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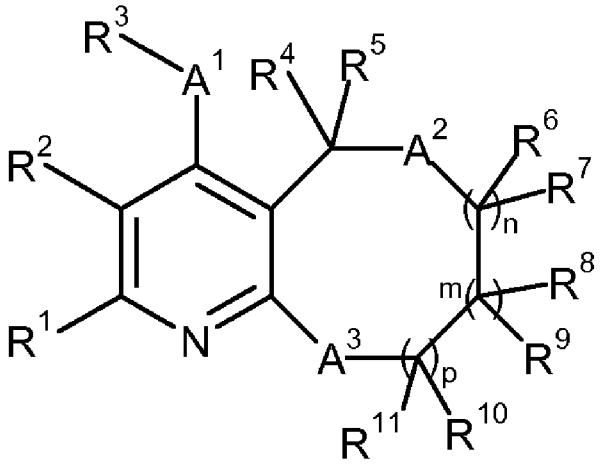

(I)

(57) Abstract: The invention provides novel compounds having the general formula (I) wherein R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11}, A^1, A^2, A^3, m, n and p are as described herein, compositions including the compounds and methods of using the compounds.

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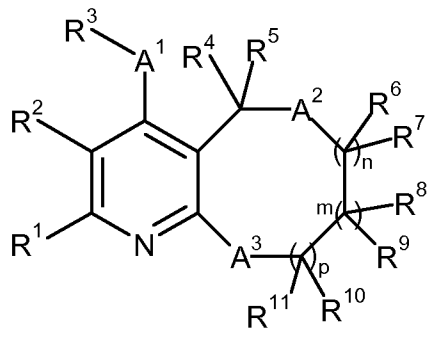
New bicyclicpyridine derivatives

The present invention relates to organic compounds useful for therapy or prophylaxis in a mammal, and in particular to fatty acid binding protein (FABP) 4 and/or 5 inhibitors, more particularly dual FABP 4/5 inhibitors for the treatment or prophylaxis of e.g. type 2 diabetes, atherosclerosis, chronic kidney diseases, non-alcoholic steatohepatitis and cancer.

The present invention provides novel compounds of formula (I)



(I)

wherein

R^1 is alkyl, haloalkyl, cycloalkyl, substituted cycloalkyl, alkoxy, alkoxyalkyl, alkoxyalkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, carboxy, carboxyalkyl, haloalkyl, haloalkoxy, haloalkoxyalkyl, cycloalkoxy, substituted cycloalkoxy, cycloalkoxylalkyl, substituted cycloalkoxyalkyl, hydroxyalkyl, aryl, substituted aryl, heterocycloalkyl, substituted heterocycloalkyl, heterocycloalkoxy, substituted heterocycloalkoxy, heterocycloalkylalkoxy, substituted heterocycloalkylalkoxy, heteroaryl, substituted heteroaryl, amino, substituted amino, aminocarbonyl or substituted aminocarbonyl, wherein substituted cycloalkyl, substituted cycloalkoxy, substituted cycloalkoxyalkyl, substituted aryl, substituted heterocycloalkyl, substituted heterocycloalkoxy, substituted heterocycloalkylalkoxy and substituted heteroaryl are substituted with one to three substituents independently selected from hydroxy, oxo, halogen, alkyl, cycloalkyl, haloalkyl, alkylcycloalkyl, cycloalkylalkyl, alkylcycloalkylalkyl, hydroxyalkyl, alkylsulfonyl, alkylsulfonylalkyl, alkoxycarbonyl, alkoxy and alkoxyalkyl and wherein substituted amino and substituted aminocarbonyl are substituted on the nitrogen atom with one to two substituents independently selected

from alkyl, cycloalkyl, haloalkyl, alkylcycloalkyl, cycloalkylalkyl, alkylcycloalkylalkyl, hydroxyalkyl and alkoxyalkyl;

R^2 is -COOH, tetrazol-5-yl, [1,3,4]oxadiazol-2-on-5-yl, [1,3,4]oxadiazole-2-thion-5-yl, [1,2,4]oxadiazol-5-on-3-yl, [1,2,4]oxadiazole-5-thion-3-yl, [1,2,3,5]oxathiadiazole-2-oxide-4-yl, [1,2,4]thiadiazol-5-on-3-yl, isoxazol-3-ol-5-yl, 5-alkylisoxazol-3-ol-4-yl, 5-cycloalkylisoxazol-3-ol-4-yl, furazan-3-ol-4-yl, 5-alkylsulfonylamino-[1,3,4]oxadiazol-2-yl, 5-cycloalkylsulfonylamino-[1,3,4]oxadiazol-2-yl, 5-alkylsulfonylamino-[1,2,4]triazol-3-yl, 5-cycloalkylsulfonylamino-[1,2,4]triazol-3-yl, 5-alkylisothiazol-3-ol-4-yl, 5-cycloalkylisothiazol-3-ol-4-yl, [1,2,5]thiadiazol-3-ol-4-yl, 1,4-dihydro-tetrazol-5-on-1-yl, tetrazol-5-ylcarbamoyl, tetrazole-5-carbonyl, [1,2,4]oxadiazolidine-3,5-dion-2-y, [1,2,4]oxadiazol-5-on-3-yl, 2,4-dihydro-[1,2,4]triazol-3-on-5-sulfanyl, [1,2,4]triazole-3-sulfanyl, [1,2,4]triazole-3-sulfinyl, [1,2,4]triazole-3-sulfonyl, 4-alkyl-pyrazol-1-ol-5-yl, 4-cycloalkyl-pyrazol-1-ol-5-yl, 4-alkyl-[1,2,3]triazol-1-ol-5-yl, 4-cycloalkyl-[1,2,3]triazol-1-ol-5-yl, 5-alkyl-imidazol-1-ol-2-yl, 5-cycloalkyl-imidazol-1-ol-2-yl, 4-alkyl-imidazol-1-ol-5-yl, 4-cycloalkyl-imidazol-1-ol-5-yl, 4-alkyl-1,1-dioxo-1λ^6-[1,2,5]thiadiazolidin-3-on-5-yl, 4,4-dialkyl-1,1-dioxo-1λ^6-[1,2,5]thiadiazolidin-3-on-5-yl, 4-cycloalkyl-1,1-dioxo-1λ^6-[1,2,5]thiadiazolidin-3-on-5-yl, 4,4-dicycloalkyl-1,1-dioxo-1λ^6-[1,2,5]thiadiazolidin-3-on-5-yl, thiazolidine-2,4-dion-5-yl, oxazolidine-2,4-dion-5-yl, 3-[1-hydroxy-meth-(E)-ylidene]-pyrrolidine-2,4-dion-1-yl, 3-[1-hydroxy-meth-(Z)-ylidene]-pyrrolidine-2,4-dion-1-yl, 5-methyl-4-hydroxyfuran-2-on-3-yl, 5,5-dialkyl-4-hydroxyfuran-2-on-3-yl, 5-cycloalkyl-4-hydroxyfuran-2-on-3-yl, 5,5-dicycloalkyl-4-hydroxyfuran-2-on-3-yl, 3-hydroxycyclobut-3-ene-1,2-dion-4-yl or 3-hydroxycyclobut-3-ene-1,2-dion-4-amino;

R^3 is phenyl, substituted phenyl, substituted dihydropyridinyl, heteroaryl or substituted heteroaryl, wherein substituted phenyl, substituted dihydropyridinyl and substituted heteroaryl are substituted with one to three substituents independently selected from hydroxy, oxo, halogen, alkyl, cycloalkyl, haloalkyl, haloalkoxy, alkylcycloalkyl, cycloalkylalkyl, alkylcycloalkylalkyl, hydroxyalkyl, hydroxyalkoxy, alkoxy, alkoxyalkyl, alkylsulfonyl, amino and amino substituted on the nitrogen atom with one to two substituents independently selected from alkyl, cycloalkyl, haloalkyl, alkylcycloalkyl, cycloalkylalkyl, alkylcycloalkylalkyl, hydroxyalkyl and alkoxyalkyl;

A^1 is a bond or $CR^{12}R^{13}$;

A^2 is $-CR^{14}R^{15}-$, $-NR^{16}-$, -O-, -S-, -S(O)- or $-S(O)_2-$;

A^3 is $-CR^{17}R^{18}-$, $-C(O)NR^{19}-$, $-NR^{19}-$, -O-, -S-, -S(O)- or $-S(O)_2-$;

R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11}, R^{14}, R^{15}, R^{17} and R^{18} are independently selected from H, halogen, alkyl, alkoxy, cycloalkyl, cycloalkylalkoxy, haloalkoxy and haloalkyl.

