(1*r*,4*r*)-4-(dimethylamino)cyclohexyl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride;

2-(6-{methyl[(3*S*)-1-methylpiperidin-3-yl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride;

2-{6-[(azetidin-3-yl)(methyl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride;

2-[6-(1,7-diazaspiro[3.5]nonan-1-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride;

2-{6-[(3,3-dimethylpiperidin-4-yl)(methyl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride;

2-{6-[(2-azaspiro[3.3]heptan-6-yl)(methyl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride;

5-{2-[(2*R*,4*r*,6*S*)-2,6-dimethylpiperidin-4-yl]-4-fluoro-1,3-benzothiazol-6-yl}-2,7-dimethyl[1,3]oxazolo[5,4-b]pyridine hydrochloride;

2-{6-[methyl(1,3,3-trimethylpiperidin-4-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride;

2-(6-{methyl[(1*s*,3*s*)-3-(methylamino)cyclobutyl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride;

2-{6-[(3a*R*,7a*S*)-octahydro-1*H*-pyrrolo[2,3-c]pyridin-1-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride;

2-[6-(1,6-diazaspiro[3.5]nonan-1-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride;

2-(6-{[(1*s*,3*s*)-3-(dimethylamino)cyclobutyl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride;

2-(6-{[(3*R*,4*R*)-3-fluoropiperidin-4-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol formate;

5-(1*H*-pyrazol-4-yl)-2-{6-[(pyrrolidin-3-yl)amino][1,3]thiazolo[4,5-c]pyridazin-3-yl}phenol formate;

2-[6-(2,6-diazaspiro[3.3]heptan-2-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(3-fluoro-1*H*-pyrazol-4-yl)phenol formate;

2-{6-[(3a*R*,7a*S*)-6-methyloctahydro-1*H*-pyrrolo[2,3-c]pyridin-1-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride;

2-[6-(6-methyl-1,6-diazaspiro[3.5]nonan-1-yl)[1,3]thiazolo[4,5-c]pyridazin-3-yl]-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride;

2-(6-{[(2*S*,4*S*)-2-(hydroxymethyl)piperidin-4-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride;

2-(6-{[(2*S*,4*S*)-2-(hydroxymethyl)-1-methylpiperidin-4-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride;

2-(6-{methyl[(1*r*,3*r*)-3-(methylamino)cyclobutyl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol dihydrochloride;

N-(1,2-dimethylpiperidin-4-yl)-6-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-*N*-methyl[1,3]thiazolo[4,5-c]pyridin-2-amine trifluoroacetate;

2-{6-[(1*S*,6*R*)-3,8-diazabicyclo[4.2.0]octan-8-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol trifluoroacetate;

2-{6-[(1*S*,6*R*)-3-methyl-3,8-diazabicyclo[4.2.0]octan-8-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol trifluoroacetate;

2-{6-[(1*R*,6*S*)-3,8-diazabicyclo[4.2.0]octan-8-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol trifluoroacetate;

2-{6-[(1*R*,6*S*)-3-methyl-3,8-diazabicyclo[4.2.0]octan-8-yl][1,3]thiazolo[4,5-c]pyridazin-3-yl}-5-(1*H*-pyrazol-4-yl)phenol trifluoroacetate;

2-(6-{methyl[(2*S*,4*S*)-2-methylpiperidin-4-yl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol trifluoroacetate;

2-(6-{[(2*S*,4*S*)-1,2-dimethylpiperidin-4-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol trifluoroacetate;

2-(6-{methyl[(2*R*,4*S*)-2-methylpiperidin-4-yl]amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol trifluoroacetate, and

2-(6-{[(2*R*,4*S*)-1,2-dimethylpiperidin-4-yl](methyl)amino}[1,3]thiazolo[4,5-c]pyridazin-3-yl)-5-(1*H*-pyrazol-4-yl)phenol trifluoroacetate;

or a form thereof.

8. A method for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of the compound of any of claims 1, 6, or 7.

9. The method of claim 8, wherein the effective amount of the compound is in a range of from about 0.001 mg/kg/day to about 500 mg/kg/day.

10. A use of the compound of any of claims 1, 6, or 7 for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of the compound.

11. The use of claim 10, wherein the effective amount of the compound is in a range of from about 0.001 mg/kg/day to about 500 mg/kg/day.

12. A use of the compound of any of claims 1, 6, or 7 in the manufacture of a medicament for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of the medicament.

13. The use of claim 12, wherein the effective amount of the compound in the medicament is in a range of from about 0.001 mg/kg/day to about 500 mg/kg/day.

14. A use of the compound of any of claims 1, 6, or 7 in the preparation of a pharmaceutical composition for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of the compound of Formula (I) or Formula (II), or a form thereof in admixture with one or more of the pharmaceutically acceptable excipients.

15. The use of claim 14, wherein the effective amount of the compound in the pharmaceutical composition is in a range of from about 0.001 mg/kg/day to about 500 mg/kg/day.

16. A pharmaceutical composition for use in treating or ameliorating HD comprising an effective amount of the compound of claim 1 and a pharmaceutically acceptable excipient.

17. A pharmaceutical composition for use in treating or ameliorating HD comprising an effective amount of the compound of claims 6 or 7 and a pharmaceutically acceptable excipient.