

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to United States provisional patent application no. 61/890,718, filed on October 14, 2013. That application is incorporated by reference herein.

BACKGROUND

[0002] Field of the Disclosure

[0003] Embodiments of the disclosure relate to selectively substituted quinoline compounds and pharmaceutical agents comprising one or more of those compounds as active ingredient(s). More particularly, embodiments of the disclosure relate to those compounds that act as an antagonist or inhibitor for Toll-like receptors (TLR) 7 and 8, and their use in a pharmaceutical composition effective for treatment of systemic lupus erythematosus (SLE) and lupus nephritis.

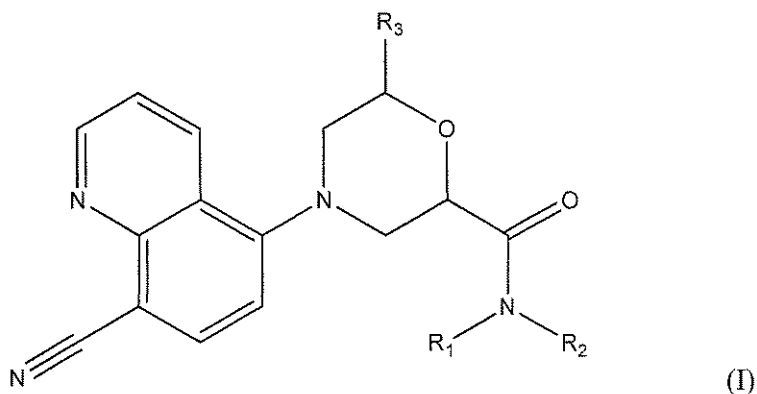
[0004] Description of Related Art

[0005] Systemic lupus erythematosus (SLE) and lupus nephritis are autoimmune diseases characterized by inflammation and tissue damage. For example, SLE may cause damage to the skin, liver, kidneys, joints, lungs, and central nervous system. SLE sufferers may experience general symptoms such as extreme fatigue, painful and swollen joints, unexplained fever, skin rash, and kidney dysfunction. Because organ involvement differs amongst patients, symptoms may vary. SLE is predominantly a disease of younger women, with peak onset between 15-40 years of age and an approximate 10-fold higher prevalence in women vs. men.

[0006] Current treatments for SLE typically involve immunomodulatory drugs such as belimumab, hydroxychloroquine, prednisone, and cyclophosphamide. All of these drugs may have dose-limiting side effects, and many patients still have poorly controlled disease.

BRIEF SUMMARY OF THE DISCLOSURE

[0007] ~~Embodiments of the disclosure provide compounds and methods of use for preventing or treating diseases or conditions characterized by Toll-like receptor 7 or 8 activation in patients. In one aspect, there is provided One embodiment features a compound of formula (I) or pharmaceutically acceptable salt thereof:~~



wherein at least one of R_1 and R_2 is $-H$, methyl, or ethyl, and the other is

$-H$; or the other is

C_1-C_6 alkyl that is optionally substituted with:

$-OH$, methoxy, ethoxy, $-OCH(CH_3)_2$, $-O(CH_2)_2CH_3$, phenyl, furanyl, $-O(CH_2)_2OH$, phenoxy, methylthio, $-F$, $-N(CH_3)_2$, cyano, pyridinyloxy, fluorophenoxy, isochromanyl, phenol, benzylamino, $-NHCH_3$, oxo-, amino, carboxyl, 7-member spiroaminyl, a three to six member cycloalkyl, saturated or unsaturated and optionally including one or more heteroatoms selected from O and N, and optionally substituted at one or more C or N atoms by methyl, cyano, fluoro, methylamino, or trifluoromethyl; or the other is

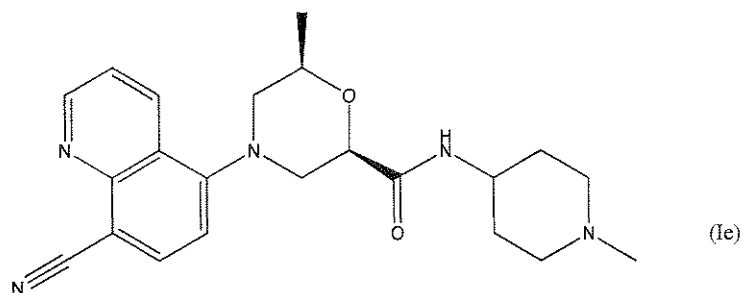
C_3-C_7 cycloalkane, saturated or unsaturated, optionally bridged, optionally including one or more heteroatoms selected from O, S, and N, and optionally substituted at one or more C or N atoms by methyl, ethyl, pyridinyl, azetidiny, acetamidyl, carboxamidyl, cyano, fluoro, methylamino, or trifluoromethyl; or

R_1 and R_2 , together with the nitrogen atom to which they are attached, form an 8 to 11 member spirodiamine, an 8 member bicyclodiamine, a 7 member spiroxamine, a piperidinyl optionally substituted with ethyl, or a four to six member cycloalkyl, optionally substituted with at least one of carboxamidyl, aminomethyl, methyl, (ethylamino)methyl, (dimethylamino)methyl, dimethylamino, (methylamino)methyl, and amino; and wherein

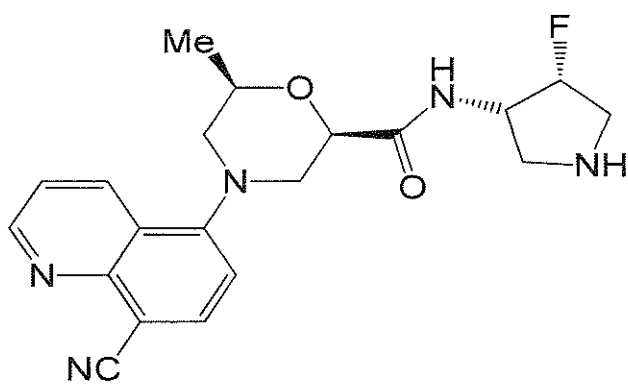
R_3 is $-H$ or methyl.

[0008] In a further ~~embodiment~~ example the compound is a compound of Formula (I), having the stereochemistry set forth in one of Formula (Ia), (Ib), (Ic), or (Id), having the same substituent options as set forth above for Formula (Ia):

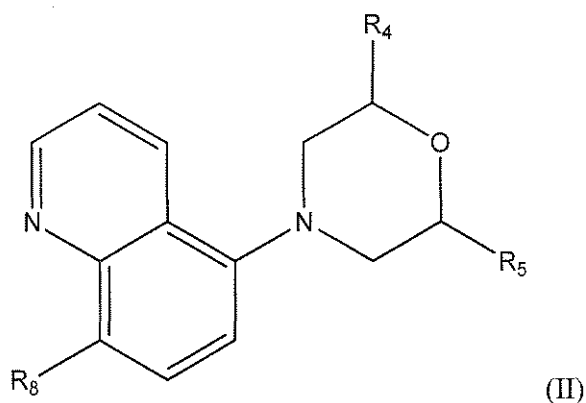
[0009] A further ~~embodiment example~~ provides a compound of Formula (Ie) (relative stereochemistry indicated):



[0009a] In one aspect, there is provided a compound as shown below or a pharmaceutically acceptable salt thereof, with relative stereochemistry indicated:



[0010] In a further ~~aspect, there is provided~~~~embodiment the compound is~~ a compound of Formula (II) or pharmaceutically acceptable salt thereof:



wherein

R_4 is ~~H or~~ methyl;

R₅ is C₁-C₅ alkyl that is saturated, partially saturated, or unsaturated, and that is optionally substituted with:

-H, -Cl, -F, -OH, -NH₂, oxo-, -N(CH₂CH₃)₂, phenyl, cyclohexyl, phenyltriazolyl, cyclohexyltriazolyl, pyridinyl, pyrrolidinyl,

morpholinyl optionally substituted with methyl or hydroxymethyl,

-O-, substituted with:

C₁-C₆ alkyl, methylphenyl, methylcyclohexyl, pyridinyl, diazinyl, or phenyl optionally substituted with -F or methyl,

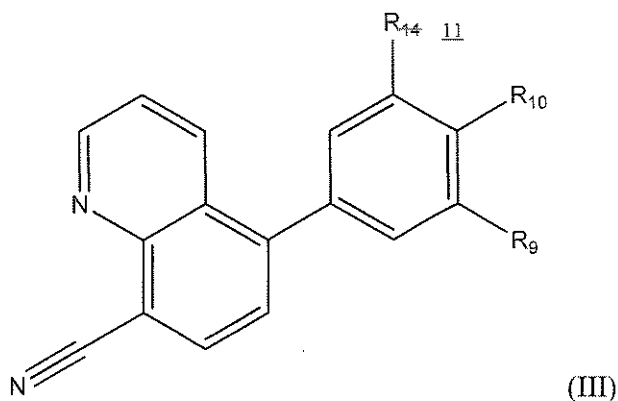
-NH-, substituted with:

C₂-C₇ alkyl that is linear, branched, or cyclic, saturated or unsaturated, and optionally substituted with oxo-, phenyl, methyl, or -OH,

pyridinyl optionally substituted with methyl, methoxy, phenyl, or amino,

diazinyl optionally substituted with ethyl,

[0011] A further ~~embodiment aspect~~ provides a compound of Formula (III) or pharmaceutically acceptable salt thereof:



wherein

R₁₁ is H or methyl;

R₁₀ is H or, when both R₁₄ and R₉ are H, is methyl-1,4'-bipiperidinyl;

R₉ is -H or is -CH₂- substituted by 1,4'-bipiperidinyl, oxo-, hydroxyl, methylpyridinyl, or piperidinyl optionally substituted with hydroxyl, -N(CH₃)₂, or piperidinyl.

[0012] In a further ~~embodiment one example~~ the compound is selected from rel-(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-N-((3*R*,4*S*)-4-fluoropyrrolidin-3-yl)-6-methylmorpholine-2-carboxamide hydrochloride, (2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-N-(1-methylpiperidin-4-yl)morpholine-2-carboxamide, 5-((2*S*,6*R*)-2-([1,4'-bipiperidin]-1'-ylmethyl)-6-methylmorpholino)quinoline-8-carbonitrile, and 5-((2*R*,7*R*)-2-(hydroxymethyl)-7-methyl-1,4-oxazepan-4-yl)quinoline-8-carbonitrile.

[0013] In a further ~~embodiment example~~ the compound or pharmaceutically effective salt thereof of the preceding paragraph has an IC₅₀ less than or equal to 20 nM against human TLR7 receptors expressed in a HEK-293 cell line. In a further ~~example embodiment~~ the compound or pharmaceutically effective salt thereof of the preceding paragraph of this disclosure has an IC₅₀ less than or equal to 100 nM against human TLR7 receptors expressed in a HEK-293 cell line. In a further ~~example embodiment~~ the IC₅₀ against human TLR7 receptors expressed in a HEK-293 cell line is measured by (1) plating cells of the HEK-293 cell line stably expressing TLR7 in Dulbecco's modified Eagle's medium containing 10 % fetal bovine serum at a density of 2.22X10⁵ cells/ml into a 384-well plate and incubating for 2 days at 37 °C, 5 % CO₂; (2) adding the compound or pharmaceutically acceptable salt thereof and incubating the cells for 30 minutes; (3) adding CL097 (InvivoGen) at 3ug/ml and

incubating the cells for approximately 20 hours; and (4) quantifying NF-kappaB dependent reporter activation by measuring luminescence.

[0014] In further embodiments of the disclosure, compounds have an IC₅₀ against human TLR7 receptors expressed in a HEK-293 cell line less than or equal to 200 nM, less than or equal to 180 nM, less than or equal to 160 nM, less than or equal to 140 nM, less than or equal to 120 nM, less than or equal to 100 nM, less than or equal to 80 nM, less than or equal to 60 nM, less than or equal to 40 nM, or less than or equal to 20 nM. In further embodiments of the disclosure, compounds have an IC₅₀ against human TLR7 receptors expressed in a HEK-293 cell line from 10 nM to 30 nM, from 10 nM to 50 nM, from 10 nM to 100 nM, from 30 nM to 50 nM, from 30 nM to 100 nM, or from 50 nM to 100 nM. In further embodiments the IC₅₀ against human TLR7 receptors expressed in a HEK-293 cell line is measured by (1) plating cells of the HEK-293 cell line stably expressing TLR7 in Dulbecco's modified Eagle's medium containing 10 % fetal bovine serum at a density of 2.22X10⁵ cells/ml into a 384-well plate and incubating for 2 days at 37 °C, 5 % CO₂; (2) adding the compound or pharmaceutically acceptable salt thereof and incubating the cells for 30 minutes; (3) adding CL097 (InvivoGen) at 3ug/ml and incubating the cells for approximately 20 hours; and (4) quantifying NF-kappaB dependent reporter activation by measuring luminescence.

[0014a] In one aspect, there is provided the compound or pharmaceutically acceptable salt of the present invention for use in the treatment of lupus. In another aspect, there is provided the compound or pharmaceutically acceptable salt of the present invention for use in antagonizing TLR7. In a further aspect, there is provided the compound or pharmaceutically acceptable salt of any of the present invention for use in antagonizing TLR8. In another aspect, there is provided a pharmaceutical composition comprising at least one compound or pharmaceutically acceptable salt of the present invention and at least one pharmaceutically acceptable carrier. In another aspect, there is provided the compound or pharmaceutically acceptable salt of any of the present invention for use in the treatment of a systematic lupus erythematosus, cutaneous lupus, or neuropsychiatric lupus.

[0015] ~~Further embodiments~~ examples provide methods for treatment of lupus, including but not limited to treatment of systemic lupus erythematosus, cutaneous lupus, neuropsychiatric lupus, fetal heart block, and antiphospholipid syndrome, including administering a pharmaceutically effective amount of a compound or pharmaceutically acceptable salt of the disclosure.

[0016] Further ~~example~~~~embediments~~ provide methods for antagonizing TLR7, including administering a pharmaceutically effective amount of a compound or pharmaceutically acceptable salt of the disclosure.

[0017] Further ~~example~~~~embediments~~ provide methods for antagonizing TLR8, including administering a pharmaceutically effective amount of a compound or pharmaceutically acceptable salt of the disclosure.

[0018] Further ~~example~~~~embediments~~ provide pharmaceutical compositions comprising at least one compound or pharmaceutically acceptable salt of the disclosure and at least one pharmaceutically acceptable carrier.

[0019] Further ~~embediments~~~~examples~~ provide methods for treatment of systemic lupus erythematosus or lupus, including administering a pharmaceutically effective amount of a compound or pharmaceutically acceptable salt of the disclosure.

[0020] Further ~~example~~~~embediments~~ provide methods for antagonizing TLR7, including administering a pharmaceutically effective amount of a compound or pharmaceutically acceptable salt of the disclosure.

[0021] Further ~~embediments~~~~examples~~ provide methods for antagonizing TLR8, including administering a pharmaceutically effective amount of a compound or pharmaceutically acceptable salt of the disclosure.

[0022] Further ~~embediments~~~~examples~~ provide pharmaceutical compositions comprising at least one compound or pharmaceutically acceptable salt of the disclosure and at least one pharmaceutically acceptable carrier.

[0023] The term “optionally substituted,” as used herein, means that the subject structure may include, but is not required to include, one or more substituents independently selected from lower alkyl, methoxy-, -OH, -NH₂, -CH₂-NH-CH₂, -OCH₂CH₂CH₃, or -OCH(CH₃)₂. If the optionally substituted moiety is cyclic, then the optional substitution may be a methyl bridge between two atoms in the ring.

[0024] The symbol “C(O)” as used herein refers to a carbonyl group having the formula C=O.

[0025] Unless otherwise specified, “a” and “an” as used in this disclosure, including the claims, mean “one or more.”