R^{12} and R^{13} are independently selected from hydrogen, alkyl, cycloalkyl and haloalkyl.

R^{16} and R^{19} are independently selected from hydrogen, alkyl, cycloalkyl, haloalkyl and alkylcarbonyl.

n, m and p are independently selected from zero and 1;

or pharmaceutically acceptable salts.

FABP4 (aP2) and FABP5 (mal1) are members of the fatty acid binding protein family. FABPs are proteins of 14-15 KDa that act as chaperones for fatty acids in the aqueous cytosolic environment and facilitate their movement between cellular compartments. So far at least nine members of this family have been identified with a tissue-specific pattern of expression. FABP4 is mainly expressed in adipose tissue and macrophages, but also in other cell types, whereas FABP5 is expressed in a wide range of tissues and organs. FABPs are responsible for the transfer of fatty acids to different cell compartments and are thus implicated in key cellular functions such as lipid storage in adipocytes, fatty acid oxidation in mitochondria, ER signaling, fatty acid-dependent gene expression, regulation of cytosolic enzymes activity, modulation of inflammatory response and leukotriene synthesis. Plasma FABP4 is secreted by adipose tissue in mice and secretion is de-regulated in obesity and blocking of plasma FABP4 in vivo by antibodies improves insulin sensitivity.

Several genetic evidences in human support a role of FABP4 and FABP5 in metabolic diseases. A mutation in the FABP4 promoter (SNP T-87C) leading to 50% reduction in gene expression is associated to reduced cardiovascular diseases (CVDs) and type 2 diabetes (T2D) risk and to reduced plasma triglycerides (TGs). Two mutations in FABP5 gene, one in the 5`UTR (rs454550), one in the promoter (nSNP), are associated, respectively to increased (OR 4.24) and decreased risk (OR 0.48) of T2D. In addition, it was shown that FABP4 protein and mRNA levels in atherosclerotic plaque macrophages are associated to plaques instability and CV death. Finally, a large number of publications report an association between FABP4 and FABP5

plasma levels and severity of metabolic diseases. Elevated FABP4 plasma levels are associated with atherogenic dyslipidemia, reduced endothelial function, increased intima-media (IM) thickness, metabolic syndrome, obesity and insulin resistance IR. Elevated FABP5 plasma levels are associated to metabolic syndrome.

Genetic and pharmacological studies in mice largely confirm the human evidences. It was demonstrated that loss-of-function in FABP4 and FABP5 improves insulin sensitivity, lowers glucose, and protects against atherosclerosis. FABP4 knockout mice on high fat diet showed metabolic improvement that was tempered by compensatory up-regulation of FABP5 in adipose. Mice with a deletion of FABP5 gene on high fat (HF) diet showed body weight reduction and improved glucose and insulin tolerance. The FABP4/FABP5 double-knockout mice were strongly protected from hyperglycemia, insulin resistance, and hepatic steatosis. In addition, in an ApoE deficient background, FABP4 and FABP5 deletion was highly protective against the development of atherosclerosis and increased longevity. A specific FABP4 inhibitor (BMS309403), showed in a clamp study in ob/ob mice a reduction of hepatic glucose production, increased glucose uptake in muscle and adipose and reduction in hepatic steatosis, but no change in body weight and energy consumption. Also, it showed a decrease in atherosclerotic plaques formation in ApoE KO mice. A dual FABP4/5 inhibitor, Compound 3 described in *J. Lipid Res.* **2011**, *52*, 646, showed in mice under HF diet a reduction in plasma triglycerides and free fatty acids, but no improvement in insulin and glucose tolerance.

Objects of the present invention are the compounds of formula (I) and their aforementioned salts and esters and their use as therapeutically active substances, a process for the manufacture of the said compounds, intermediates, pharmaceutical compositions, medicaments containing the said compounds, their pharmaceutically acceptable salts or esters, the use of the said compounds, salts or esters for the treatment or prophylaxis of illnesses, especially in the treatment or prophylaxis of type 2 diabetes, metabolic syndrome, atherosclerosis, dyslipidemia, liver diseases involving inflammation, steatosis and/or fibrosis, such as non-alcoholic fatty liver disease, in particular non-alcoholic steatohepatitis, obesity, lipodystrophy, such as genetic and iatrogenic lipodystrophy, cancer, eye diseases supported by endothelial proliferation and angiogenesis, such as macular degeneration and retinopathy, lung diseases, such as asthma, bronchopulmonary dysplasia and chronic obstructive pulmonary disease, sarcoidosis, chronic renal diseases, such as vasculitis, focal segmental glomerulosclerosis, diabetic nephropathy, lupus nephritis, polycystic kidney disease and drug or toxin-induced chronic tubulointerstitial nephritis, chronic inflammatory and autoimmune

inflammatory diseases, preeclampsia and polycystic ovary syndrome, and the use of the said compounds, salts or esters for the production of medicaments for the treatment or prophylaxis of of type 2 diabetes, metabolic syndrome, atherosclerosis, dyslipidemia, liver diseases involving inflammation, steatosis and/or fibrosis, such as non-alcoholic fatty liver disease, in particular non-alcoholic steatohepatitis, obesity, lipodystrophy, such as genetic and iatrogenic lipodystrophy, cancer, eye diseases supported by endothelial proliferation and angiogenesis, such as macular degeneration and retinopathy, lung diseases, such as asthma, bronchopulmonary dysplasia and chronic obstructive pulmonary disease, sarcoidosis, chronic renal diseases, such as vasculitis, focal segmental glomerulosclerosis, diabetic nephropathy, lupus nephritis, polycystic kidney disease and drug or toxin-induced chronic tubulointerstitial nephritis, chronic inflammatory and autoimmune inflammatory diseases, preeclampsia and polycystic ovary syndrome.

Compounds of the present invention are FABP 4 and/or 5 inhibitors, more particularly dual FABP 4 and 5 inhibitors. Some particular compounds of formula (I) of the present invention are also selective FABP 4 and/or 5 inhibitors compared to FABP 3 and/or 1.

The term “alkoxy” denotes a group of the formula -O-R’, wherein R’ is an alkyl group. Examples of alkoxy group include methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, isobutoxy and tert-butoxy. Particular alkoxy group include methoxy, ethoxy and isopropoxy. More particular, alkoxy group is methoxy.

