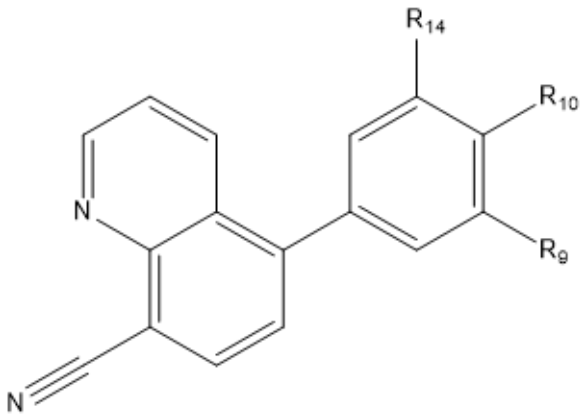
[0011] A further example provides a compound of Formula (III):



(III)

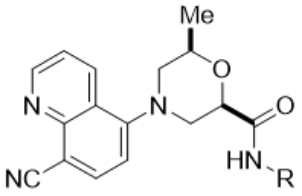
wherein

R_{11} is H or methyl;

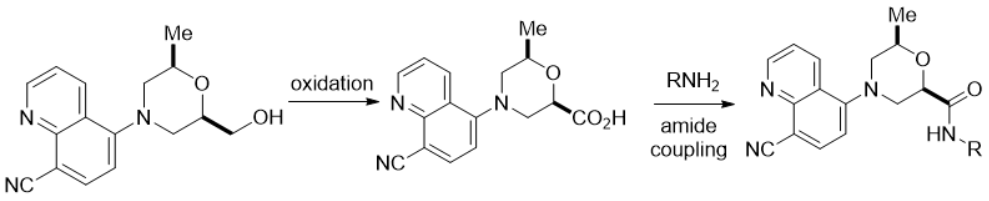
R_{10} is H or, when both R_{14} and R_9 are H, is methyl-1,4'-bipiperidinyl;

R_9 is –H or is $–CH_2$- substituted by 1,4'-bipiperidinyl, oxo-, hydroxyl, methylpyridinyl, or piperidinyl optionally substituted with hydroxyl, $-N(CH_3)_2$, or piperidinyl.

[0011a] In one aspect, the present disclosure refers to a method of preparing a compound of formula

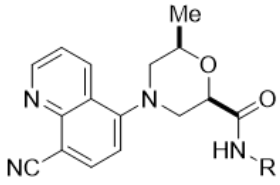


which method comprises the following steps:-



wherein the oxidation conditions comprise reacting the starting compound with 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO) and iodobenzene diacetate ($PhI(OAc)_2$), and wherein R 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 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, azetidinyl, acetamidyl, carboxamidyl, cyano, fluoro, methylamino, or trifluoromethyl.

[0011b] In another aspect, the present disclosure refers to a compound of formula 

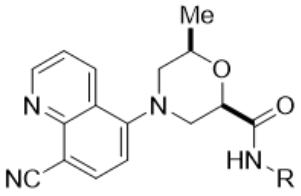
wherein R is C_1-C_6 alkyl that is optionally substituted with: –OH, methoxy, ethoxy, -$OCH(CH_3)_2$, -$O(CH_2)_2CH_3$, phenyl, furanyl, -$O(CH_2)_2OH$, phenoxy, methylthio, -F, -$N(CH_3)_2$, cyano, pyridinyloxy, fluorophenoxy, isochromanyl, phenol, benzylamino, -$NHCH_3$, oxo-, amino, carboxyl, 7-member 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 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, azetidinyl, acetamidyl, carboxamidyl, cyano, fluoro, methylamino, or trifluoromethyl; or a pharmaceutically acceptable salt thereof.