[0026] As used herein, “lower alkyl” refers to straight, or, in the case of three- and four-carbon groups, straight, branched, or cyclic saturated hydrocarbons having between one and four carbon atoms.

[0027] As used herein, the term “attached through a nitrogen” when referring to a heterocyclic moiety including nitrogen, means that a point of attachment of the moiety to another structure is through a nitrogen that is part of the heterocycle.

[0028] As used herein, the term “TLR7/8” means “TLR7 and TLR8” or “TLR7 or TLR8” or “TLR7 and/or TLR8.” The particular meaning can be understood by a person skilled in the art based upon the context in which “TLR7/8” appears.

[0029] Heterocyclic moieties recited herein include azetidiny, pyrrolidinyl, piperidinyl, methylazetidiny, pyrazolyl, piperazinyl, morpholinyl, thiazolyl, pyrrolopyrrolyl, imidazolidinyl, and isothiazolyl. Where a heterocyclic group is mentioned, unless otherwise indicated it will be understood that the heterocyclic atom(s) in the group may be at any position in the group. It will further be understood that imidazolyl, pyrazolyl, thiazolyl, and pyrrolyl may be unsaturated or partially unsaturated. An ~~embodiment~~-example of the disclosure may include a pharmaceutical composition that includes one or more compounds of the disclosure with a pharmaceutically acceptable excipient. These pharmaceutical compositions may be used to treat or prevent a disease or condition characterized by TLR7/8 activation in a patient, typically a human patient, who has or is predisposed to have such a condition or disease. Examples of diseases or conditions characterized by TLR7/8 activation include systemic lupus erythematosus (SLE) and lupus nephritis.

[0030] As used herein, “effective amount” of a compound of an ~~example~~embodiment of the disclosure is effective amount of the above-identified compounds in an amount sufficient to treat or prevent SLE and lupus nephritis.

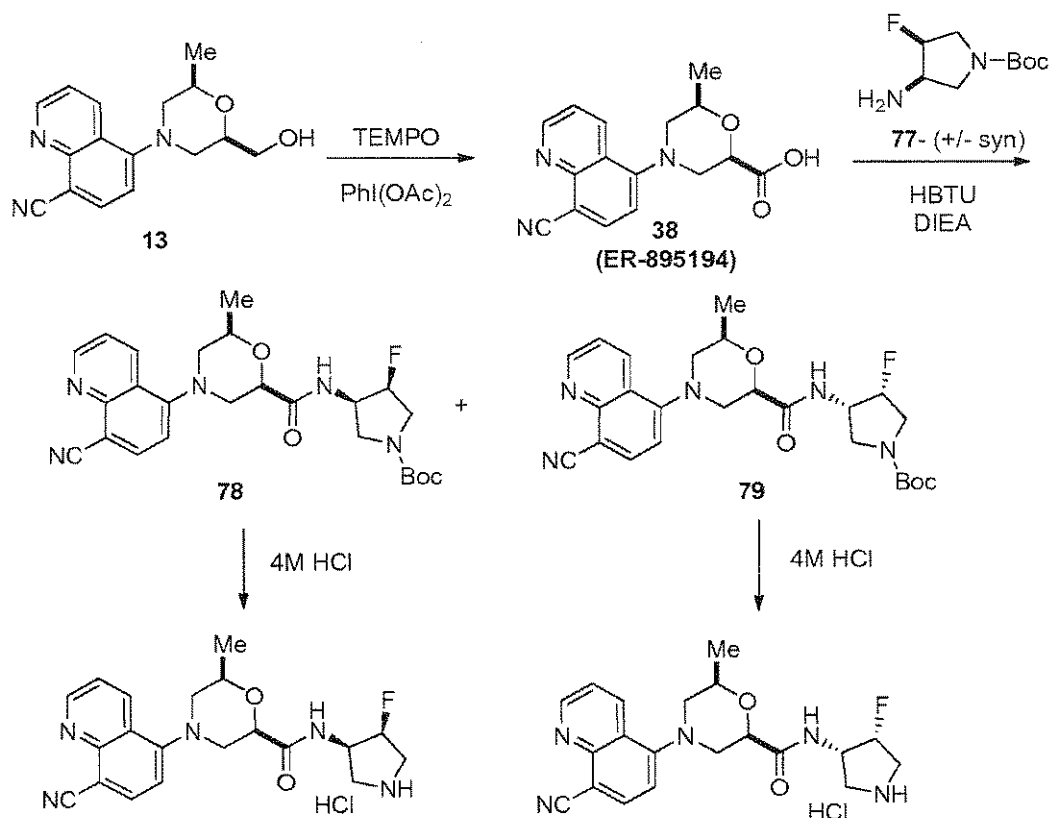
[0031] ~~Embodiments~~-Examples presented herein may include asymmetric or chiral centers. ~~Examples~~Embodiments include the various stereoisomers and mixtures thereof. Individual stereoisomers of compounds of ~~example~~embodiments of the disclosure may be prepared synthetically from commercially available starting materials that contain asymmetric or chiral centers, or by preparation of mixtures of enantiomeric compounds followed by resolution of those compounds. Suitable methods of resolution include attachment of a racemic mixture of enantiomers, designated (+/-), to a chiral auxiliary, separation of the resulting diastereomer by chromatography or recrystallization and separation of the optically pure product from the auxiliary; or direct separation of the mixture of optical enantiomers on chiral chromatographic columns.

[0032] ~~Examples~~Embodiments of the disclosure also include a pharmaceutical composition including any compound of the disclosure as well as a pharmaceutically acceptable excipient. The pharmaceutical compositions can be used to treat or prevent SLE

and lupus nephritis. Therefore, ~~embodiments~~ examples of the disclosure may also feature a method for treating or preventing SLE or lupus nephritis in a human patient having or predisposed to having lupus nephritis or SLE.

[0033] ~~Embodiments~~ Examples of the disclosure include pharmaceutically acceptable salts of the compounds presented herein. The term “pharmaceutically acceptable salt” refers to those salts that are, within the scope of sound medical judgment, suitable for use in contact with the tissues of humans and animals without undue toxicity, irritation, or allergic response. Pharmaceutically acceptable salts are well known in the art. For example, S. M. Berge, et al., describes pharmaceutically acceptable salts in detail in *J. Pharmaceutical Sciences* 66:1-19, 1977. Salts can be prepared in situ during final isolation and purification of a compound or separately by reacting a free base group with a suitable organic acid. Representative acid addition salts include acetate, adipate, alginate, ascorbate, aspartate, benzenesulfonate, benzoate, bisulfate, borate, butyrate, camphorate, camphersulfonate, citrate,

[0403] Scheme 19



[0404] ~~ER-899742-HCl~~ ~~ER-899745-HCl~~ ~~ER-899745-HCl~~ ~~ER-899742-HCl~~

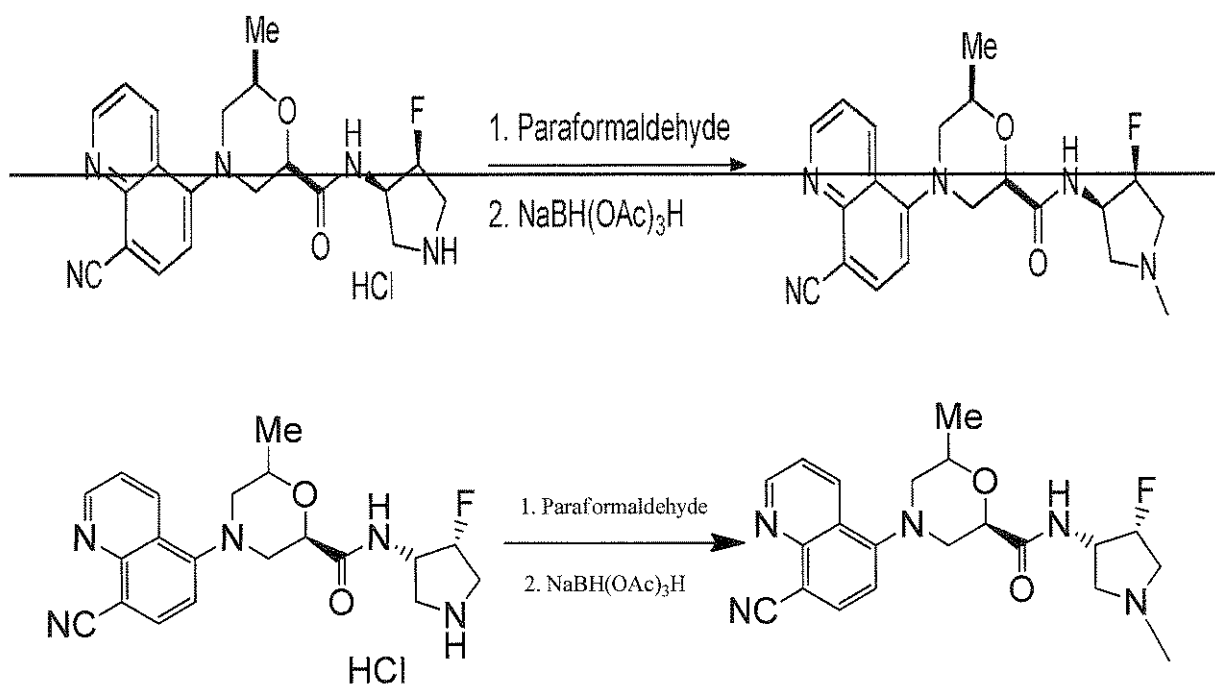
[0405] **ER-895194** or 38: To a stirred solution of 13 (231.0 g, 815.3 mmol) in DCM (3.93 L) at 0 – 5 °C was added iodobenzene diacetate (525 g, 1630.6 mmol) while maintaining the temperature at < 5 °C. TEMPO (25.4 g, 162.8 mmol) was added followed by water (151 mL) after which time the resulting reaction mixture was warmed to 10 °C, stirred for 30 minutes and then allowed to warm to rt and stirred for 15 h. The completed reaction was cooled to < 15 °C and quenched by the slow addition of 1.34 L of a 10 % (w/v) solution of sodium thiosulfate in water while maintaining the reaction temperature ≤ 15 °C followed by additional stirring at rt for 45 min. The pH of the quenched reaction was adjusted to pH 9 by the slow addition of 1M sodium hydroxide in water while maintaining the temperature at ≤ 25 °C. The stirring layers were separated and the organic layer was washed with water (560 mL). 1-Butanol (2.31 L) was added to the combined aqueous layers after which time the mixture was cooled to 10 – 15 °C followed by the slow addition of 5 M sulfuric acid (231 mL) maintaining the temperature at ≤ 25 °C to obtain an approximate pH 5. The resultant layers were separated and the aqueous layer was extracted 3 times with 1-butanol (2.31 L) while maintaining the pH of the aqueous layer approximately pH 5 between extractions. The combined aqueous layers were concentrated while warming to 50 – 55 °C after which time the resultant yellow solid-slurry was concentrated via azeotrope three times with *n*-heptane

[0557] **ER-899477** (78 mg, 0.196 mmol, 58.3 % yield as a diastereomeric mixture) was prepared in a similar manner to **ER-899464** starting with **38** (100 mg, 0.336 mmol) and a racemic mixture of (3*S*,4*R*)-*tert*-butyl 3-amino-4-fluoropiperidine-1-carboxylate and (3*R*,4*S*)-*tert*-butyl 3-amino-4-fluoropiperidine-1-carboxylate (220 mg, 1.009 mmol).

[0558] **ER-895415** as an example for **Compound 41** in **Scheme 11**: To a stirred solution of **38** (1.10 g, 3.70 mmol) in DCM (5 mL) at 0 °C was added oxalyl chloride (1.0 mL, 11.42 mmol) dropwise over 2 min. The reaction mixture was allowed to warm to rt and stir for 1 h after which time the reaction was concentrated and dried in vacuo. The dried syrup was cooled to 0 °C followed by the slow addition of MeOH (5 mL) with stirring. The completed reaction was concentrated to dry, diluted with DCM (10 mL), washed with saturated sodium sulfite (3 mL), brine (3 mL) and then dried over Na₂SO₄, filtered and concentrated to dry. The crude product was purified over silica gel (eluting with a 0 – 50 % EtOAc in heptane gradient) to provide **ER-895415** (894 mg, 2.81 mmol, 76 % yield) after combining the desired fractions, concentrating and drying in vacuo.

[0559] Preparation of example **ER-899332** following **Scheme 21**:

[0560] **Scheme 21**



[0561] **ER-899742472**

ER-899332

[0562] The solution of **ER-899742472**-HCl (49.8 mg, .119 mmol) and paraformaldehyde (8.90 mg, .297 mmol) in DCM (0.5 mL) was stirred at room for 1 hr. Sodium triacetoxyborohydride (62.8 mg, .297 mmol) was added and resulting solution was stirred at rt for 2 days. After the solvents were removed, the crude was chromatographed on silica (15% MeOH in DCM) to give **ER-899332** (8.16 mg, 0.021 mmol, 18.3 % yield).

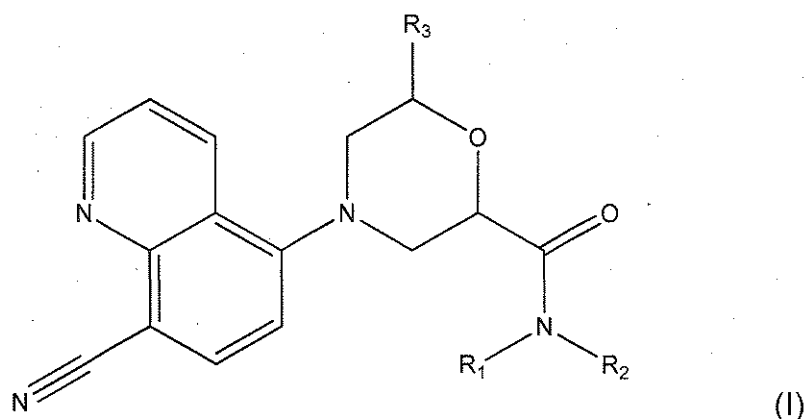
[0563] **ER-899457** (50 mg, 0.117 mmol, 97 % yield) was prepared in a similar manner to **ER-899332** starting with **ER-899336** (50 mg, 0.122 mmol) .