The term “alkoxyalkoxy” denotes an alkoxy group wherein at least one of the hydrogen atoms of the alkoxy group has been replaced by another alkoxy group. Example of alkoxyalkoxy group includes methoxyethoxy,

The term “alkoxyalkyl” denotes an alkyl group wherein at least one of the hydrogen atoms of the alkyl group has been replaced by an alkoxy group. Exemplary alkoxyalkyl groups include methoxymethyl, ethoxymethyl, methoxyethyl, methoxydimethylethyl, methoxymethylpentanyl, methoxymethylpropanyl, ethoxyethyl, methoxypropyl and ethoxypropyl. Particular alkoxyalkyl groups include methoxymethyl and 2-methoxy-1,1-dimethylethyl.

The term “alkoxycarbonyl” denotes a group of the formula -C(O)-R’, wherein R’ is an alkoxy group. Examples of alkoxycarbonyl groups include groups of the formula -C(O)-R’, wherein R’ is methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, isobutoxy and tert-

butoxy. Particular alkoxycarbonyl group is a group of the formula -C(O)-R', wherein R' is tert-butoxy.

The term "alkoxycarbonylalkyl" denotes an alkyl group wherein one of the hydrogen atoms of the alkyl group has been replaced by an alkoxycarbonyl group. Particular alkoxycarbonylalkyl includes 2-tert-butoxy-1,1-dimethyl-2-oxo-ethyl.

The term "alkyl" denotes a monovalent linear or branched saturated hydrocarbon group of 1 to 12 carbon atoms, in particular of 1 to 7 carbon atoms, more particular of 1 to 4 carbon atoms, for example, methyl, ethyl, propyl, isopropyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, ethylpropyl and dimethylpropyl. Particular alkyl groups include methyl, ethyl, propyl, isopropyl, n-butyl, sec-butyl, tert-butyl, ethylpropyl and dimethylpropyl. Further particular alkyl groups include methyl and ethylpropyl.

The term "alkylcarbonyl" denotes a group of the formula -C(O)-R', wherein R' is an alkyl group. Examples of alkylcarbonyl groups include groups of the formula -C(O)-R', wherein R' is methyl, ethyl, propyl, isopropyl, n-butyl, iso-butyl, sec-butyl and tert-butyl. Particular alkylcarbonyl group is a group of the formula -C(O)-R', wherein R' is methyl.

The term "alkylcycloalkyl" denotes a cycloalkyl group wherein at least one of the hydrogen atoms of the cycloalkyl group is replaced by an alkyl group. Examples of alkylcycloalkyl include methyl-cyclopropyl, dimethyl-cyclopropyl, methyl-cyclobutyl, dimethyl-cyclobutyl, methyl-cyclopentyl, dimethyl-cyclopentyl, methyl-cyclohexyl and dimethyl-cyclohexyl. Particular alkylcycloalkyl groups include methyl-cyclopropyl and dimethyl-cyclopropyl.

The term "alkylcycloalkylalkyl" denotes an alkyl group wherein at least one of the hydrogen atoms of the alkyl group is replaced by an alkylcycloalkyl group. Examples of alkylcycloalkylalkyl include methyl-cyclopropylmethyl, dimethyl-cyclopropylmethyl, methyl-cyclopropylethyl, dimethyl-cyclopropylethyl, methyl-cyclobutylmethyl, dimethyl-cyclobutylmethyl, methyl-cyclobutylethyl, dimethyl-cyclobutylethyl, methyl-cylopentylmethyl, dimethyl-cylopentylmethyl, methyl-cyclopentylethyl, dimethyl-cyclopentylethyl, methyl-cyclohexylmethyl, dimethyl-cyclohexylmethyl, methyl-cyclohexylethyl, dimethyl-cyclohexylethyl, methyl-cycloheptylmethyl, dimethyl-cycloheptylmethyl, methyl-cycloheptylethyl, dimethyl-cycloheptylethyl, methyl-cyclooctylmethyl, dimethyl-cyclooctylmethyl, methyl-cyclooctylethyl and dimethyl-cyclooctylethyl.

The term "alkylsulfonyl" denotes a group of the formula -$S(O)_2$-R', wherein R' is an alkyl group. Examples of alkylsulfonyl groups include groups of the formula -$S(O)_2$-R', wherein R' is methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl and tert-butyl. Particular example is a group of the formula -$S(O)_2$-R', wherein R' is methyl.

The term "alkylsulfonylalkyl" denotes an alkyl group wherein one of the hydrogen atoms of the alkyl group has been replaced by an alkylsulfonyl group. Particular example of alkylsulfonylalkyl is methylsulfonylmethyl.The term "alkylsulfonylamino" denotes a group of formula -NH-$S(O)_2$-R' wherein R' is an alkyl group. Examples of alkylsulfonylamino include methylsulfonylamino, ethylsulfonylamino, propylsulfonylamino, isopropylsulfonylamino, n-butylsulfonylamino, iso-butylsulfonylamino, sec-butylsulfonylamino, and tert-butylsulfonylamino

The term "amino" denotes a -NH_2 group.

The term "aminocarbonyl" denotes a group of the formula -C(O)-NH_2

The term "aryl" denotes a monovalent aromatic carbocyclic mono- or bicyclic ring system comprising 6 to 10 carbon ring atoms. Examples of aryl moieties include phenyl and naphthyl. Particular aryl group is phenyl.

The term "carbonyl" denotes a -C(O)- group.

The term "cycloalkoxy" denotes a group of the formula -O-R', wherein R' is a cycloalkyl group. Examples of cycloalkoxy group include cyclopropoxy, cyclobutoxy, cyclopentyloxy, cyclohexyloxy, cycloheptyloxy and cyclooctyloxy. Particular cycloalkoxy group is cyclopentyloxy.

The term "cycloalkoxyalkyl" denotes an alkyl group wherein at least one of the hydrogen atoms of the alkyl group has been replaced by a cycloalkoxy group. Examples of cycloalkoxyalkyl group include cyclopropoxymethyl, cyclopropoxyethyl, cyclobutoxymethyl, cyclobutoxyethyl, cyclopentyloxymethyl, cyclopentyloxyethyl, cyclohexyloxymethyl, cyclohexyloxyethyl, cycloheptyloxymethyl, cycloheptyloxyethyl, cyclooctyloxymethyl and cyclooctyloxyethyl.

The term "cycloalkyl" denotes a monovalent saturated monocyclic or bicyclic hydrocarbon group of 3 to 10 ring carbon atoms, particularly a monovalent saturated monocyclic hydrocarbon group of 3 to 8 ring carbon atoms. Bicyclic means consisting of two saturated or partially saturated carbocycles having two carbon atoms in common. Particular cycloalkyl groups are cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and cycloheptenyl. Further particular cycloalkyl groups are cyclobutyl, cyclopentyl and cyclohexyl.

The term "cycloalkylalkoxy" denotes an alkoxy group wherein at least one of the hydrogen atoms of the alkoxy group is replaced by a cycloalkyl group. Examples of cycloalkylalkoxy include cyclopropylmethoxy, cyclobutylmethoxy, cyclopentylmethoxy, cyclohexylmethoxy, cycloheptylmethoxy and cyclooctylmethoxy.

The term "cycloalkylalkyl" denotes an alkyl group wherein at least one of the hydrogen atoms of the alkyl group is replaced by a cycloalkyl group. Examples of cycloalkylalkyl include cyclopropylmethyl, cyclopropylethyl, cyclobutylpropyl and cyclopentylbutyl.

The term "cycloalkylsulfonylamino" denotes a group of formula -NH-S(O)$_2$-R' wherein R' is a cycloalkyl group. Examples of cycloalkylsulfonylamino include cyclopropylsulfonylamino, cyclobutanylsulfonylamino, cyclopentylsulfonylamino or cyclohexylsulfonylamino.