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

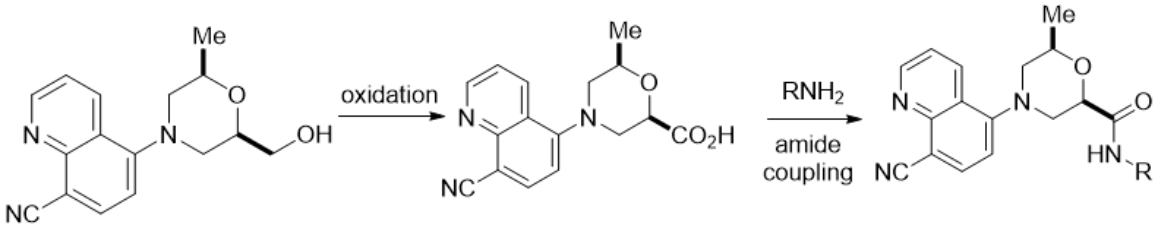
[0013] In a further example the compound or pharmaceutically effective salt thereof of the preceding paragraph has an IC50 less than or equal to 20 nM against human TLR7 receptors expressed in a HEK-293 cell line. In a further example the compound or pharmaceutically effective salt thereof of the preceding 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 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 % CO_2; (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.

We claim:

1. A method of preparing a compound of formula



which method comprises the following steps:-



wherein the oxidation conditions comprise reacting the starting compound with 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO) and iodobenzene diacetate ($PhI(OAc)_2$), and wherein R 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

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, azetidinyl, acetamidyl, carboxamidyl, cyano, fluoro, methylamino, or trifluoromethyl.

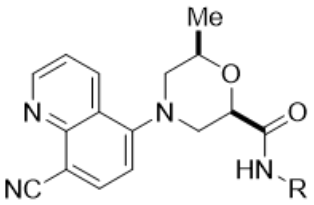
2. A method according to claim 1, which further comprises one or two additional steps to modify the R group to a different group R', wherein R' is

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

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, azetidinyl, acetamidyl, carboxamidyl, cyano, fluoro, methylamino, or trifluoromethyl.

3. A compound of formula



wherein R 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

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, azetidinyl, acetamidyl, carboxamidyl, cyano, fluoro, methylamino, or trifluoromethyl;

or a pharmaceutically acceptable salt thereof.

4. A compound according to claim 3, or a pharmaceutically acceptable salt thereof, wherein R is selected from

ethyl,
isopropyl,
3,4-difluorobenzyl,
cyclopropyl,
2-hydroxyethyl,
2-methoxyethyl,
(*R*)-2-hydroxypropyl,
(*S*)-1-hydroxypropan-2-yl,
(*R*)-1-hydroxypropan-2-yl,
(*S*)-1-hydroxybutan-2-yl,
(*S*)-1-hydroxy-3-methylbutan-2-yl,
(*S*)-2-hydroxy-1-phenylethyl,
(*R*)-2-hydroxy-1-phenylethyl,
2-hydroxybutyl,
2-ethoxyethyl,
(*R*)-1-hydroxybutan-2-yl,
1,3-dihydroxypropan-2-yl,
2,3-dihydroxypropyl,
((*R*)-tetrahydrofuran-2-yl)methyl,

(tetrahydrofuran-2-yl)methyl,
2-propoxyethyl,
(*R*)-1-hydroxypentan-2-yl,
2-isopropoxyethyl,
1-methoxybutan-2-yl,
2-(2-fluorophenyl)-2-hydroxyethyl,
(*R*)-1-hydroxy-3-methylbutan-2-yl,
2,2-dimethoxyethyl,
2-(2-hydroxyethoxy)ethyl,
1-hydroxyhexan-2-yl,
(*S*)-1-hydroxy-3,3-dimethylbutan-2-yl;
(*S*)-1-hydroxyhexan-2-yl,
(*2S,3S*)-1-hydroxy-3-methylpentan-2-yl,
(*S*)-1-hydroxy-4-methylpentan-2-yl,
(*R*)-1-hydroxy-4-methylpentan-2-yl,
((4-methylmorpholin-2-yl)methyl,
(*S*)-1-hydroxy-4-(methylthio)butan-2-yl,
2-phenoxyethyl,
(*S*)-1-hydroxy-3-phenylpropan-2-yl,
2-phenoxypropyl,
2-hydroxy-3-phenylpropyl,
(2-(pyridin-3-yloxy)propyl,
2-(4-fluorophenoxy)ethyl,
2-(3-fluorophenyl)-2-hydroxyethyl,
(S)-1-cyclohexyl-3-hydroxypropan-2-yl,
isochroman-1-ylmethyl,
2-hydroxy-3-phenoxypropyl,
(*1S*)-1,3-dihydroxy-1-phenylpropan-2-yl,
2-hydroxy-3-(piperazin-1-yl)propyl,
azetidin-3-yl,
(*S*)-pyrrolidin-3-yl,
(*R*)-pyrrolidin-3-yl,