[0564] **ER-899836**: A stirred solution of **ER-899477** (76 mg, .191 mmol) in solution of 37 % formaldehyde in water (0.5 g, 16.652 mmol) and formic acid (0.5 ml, 13.036 mmol) was warmed to 80 °C for 3 h after which time the completed reaction is cooled to rt. The mixture was azeotroped to dryness four times with toluene (2 mL each) and the resultant

Claims

We claim:

1. A compound of formula (I) or pharmaceutically acceptable salt thereof:



wherein at least one of R_1 and R_2 is $-H$, methyl, or ethyl, and the other is $-H$; or the other is

C_1 - C_6 alkyl that is optionally substituted with:

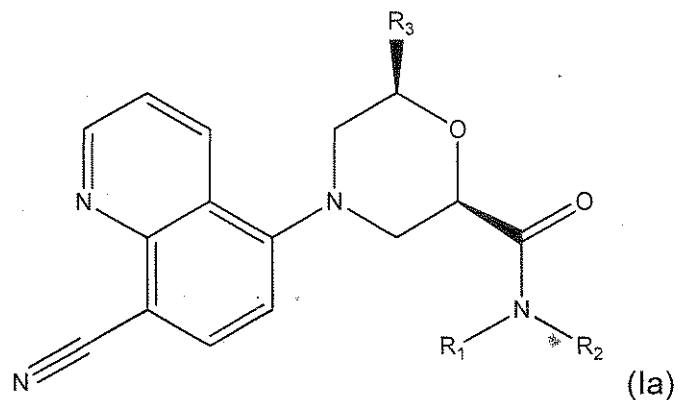
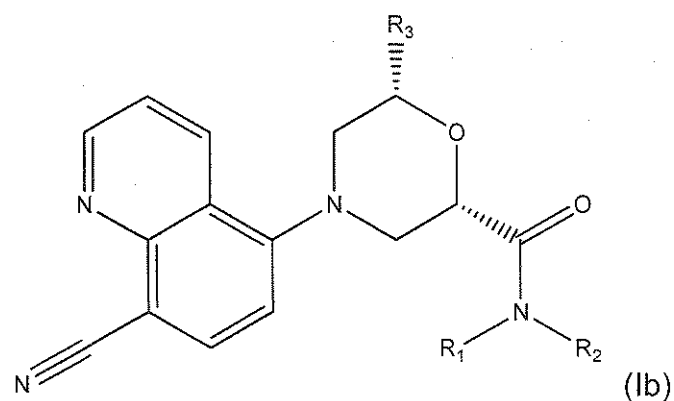
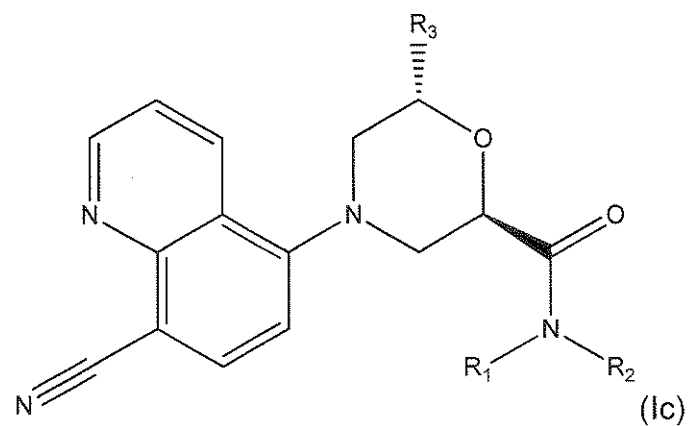
$-OH$, methoxy, ethoxy, $-OCH(CH_3)_2$, $-O(CH_2)_2CH_3$, phenyl, furanyl, $-O(CH_2)_2OH$, phenoxy, methylthio, $-F$, $-N(CH_3)_2$, cyano, pyridinyloxy, fluorophenoxy, isochromanyl, phenol, benzylamino, $-NHCH_3$, oxo-, amino, carboxyl, 7-member spiroaminyl, a three to six member cycloalkyl, saturated or unsaturated and optionally including one or more heteroatoms selected from O and N, and optionally substituted at one or more C or N atoms by methyl, cyano, fluoro, methylamino, or trifluoromethyl; or the other is

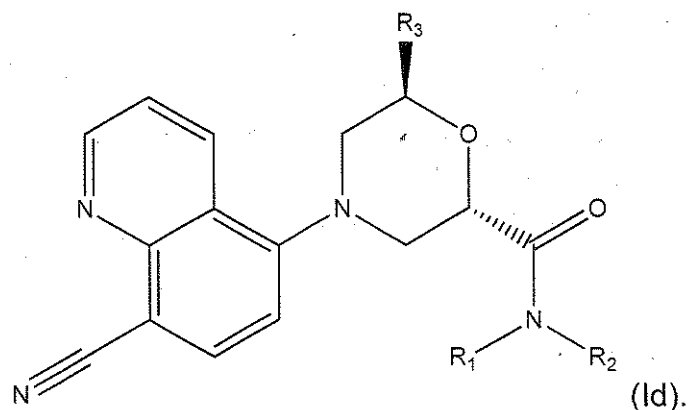
C_3 - C_7 cycloalkane, saturated or unsaturated, optionally bridged, optionally including one or more heteroatoms selected from O, S, and N, and optionally substituted at one or more C or N atoms by methyl, ethyl, pyridinyl, azetidiny, acetamidyl, carboxamidyl, cyano, fluoro, methylamino, or trifluoromethyl; or

R_1 and R_2 , together with the nitrogen atom to which they are attached, form an 8 to 11 member spirodiamine, an 8 member bicyclodiamine, a 7 member spiroxamine, a piperidinyl optionally substituted with ethyl, or a four to six member cycloalkyl, optionally substituted with at least one of carboxamidyl, aminomethyl, methyl, (ethylamino)methyl,

(dimethylamino)methyl, dimethylamino, (methylamino)methyl, and amino; and wherein R_3 is $-H$ or methyl.

2. The compound or pharmaceutically acceptable salt of claim 1, wherein said compound or salt has a stereochemical configuration selected from one of those shown in the group consisting of Formula (1a), Formula (1b), Formula (1c), and Formula (1d):





3. The compound or pharmaceutically acceptable salt of claim 1, wherein said compound or salt is selected from the group consisting of: *

5-((2*R*,6*R*)-2-formyl-6-methylmorpholino)quinoline-8-carbonitrile;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-ethyl-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-isopropyl-6-methylmorpholine-2-carboxamide;

5-((2*R*,6*R*)-2-formyl-6-methylmorpholino)quinoline-8-carbonitrile;

(2*R*,6*R*)-methyl 4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxylate;

(6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide;

5-((2*R*,6*R*)-2-((*S*)-3-ethylpiperazine-1-carbonyl)-6-methylmorpholino)quinoline-8-carbonitrile;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(3,4-difluorobenzyl)-6-methylmorpholine-2-carboxamide;

5-((2*R*,6*R*)-2-((*S*)-3-aminopyrrolidine-1-carbonyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-(azetidine-1-carbonyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-([1,4'-bipiperidine]-1'-carbonyl)-6-methylmorpholino)quinoline-8-carbonitrile;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-cyclopropyl-6-methylmorpholine-2-carboxamide;

5-((2*R*,6*R*)-2-(3-aminoazetidine-1-carbonyl)-6-methylmorpholino)quinoline-8-carbonitrile;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-hydroxyethyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-methoxyethyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*R*)-2-hydroxypropyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*S*)-1-hydroxypropan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*R*)-1-hydroxypropan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*S*)-1-hydroxybutan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*S*)-1-hydroxy-3-methylbutan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*S*)-2-hydroxy-1-phenylethyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*R*)-2-hydroxy-1-phenylethyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-hydroxybutyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-ethoxyethyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*R*)-1-hydroxybutan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(1,3-dihydroxypropan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2,3-dihydroxypropyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(((*R*)-tetrahydrofuran-2-yl)methyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((tetrahydrofuran-2-yl)methyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(2-propoxyethyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*R*)-1-hydroxypentan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-isopropoxyethyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(1-methoxybutan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-(2-fluorophenyl)-2-hydroxyethyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*R*)-1-hydroxy-3-methylbutan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2,2-dimethoxyethyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-(2-hydroxyethoxy)ethyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((1*S*,2*S*)-2-hydroxycyclohexyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-hydroxycyclohexyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(1-hydroxyhexan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*S*)-1-hydroxy-3,3-dimethylbutan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*S*)-1-hydroxyhexan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((2*S*,3*S*)-1-hydroxy-3-methylpentan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*S*)-1-hydroxy-4-methylpentan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*R*)-1-hydroxy-4-methylpentan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((4-methylmorpholin-2-yl)methyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*S*)-1-hydroxy-4-(methylthio)butan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(2-phenoxyethyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*S*)-1-hydroxy-3-phenylpropan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(2-phenoxypropyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-hydroxy-3-phenylpropyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(2-(pyridin-3-yloxy)propyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-(4-fluorophenoxy)ethyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-(3-fluorophenyl)-2-hydroxyethyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*S*)-1-cyclohexyl-3-hydroxypropan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(isochroman-1-ylmethyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-hydroxy-3-phenoxypropyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((1*S*,2*R*)-1-hydroxy-1-(4-hydroxyphenyl)propan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((1*S*)-1,3-dihydroxy-1-phenylpropan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-hydroxy-3-(piperazin-1-yl)propyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-*N*-(azetidin-3-yl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*S*)-pyrrolidin-3-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*R*)-pyrrolidin-3-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*S*)-piperidin-3-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*R*)-piperidin-3-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*S*)-pyrrolidin-2-ylmethyl)morpholine-2-carboxamide;

(2*R*,6*R*)-*N*-(2-(benzylamino)ethyl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(pyridin-2-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(6-methylpyridin-2-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(5-methylisoxazol-3-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(2,2,2-trifluoroethyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2,2-difluoroethyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(3,3,3-trifluoropropyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-(dimethylamino)-2-methylpropyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*S*)-morpholin-2-ylmethyl)morpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(((*S*)-4-methylmorpholin-2-yl)methyl)morpholine-2-carboxamide acetic acetate;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-fluoroethyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(3-fluoropropyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*S*)-1,1,1-trifluoropropan-2-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*R*)-1,1,1-trifluoropropan-2-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(1,3-dimethyl-1*H*-pyrazol-5-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(1-methyl-1*H*-pyrazol-5-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-*N*-(cyanomethyl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-*N*-(1-cyanocyclopropyl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(1,2,4-thiadiazol-5-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(3-methyl-1,2,4-thiadiazol-5-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(piperidin-4-yl)morpholine-2-carboxamide;

5-((2*R*,6*R*)-2-methyl-6-(2,6-diazaspiro[3.4]octane-2-carbonyl)morpholino)quinoline-8-carbonitrile hydrochloride;

5-((2*R*,6*R*)-2-methyl-6-(3-((methylamino)methyl)azetidine-1-carbonyl)morpholino)quinoline-8-carbonitrile hydrochloride;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((4-fluoropiperidin-4-yl)methyl)-6-methylmorpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-*N*-(azetidin-3-ylmethyl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide hydrochloride;

5-((2*R*,6*R*)-2-methyl-6-(2,6-diazaspiro[3.5]nonane-2-carbonyl)morpholino)quinoline-8-carbonitrile hydrochloride;

5-((2*R*,6*R*)-2-methyl-6-(1,6-diazaspiro[3.4]octane-1-carbonyl)morpholino)quinoline-8-carbonitrile hydrochloride;

5-((2*R*,6*R*)-2-methyl-6-(1,7-diazaspiro[4.4]nonane-7-carbonyl)morpholino)quinoline-8-carbonitrile hydrochloride;

(2*R*,6*R*)-*N*-(3-carbamoyl-1-methyl-1*H*-pyrazol-4-yl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(oxetan-3-ylmethyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(tetrahydro-2*H*-pyran-4-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(tetrahydrofuran-3-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((3-methyloxetan-3-yl)methyl)morpholine-2-carboxamide;

5-((2*R*,6*R*)-2-methyl-6-(2-oxa-6-azaspiro[3.3]heptane-6-carbonyl)morpholino)quinoline-8-carbonitrile;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(oxetan-3-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-*N*-((3-(aminomethyl)oxetan-3-yl)methyl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(oxetan-2-ylmethyl)morpholine-2-carboxamide;

5-((2*R*,6*R*)-2-methyl-6-(piperazine-1-carbonyl)morpholino)quinoline-8-carbonitrile hydrochloride;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(2-(methylamino)ethyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*S*)-3,3,3-trifluoro-2-hydroxypropyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*R*)-3,3,3-trifluoro-2-hydroxypropyl)morpholine-2-carboxamide;

Methyl 2-((2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamido)acetate;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-(dimethylamino)ethyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*S*)-4,4,4-trifluoro-3-hydroxybutyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*R*)-4,4,4-trifluoro-3-hydroxybutyl)morpholine-2-carboxamide;

(2*R*,6*R*)-*N*-(3-amino-4,4,4-trifluorobutyl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide;

2-((2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamido)acetic acid;

1-((2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carbonyl)azetidine-3-carboxamide;

5-((2*R*,6*R*)-2-methyl-6-(2,7-diazaspiro[4.4]nonane-2-carbonyl)morpholino)quinoline-8-carbonitrile hydrochloride;

5-((2*R*,6*R*)-2-methyl-6-(3,9-diazaspiro[5.5]undecane-3-carbonyl)morpholino)quinoline-8-carbonitrile hydrochloride;

(2*R*,6*R*)-*N*-(3-carbamoylpyridin-4-yl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*R*)-morpholin-2-ylmethyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(pyridin-4-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(pyridin-3-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(1-(piperidin-4-yl)-1*H*-pyrazol-4-yl)morpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-*N*-(1-(azetidin-3-yl)-1*H*-pyrazol-4-yl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-*N*-((1*H*-pyrazol-5-yl)methyl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-*N*-((1*H*-pyrazol-4-yl)methyl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((3-(trifluoromethyl)pyridin-2-yl)methyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(1-(pyridin-2-yl)ethyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(pyridin-2-ylmethyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((6-methylpyridin-2-yl)methyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((1-methylpiperidin-2-yl)methyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((3-methylpyridin-2-yl)methyl)morpholine-2-carboxamide;

(2*R*,6*R*)-*N*-(4-cyano-1*H*-pyrazol-3-yl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((3*S*,4*R*)-4-fluoro-1-methylpyrrolidin-3-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((3*S*,4*R*)-4-fluoropiperidin-3-yl)-*N*,6-dimethylmorpholine-2-carboxamide hydrochloride;

5-((2*R*,6*R*)-2-(3-(aminomethyl)azetidine-1-carbonyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-(3-((ethylamino)methyl)azetidine-1-carbonyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-(3-((dimethylamino)methyl)azetidine-1-carbonyl)-6-methylmorpholino)quinoline-8-carbonitrile;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(1-methylazepan-4-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(((2*R*,6*R*)-6-methylmorpholin-2-yl)methyl)morpholine-2-carboxamide;

5-((2*R*,6*R*)-2-methyl-6-(octahydropyrrolo[3,4-*c*]pyrrole-2-carbonyl)morpholino)quinoline-8-carbonitrile;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*R*)-pyrrolidin-2-ylmethyl)morpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*S*)-piperidin-2-ylmethyl)morpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-*N*-((1*R*,3*R*,5*S*)-8-azabicyclo[3.2.1]octan-3-yl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-*N*-(azepan-4-yl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-*N*-((1*R*,5*S*,6*S*)-3-azabicyclo[3.1.0]hexan-6-yl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-6-dimethylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(((2*S*,6*R*)-4,6-dimethylmorpholin-2-yl)methyl)-6-methylmorpholine-2-carboxamide;

5-((2*R*,6*R*)-2-(4-(dimethylamino)piperidine-1-carbonyl)-6-methylmorpholino)quinoline-8-carbonitrile;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(1-methylpiperidin-4-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((3*S*,4*R*)-4-fluoropyrrolidin-3-yl)-6-methylmorpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((3*S*,4*R*)-4-fluoropiperidin-3-yl)-6-methylmorpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(2-azaspiro[3.3]heptan-6-yl)morpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-*N*-(1-(2-amino-2-oxoethyl)piperidin-4-yl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide;

5-((2*R*,6*R*)-2-(4-aminopiperidine-1-carbonyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-(4-amino-4-methylpiperidine-1-carbonyl)-6-methylmorpholino)quinoline-8-carbonitrile;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*,6-dimethyl-*N*-((*R*)-piperidin-3-yl)morpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-*N*-(2-carbamoylpyridin-4-yl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*,6-dimethyl-*N*-((*S*)-piperidin-3-yl)morpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(1-ethylpiperidin-4-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(1-ethylpiperidin-3-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*R*)-1-methylpiperidin-3-yl)morpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(4-methylpiperidin-4-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-*N*-(2-amino-2-methylpropyl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide;

rel-(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((3*R*,4*S*)-4-fluoropyrrolidin-3-yl)-6-methylmorpholine-2-carboxamide hydrochloride;

rel-(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((3*S*,4*R*)-4-fluoropyrrolidin-3-yl)-6-methylmorpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-*N*-(azepan-3-yl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide hydrochloride;

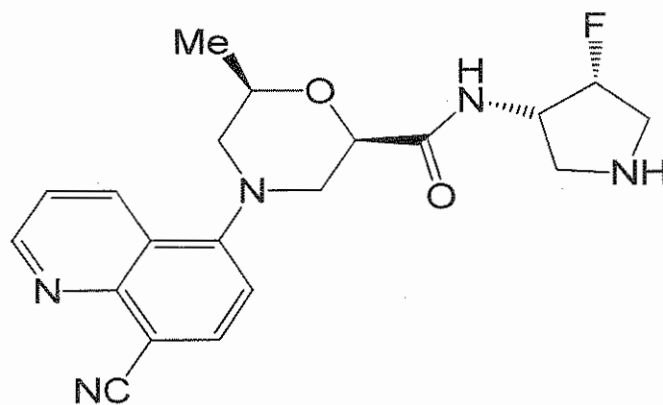
(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(1-methylazepan-3-yl)morpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(1,4-dimethylpiperidin-4-yl)-6-methylmorpholine-2-carboxamide; and

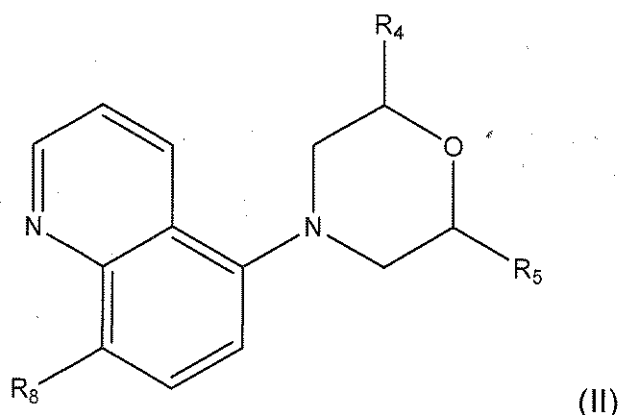
(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(4-fluoro-1-methylpiperidin-3-yl)-6-methylmorpholine-2-carboxamide hydrochloride.