The term "haloalkoxy" denotes an alkoxy group wherein at least one of the hydrogen atoms of the alkoxy group has been replaced by same or different halogen atoms. The term "perhaloalkoxy" denotes an alkoxy group where all hydrogen atoms of the alkoxy group have been replaced by the same or different halogen atoms. Examples of haloalkoxy include fluoromethoxy, difluoromethoxy, trifluoromethoxy, trifluoroethoxy, trifluoromethylethoxy, trifluorodimethylethoxy and pentafluoroethoxy. Particular haloalkoxy groups are trifluoromethoxy, trifluoroethoxy and trifluoromethylethoxy.

The term "haloalkoxyalkyl" denotes an alkyl group wherein at least one of the hydrogen atoms of the alkyl group has been replaced by a haloalkoxy group. Examples of haloalkoxyalkyl include fluoromethoxymethyl, difluoromethoxymethyl, trifluoromethoxymethyl, fluoroethoxymethyl, difluoroethoxymethyl, trifluoroethoxymethyl, fluoromethoxyethyl, difluoromethoxyethyl, trifluoromethoxyethyl, fluoroethoxyethyl, difluoroethoxyethyl, trifluoroethoxyethyl, fluoromethoxypropyl, difluoromethoxypropyl, trifluoromethoxypropyl,

fluoroethoxypropyl, difluoroethoxypropyl and trifluoroethoxypropyl. Particular haloalkoxyalkyl group is 2,2-difluoroethoxyethyl.

The term "haloalkyl" denotes an alkyl group wherein at least one of the hydrogen atoms of the alkyl group has been replaced by same or different halogen atoms. The term "perhaloalkyl" denotes an alkyl group where all hydrogen atoms of the alkyl group have been replaced by the same or different halogen atoms. Examples of haloalkyl include fluoromethyl, difluoromethyl, trifluoromethyl, trifluoroethyl, trifluoromethylethyl and pentafluoroethyl. Particular haloalkyl groups are trifluoromethyl and trifluoroethyl.

The term "halogen" and "halo" are used interchangeably herein and denote fluoro, chloro, bromo, or iodo. Particular halogens are chloro and fluoro. More particular halogen is fluoro.

The term "heteroaryl" denotes a monovalent aromatic heterocyclic mono- or bicyclic ring system of 5 to 12 ring atoms, comprising 1, 2, 3 or 4 heteroatoms selected from N, O and S, the remaining ring atoms being carbon. Examples of heteroaryl moieties include pyrrolyl, furanyl, thienyl, imidazolyl, oxazolyl, thiazolyl, triazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, pyridinyl, pyrazinyl, pyrazolyl, pyridazinyl, pyrimidinyl, triazinyl, azepinyl, diazepinyl, isoxazolyl, benzofuranyl, isothiazolyl, benzothienyl, indolyl, isoindolyl, isobenzofuranyl, benzimidazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl, benzisothiazolyl, benzoxadiazolyl, benzothiadiazolyl, benzotriazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, or quinoxalinyl. Particular heteroaryl groups are furanyl, thienyl, imidazolyl, thiazolyl, triazolyl, tetrazolyl, pyridinyl, pyrazolyl, pyridazinyl, pyrimidinyl and isoxazolyl.

In the case of R^1, particular heteroaryl is furanyl.

In the case of R^3, particular heteroaryl are thienyl, imidazolyl, thiazolyl, triazolyl, tetrazolyl, pyridinyl, pyrazolyl, pyridazinyl, pyrimidinyl and isoxazolyl. Also particular heteroaryl are oxazolyl, indolyl, pyridinonyl and indazolyl,

The term "heterocycloalkoxy" denotes a group of the formula -O-R', wherein R' is a heterocycloalkyl group. Particular R' are tetrahydrofuranyl and tetrahydro-2H-pyranyl. Further particular R' is tetrahydrofuranyl.

The term "heterocycloalkyl" denotes a monovalent saturated or partly unsaturated mono- or bicyclic ring system of 4 to 9 ring atoms, comprising 1, 2, or 3 ring heteroatoms selected from N, O and S, the remaining ring atoms being carbon. Bicyclic means consisting of two cycles

having two ring atoms in common, i.e. the bridge separating the two rings is either a single bond or a chain of one or two ring atoms. Examples for monocyclic saturated heterocycloalkyl are 4,5-dihydro-oxazolyl, oxetanyl, azetidinyl, pyrrolidinyl, tetrahydrofuranyl, tetrahydro-thienyl, pyrazolidinyl, imidazolidinyl, oxazolidinyl, isoxazolidinyl, thiazolidinyl, piperidinyl, tetrahydropyranyl, tetrahydrothiopyranyl, piperazinyl, morpholinyl, thiomorpholinyl, 1,1-dioxo-thiomorpholin-4-yl, azepanyl, diazepanyl, homopiperazinyl or oxazepanyl. Examples for bicyclic saturated heterocycloalkyl are 8-aza-bicyclo[3.2.1]octyl, quinuclidinyl, 8-oxa-3-aza-bicyclo[3.2.1]octyl, 9-aza-bicyclo[3.3.1]nonyl, 3-oxa-9-aza-bicyclo[3.3.1]nonyl, or 3-thia-9-aza-bicyclo[3.3.1]nonyl. Examples for partly unsaturated heterocycloalkyl are dihydrofuryl, imidazolinyl, dihydro-oxazolyl, tetrahydro-pyridinyl, or dihydropyranyl. Particular examples of heterocycloalkyl group are azetidinyl, pyrrolidinyl, tetrahydrofuranyl, piperidinyl and tetrahydropyranyl. Further particular examples of heterocycloalkyl group are tetrahydrofuranyl and piperidinyl.

The term “heterocycloalkylalkoxy” denotes an alkoxy group wherein at least one of the hydrogen atoms of the alkoxy group is replaced by a heterocycloalkyl group. Particular example of heterocycloalkylalkoxy is tetrahydrofuranylmethyl.

The term “hydroxy” denotes a -OH group.

The term “hydroxyalkoxy” denotes an alkoxy group wherein at least one of the hydrogen atoms of the alkoxy group has been replaced by a hydroxy group. Examples of hydroxyalkoxy include hydroxyethoxy, hydroxypropoxy, hydroxymethylpropoxy and dihydroxypropoxy. Particluar example of hydroxyalkoxy group is hydroxyethoxy.

The term “hydroxyalkyl” denotes an alkyl group wherein at least one of the hydrogen atoms of the alkyl group has been replaced by a hydroxy group. Examples of hydroxyalkyl include hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxymethylpropyl and dihydroxypropyl. Particular examples are hydroxymethyl and hydroxyethyl.

The term “carboxy” denotes a COOH group.

The term “carboxyalkyl” denotes an alkyl group wherein one of the hydrogen atoms of the alkyl group has been replaced by a carboxy group. Particular carboxyalkyl group is 1-carboxy-1-methyl-ethyl.

The term “oxo” denotes a =O group.

The term “sulfonyl” denotes a -$S(O)_2$- group.

The term "pharmaceutically acceptable salts" refers to those salts which retain the biological effectiveness and properties of the free bases or free acids, which are biologically or otherwise undesirable. The salts are formed with inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid and the like, in particular hydrochloric acid, and organic acids such as acetic acid, propionic acid, glycolic acid, pyruvic acid, oxalic acid, maleic acid, malonic acid, succinic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, cinnamic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, salicylic acid, N-acetylcystein and the like. In addition these salts may be prepared by addition of an inorganic base or an organic base to the free acid. Salts derived from an inorganic base include, but are not limited to, the sodium, potassium, lithium, ammonium, calcium, magnesium salts and the like. Salts derived from organic bases include, but are not limited to salts of primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines and basic ion exchange resins, such as isopropylamine, trimethylamine, diethylamine, triethylamine, tripropylamine, ethanolamine, lysine, arginine, N-ethylpiperidine, piperidine, polyimine resins and the like. Particular pharmaceutically acceptable salts of compounds of formula (I) are the hydrochloride salts, methanesulfonic acid salts and citric acid salts. Particular pharmaceutically acceptable salts of compounds of formula (I) are also the sodium and potassium salts.