(*S*)-piperidin-3-yl,
(*R*)-piperidin-3-yl,
(*S*)-pyrrolidin-2-ylmethyl,
2-(benzylamino)ethyl,
pyridin-2-yl,
6-methylpyridin-2-yl,
5-methylisoxazol-3-yl,
2,2,2-trifluoroethyl,
2,2-difluoroethyl,
3,3,3-trifluoropropyl,
(2-(dimethylamino)-2-methylpropyl,
(*S*)-morpholin-2-ylmethyl,
((*S*)-4-methylmorpholin-2-yl)methyl,
2-fluoroethyl,
3-fluoropropyl,
(*S*)-1,1,1-trifluoropropan-2-yl,
(*R*)-1,1,1-trifluoropropan-2-yl,
1,3-dimethyl-1*H*-pyrazol-5-yl,
1-methyl-1*H*-pyrazol-5-yl,
cyanomethyl,1-cyanocyclopropyl,
1,2,4-thiadiazol-5-yl,
3-methyl-1,2,4-thiadiazol-5-yl,
piperidin-4-yl,
(4-fluoropiperidin-4-yl)methyl,
azetidin-3-ylmethyl,
3-carbamoyl-1-methyl-*1H*-pyrazol-4-yl,
oxetan-3-ylmethyl,
tetrahydro-2*H*-pyran-4-yl,
tetrahydrofuran-3-yl,
(3-methyloxetan-3-yl)methyl,
oxetan-3-yl(3-(aminomethyl)oxetan-3-yl)methyl,
oxetan-2-ylmethyl,

2-(methylamino)ethyl,
(S)-3,3,3-trifluoro-2-hydroxypropyl,
(R)-3,3,3-trifluoro-2-hydroxypropyl,
2-(dimethylamino)ethyl,
(S)-4,4,4-trifluoro-3-hydroxybutyl,
(R)-4,4,4-trifluoro-3-hydroxybutyl,
3-amino-4,4,4-trifluorobutyl,
acetic acid,
3-carbamoylpyridin-4-yl,
(R)-morpholin-2-ylmethyl,
pyridin-4-yl,
pyridin-3-yl,
1-(piperidin-4-yl)-*1H*-pyrazol-4-yl,
1-(azetidin-3-yl)-*1H*-pyrazol-4-yl,
(1H-pyrazol-5-yl)methyl,
(1H-pyrazol-4-yl)methyl,
(3-(trifluoromethyl)pyridin-2-yl)methyl,
1-(pyridin-2-yl)ethyl,
pyridin-2-ylmethyl,
(6-methylpyridin-2-yl)methyl,
(1-methylpiperidin-2-yl)methyl,
(3-methylpyridin-2-yl)methyl,
4-cyano-*1H*-pyrazol-3-yl,
(*3S,4R*)-4-fluoro-1-methylpyrrolidin-3-yl,-
(*3S,4R*)-4-fluoropiperidin-3-yl,
((*2R,6R*)-6-methylmorpholin-2-yl)methyl,
(R)-pyrrolidin-2-ylmethyl,
(S)-piperidin-2-ylmethyl,
(*1R,5S,6S*)-3-azabicyclo[3.1.0]hexan-6-yl,
methyl,
((*2S,6R*)-4,6-dimethylmorpholin-2-yl)methyl
1-methylpiperidin-4-yl,

(*3S,4R*)-4-fluoropiperidin-3-yl,
1-(2-amino-2-oxoethyl)piperidin-4-yl,
2-carbamoylpyridin-4-yl,
(S)-piperidin-3-yl,
1-ethylpiperidin-4-yl,
1-ethylpiperidin-3-yl,
(R)-1-methylpiperidin-3-yl,
4-methylpiperidin-4-yl,
2-amino-2-methylpropyl,
(*3R,4S*)-4-fluoropyrrolidin-3-yl,
(*3S,4R*)-4-fluoropyrrolidin-3-yl,
azepan-3-yl;
1-methylazepan-3-yl,
1,4-dimethylpiperidin-4-yl and
4-fluoro-1-methylpiperidin-3-yl.