4. The compound or pharmaceutically acceptable salt of claim 3, wherein said compound or salt is selected from the group consisting of rel-(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((3*R*,4*S*)-4-fluoropyrrolidin-3-yl)-6-methylmorpholine-2-carboxamide hydrochloride and (2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(1-methylpiperidin-4-yl)morpholine-2-carboxamide.

5. A compound as shown below or a pharmaceutically acceptable salt thereof, with relative stereochemistry indicated:



6. A compound of Formula (II) or pharmaceutically acceptable salt thereof:



wherein

R_4 is methyl;

R_5 is C_1 - C_5 alkyl that is saturated, partially saturated, or unsaturated, and that is optionally substituted with:

-H, -Cl, -F, -OH, - NH_2 , oxo-, - $N(CH_2CH_3)_2$, phenyl, cyclohexyl, phenyltriazolyl, cyclohexyltriazolyl, pyridinyl, pyrrolidinyl,

morpholinyl optionally substituted with methyl or hydroxymethyl,

-O-, substituted with:

C_1 - C_6 alkyl, methylphenyl, methylcyclohexyl, pyridinyl, diazinyl, or phenyl optionally substituted with -F or methyl,

-NH-, substituted with:

C_2 - C_7 alkyl that is linear, branched, or cyclic, saturated or unsaturated, and optionally substituted with oxo-, phenyl, methyl, or -OH,

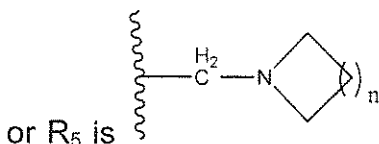
pyridinyl optionally substituted with methyl, methoxy, phenyl, or amino,

diazinyl optionally substituted with ethyl,

benzoimidazolyl, methylphenyl, phenylpyrazolyl, naphthyridyl,

phenyl optionally substituted with -F, methyl, ethyl, or ethoxy,

imidazolidinyl optionally substituted with methyl



, wherein n is 1-3, and wherein the cyclic amine is optionally substituted with

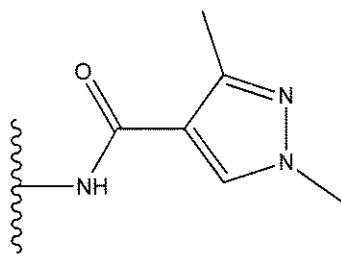
C₁-C₃ alkyl optionally substituted with

-OH, -F, phenyl, -NH₂, cyclohexyl, -N(CH₃)₂, -C(O)NH₂,
methylsulfonamidyl, benzenesulfonamidyl, methylbenzenesulfonamidyl, or
pyrrolidinyl optionally substituted with methyl or hydroxyl, or

-NHC(O)R₆, wherein R₆ is

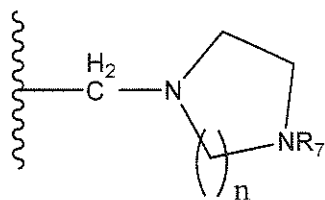
C₁-C₅ alkyl, phenyl, pyridinyl, fluorophenyl, methylsulfonyl,
fluorobenzenesulfonyl, dimethyl pyrazole sulfonyl, or
pyrazolyl optionally substituted with methyl;

piperidinyl optionally substituted with -C(O)CH₃, -C(O)CH₂CH₃, methyl, oxo-,



C(O)Ph, -NH₂, -NH-C(O)CH₃, or

piperazinyl optionally substituted with -C(O)OC(CH₃)₃, methyl, -C(O)CH₃, -
C(O)Ph, C(O)CH(CH₃)₂, -C(O)CH₃, or methylsulfonyl; or



R₅ is , where n is 1 or 2, and wherein the cyclic diamine is
optionally substituted on at least one carbon atom with

methyl, oxo-, -N(CH₃)₂, amino, -CH₂CH₃, or

piperidinyl optionally substituted with methyl, -C(O)CH₃, -C(O)CH(CH₃)₂, -
C(O)Ph, or -C(O)OC(CH₃)₃, and

wherein R₇ is -H, phenyl, -C(O)CH₃, C₁-C₃ alkyl, -C(O)NH₂, or -C(O)Ph; and

R₈ is methoxy or cyano.

7. The compound or pharmaceutically acceptable salt of claim 6, wherein said
compound or salt is selected from the group consisting of:

5-((2*R*,6*S*)-2,6-dimethylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2,6-dimethylmorpholino)quinoline-8-carbonitrile dihydrochloride;

5-((2*R*,6*S*)-2,6-dimethylmorpholino)quinoline-8-carbonitrile methanesulfonate;
 5-((2*R*,6*S*)-2,6-dimethylmorpholino)quinoline-8-carbonitrile bis(2,2,2-trifluoro-
 acetate);
 5-((2*R*,6*S*)-2,6-dimethylmorpholino)quinoline-8-carbonitrile bis(sulfonate);
 5-((2*R*,6*S*)-2,6-dimethylmorpholino)quinoline-8-carbonitrile sulfonate;
 5-((2*S*,6*R*)-2,6-dimethylmorpholino)quinoline-8-carbonitrile 2,3-dihydroxy-
 succinate;
 5-((2*S*,6*R*)-2,6-dimethylmorpholino)quinoline-8-carbonitrile dimethanesulfonate;
N-((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)acetamide;
N-((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)pivalamide;
 5-((2*S*,6*S*)-2,6-dimethylmorpholino)quinoline-8-carbonitrile;
 5-((2*S*,6*R*)-2-(aminomethyl)-6-methylmorpholino)quinoline-8-carbonitrile;
 5-(2-(hydroxymethyl)-6-methylmorpholino)quinoline-8-carbonitrile;
 (2*R*,6*S*)-4-(8-methoxyquinolin-5-yl)-2,6-dimethylmorpholine;
 5-((2*R*,6*S*)-2,6-dimethylmorpholino)quinoline-8-carboxamide;
 5-((2*R*,6*R*)-2-(hydroxymethyl)-6-methylmorpholino)quinoline-8-carbonitrile;
 5-((2*R*,6*R*)-2-(methoxymethyl)-6-methylmorpholino)quinoline-8-carbonitrile;
 5-((2*R*,6*R*)-2-((benzyloxy)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;
 5-((2*R*,6*R*)-2-(fluoromethyl)-6-methylmorpholino)quinoline-8-carbonitrile;
 5-((2*R*,6*R*)-2-(ethoxymethyl)-6-methylmorpholino)quinoline-8-carbonitrile;
 5-((2*R*,6*R*)-2-(isopropoxymethyl)-6-methylmorpholino)quinoline-8-carbonitrile;
 5-((2*R*,6*R*)-2-(isobutoxymethyl)-6-methylmorpholino)quinoline-8-carbonitrile;
 5-((2*R*,6*R*)-2-(chloromethyl)-6-methylmorpholino)quinoline-8-carbonitrile;
 5-((2*R*,6*R*)-2-((hexyloxy)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;
 5-((2*R*,6*R*)-2-((cyclohexylmethoxy)methyl)-6-methylmorpholino)quinoline-8-
 carbonitrile;
 5-((2*R*,6*S*)-2-methyl-6-propylmorpholino)quinoline-8-carbonitrile;
 5-((2*S*,6*S*)-2-(fluoromethyl)-6-methylmorpholino)quinoline-8-carbonitrile;
 5-((2*S*,6*S*)-2-(chloromethyl)-6-methylmorpholino)quinoline-8-carbonitrile;
 5-((2*R*,6*R*)-2-((2,6-dimethylphenoxy)methyl)-6-methylmorpholino)quinoline-8-
 carbonitrile;

5-((2*R*,6*S*)-2,6-diethylmorpholino)quinoline-8-carbonitrile;
 5-((2*R*,6*S*)-2-methyl-6-pentylmorpholino)quinoline-8-carbonitrile;
 5-((2*R*,6*R*)-2-formyl-6-methylmorpholino)quinoline-8-carbonitrile;
 5-((2*R*,6*R*)-2-((benzyloxy)methyl)-6-ethylmorpholino)quinoline-8-carbonitrile;
N-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)-2-phenylpropanamide;
 5-((2*R*,6*R*)-2-(1-hydroxyallyl)-6-methylmorpholino)quinoline-8-carbonitrile;
 5-((2*R*,6*R*)-2-((*S*)-1-hydroxyallyl)-6-methylmorpholino)quinoline-8-carbonitrile;
N-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)-1-phenylcyclobutanecarboxamide;
 5-((2*R*,6*R*)-2-((*R*)-1-hydroxyallyl)-6-methylmorpholino)quinoline-8-carbonitrile;
 5-((2*R*,6*S*)-2-methyl-6-(pyrrolidin-1-ylmethyl)morpholino)quinoline-8-carbonitrile;
 5-((2*S*,6*R*)-2-((diethylamino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;
 5-((2*S*,6*R*)-2-((benzylamino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;
 5-((2*R*,6*R*)-2-methyl-6-(phenoxymethyl)morpholino)quinoline-8-carbonitrile;
 5-((2*R*,6*R*)-2-methyl-6-((*m*-tolylloxy)methyl)morpholino)quinoline-8-carbonitrile;
 5-((2*R*,6*R*)-2-methyl-6-((*p*-tolylloxy)methyl)morpholino)quinoline-8-carbonitrile;
 5-((2*R*,6*R*)-2-(1-hydroxypropyl)-6-methylmorpholino)quinoline-8-carbonitrile;
 5-((2*R*,6*R*)-2-((*R*)-1-hydroxypentyl)-6-methylmorpholino)quinoline-8-carbonitrile;
 5-((2*R*,6*R*)-2-((*S*)-1-hydroxypentyl)-6-methylmorpholino)quinoline-8-carbonitrile;
 5-((2*R*,6*R*)-2-((*R*)-cyclohexyl(hydroxy)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;
 5-((2*R*,6*R*)-2-((*S*)-cyclohexyl(hydroxy)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;
N-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)-2-phenylacetamide;
 5-((2*R*,6*R*)-2-((*R*)-1-hydroxy-2-phenylethyl)-6-methylmorpholino)quinoline-8-carbonitrile;
 5-((2*R*,6*R*)-2-((*S*)-1-hydroxy-2-phenylethyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-((*R*)-1-hydroxy-3-phenylpropyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-((*S*)-1-hydroxy-3-phenylpropyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((phenylamino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((*m*-tolylamino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((*o*-tolylamino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((*p*-tolylamino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-((3,4-difluorophenoxy)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-((3-fluorophenoxy)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((1,2-dimethyl-1*H*-benzo[d]imidazol-5-yl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((1-ethyl-2-methyl-1*H*-benzo[d]imidazol-5-yl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((cyclohexylamino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-((2-fluorophenoxy)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-methyl-6-propionylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-(cyclohexanecarbonyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-methyl-6-(3-phenylpropanoyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-methyl-6-((*o*-tolylloxy)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((pyrimidin-2-ylamino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((pyridin-2-ylamino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((6-methylpyridin-2-yl)amino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((5-methylpyridin-2-yl)amino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((*R*)-2-(hydroxymethyl)pyrrolidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-((2,2-dimethylpyrrolidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((2-isopropylpyrrolidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((*S*)-2-methylpyrrolidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((*S*)-3-phenylpyrrolidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((*R*)-3-methylpyrrolidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((*S*)-3-hydroxypyrrolidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((4-methylpyridin-2-yl)amino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((3-phenylpyrrolidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((6-methoxypyridin-3-yl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((*R*)-2-methylpyrrolidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((2,5-dimethylpyrrolidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((4-methoxypyridin-2-yl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((6-methoxypyridin-2-yl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((1-phenyl-1*H*-pyrazol-5-yl)amino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((*S*)-2-(hydroxymethyl)pyrrolidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((*R*)-3-hydroxypyrrolidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((*S*)-3-methylpyrrolidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((3,3-dimethylpyrrolidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-methyl-6-((*R*)-3-phenyl-1-(pyrrolidin-1-yl)propyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-methyl-6-(((*S*)-3-phenyl-1-(pyrrolidin-1-yl)propyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((3-methoxypyridin-2-yl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((*R*)-3-hydroxypiperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((2*R*,6*S*)-2,6-dimethylpiperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((*S*)-3-hydroxypiperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((4-hydroxypiperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((2-(hydroxymethyl)piperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((2-methylpiperidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((2-ethylpiperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((2,3-dimethylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((pyridin-3-ylamino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((pyridin-4-ylamino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((*S*)-2-(trifluoromethyl)pyrrolidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((4-methylpiperidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((4,4-difluoropiperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((4-phenylpiperidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((4-fluoropiperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((cyclopentylamino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((3-methylcyclohexyl)amino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((3-methylpyridin-2-yl)amino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-ethyl-6-(hydroxymethyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((4-phenylpyridin-2-yl)amino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(piperazin-1-ylmethyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((4-phenylpiperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((6-aminopyridin-2-yl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((2,5-dimethylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((4-acetylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((2*S*,4*R*)-4-hydroxy-2-(hydroxymethyl)pyrrolidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((*R*)-2-methylpiperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((*R*)-3-methylpiperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((*S*)-3-methylpiperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((2*R*,5*R*)-2,5-dimethylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((2*R*,5*S*)-2,5-dimethylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((4-methylcyclohexyl)amino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((cyclobutylamino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((cycloheptylamino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((4-hydroxycyclohexyl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((2-hydroxycyclopentyl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((2-methylcyclohexyl)amino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((5-phenylpyridin-2-yl)amino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((3-phenylpyridin-2-yl)amino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((1*S*,3*R*)-3-hydroxycyclopentyl)amino)methyl)-6-methylmorpholinoquinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((3-ethoxypyridin-2-yl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((2-phenylpyridin-4-yl)amino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((6-phenylpyridin-2-yl)amino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((2-methyl-5-oxopiperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((4-methylpiperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((4-propylpiperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((4-(dimethylamino)piperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-([1,4'-bipiperidin]-1'-ylmethyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-([1,4'-bipiperidin]-1'-ylmethyl)-6-methylmorpholino)quinoline-8-carbonitrile dihydrochloride;