"Pharmaceutically acceptable esters" means that compounds of general formula (I) may be derivatised at functional groups to provide derivatives which are capable of conversion back to the parent compounds in vivo. Examples of such compounds include physiologically acceptable and metabolically labile ester derivatives, such as methoxymethyl esters, methylthiomethyl esters and pivaloyloxymethyl esters. Additionally, any physiologically acceptable equivalents of the compounds of general formula (I), similar to the metabolically labile esters, which are capable of producing the parent compounds of general formula (I) in vivo, are within the scope of this invention.

The term “protecting group” (PG) denotes the group which selectively blocks a reactive site in a multifunctional compound such that a chemical reaction can be carried out selectively at another unprotected reactive site in the meaning conventionally associated with it in synthetic chemistry. Protecting groups can be removed at the appropriate point. Exemplary protecting groups are amino-protecting groups, carboxy-protecting groups or hydroxy-protecting groups.

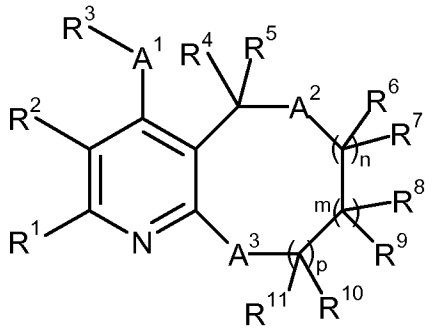
Particular protecting groups are the tert-butoxycarbonyl (Boc), benzyloxycarbonyl (Cbz), fluorenylmethoxycarbonyl (Fmoc) and benzyl (Bn). Further particular protecting groups are the tert-butoxycarbonyl (Boc) and the fluorenylmethoxycarbonyl (Fmoc). More particular protecting group is the tert-butoxycarbonyl (Boc).

The compounds of formula (I) can contain several asymmetric centers and / or stereoaxis and can be present in the form of optically pure enantiomers, mixtures of enantiomers such as, for example, racemates, optically pure diastereoisomers, mixtures of diastereoisomers, diastereoisomeric racemates or mixtures of diastereoisomeric racemates.

According to the Cahn-Ingold-Prelog Convention the asymmetric carbon atom can be of the "R" or "S" configuration.

Also an embodiment of the present invention are compounds according to formula (I) as described herein and pharmaceutically acceptable salts or esters thereof, in particular compounds according to formula (I) as described herein and pharmaceutically acceptable salts thereof, more particularly compounds according to formula (I) as described herein.

An embodiment of the present invention are compounds of formula (I)



(I)

wherein

R^1 is alkyl, haloalkyl, cycloalkyl, substituted cycloalkyl, alkoxy, alkoxyalkyl, haloalkoxy, haloalkoxyalkyl, cycloalkoxy, substituted cycloalkoxy, cycloalkoxylalkyl, substituted cycloalkoxyalkyl, hydroxyalkyl, aryl, substituted aryl, heterocycloalkyl, substituted heterocycloalkyl, heteroaryl, substituted heteroaryl, amino, substituted amino, aminocarbonyl or substituted aminocarbonyl, wherein substituted cycloalkyl, substituted cycloalkoxy, substituted cycloalkoxyalkyl, substituted aryl, substituted heterocycloalkyl and substituted heteroaryl are substituted with one to three

substituents independently selected from hydroxy, oxo, halogen, alkyl, cycloalkyl, haloalkyl, alkylcycloalkyl, cycloalkylalkyl, alkylcycloalkylalkyl, hydroxyalkyl, alkoxy and alkoxyalkyl and wherein substituted amino and substituted aminocarbonyl are substituted on the nitrogen atom with one to two substituents independently selected from alkyl, cycloalkyl, haloalkyl, alkylcycloalkyl, cycloalkylalkyl, alkylcycloalkylalkyl, hydroxyalkyl and alkoxyalkyl;

R^2 is -COOH, tetrazol-5-yl, [1,3,4]oxadiazol-2-on-5-yl, [1,3,4]oxadiazole-2-thion-5-yl, [1,2,4]oxadiazol-5-on-3-yl, [1,2,4]oxadiazole-5-thion-3-yl, [1,2,3,5]oxathiadiazole-2-oxide-4-yl, [1,2,4]thiadiazol-5-on-3-yl, isoxazol-3-ol-5-yl, 5-alkylisoxazol-3-ol-4-yl, 5-cycloalkylisoxazol-3-ol-4-yl, furazan-3-ol-4-yl, 5-alkylsulfonylamino-[1,3,4]oxadiazol-2-yl, 5-cycloalkylsulfonylamino-[1,3,4]oxadiazol-2-yl, 5-alkylsulfonylamino-[1,2,4]triazol-3-yl, 5-cycloalkylsulfonylamino-[1,2,4]triazol-3-yl, 5-alkylisothiazol-3-ol-4-yl, 5-cycloalkylisothiazol-3-ol-4-yl, [1,2,5]thiadiazol-3-ol-4-yl, 1,4-dihydro-tetrazol-5-on-1-yl, tetrazol-5-ylcarbamoyl, tetrazole-5-carbonyl, [1,2,4]oxadiazolidine-3,5-dion-2-y, [1,2,4]oxadiazol-5-on-3-yl, 2,4-dihydro-[1,2,4]triazol-3-on-5-sulfanyl, [1,2,4]triazole-3-sulfanyl, [1,2,4]triazole-3-sulfinyl, [1,2,4]triazole-3-sulfonyl, 4-alkyl-pyrazol-1-ol-5-yl, 4-cycloalkyl-pyrazol-1-ol-5-yl, 4-alkyl-[1,2,3]triazol-1-ol-5-yl, 4-cycloalkyl-[1,2,3]triazol-1-ol-5-yl, 5-alkyl-imidazol-1-ol-2-yl, 5-cycloalkyl-imidazol-1-ol-2-yl, 4-alkyl-imidazol-1-ol-5-yl, 4-cycloalkyl-imidazol-1-ol-5-yl, 4-alkyl-1,1-dioxo-1λ^6-[1,2,5]thiadiazolidin-3-on-5-yl, 4,4-dialkyl-1,1-dioxo-1λ^6-[1,2,5]thiadiazolidin-3-on-5-yl, 4-cycloalkyl-1,1-dioxo-1λ^6-[1,2,5]thiadiazolidin-3-on-5-yl, 4,4-dicycloalkyl-1,1-dioxo-1λ^6-[1,2,5]thiadiazolidin-3-on-5-yl, thiazolidine-2,4-dion-5-yl, oxazolidine-2,4-dion-5-yl, 3-[1-hydroxy-meth-(E)-ylidene]-pyrrolidine-2,4-dion-1-yl, 3-[1-hydroxy-meth-(Z)-ylidene]-pyrrolidine-2,4-dion-1-yl, 5-methyl-4-hydroxyfuran-2-on-3-yl, 5,5-dialkyl-4-hydroxyfuran-2-on-3-yl, 5-cycloalkyl-4-hydroxyfuran-2-on-3-yl, 5,5-dicycloalkyl-4-hydroxyfuran-2-on-3-yl, 3-hydroxycyclobut-3-ene-1,2-dion-4-yl or 3-hydroxycyclobut-3-ene-1,2-dion-4-amino;