5-((2*S*,6*R*)-2-(((*R*)-3-aminopiperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

(2*R*,6*S*)-4-(8-chloro-1,7-naphthyridin-5-yl)-2,6-dimethylmorpholine;

5-((2*S*,6*R*)-2-((4-aminopiperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((5-fluoropyrimidin-2-yl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(piperidin-1-ylmethyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(morpholinomethyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((2*S*,6*R*)-2,6-dimethylmorpholino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((2*R*,6*R*)-2-(hydroxymethyl)-6-methylmorpholino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((4-(pyridin-2-yl)piperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((4-(pyridin-4-yl)piperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)acetamide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)acetamide hydrochloride;

5-((2*S*,6*R*)-2-(((1,8-naphthyridin-2-yl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidine-4-carboxamide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)benzamide;

5-((2*S*,6*R*)-2-((4-isopropylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

4-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperazine-1-carboxamide;

5-((2*S*,6*R*)-2-((4-cyclohexylpiperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((4-(pyrrolidin-1-yl)piperidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-((4-cyclohexyl-1*H*-1,2,3-triazol-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-methyl-6-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((2-oxo-[1,4'-bipiperidin]-1'-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((5-ethylpyrimidin-2-yl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((6-amino-3,5-dimethylpyridin-2-yl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((pyrazin-2-ylamino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((1,3-dimethyl-1*H*-pyrazol-5-yl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,7*R*)-2-(hydroxymethyl)-7-methyl-1,4-oxazepan-4-yl)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((4-ethylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((3-(pyrrolidin-1-yl)azetidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((3-(piperidin-1-yl)azetidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((*R*)-2,4-dimethylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((4-(hydroxymethyl)piperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((*R*)-[1,3'-bipyrrolidin]-1'-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((*R*)-3-(piperidin-1-yl)pyrrolidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((4-methyl-1,4-diazepan-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((4-benzoylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)nicotinamide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)isonicotinamide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)picolinamide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)hexanamide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)isobutyramide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)isobutyramide hydrochloride;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)pivalamide;

5-((2*S*,7*R*)-2-([1,4'-bipiperidin]-1'-ylmethyl)-7-methyl-1,4-oxazepan-4-yl)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((4-morpholinopiperidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

tert-butyl 4-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)piperazine-1-carboxylate;

tert-butyl 4-(4-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperazin-1-yl)piperidine-1-carboxylate;

5-((2*R*,6*S*)-2-methyl-6-((4-(piperazin-1-yl)piperidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((4-(piperidin-4-yl)piperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((3-(4-methylpiperazin-1-yl)azetidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-([4,4'-bipiperidin]-1-ylmethyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((1'-acetyl-[4,4'-bipiperidin]-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((1'-methyl-[4,4'-bipiperidin]-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((3-(piperazin-1-yl)azetidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((3-(4-acetylpiperazin-1-yl)azetidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((1'-isobutyryl-[4,4'-bipiperidin]-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((3-(4-benzoylpiperazin-1-yl)azetidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((1'-benzoyl-[4,4'-bipiperidin]-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((4-(1-methylpiperidin-4-yl)piperazin-1-yl)methyl)-morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((4-(1-acetylpiperidin-4-yl)piperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((4-(1-isobutyrylpiperidin-4-yl)piperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((4-(1-benzoylpiperidin-4-yl)piperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((3-(4-isobutyrylpiperazin-1-yl)azetidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((4-(4-acetylpiperazin-1-yl)piperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((4-(4-isobutyrylpiperazin-1-yl)piperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((4-(4-benzoylpiperazin-1-yl)piperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((4-(4-methylpiperazin-1-yl)piperidin-1-yl)methyl)-morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((4-(4-methylpiperazin-1-yl)piperidin-1-yl)methyl)-morpholino)quinoline-8-carbonitrile trihydrochloride;

5-((2*S*,6*R*)-2-([1,4'-bipiperidin]-1'-ylmethyl)-6-methylmorpholino)-2-methyl-quinoline-8-carbonitrile;

N-((*R*)-1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)-pyrrolidin-3-yl)acetamide;

N-((*R*)-1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)-pyrrolidin-3-yl)isobutyramide;

5-((2*R*,6*S*)-2-methyl-6-(((*S*)-3-(piperidin-1-yl)pyrrolidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((*S*)-3-(piperidin-1-yl)pyrrolidin-1-yl)methyl)morpholino)-quinoline-8-carbonitrile dihydrochloride;

5-((2*R*,6*S*)-2-methyl-6-((3-morpholinoazetidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((3-((*S*)-2-methylpyrrolidin-1-yl)azetidin-1-yl)methyl)-morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((*S*)-2-methylpiperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((*S*)-2,4-dimethylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((*R*)-3,4-dimethylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((*S*)-3,4-dimethylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((*S*)-3-ethylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((*S*)-3-ethylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile dihydrochloride;

5-((2*S*,6*R*)-2-(((*S*)-3-ethyl-4-methylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((4-(azepan-1-yl)piperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((*S*)-[1,3'-bipyrrolidin]-1'-ylmethyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((3-(4-aminopiperidin-1-yl)azetidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

N-(1-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)-azetidin-3-yl)piperidin-4-yl)acetamide;

5-((2*R*,6*S*)-2-methyl-6-((3-(4-(methylsulfonyl)piperazin-1-yl)azetidin-1-yl)methyl)-morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((3-((*S*)-3-hydroxypyrrolidin-1-yl)azetidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)-1,3-dimethyl-1*H*-pyrazole-4-carboxamide;

N-(1-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)-azetidin-3-yl)piperidin-4-yl)-1,3-dimethyl-1*H*-pyrazole-4-carboxamide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)methanesulfonamide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)benzenesulfonamide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)-4-fluorobenzenesulfonamide;

5-((2*S*,6*R*)-2-((3-aminoazetidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)azetidin-3-yl)acetamide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)azetidin-3-yl)-4-fluorobenzamide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)azetidin-3-yl)methanesulfonamide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)azetidin-3-yl)-4-fluorobenzenesulfonamide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)azetidin-3-yl)-1,3-dimethyl-1*H*-pyrazole-4-sulfonamide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)-1,3-dimethyl-1*H*-pyrazole-4-sulfonamide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)azetidin-3-yl)isobutyramide;

5-((2*R*,6*S*)-2-methyl-6-(((*S*)-2-methyl-5-oxopiperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((*R*)-2-methyl-5-oxopiperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((*R*)-2-methyl-3-oxopiperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((*S*)-2-methyl-3-oxopiperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((2,4,5-trimethylpiperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((2,3,4-trimethylpiperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

N-((*R*)-1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)pyrrolidin-3-yl)benzamide;

5-((2*S*,6*R*)-2-(((*R*)-3-(dimethylamino)pyrrolidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

N-((*S*)-1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)-pyrrolidin-3-yl)acetamide;

N-((*S*)-1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)-pyrrolidin-3-yl)isobutyramide;

N-((*S*)-1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)-pyrrolidin-3-yl)benzamide;

5-((2*S*,6*R*)-2-(((*S*)-3-(dimethylamino)pyrrolidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-methyl-6-((pyrazin-2-yloxy)methyl)morpholino)quinoline-8-carbonitrile;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)azetid-3-yl)benzamide;

5-((2*S*,6*R*)-2-((3,3-dimethylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile dihydrochloride;

5-((2*R*,6*S*)-2-methyl-6-((3,3,4-trimethylpiperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile dihydrochloride;

5-((2*R*,6*R*)-2-((*R*)-1-hydroxyethyl)-6-methylmorpholino)quinoline-8-carbonitrile;

1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)-*N*-ethylpiperidine-4-carboxamide;

1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)-*N*-ethylpiperidine-4-carboxamide hydrochloride;

5-((2*R*,6*R*)-2-((*S*)-1-hydroxyethyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-methyl-6-((pyridin-2-yloxy)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-methyl-6-((pyrimidin-2-yloxy)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-methyl-6-((*R*)-1-(pyrimidin-2-yloxy)ethyl)morpholino)quinoline-8-carbonitrile;

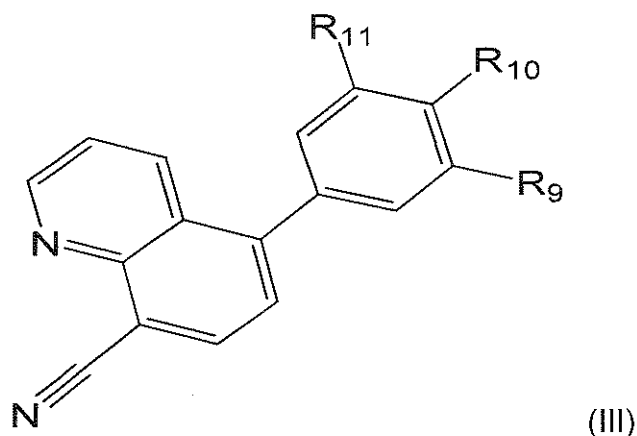
5-((2*R*,6*R*)-2-methyl-6-((*S*)-1-(pyrimidin-2-yloxy)ethyl)morpholino)quinoline-8-carbonitrile; and

5-((2*R*,6*R*)-2-((*S*)-hydroxy(pyridin-2-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile.

8. The compound or pharmaceutically acceptable salt of claim 6, wherein said compound or salt is selected from the group consisting of 5-((2*S*,6*R*)-2-([1,4'-

bipiperidin]-1'-ylmethyl)-6-methylmorpholino)quinoline-8-carbonitrile and 5-((2*R*,7*R*)-2-(hydroxymethyl)-7-methyl-1,4-oxazepan-4-yl)quinoline-8-carbonitrile.

9. A compound of Formula (III) or pharmaceutically acceptable salt thereof:



wherein

R_{11} is H or methyl;

R_{10} is H or, when both R_{11} and R_9 are H, is methyl-1,4'-bipiperidinyl;

R_9 is -H or is -CH₂- substituted by 1,4'-bipiperidinyl, oxo-, hydroxyl, methylpyridinyl, or piperidinyl optionally substituted with hydroxyl, -N(CH₃)₂, or piperidinyl.

10. The compound or pharmaceutically acceptable salt of claim 9, wherein said compound or salt is selected from the group consisting of:

5-(3-([1,4'-bipiperidin]-1'-ylmethyl)phenyl)quinoline-8-carbonitrile;

5-(4-([1,4'-bipiperidin]-1'-ylmethyl)phenyl)quinoline-8-carbonitrile;

5-(3-formyl-5-methylphenyl)quinoline-8-carbonitrile;

5-(3-(hydroxymethyl)-5-methylphenyl)quinoline-8-carbonitrile;

5-(3-(chloromethyl)-5-methylphenyl)quinoline-8-carbonitrile;

5-(3-((4-hydroxypiperidin-1-yl)methyl)-5-methylphenyl)quinoline-8-carbonitrile;

5-(3-((4-(dimethylamino)piperidin-1-yl)methyl)-5-methylphenyl)quinoline-8-carbonitrile;

5-(3-methyl-5-((4-methylpiperazin-1-yl)methyl)phenyl)quinoline-8-carbonitrile;
and
5-(3-([1,4'-bipiperidin]-1'-ylmethyl)-5-methylphenyl)quinoline-8-carbonitrile.

11. The compound or pharmaceutically acceptable salt of any of claims 1-10 for use in the treatment of lupus.
12. The compound of claim 11, wherein said compound is to be administered as a pharmaceutically acceptable salt.
13. The compound or pharmaceutically acceptable salt of any of claims 1-10 for use in antagonizing TLR7.
14. The compound or pharmaceutically acceptable salt of any of claims 1-10 for use in antagonizing TLR8.
15. A pharmaceutical composition comprising at least one compound or pharmaceutically acceptable salt of any of claims 1-10 and at least one pharmaceutically acceptable carrier.
16. The pharmaceutical composition of claim 15, wherein said compound or pharmaceutically acceptable salt thereof has an IC₅₀ less than or equal to 100 nM against human TLR7 receptors in a HEK-293 cell line.
17. The pharmaceutical composition of claim 15, wherein said compound or pharmaceutically acceptable salt thereof has an IC₅₀ less than or equal to 20 nM against human TLR7 receptors expressed in a HEK-293 cell line.
18. The pharmaceutical composition of claim 15, wherein said compound or pharmaceutically acceptable salt thereof has an IC₅₀ less than or equal to 5 nM against human TLR7 receptors expressed in a HEK-293 cell line.

19. The pharmaceutical composition of any of claims 16-18, wherein the IC50 against human TLR7 receptors expressed in a HEK-293 cell line is measured by (1) plating cells of the HEK-293 cell line stably expressing TLR7 in a Dulbecco's modified Eagle's medium containing 10% fetal bovine serum at a density of 2.22X10⁵ cells/ml into a 384-well plate and incubating for 2 days at 37°C, 5% CO₂; (2) adding the compound or pharmaceutically acceptable salt thereof and incubating the cells for 30 minutes; (3) adding CL097 (InvivoGen) at 3ug/ml and incubating the cells for approximately 20 hours; and (4) quantifying NF-kappaB dependent reporter activation by measuring luminescence.

20. The compound or pharmaceutically acceptable salt of any of claims 1-10 for use in the treatment of a systematic lupus erythematosus, cutaneous lupus, or neuropsychiatric lupus.

21. The compound of claim 20, wherein said compound is administered as a pharmaceutically acceptable salt.

22. A pharmaceutically acceptable salt of Claim 5, wherein the pharmaceutically acceptable salt, with relative stereochemistry indicated, is Rel-(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((3*S*,4*R*)-4-fluoropyrrolidin-3-yl)-6-methylmorpholine-2-carboxamide hydrochloride.

23. The pharmaceutically acceptable salt of claim 22 for use in the treatment of lupus.

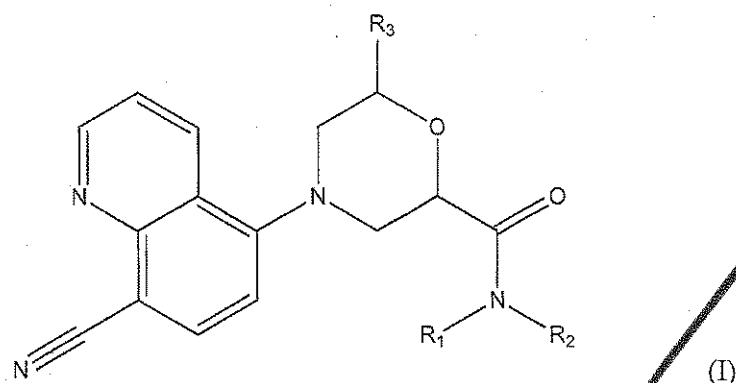
24. A pharmaceutical composition comprising the pharmaceutically acceptable salt of claim 22 and at least one pharmaceutically acceptable carrier.

25. The pharmaceutically acceptable salt of claim 22 for use in the treatment of a systematic lupus erythematosus, cutaneous lupus, or neutopsychiatric lupus.

26. The pharmaceutically acceptable salt of claim 22 for use in antagonizing TLR7.
27. The pharmaceutically acceptable salt of claim 22 for use in antagonizing TLR8.
28. The compound or pharmaceutically acceptable salt of claim 5 for use in the treatment of lupus.
29. A pharmaceutical composition comprising the pharmaceutically acceptable salt of claim 5 and at least one pharmaceutically acceptable carrier.
30. The compound or pharmaceutically acceptable salt of claim 5 for use in the treatment of a systematic lupus erythematosus, cutaneous lupus, or neutropsychiatric lupus.
31. The compound or pharmaceutically acceptable salt of claim 5 for use in antagonizing TLR7.
32. The compound or pharmaceutically acceptable salt of claim 5 for use in antagonizing TLR8.