R^3 is phenyl, substituted phenyl, substituted dihydropyridinyl, heteroaryl or substituted heteroaryl, wherein substituted phenyl, substituted dihydropyridinyl and substituted heteroaryl are substituted with one to three substituents independently selected from hydroxy, oxo, halogen, alkyl, cycloalkyl, haloalkyl, alkylcycloalkyl, cycloalkylalkyl, alkylcycloalkylalkyl, hydroxyalkyl, hydroxyalkoxy, alkoxy, alkoxyalkyl, amino and amino substituted on the nitrogen atom with one to two substituents independently

selected from alkyl, cycloalkyl, haloalkyl, alkylcycloalkyl, cycloalkylalkyl, alkylcycloalkylalkyl, hydroxyalkyl and alkoxyalkyl;

A^1 is a bond or $CR^{12}R^{13}$;

A^2 is $-CR^{14}R^{15}-$, $-NR^{16}-$, -O-, -S-, -S(O)- or $-S(O)_2-$;

A^3 is $-CR^{17}R^{18}-$, $-C(O)NR^{19}-$, $-NR^{19}-$, -O-, -S-, -S(O)- or $-S(O)_2-$;

R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11}, R^{14}, R^{15}, R^{17} and R^{18} are independently selected from H, halogen, alkyl, alkoxy, cycloalkyl, cycloalkylalkoxy, haloalkoxy and haloalkyl.

R^{12} and R^{13} are independently selected from hydrogen, alkyl, cycloalkyl and haloalkyl.

R^{16} and R^{19} are independently selected from hydrogen, alkyl, cycloalkyl, haloalkyl and alkylcarbonyl.

n, m and p are independently selected from zero and 1;

and pharmaceutically acceptable salts.

Also further embodiment of the present invention are compounds according to formula (I) as described herein, wherein R^1 is alkyl, cycloalkyl, substituted cycloalkyl, alkoxy, alkoxyalkyl, alkoxyalkoxy, alkoxycarbonylalkyl, carboxyalkyl, haloalkyl, haloalkoxy, substituted aryl, heterocycloalkyl, substituted heterocycloalkyl, heterocycloalkoxy, substituted heterocycloalkylalkoxy, heteroaryl, substituted heteroaryl, amino or substituted amino, wherein substituted cycloalkyl, substituted aryl, substituted heterocycloalkyl, substituted heterocycloalkylalkoxy and substituted heteroaryl are substituted with one to three substituents independently selected from halogen, alkyl, haloalkyl, hydoxyalkyl, alkylsulfonylalkyl, alkoxycarbonyl and alkoxyalkyl and wherein substituted amino is substituted on the nitrogen atom with two alkyl.

A further embodiment of the present invention are compounds according to formula (I) as described herein, wherein R^1 is alkyl, cycloalkyl, substituted cycloalkyl, alkoxyalkyl, substituted aryl, heterocycloalkyl, substituted heterocycloalkyl, heteroaryl, amino or substituted amino, wherein substituted cycloalkyl, substituted aryl and substituted heterocycloalkyl are substituted with one to three substituents independently selected from halogen, alkyl, haloalkyl and alkoxyalkyl and wherein substituted amino is substituted on the nitrogen atom with two alkyl.

A particular embodiment of the present invention are compounds according to formula (I) as described herein, wherein R^1 is cycloalkyl, substituted cycloalkyl, heterocycloalkyl, substituted heterocycloalkyl, heterocycloalkylalkoxy or substituted amino, wherein substituted cycloalkyl and substituted heterocycloalkyl are substituted with one alkyl or alkoxyalkyl and wherein substituted amino is substituted on the nitrogen atom with two alkyl.

A particular embodiment of the present invention are compounds according to formula (I) as described herein, wherein R^1 is cycloalkyl, substituted cycloalkyl, heterocycloalkyl or substituted amino, wherein substituted cycloalkyl is substituted with one alkoxyalkyl and wherein substituted amino is substituted on the nitrogen atom with two substituents independently selected alkyl.

A further particular embodiment of the present invention are compounds according to formula (I) as described herein, wherein R^1 is cyclopentyl, substituted cyclopentyl, tetrahydrofuranyl, substituted tetrahydrofuranyl, tetrahydrofuranyloxy, piperidinyl or substituted amino, wherein substituted cyclopentyl and substituted tetrahydrofuranyl are substituted with one alkyl or alkoxyalkyl and wherein substituted amino is substituted on the nitrogen atom with two alkyl.

A particular embodiment of the present invention are compounds according to formula (I) as described herein, wherein R^1 is cyclopentyl, substituted cyclopentyl, tetrahydrofuranyl, piperidinyl or substituted amino, wherein substituted cyclopentyl is substituted with one alkoxyalkyl and wherein substituted amino is substituted on the nitrogen atom with two substituents independently selected alkyl.

In a further embodiment of the present invention are compounds according to formula (I) as described herein, wherein R^2 is -COOH, tetrazol-5-yl or [1,3,4]oxadiazol-2-thion-5-yl.

Another further embodiment of the present invention are compounds according to formula (I) as described herein, wherein R^2 is tetrazol-5-yl.

Another embodiment of the present invention are compounds according to formula (I) as described herein, wherein R^3 is phenyl, substituted phenyl, substituted dihydropyridinyl, heteroaryl or substituted heteroaryl, wherein substituted phenyl, substituted dihydropyridinyl and substituted heteroaryl are substituted with one to three substituents independently selected from hydroxy, oxo, halogen, alkyl, cycloalkyl, haloalkyl, haloalkoxy, hydroxyalkoxy, alkoxy, alkylsulfonyl and amino substituted on the nitrogen atom with one to two substituents

independently selected from alkyl, cycloalkyl, haloalkyl, alkylcycloalkyl, cycloalkylalkyl, alkylcycloalkylalkyl, hydroxyalkyl and alkoxyalkyl.

Another embodiment of the present invention are compounds according to formula (I) as described herein, wherein R^3 is phenyl, substituted phenyl, substituted dihydropyridinyl, heteroaryl or substituted heteroaryl, wherein substituted phenyl, substituted dihydropyridinyl and substituted heteroaryl are substituted with one to three substituents independently selected from oxo, halogen, alkyl, cycloalkyl, haloalkyl, hydroxyalkoxy and alkoxy.

Another particular embodiment of the present invention are compounds according to formula (I) as described herein, wherein R^3 is phenyl, substituted phenyl or substituted heteroaryl, wherein substituted phenyl and substituted heteroaryl are substituted with one to three substituents independently selected from halogen and alkyl.

The present invention also relates to compounds according to formula (I) as described herein, wherein R^3 is phenyl, substituted phenyl, substituted pyrazolyl or substituted pyridinyl, wherein substituted phenyl, substituted pyrazolyl and substituted pyridinyl are substituted with one to three substituents independently selected from halogen and alkyl.

A further particular embodiment of the present invention are compounds according to formula (I) as described herein, wherein R^3 is substituted pyrazolyl or substituted pyridinyl, wherein substituted pyrazolyl and substituted pyridinyl are substituted with one alkyl.

A particular embodiment of the present invention are compounds according to formula (I) as described herein, wherein R^3 is pyridinyl substituted with one alkyl or halogen.

A more particular embodiment of the present invention are compounds according to formula (I) as described herein, wherein R^3 is pyridinyl substituted with one alkyl.

Also an embodiment of the present invention are compounds according to formula (I) as described herein, wherein A^1 is a bond.