We claim:

1. A compound of formula (I):



wherein at least one of R_1 and R_2 is -H, methyl, or ethyl, and the other is

-H; or the other is

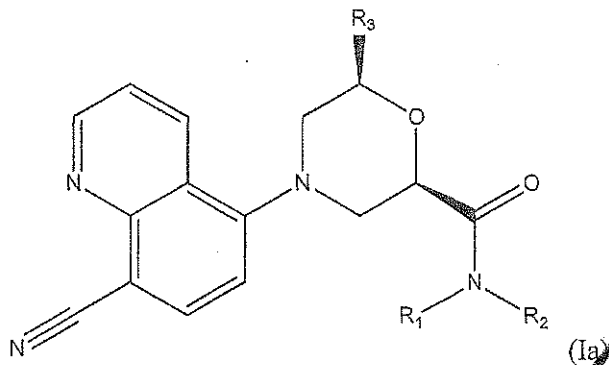
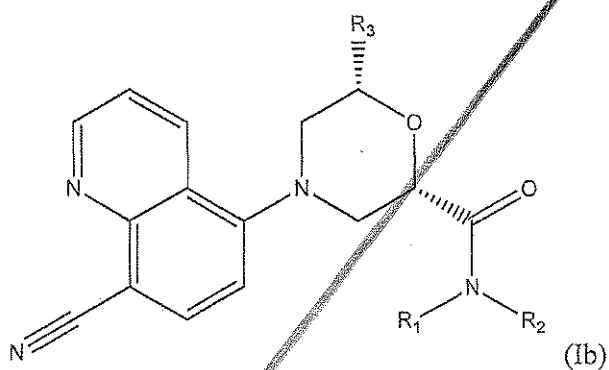
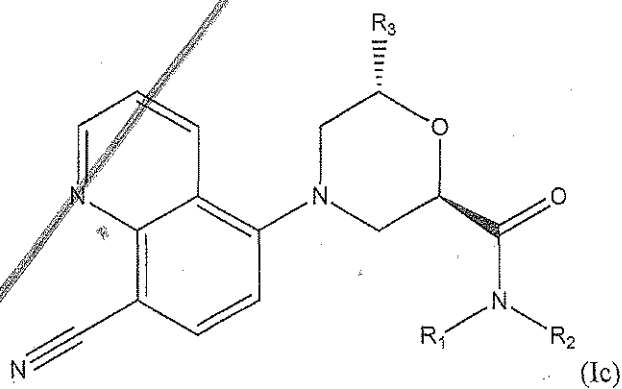
C_1 - C_6 alkyl that is optionally substituted with:

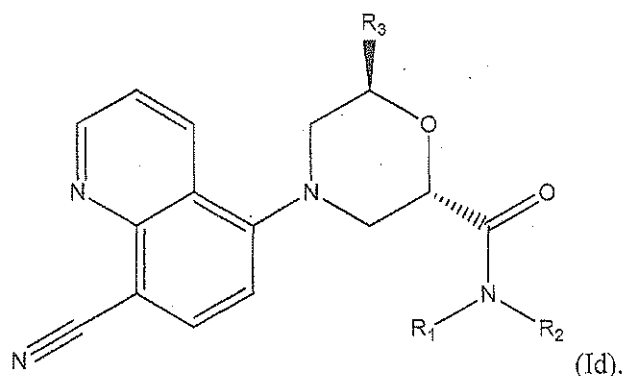
-OH, methoxy, ethoxy, $-OCH(CH_3)_2$, $-O(CH_2)_2CH_3$, phenyl, furanyl, $-O(CH_2)_2OH$, phenoxy, methylthio, -F, $-N(CH_3)_2$, cyano, pyridinyloxy, fluorophenoxy, isochromanyl, phenol, benzylamino, $-NHCH_3$, oxo-, amino, carboxyl, 7-member spiroaminyl, a three to six member cycloalkyl, saturated or unsaturated and optionally including one or more heteroatoms selected from O and N, and optionally substituted at one or more C or N atoms by methyl, cyano, fluoro, methylamino, or trifluoromethyl; or the other is

C_3 - C_7 cycloalkane, saturated or unsaturated, optionally bridged, optionally including one or more heteroatoms selected from O, S, and N, and optionally substituted at one or more C or N atoms by methyl, ethyl, pyridinyl, azetidyl, acetamidyl, carboxamidyl, cyano, fluoro, methylamino, or trifluoromethyl; or

R_1 and R_2 , together with the nitrogen atom to which they are attached, form an 8 to 11 member spirodiamine, an 8 member bicycldiamine, a 7 member spiroxamine, a piperidinyl optionally substituted with ethyl, or a four to six member cycloalkyl, optionally substituted with at least one of carboxamidyl, aminomethyl, methyl, (ethylamino)methyl, (dimethylamino)methyl, dimethylamino, (methylamino)methyl, and amino; and wherein R_3 is -H or methyl.

2. The compound of formula 1, wherein said compound has a stereochemical configuration selected from one of those shown in the group consisting of Formula (Ia), Formula (Ib), Formula (Ic), and Formula (Id):





3. The compound of claim 1, wherein said compound is selected from the group consisting of:

- 5-((2*R*, 6*R*)-2-formyl-6-methylmorpholino)quinoline-8-carbonitrile;
- (2*R*, 6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-ethyl-6-methylmorpholine-2-carboxamide;
- (2*R*, 6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-isopropyl-6-methylmorpholine-2-carboxamide;
- 5-((2*R*, 6*R*)-2-formyl-6-methylmorpholino)quinoline-8-carbonitrile;
- (2*R*, 6*R*)-methyl 4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxylate;
- (6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide;
- 5-((2*R*, 6*R*)-2-((*S*)-3-ethylpiperazine-1-carbonyl)-6-methylmorpholino)quinoline-8-carbonitrile;
- (2*R*, 6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(3,4-difluorobenzyl)-6-methylmorpholine-2-carboxamide;
- 5-((2*R*, 6*R*)-2-((*S*)-3-aminopyrrolidine-1-carbonyl)-6-methylmorpholino)quinoline-8-carbonitrile;
- 5-((2*R*, 6*R*)-2-(azetidine-1-carbonyl)-6-methylmorpholino)quinoline-8-carbonitrile;
- 5-((2*R*, 6*R*)-2-([1,4'-bipiperidine]-1'-carbonyl)-6-methylmorpholino)quinoline-8-carbonitrile;
- (2*R*, 6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-cyclopropyl-6-methylmorpholine-2-carboxamide;
- 5-((2*R*, 6*R*)-2-(3-aminoazetidine-1-carbonyl)-6-methylmorpholino)quinoline-8-carbonitrile;
- (2*R*, 6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-hydroxyethyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-methoxyethyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*R*)-2-hydroxypropyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*S*)-1-hydroxypropan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*R*)-1-hydroxypropan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*S*)-1-hydroxybutan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*S*)-1-hydroxy-3-methylbutan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*S*)-2-hydroxy-1-phenylethyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*R*)-2-hydroxy-1-phenylethyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-hydroxybutyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-ethoxyethyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*R*)-1-hydroxybutan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(1,3-dihydroxypropan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2,3-dihydroxypropyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(((*R*)-tetrahydrofuran-2-yl)methyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((tetrahydrofuran-2-yl)methyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(2-propoxyethyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*R*)-1-hydroxypentan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-isopropoxyethyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(1-methoxybutan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-(2-fluorophenyl)-2-hydroxyethyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*R*)-1-hydroxy-3-methylbutan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2,2-dimethoxyethyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-(2-hydroxyethoxy)ethyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((1*S*,2*S*)-2-hydroxycyclohexyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-hydroxycyclohexyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(1-hydroxyhexan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*S*)-1-hydroxy-3,3-dimethylbutan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*S*)-1-hydroxyhexan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((2*S*,3*S*)-1-hydroxy-3-methylpentan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*S*)-1-hydroxy-4-methylpentan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*R*)-1-hydroxy-4-methylpentan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((4-methylmorpholin-2-yl)methyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*S*)-1-hydroxy-4-(methylthio)butan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(2-phenoxyethyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*S*)-1-hydroxy-3-phenylpropan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(2-phenoxypropyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-hydroxy-3-phenylpropyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(2-(pyridin-3-yloxy)propyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-(4-fluorophenoxy)ethyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-(3-fluorophenyl)-2-hydroxyethyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((*S*)-1-cyclohexyl-3-hydroxypropan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(isochroman-1-ylmethyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-hydroxy-3-phenoxypropyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((1*S*,2*R*)-1-hydroxy-1-(4-hydroxyphenyl)propan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((1*S*)-1,3-dihydroxy-1-phenylpropan-2-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-hydroxy-3-(piperazin-1-yl)propyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-*N*-(azetidin-3-yl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*S*)-pyrrolidin-3-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*R*)-pyrrolidin-3-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*S*)-piperidin-3-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*R*)-piperidin-3-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*S*)-pyrrolidin-2-ylmethyl)morpholine-2-carboxamide;

(2*R*,6*R*)-*N*-(2-(benzylamino)ethyl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(pyridin-2-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(6-methylpyridin-2-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(5-methylisoxazol-3-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(2,2,2-trifluoroethyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2,2-difluoroethyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(3,3,3-trifluoropropyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-(dimethylamino)-2-methylpropyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*S*)-morpholin-2-ylmethyl)morpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(((*S*)-4-methylmorpholin-2-yl)methyl)morpholine-2-carboxamide acetic acetate;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-fluoroethyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(3-fluoropropyl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*S*)-1,1,1-trifluoropropan-2-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*R*)-1,1,1-trifluoropropan-2-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(1,3-dimethyl-1*H*-pyrazol-5-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(1-methyl-1*H*-pyrazol-5-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-*N*-(cyanomethyl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-*N*-(1-cyanocyclopropyl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(1,2,4-thiadiazol-5-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(3-methyl-1,2,4-thiadiazol-5-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(piperidin-4-yl)morpholine-2-carboxamide;

5-((2*R*,6*R*)-2-methyl-6-(2,6-diazaspiro[3.4]octane-2-carbonyl)morpholino)quinoline-8-carbonitrile hydrochloride;

5-((2*R*,6*R*)-2-methyl-6-(3-((methylamino)methyl)azetidine-1-carbonyl)morpholino)quinoline-8-carbonitrile hydrochloride;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((4-fluoropiperidin-4-yl)methyl)-6-methylmorpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-*N*-(azetidin-3-ylmethyl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide hydrochloride;

5-((2*R*,6*R*)-2-methyl-6-(2,6-diazaspiro[3.5]nonane-2-carbonyl)morpholino)quinoline-8-carbonitrile hydrochloride;

5-((2*R*,6*R*)-2-methyl-6-(1,6-diazaspiro[3.4]octane-1-carbonyl)morpholino)quinoline-8-carbonitrile hydrochloride;

5-((2*R*,6*R*)-2-methyl-6-(1,7-diazaspiro[4.4]nonane-7-carbonyl)morpholino)quinoline-8-carbonitrile hydrochloride;

(2*R*,6*R*)-*N*-(3-carbamoyl-1-methyl-1*H*-pyrazol-4-yl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(oxetan-3-ylmethyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(tetrahydro-2*H*-pyran-4-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(tetrahydrofuran-3-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((3-methyloxetan-3-yl)methyl)morpholine-2-carboxamide;

5-((2*R*, 6*R*)-2-methyl-6-(2-oxa-6-azaspiro[3.3]heptane-6-carbonyl)morpholino)quinoline-8-carbonitrile;

(2*R*, 6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(oxetan-3-yl)morpholine-2-carboxamide;

(2*R*, 6*R*)-*N*-((3-(aminomethyl)oxetan-3-yl)methyl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide;

(2*R*, 6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(oxetan-2-ylmethyl)morpholine-2-carboxamide;

5-((2*R*, 6*R*)-2-methyl-6-(piperazine-1-carbonyl)morpholino)quinoline-8-carbonitrile hydrochloride;

(2*R*, 6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(2-(methylamino)ethyl)morpholine-2-carboxamide;

(2*R*, 6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*S*)-3,3,3-trifluoro-2-hydroxypropyl)morpholine-2-carboxamide;

(2*R*, 6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*R*)-3,3,3-trifluoro-2-hydroxypropyl)morpholine-2-carboxamide;

methyl 2-((2*R*, 6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamido)acetate;

(2*R*, 6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(2-(dimethylamino)ethyl)-6-methylmorpholine-2-carboxamide;

(2*R*, 6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*S*)-4,4,4-trifluoro-3-hydroxybutyl)morpholine-2-carboxamide;

(2*R*, 6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*R*)-4,4,4-trifluoro-3-hydroxybutyl)morpholine-2-carboxamide;

(2*R*, 6*R*)-*N*-(3-amino-4,4,4-trifluorobutyl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide;

2-((2*R*, 6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamido)acetic acid;

1-((2*R*, 6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carbonyl)azetidine-3-carboxamide;

5-((2*R*, 6*R*)-2-methyl-6-(2,7-diazaspiro[4.4]nonane-2-carbonyl)morpholino)quinoline-8-carbonitrile hydrochloride;

5-((2*R*, 6*R*)-2-methyl-6-(3,9-diazaspiro[5.5]undecane-3-carbonyl)morpholino)quinoline-8-carbonitrile hydrochloride;

(2*R*,6*R*)-*N*-(3-carbamoylpyridin-4-yl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*R*)-morpholin-2-ylmethyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(pyridin-4-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(pyridin-3-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(1-(piperidin-4-yl)-1*H*-pyrazol-4-yl)morpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-*N*-(1-(azetidin-3-yl)-1*H*-pyrazol-4-yl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-*N*-((1*H*-pyrazol-5-yl)methyl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-*N*-((1*H*-pyrazol-4-yl)methyl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((3-(trifluoromethyl)pyridin-2-yl)methyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(1-(pyridin-2-yl)ethyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(pyridin-2-ylmethyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((6-methylpyridin-2-yl)methyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((1-methylpiperidin-2-yl)methyl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((3-methylpyridin-2-yl)methyl)morpholine-2-carboxamide;

(2*R*,6*R*)-*N*-(4-cyano-1*H*-pyrazol-3-yl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((3*S*,4*R*)-4-fluoro-1-methylpyrrolidin-3-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((3*S*,4*R*)-4-fluoropiperidin-3-yl)-*N*,6-dimethylmorpholine-2-carboxamide hydrochloride;

5-((2*R*,6*R*)-2-(3-(aminomethyl)azetidine-1-carbonyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-(3-((ethylamino)methyl)azetidine-1-carbonyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-(3-((dimethylamino)methyl)azetidine-1-carbonyl)-6-methylmorpholino)quinoline-8-carbonitrile;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(1-methylazepan-4-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(((2*R*,6*R*)-6-methylmorpholin-2-yl)methyl)morpholine-2-carboxamide;

5-((2*R*,6*R*)-2-methyl-6-(octahydropyrrolo[3,4-*c*]pyrrole-2-carbonyl)morpholino)quinoline-8-carbonitrile;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*R*)-pyrrolidin-2-ylmethyl)morpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*S*)-piperidin-2-ylmethyl)morpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-*N*-((1*R*,3*R*,5*S*)-8-azabicyclo[3.2.1]octan-3-yl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-*N*-(azepan-4-yl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-*N*-((1*R*,5*S*,6*S*)-3-azabicyclo[3.1.0]hexan-6-yl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-6-dimethylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(((2*S*,6*R*)-4,6-dimethylmorpholin-2-yl)methyl)-6-methylmorpholine-2-carboxamide;

5-((2*R*,6*R*)-2-(4-(dimethylamino)piperidine-1-carbonyl)-6-methylmorpholino)quinoline-8-carbonitrile;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(1-methylpiperidin-4-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((3*S*,4*R*)-4-fluoropyrrolidin-3-yl)-6-methylmorpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((3*S*,4*R*)-4-fluoropiperidin-3-yl)-6-methylmorpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(2-azaspiro[3.3]heptan-6-yl)morpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-*N*-(1-(2-amino-2-oxoethyl)piperidin-4-yl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide;

5-((2*R*,6*R*)-2-(4-aminopiperidine-1-carbonyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-(4-amino-4-methylpiperidine-1-carbonyl)-6-methylmorpholino)quinoline-8-carbonitrile;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*,6-dimethyl-*N*-((*R*)-piperidin-3-yl)morpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-*N*-(2-carbamoylpyridin-4-yl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-6-dimethyl-*N*-((*S*)-piperidin-3-yl)morpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(1-ethylpiperidin-4-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(1-ethylpiperidin-3-yl)-6-methylmorpholine-2-carboxamide;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-((*R*)-1-methylpiperidin-3-yl)morpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(4-methylpiperidin-4-yl)morpholine-2-carboxamide;

(2*R*,6*R*)-*N*-(2-amino-2-methylpropyl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide;

rel-(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((3*R*,4*S*)-4-fluoropyrrolidin-3-yl)-6-methylmorpholine-2-carboxamide hydrochloride;

rel-(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((3*S*,4*R*)-4-fluoropyrrolidin-3-yl)-6-methylmorpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-*N*-(azepan-3-yl)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholine-2-carboxamide hydrochloride;

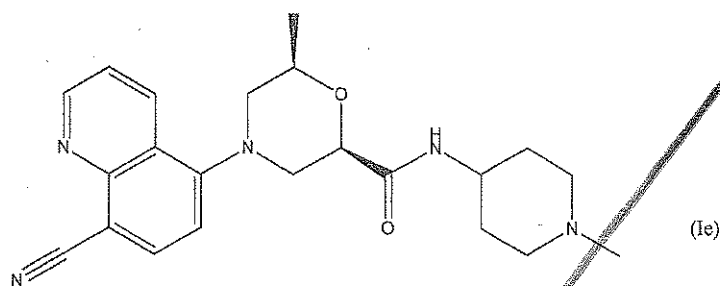
(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(1-methylazepan-3-yl)morpholine-2-carboxamide hydrochloride;

(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(1,4-dimethylpiperidin-4-yl)-6-methylmorpholine-2-carboxamide; and

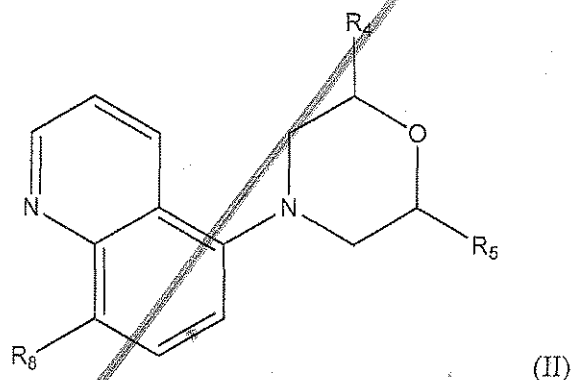
(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-(4-fluoro-1-methylpiperidin-3-yl)-6-methylmorpholine-2-carboxamide hydrochloride.

4. The compound of claim 3, wherein said compound is selected from the group consisting of *rel*-(2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-*N*-((3*R*,4*S*)-4-fluoropyrrolidin-3-yl)-6-methylmorpholine-2-carboxamide hydrochloride and (2*R*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methyl-*N*-(1-methylpiperidin-4-yl)morpholine-2-carboxamide.

5. A compound of Formula (Ie), with relative stereochemistry indicated:



6. A compound of Formula (II):



wherein

R_4 is -H or methyl;

R_5 is C_1 - C_5 alkyl that is saturated, partially saturated, or unsaturated, and that is optionally substituted with:

H, -Cl, -F, -OH, -NH₂, oxo-, -N(CH₂CH₃)₂, phenyl, cyclohexyl, phenyltriazolyl, cyclohexyltriazolyl, pyridinyl, pyrrolidinyl,

morpholinyl optionally substituted with methyl or hydroxymethyl,

-O-, substituted with:

C₁-C₆ alkyl, methylphenyl, methylcyclohexyl, pyridinyl, diazinyl, or phenyl optionally substituted with -F or methyl,

-NH-, substituted with:

C₂-C₇ alkyl that is linear, branched, or cyclic, saturated or unsaturated, and optionally substituted with oxo-, phenyl, methyl, or -OH,

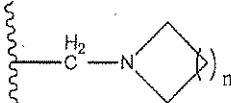
pyridinyl optionally substituted with methyl, methoxy, phenyl, or amino,

diazinyl optionally substituted with ethyl,

benzimidazolyl, methylphenyl, phenylpyrazolyl, naphthyridyl,

phenyl optionally substituted with -F, methyl, ethyl, or ethoxy

imidazolidinyl optionally substituted with methyl

or R₅ is , wherein n is 1-3, and wherein the cyclic amine is optionally substituted with

C₁-C₃ alkyl optionally substituted with

-OH, -F, phenyl, -NH₂, cyclohexyl, -N(CH₃)₂, -C(O)NH₂, methylsulfonamidyl, benzenesulfonamidyl, methylbenzenesulfonamidyl, or

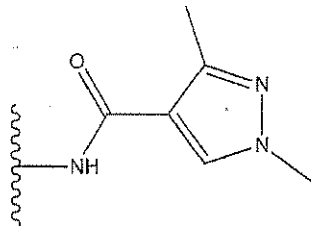
pyrrolidinyl optionally substituted with methyl or hydroxyl, or

-NHC(O)R₆, wherein R₆ is

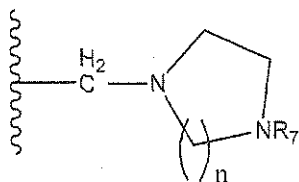
C₁-C₅ alkyl, phenyl, pyridinyl, fluorophenyl, methylsulfonyl, fluorobenzenesulfonyl, dimethyl pyrazole sulfonyl, or

pyrazolyl optionally substituted with methyl;

piperidinyl optionally substituted with -C(O)CH₃, -C(O)CH₂CH₃, methyl, oxo-,

C(O)Ph, -NH₂, NH-C(O)CH₃, or 

piperazinyl optionally substituted with -C(O)OC(CH₃)₃, methyl, -C(O)CH₃, -C(O)Ph, C(O)CH(CH₃)₂, -C(O)CH₃, or methylsulfonyl; or



R_5 is , where n is 1 or 2, and wherein the cyclic diamine is optionally substituted on at least one carbon atom with

methyl, oxo-, $-N(CH_3)_2$, amino, $-CH_2CH_3$, or

piperidinyl optionally substituted with methyl, $-C(O)CH_3$, $-C(O)CH(CH_3)_2$, $-C(O)Ph$, or $-C(O)OC(CH_3)_3$, and

wherein R_7 is $-H$, phenyl, $-C(O)CH_3$, C_1 - C_3 alkyl, $-C(O)NH_2$, or $-C(O)Ph$; and

R_8 is methoxy or cyano.

7. The compound of claim 3, wherein said compound is selected from the group consisting of:

- 5-((2*R*,6*S*)-2,6-dimethylmorpholino)quinoline-8-carbonitrile;
- 5-((2*R*,6*S*)-2,6-dimethylmorpholino)quinoline-8-carbonitrile dihydrochloride;
- 5-((2*R*,6*S*)-2,6-dimethylmorpholino)quinoline-8-carbonitrile methanesulfonate;
- 5-((2*R*,6*S*)-2,6-dimethylmorpholino)quinoline-8-carbonitrile bis(2,2,2-trifluoroacetate);
- 5-((2*R*,6*S*)-2,6-dimethylmorpholino)quinoline-8-carbonitrile bis(sulfonate);
- 5-((2*R*,6*S*)-2,6-dimethylmorpholino)quinoline-8-carbonitrile sulfonate;
- 5-((2*S*,6*R*)-2,6-dimethylmorpholino)quinoline-8-carbonitrile 2,3-dihydroxysuccinate;
- 5-((2*S*,6*R*)-2,6-dimethylmorpholino)quinoline-8-carbonitrile dimethanesulfonate;
- 5-(2-(chloromethyl)morpholino)quinoline-8-carbonitrile;
- (*S*)-5-(2-(chloromethyl)morpholino)quinoline-8-carbonitrile;
- N*-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)acetamide;
- N*-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)pivalamide;
- 5-(2-methylmorpholino)quinoline-8-carbonitrile;
- 5-((2*S*,6*S*)-2,6-dimethylmorpholino)quinoline-8-carbonitrile;
- 5-(2-methylmorpholino)quinoline-8-carbonitrile;
- 5-((2*S*,6*R*)-2-(aminomethyl)-6-methylmorpholino)quinoline-8-carbonitrile;
- 5-(2-(hydroxymethyl)-6-methylmorpholino)quinoline-8-carbonitrile;
- (2*R*,6*S*)-4-(8-methoxyquinolin-5-yl)-2,6-dimethylmorpholine;
- 5-((2*R*,6*S*)-2,6-dimethylmorpholino)quinoline-8-carboxamide;

(*R*)-5-(2-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-(hydroxymethyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-(methoxymethyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-((benzyloxy)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-(fluoromethyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-(ethoxymethyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-(isopropoxymethyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-(isobutoxymethyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-(chloromethyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-((hexyloxy)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-((cyclohexylmethoxy)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*S*)-2-methyl-6-propylmorpholino)quinoline-8-carbonitrile;
5-((2*S*,6*S*)-2-(fluoromethyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*S*,6*S*)-2-(chloromethyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-((2,6-dimethylphenoxy)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*S*)-2,6-diethylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*S*)-2-methyl-6-pentylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-formyl-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-((benzyloxy)methyl)-6-ethylmorpholino)quinoline-8-carbonitrile;
N-((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)-2-phenylpropanamide;
5-((2*R*,6*R*)-2-(1-hydroxyallyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-((*S*)-1-hydroxyallyl)-6-methylmorpholino)quinoline-8-carbonitrile;
N-((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)-1-phenylcyclobutanecarboxamide;
5-((2*R*,6*R*)-2-((*R*)-1-hydroxyallyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*S*)-2-methyl-6-(pyrrolidin-1-ylmethyl)morpholino)quinoline-8-carbonitrile;
5-((2*S*,6*R*)-2-((diethylamino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*S*,6*R*)-2-((benzylamino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-methyl-6-(phenoxymethyl)morpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-methyl-6-((*m*-tolylloxy)methyl)morpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-methyl-6-((*p*-tolylloxy)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-(1-hydroxypropyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-((*R*)-1-hydroxypentyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-((*S*)-1-hydroxypentyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-((*R*)-cyclohexyl(hydroxy)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-((*S*)-cyclohexyl(hydroxy)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;
N-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)-2-phenylacetamide;
5-((2*R*,6*R*)-2-((*R*)-1-hydroxy-2-phenylethyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-((*S*)-1-hydroxy-2-phenylethyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-((*R*)-1-hydroxy-3-phenylpropyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-((*S*)-1-hydroxy-3-phenylpropyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*S*)-2-methyl-6-((phenylamino)methyl)morpholino)quinoline-8-carbonitrile;
5-((2*R*,6*S*)-2-methyl-6-((*m*-tolylamino)methyl)morpholino)quinoline-8-carbonitrile;
5-((2*R*,6*S*)-2-methyl-6-((*o*-tolylamino)methyl)morpholino)quinoline-8-carbonitrile;
5-((2*R*,6*S*)-2-methyl-6-((*p*-tolylamino)methyl)morpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-((3,4-difluorophenoxy)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-((3-fluorophenoxy)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*S*,6*R*)-2-(((1,2-dimethyl-1*H*-benzo[d]imidazol-5-yl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*S*,6*R*)-2-(((1-ethyl-2-methyl-1*H*-benzo[d]imidazol-5-yl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*S*,6*R*)-2-((cyclohexylamino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-((2-fluorophenoxy)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-methyl-6-propionylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-(cyclohexanecarbonyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-methyl-6-(3-phenylpropanoyl)morpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-methyl-6-((*o*-tolylloxy)methyl)morpholino)quinoline-8-carbonitrile;
5-((2*R*,6*S*)-2-methyl-6-((pyrimidin-2-ylamino)methyl)morpholino)quinoline-8-carbonitrile;
5-((2*R*,6*S*)-2-methyl-6-((pyridin-2-ylamino)methyl)morpholino)quinoline-8-carbonitrile;
5-((2*R*,6*S*)-2-methyl-6-(((6-methylpyridin-2-yl)amino)methyl)morpholino)quinoline-8-carbonitrile;
5-((2*R*,6*S*)-2-methyl-6-(((5-methylpyridin-2-yl)amino)methyl)morpholino)quinoline-8-carbonitrile;
5-((2*S*,6*R*)-2-(((*R*)-2-(hydroxymethyl)pyrrolidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*R*)-2-((2,2-dimethylpyrrolidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*S*,6*R*)-2-((2-isopropylpyrrolidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*S*)-2-methyl-6-(((*S*)-2-methylpyrrolidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;
5-((2*R*,6*S*)-2-methyl-6-(((*S*)-3-phenylpyrrolidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;
5-((2*R*,6*S*)-2-methyl-6-(((*R*)-3-methylpyrrolidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;
5-((2*S*,6*R*)-2-(((*S*)-3-hydroxypyrrolidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*S*)-2-methyl-6-(((4-methylpyridin-2-yl)amino)methyl)morpholino)quinoline-8-carbonitrile;
5-((2*R*,6*S*)-2-methyl-6-((3-phenylpyrrolidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;
5-((2*S*,6*R*)-2-(((6-methoxypyridin-3-yl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;
5-((2*R*,6*S*)-2-methyl-6-(((*R*)-2-methylpyrrolidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((2,5-dimethylpyrrolidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((4-methoxypyridin-2-yl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((6-methoxypyridin-2-yl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((1-phenyl-1*H*-pyrazol-5-yl)amino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((*S*)-2-(hydroxymethyl)pyrrolidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((*R*)-3-hydroxypyrrolidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((*S*)-3-methylpyrrolidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((3,3-dimethylpyrrolidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-methyl-6-((*R*)-3-phenyl-1-(pyrrolidin-1-yl)propyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-methyl-6-((*S*)-3-phenyl-1-(pyrrolidin-1-yl)propyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((3-methoxypyridin-2-yl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((*R*)-3-hydroxypiperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((2*R*,6*S*)-2,6-dimethylpiperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((*S*)-3-hydroxypiperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((4-hydroxypiperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((2-(hydroxymethyl)piperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((2-methylpiperidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*, 6*R*)-2-((2-ethylpiperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*, 6*R*)-2-((2,3-dimethylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*, 6*S*)-2-methyl-6-((pyridin-3-ylamino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*, 6*S*)-2-methyl-6-((pyridin-4-ylamino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*, 6*S*)-2-methyl-6-(((*S*)-2-(trifluoromethyl)pyrrolidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*, 6*S*)-2-methyl-6-((4-methylpiperidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*, 6*R*)-2-((4,4-difluoropiperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*, 6*S*)-2-methyl-6-((4-phenylpiperidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*, 6*R*)-2-((4-fluoropiperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*, 6*R*)-2-((cyclopentylamino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*, 6*S*)-2-methyl-6-(((3-methylcyclohexyl)amino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*, 6*S*)-2-methyl-6-(((3-methylpyridin-2-yl)amino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*, 6*R*)-2-ethyl-6-(hydroxymethyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*, 6*S*)-2-methyl-6-(((4-phenylpyridin-2-yl)amino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*, 6*S*)-2-methyl-6-(piperazin-1-ylmethyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*, 6*S*)-2-methyl-6-((4-phenylpiperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*, 6*R*)-2-(((6-aminopyridin-2-yl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*, 6*R*)-2-((2,5-dimethylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((4-acetylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((2*S*,4*R*)-4-hydroxy-2-(hydroxymethyl)pyrrolidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((*R*)-2-methylpiperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((*R*)-3-methylpiperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((*S*)-3-methylpiperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((2*R*,5*R*)-2,5-dimethylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((2*R*,5*S*)-2,5-dimethylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((4-methylcyclohexyl)amino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((cyclobutylamino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((cycloheptylamino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((4-hydroxycyclohexyl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((2-hydroxycyclopentyl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((2-methylcyclohexyl)amino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((5-phenylpyridin-2-yl)amino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((3-phenylpyridin-2-yl)amino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((1*S*,3*R*)-3-hydroxycyclopentyl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((3-ethoxypyridin-2-yl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*, 6*S*)-2-methyl-6-(((2-phenylpyridin-4-yl)amino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*, 6*S*)-2-methyl-6-(((6-phenylpyridin-2-yl)amino)methyl)morpholino)quinoline-8-carbonitrile;