The present invention also relates to compounds according to formula (I) as described herein, wherein A^2 is $-CR^{14}R^{15}-$, $-NR^{16}-$, -O- or -S-.

The present invention also relates to compounds according to formula (I) as described herein, wherein A^2 is $-CR^{14}R^{15}-$, $-NR^{16}-$ or -O-.

Another embodiment of the present invention are compounds according to formula (I) as described herein, wherein A^2 is $-CR^{14}R^{15}$.

A further particular embodiment of the present invention are compounds according to formula (I) as described herein, wherein is A^3 is $-CR^{17}R^{18}-$, $-C(O)NR^{19}-$ or $-NR^{19}$.

A further particular embodiment of the present invention are compounds according to formula (I) as described herein, wherein is A^3 is $-CR^{17}R^{18}-$ or $-NR^{19}$.

A particular embodiment of the present invention are compounds according to formula (I) as described herein, wherein A^3 is $-CR^{17}R^{18}-$.

Also an embodiment of the present invention are compounds according to formula (I) as described herein, wherein n is 1.

A further particular embodiment of the present invention are compounds according to formula (I) as described herein, wherein p is zero.

The present invention also relates to compounds according to formula (I) as described herein, wherein R^4, R^5, R^6, R^7, R^8, R^9, R^{10} and R^{11} are H.

Another embodiment of the present invention are compounds according to formula (I) as described herein, wherein R^4 and R^5 are H.

The present invention also relates to compounds according to formula (I) as described herein, wherein R^6 and R^7 are H.

Also an embodiment of the present invention are compounds according to formula (I) as described herein, wherein R^8 and R^9 are H.

Also an embodiment of the present invention are compounds according to formula (I) as described herein, wherein R^{10} and R^{11} are H.

Another embodiment of the present invention are compounds according to formula (I) as described herein, wherein R^{14} is H, halogen, alkyl, alkoxy or haloalkyl.

A particular embodiment of the present invention are compounds according to formula (I) as described herein, wherein R^{15} is H, halogen or alkyl.

A further particular embodiment of the present invention are compounds according to formula (I) as described herein, wherein R^{14} and R^{15} are independently selected from H, halogen and alkyl.

A particular embodiment of the present invention are compounds according to formula (I) as described herein, wherein R^{17} and R^{18} are independently selected from H and alkyl.

A more particular embodiment of the present invention are compounds according to formula (I) as described herein, wherein R^{17} and R^{18} are H.

Also a particular embodiment of the present invention are compounds according to formula (I) as described herein, wherein R^{16} is haloalkyl or alkylcarbonyl.

Also a particular embodiment of the present invention are compounds according to formula (I) as described herein, wherein R^{19} is alkyl or alkylcarbonyl.

Also an embodiment of the present invention are compounds according to formula (I) as described herein, wherein R^{16} and R^{17} are halogen.

Particular examples of compounds of formula (I) as described herein are selected from

2-isopropyl-6,8-dimethyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylic acid;

8-acetyl-2-isopropyl-6-methyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylic acid;

8-ethyl-2-isopropyl-6-methyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylic acid;

4-(3-chlorophenyl)-2-cyclohexyl-8-ethyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylic acid;

2-cyclohexyl-8-ethyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylic acid;

2-cyclopentyl-8-ethyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylic acid;

2-cyclopentyl-8-ethyl-6-methyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylic acid;

2-cyclopentyl-6,8-dimethyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylic acid;

2-isopropyl-6-methyl-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carboxylic acid;

6-ethyl-2-isopropyl-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carboxylic acid;

2-isopropyl-6,6-dimethyl-4-phenyl-5,6,7,8-tetrahydro-quinoline-3-carboxylic acid;

2-cyclopentyl-4-(6-methoxypyridin-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid;

2-cyclopentyl-4-(6-oxo-1,6-dihydropyridin-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid;

4-phenyl-2-(piperidin-1-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid;

2-(2-methylpyrrolidin-1-yl)-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid;

6-methyl-4-phenyl-2-(piperidin-1-yl)-5,6,7,8-tetrahydroquinoline-3-carboxylic acid;

2-(diethylamino)-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid;

6-methyl-2-(2-methylpyrrolidin-1-yl)-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carboxylic acid;

2-(diethylamino)-6-methyl-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carboxylic acid;

4-(3-chlorophenyl)-6-methyl-2-(pyrrolidin-1-yl)-5,6,7,8-tetrahydroquinoline-3-carboxylic acid;

4-phenyl-2-(piperidin-1-yl)-6,7-dihydro-5H-cyclopenta[b]pyridine-3-carboxylic acid;

2-(diethylamino)-4-phenyl-6,7-dihydro-5H-cyclopenta[b]pyridine-3-carboxylic acid;

4-(3-chlorophenyl)-6-methyl-2-(piperidin-1-yl)-5,6,7,8-tetrahydroquinoline-3-carboxylic acid;

5-(6-methyl-4-phenyl-2-(piperidin-1-yl)-5,6,7,8-tetrahydroquinolin-3-yl)-1,3,4-oxadiazole-2(3H)-thione;

6-methyl-4-phenyl-2-(piperidin-1-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

N,N-diethyl-6-methyl-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinolin-2-amine;

4-phenyl-2-(piperidin-1-yl)-3-(2H-tetrazol-5-yl)-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinoline;

N,N-diethyl-4-phenyl-3-(2H-tetrazol-5-yl)-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinolin-2-amine;

6-methyl-4-(1-methyl-1H-pyrazol-5-yl)-2-(piperidin-1-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

4-phenyl-2-(piperidin-1-yl)-3-(2H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

N,N-diethyl-4-phenyl-3-(2H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine;

4-(3-chlorophenyl)-2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(3-chlorophenyl)-N,N-diethyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine;

4-(1-methyl-1H-pyrazol-5-yl)-2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(4-fluorophenyl)-6-methyl-2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

4-(4-fluorophenyl)-2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-7,8-dihydro-5H-pyrano[4,3-b]pyridine;

4-(1-methyl-1H-pyrazol-5-yl)-2-(2-methylpyrrolidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(5-chlorothiophen-2-yl)-N,N-diethyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine;

4-(5-chlorothiophen-2-yl)-2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

N,N-diethyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine;

5-methyl-3-(2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)isoxazole;

N,N-diethyl-4-(5-methylisoxazol-3-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine;

4-(1-methyl-1H-pyrazol-5-yl)-2-(2-methylpyrrolidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(piperidin-1-yl)-4-(pyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

N,N-diethyl-4-(pyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine;

4-(5-methylfuran-2-yl)-2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

N,N-diethyl-4-(5-methylfuran-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine;

4-(1,5-dimethyl-1H-pyrazol-4-yl)-2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(1,5-dimethyl-1H-pyrazol-4-yl)-N,N-diethyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine;

4-(5-chlorothiophen-2-yl)-2-(3-fluoropiperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(5-chlorothiophen-2-yl)-2-(3,3-difluoropiperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(5-chlorothiophen-2-yl)-2-(4,4-difluoropiperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(5-chlorothiophen-2-yl)-2-(4-fluoropiperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(5-chlorothiophen-2-yl)-3-(1H-tetrazol-5-yl)-2-(4-(trifluoromethyl)piperidin-1-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(5-chlorothiophen-2-yl)-2-(3,3-difluoroazetidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

N,N-diethyl-4-(4-methylthiazol-5-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine;

4-methyl-5-(2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)thiazole;

N,N-diethyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8,9,10-hexahydrocycloocta[b]pyridin-2-amine;