(*S*)-5-(2-((pyridin-2-ylamino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*, 6*S*)-2-methyl-6-((2-methyl-5-oxopiperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*, 6*S*)-2-methyl-6-((4-methylpiperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*, 6*S*)-2-methyl-6-((4-propylpiperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*, 6*R*)-2-((4-(dimethylamino)piperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*, 6*R*)-2-([1,4'-bipiperidin]-1'-ylmethyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*, 6*R*)-2-([1,4'-bipiperidin]-1'-ylmethyl)-6-methylmorpholino)quinoline-8-carbonitrile dihydrochloride;

5-((2*S*, 6*R*)-2-(((*R*)-3-aminopiperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

(2*R*, 6*S*)-4-(8-chloro-1,7-naphthyridin-5-yl)-2,6-dimethylmorpholine;

5-((2*S*, 6*R*)-2-((4-aminopiperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*, 6*R*)-2-(((5-fluoropyrimidin-2-yl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*, 6*S*)-2-methyl-6-(piperidin-1-ylmethyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*, 6*S*)-2-methyl-6-(morpholinomethyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*, 6*R*)-2-(((2*S*, 6*R*)-2,6-dimethylmorpholino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*, 6*R*)-2-(((2*R*, 6*R*)-2-(hydroxymethyl)-6-methylmorpholino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*, 6*S*)-2-methyl-6-((4-(pyridin-2-yl)piperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*, 6*S*)-2-methyl-6-((4-(pyridin-4-yl)piperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)acetamide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)acetamide hydrochloride;

5-((2*S*,6*R*)-2-(((1,8-naphthyridin-2-yl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidine-4-carboxamide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)benzamide;

5-((2*S*,6*R*)-2-((4-isopropylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

4-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperazine-1-carboxamide;

5-((2*S*,6*R*)-2-((4-cyclohexylpiperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((4-(pyrrolidin-1-yl)piperidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-((4-cyclohexyl-1*H*-1,2,3-triazol-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*R*)-2-methyl-6-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((2-oxo-[1,4'-bipiperidin]-1'-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((5-ethylpyrimidin-2-yl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((6-amino-3,5-dimethylpyridin-2-yl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((pyrazin-2-ylamino)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((1,3-dimethyl-1*H*-pyrazol-5-yl)amino)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,7*R*)-2-(hydroxymethyl)-7-methyl-1,4-oxazepan-4-yl)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((4-ethylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((3-(pyrrolidin-1-yl)azetidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((3-(piperidin-1-yl)azetidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((*R*)-2,4-dimethylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((4-(hydroxymethyl)piperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((*R*)-[1,3'-bipyrrolidin]-1'-ylmethyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((*R*)-3-(piperidin-1-yl)pyrrolidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((4-methyl-1,4-diazepan-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((4-benzoylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)nicotinamide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)isonicotinamide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)picolinamide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)hexanamide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)isobutyramide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)isobutyramide hydrochloride;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)pivalamide;

5-((2*S*,7*R*)-2-([1,4'-bipiperidin]-1'-ylmethyl)-7-methyl-1,4-oxazepan-4-yl)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((4-morpholinopiperidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

tert-butyl 4-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)piperazine-1-carboxylate;

tert-butyl 4-(4-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperazin-1-yl)piperidine-1-carboxylate;

5-((2*R*,6*S*)-2-methyl-6-((4-(piperazin-1-yl)piperidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((4-(piperidin-4-yl)piperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((3-(4-methylpiperazin-1-yl)azetidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((4,4'-bipiperidin]-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((1'-acetyl-[4,4'-bipiperidin]-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((1'-methyl-[4,4'-bipiperidin]-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((3-(piperazin-1-yl)azetidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((3-(4-acetylpiperazin-1-yl)azetidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((1'-isobutyryl-[4,4'-bipiperidin]-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((3-(4-benzoylpiperazin-1-yl)azetidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((1'-benzoyl-[4,4'-bipiperidin]-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((4-(1-methylpiperidin-4-yl)piperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((4-(1-acetylpiperidin-4-yl)piperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((4-(1-isobutyrylpiperidin-4-yl)piperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((4-(1-benzoylpiperidin-4-yl)piperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((3-(4-isobutyrylpiperazin-1-yl)azetidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((4-(4-acetylpiperazin-1-yl)piperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((4-(4-isobutyrylpiperazin-1-yl)piperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((4-(4-benzoylpiperazin-1-yl)piperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((4-(4-methylpiperazin-1-yl)piperidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((4-(4-methylpiperazin-1-yl)piperidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile trihydrochloride;

5-((2*S*,6*R*)-2-([1,4'-bipiperidin]-1'-ylmethyl)-6-methylmorpholino)-2-methylquinoline-8-carbonitrile;

N-((*R*)-1-((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)pyrrolidin-3-yl)acetamide;

N-((*R*)-1-((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)pyrrolidin-3-yl)isobutyramide;

5-((2*R*,6*S*)-2-methyl-6-(((*S*)-3-(piperidin-1-yl)pyrrolidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((*S*)-3-(piperidin-1-yl)pyrrolidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile dihydrochloride;

5-((2*R*,6*S*)-2-methyl-6-((3-morpholinoazetidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((3-((*S*)-2-methylpyrrolidin-1-yl)azetidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((*S*)-2-methylpiperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((*S*)-2,4-dimethylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-((*R*)-3,4-dimethylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((*S*)-3,4-dimethylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((*S*)-3-ethylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((*S*)-3-ethylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile dihydrochloride;

5-((2*S*,6*R*)-2-(((*S*)-3-ethyl-4-methylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((4-(azepan-1-yl)piperidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((*S*)-[1,3'-bipyrrolidin]-1'-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((3-(4-aminopiperidin-1-yl)azetidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

N-(1-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)azetidin-3-yl)piperidin-4-yl)acetamide;

5-((2*R*,6*S*)-2-methyl-6-(((3-(4-(methylsulfonyl)piperazin-1-yl)azetidin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*S*,6*R*)-2-(((3-((*S*)-3-hydroxypyrrolidin-1-yl)azetidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)-1,3-dimethyl-1*H*-pyrazole-4-carboxamide;

N-(1-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)azetidin-3-yl)piperidin-4-yl)-1,3-dimethyl-1*H*-pyrazole-4-carboxamide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)methanesulfonamide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)benzenesulfonamide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)-4-fluorobenzenesulfonamide;

5-((2*S*,6*R*)-2-(((3-aminoazetidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)azetidin-3-yl)acetamide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)azetidin-3-yl)-4-fluorobenzamide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)azetidin-3-yl)methanesulfonamide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)azetidin-3-yl)-4-fluorobenzenesulfonamide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)azetidin-3-yl)-1,3-dimethyl-1*H*-pyrazole-4-sulfonamide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)piperidin-4-yl)-1,3-dimethyl-1*H*-pyrazole-4-sulfonamide;

N-(1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)azetidin-3-yl)isobutyramide;

5-((2*R*,6*S*)-2-methyl-6-(((*S*)-2-methyl-5-oxopiperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((*R*)-2-methyl-5-oxopiperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((*R*)-2-methyl-3-oxopiperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-(((*S*)-2-methyl-3-oxopiperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((2,4,5-trimethylpiperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*,6*S*)-2-methyl-6-((2,3,4-trimethylpiperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile;

N-((*R*)-1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)pyrrolidin-3-yl)benzamide;

5-((2*S*,6*R*)-2-(((*R*)-3-(dimethylamino)pyrrolidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

N-((*S*)-1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)pyrrolidin-3-yl)acetamide;

N-((*S*)-1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)pyrrolidin-3-yl)isobutyramide;

N-((*S*)-1-(((2*S*,6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)pyrrolidin-3-yl)benzamide;

5-((2*S*, 6*R*)-2-(((*S*)-3-(dimethylamino)pyrrolidin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*, 6*R*)-2-methyl-6-((pyrazin-2-yloxy)methyl)morpholino)quinoline-8-carbonitrile;

N-(1-(((2*S*, 6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)azetidin-3-yl)benzamide;

5-((2*S*, 6*R*)-2-(((3,3-dimethylpiperazin-1-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile dihydrochloride;

5-((2*R*, 6*S*)-2-methyl-6-((3,3,4-trimethylpiperazin-1-yl)methyl)morpholino)quinoline-8-carbonitrile dihydrochloride;

5-((2*R*, 6*R*)-2-((*R*)-1-hydroxyethyl)-6-methylmorpholino)quinoline-8-carbonitrile;

1-(((2*S*, 6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)-*N*-ethylpiperidine-4-carboxamide;

1-(((2*S*, 6*R*)-4-(8-cyanoquinolin-5-yl)-6-methylmorpholin-2-yl)methyl)-*N*-ethylpiperidine-4-carboxamide hydrochloride;

5-((2*R*, 6*R*)-2-((*S*)-1-hydroxyethyl)-6-methylmorpholino)quinoline-8-carbonitrile;

5-((2*R*, 6*R*)-2-methyl-6-((pyridin-2-yloxy)methyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*, 6*R*)-2-methyl-6-((pyrimidin-2-yloxy)methyl)morpholino)quinoline-8-carbonitrile;

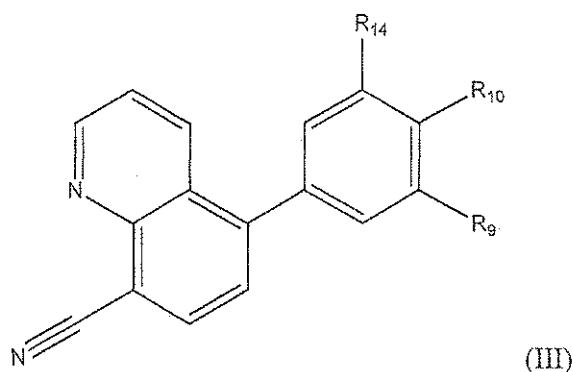
5-((2*R*, 6*R*)-2-methyl-6-((*R*)-1-(pyrimidin-2-yloxy)ethyl)morpholino)quinoline-8-carbonitrile;

5-((2*R*, 6*R*)-2-methyl-6-((*S*)-1-(pyrimidin-2-yloxy)ethyl)morpholino)quinoline-8-carbonitrile; and

5-((2*R*, 6*R*)-2-((*S*)-hydroxy(pyridin-2-yl)methyl)-6-methylmorpholino)quinoline-8-carbonitrile.

8. The compound of claim 6, wherein said compound is selected from the group consisting of 5-((2*S*, 6*R*)-2-([1,4'-bipiperidin]-1'-ylmethyl)-6-methylmorpholino)quinoline-8-carbonitrile and 5-((2*R*, 7*R*)-2-(hydroxymethyl)-7-methyl-1,4-oxazepan-4-yl)quinoline-8-carbonitrile.

9. A compound of Formula (III):



wherein

R₁₁ is H or methyl;

R₁₀ is H or, when both R₁₁ and R₉ are H, is methyl-1,4'-bipiperidinyl;

R₉ is -H or is -CH₂- substituted by 1,4'-bipiperidinyl, oxo-, hydroxyl, methylpyridinyl, or piperidinyl optionally substituted with hydroxyl, -N(CH₃)₂, or piperidinyl.

10. The compound of claim 9, wherein said compound is selected from the group consisting of:

5-(3-([1,4'-bipiperidin]-1'-ylmethyl)phenyl)quinoline-8-carbonitrile;

5-(4-([1,4'-bipiperidin]-1'-ylmethyl)phenyl)quinoline-8-carbonitrile;

5-(3-formyl-5-methylphenyl)quinoline-8-carbonitrile;

5-(3-(hydroxymethyl)-5-methylphenyl)quinoline-8-carbonitrile;

5-(3-(chloromethyl)-5-methylphenyl)quinoline-8-carbonitrile;

5-(3-((4-hydroxypiperidin-1-yl)methyl)-5-methylphenyl)quinoline-8-carbonitrile;

5-(3-((4-(dimethylamino)piperidin-1-yl)methyl)-5-methylphenyl)quinoline-8-carbonitrile;

5-(3-methyl-5-((4-methylpiperazin-1-yl)methyl)phenyl)quinoline-8-carbonitrile; and

5-(3-([1,4'-bipiperidin]-1'-ylmethyl)-5-methylphenyl)quinoline-8-carbonitrile.

11. A method for treatment of systemic lupus erythematosus or lupus, comprising administering a pharmaceutically effective amount of a compound or pharmaceutically acceptable salt of any one of claims 1-10.

12. The method of claim 11, wherein said compound is administered as a pharmaceutically acceptable salt.

13. A method for antagonizing TLR7, comprising administering a pharmaceutically effective amount of a compound or pharmaceutically acceptable salt of any one of claims 1-10.

14. A method for antagonizing TLR8, comprising administering a pharmaceutically effective amount of a compound or pharmaceutically acceptable salt of any one of claims 1-10.

15. A pharmaceutical composition comprising at least one compound or pharmaceutically acceptable salt of any one of claims 1-10 and at least one pharmaceutically acceptable carrier.

16. The pharmaceutical composition of claim 15, wherein said compound or pharmaceutically effective salt thereof has an IC₅₀ less than or equal to 100 nM against human TLR7 receptors in a HEK-293 cell line.

17. The pharmaceutical composition of claim 15, wherein said compound or pharmaceutically effective salt thereof has an IC₅₀ less than or equal to 20 nM against human TLR7 receptors expressed in a HEK-293 cell line.

18. The pharmaceutical composition of claim 15, wherein said compound or pharmaceutically effective salt thereof has an IC₅₀ less than or equal to 5 nM against human TLR7 receptors expressed in a HEK-293 cell line.

19. The pharmaceutical composition of one of claims 16-18, wherein the IC₅₀ against human TLR7 receptors expressed in a HEK-293 cell line is measured by (1) plating cells of the HEK-293 cell line stably expressing TLR7 in Dulbecco's modified Eagle's medium containing 10% fetal bovine serum at a density of 2.22X10⁵ cells/ml into a 384-well plate and incubating for 2 days at 37°C, 5% CO₂; (2) adding the compound or pharmaceutically acceptable salt thereof and incubating the cells for 30 minutes; (3) adding CL097 (InvivoGen) at 3 µg/ml and incubating the cells for approximately 20 hours; and (4) quantifying NF-kappaB dependent reporter activation by measuring luminescence.

20. A method for treatment of a systematic lupus erythematosus, cutaneous lupus, neuropsychiatric lupus, or lupus, comprising administering a pharmaceutically effective amount of a compound or pharmaceutically acceptable salt of any one of claims 1-10.

21. The method of claim 20, wherein said compound is administered as a pharmaceutically acceptable salt.