4-(5-chlorothiophen-2-yl)-2-(3,3-difluoropyrrolidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(1-methyl-1H-pyrazol-5-yl)-2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8,9,10-hexahydrocycloocta[b]pyridine;

diethyl-[4-pyrimidin-5-yl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-yl]-amine;

N,N-diethyl-4-(3-fluoropyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine;

N,N-diethyl-4-(2-methoxypyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine;

4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine;

2-propyl-4-(pyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(1-methyl-1H-pyrazol-5-yl)-2-(pentan-3-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(3-chlorophenyl)-2-cyclobutyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclohexyl-4-pyridin-4-yl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-H-cyclohepta[b]pyridine;

4-(3-chloro-phenyl)-2-cyclopentyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-H-cyclohepta[b]pyridine;

2-cyclohexyl-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

5-(2-cyclohexyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)pyridin-2(1H)-one;

5-(2-cyclohexyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)-1-ethylpyridin-2(1H)-one;

5-(2-cyclohexyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)-1-methylpyridin-2(1H)-one;

2-cyclohexyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclopentyl-4-(pyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclopentyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

1-(4-(3-chlorophenyl)-2-cyclobutyl-3-(1H-tetrazol-5-yl)-7,8-dihydro-1,6-naphthyridin-6(5H)-yl)ethanone;

2-cyclopentyl-4-(6-methoxypyridin-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-phenyl-2-(tetrahydro-2H-pyran-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclopentyl-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-phenyl-2-(tetrahydrofuran-3-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclopentyl-4-(2-methoxypyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclohexyl-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclopentyl-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-phenyl-2-(tetrahydrofuran-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclohexyl-4-(3-fluoropyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclopentyl-4-(3-fluoropyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-phenyl-2-(tetrahydro-2H-pyran-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclohexyl-4-(2-methylpyrimidin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

5-(2-cyclobutyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)-1-methylpyridin-2(1H)-one;

2-cyclohexyl-4-(pyrimidin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclopentyl-4-(pyrimidin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclopentyl-4-(2-methylpyrimidin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-(methoxymethyl)cyclopentyl)-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclopentyl-4-(pyridazin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclopentyl-4-(6-methylpyridin-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclopentyl-4-(pyridin-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-isopropyl-4-(2-isopropylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclopentyl-4-(pyrimidin-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(2-(2-cyclopentyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)phenoxy)ethanol;

2-cyclopentyl-4-(2-isopropylpyrimidin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-isopropyl-4-(2-isopropylpyrimidin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-chloropyridin-4-yl)-2-cyclopentyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-(methoxymethyl)cyclopentyl)-4-(2-methoxypyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-isopropylpyridin-4-yl)-2-(pentan-3-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(1-methyl-1H-pyrazol-5-yl)-2-(pentan-3-yl)-3-(2H-tetrazol-5-yl)-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinoline;

2-cyclohexyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinoline;

2-cyclohexyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinoline;

2-cyclohexyl-6-methyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-cyclohexyl-6-methyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-cyclopentyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinoline;

2-cyclopentyl-6,6-difluoro-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-cyclopentyl-6-methyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

4-(2-cyclohexyl-3-(2H-tetrazol-5-yl)-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinolin-4-yl)-3,5-dimethylisoxazole;

4-(2-cyclohexyl-6-methyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinolin-4-yl)-3,5-dimethylisoxazole;

2-cyclopentyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinoline;

2-cyclopentyl-4-phenyl-3-(2H-tetrazol-5-yl)-6-(2,2,2-trifluoroethyl)-5,6,7,8-tetrahydro-1,6-naphthyridine;

2-cyclopentyl-6,6-dimethyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-cyclopentyl-6-methoxy-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

6-methyl-4-(2-methylpyridin-4-yl)-2-tert-pentyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-cyclopentyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-cyclohexyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-methoxy-2-methylpropan-2-yl)-6-methyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-cyclopentyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-6,7-dihydro-5H-cyclopenta[b]pyridine;

2-cyclohexyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-6,7-dihydro-5H-cyclopenta[b]pyridine;

2-tert-butyl-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-tert-butyl-4-(3-fluorophenyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-tert-butyl-3-(1H-tetrazol-5-yl)-4-(4-(trifluoromethyl)phenyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-tert-butyl-3-(1H-tetrazol-5-yl)-4-(3-(trifluoromethyl)phenyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-tert-butyl-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(3,3-difluorocyclobutyl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-tert-butyl-4-(4-fluoro-phenyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-tert-butyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)oxazole;

2-tert-butyl-4-(1-methyl-1H-pyrazol-3-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-tert-butyl-4-(4-methyl-1H-pyrazol-5-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-tert-butyl-4-(3-cyclopropyl-1H-pyrazol-5-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-tert-butyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)-2-methyloxazole;

2-tert-butyl-4-(4-chloro-1H-pyrazol-3-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-tert-butyl-3-(1H-tetrazol-5-yl)-4-(4-(trifluoromethyl)-1H-imidazol-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-tert-butyl-3-(1H-tetrazol-5-yl)-4-(1H-1,2,3-triazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-tert-butyl-4-(2-butyl-1H-imidazol-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-furan-2-yl-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-sec-butyl-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(3-fluorophenyl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-sec-butyl-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

and pharmaceutically acceptable salts thereof.

Also particular examples of compounds of formula (I) as described herein are selected from

4-phenyl-2-(R)-tetrahydro-furan-2-yl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-phenyl-2-(S)-tetrahydro-furan-2-yl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

(R)-4-(2-chloropyridin-4-yl)-2-(tetrahydrofuran-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

(S)-4-(2-chloropyridin-4-yl)-2-(tetrahydrofuran-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-phenyl-2-(tetrahydrofuran-2-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8,9,10-hexahydrocycloocta[b]pyridine;

(S)-4-phenyl-2-(tetrahydrofuran-2-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8,9,10-hexahydrocycloocta[b]pyridine;

(R)-4-phenyl-2-(tetrahydrofuran-2-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8,9,10-hexahydrocycloocta[b]pyridine;

2-(2-methyltetrahydrofuran-2-yl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-((S)-2-methyl-tetrahydro-furan-2-yl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-((R)-2-methyl-tetrahydro-furan-2-yl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(3-methoxyphenyl)-2-(2-methyltetrahydrofuran-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(3-methoxy-phenyl)-2-((S)-2-methyl-tetrahydro-furan-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(3-methoxy-phenyl)-2-((R)-2-methyl-tetrahydro-furan-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-methylpyridin-4-yl)-2-(2-methyltetrahydrofuran-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-[(2S)-2-methyloxolan-2-yl]-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-[(2R)-2-methyloxolan-2-yl]-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(3-chlorophenyl)-2-(2-methyltetrahydrofuran-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(3-chloro-phenyl)-2-((S)-2-methyl-tetrahydro-furan-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(3-chloro-phenyl)-2-((R)-2-methyl-tetrahydro-furan-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-methylcyclopentyl)-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-methylcyclopentyl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-methoxypyridin-4-yl)-2-(1-methylcyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-(1-methylcyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)pyridin-2(1H)-one;

4-(3-chloro-phenyl)-2-(1-methyl-cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(1-methyl-1H-pyrazol-5-yl)-2-(1-methylcyclohexyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-methylcyclohexyl)-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-methoxymethyl-cyclopentyl)-4-(2-methyl-2H-pyrazol-3-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(3-fluoropyridin-4-yl)-2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-(methoxymethyl)cyclopentyl)-4-(4-methyl-1H-pyrazol-3-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(1H-indol-4-yl)-2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-chloropyridin-4-yl)-2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-ethylpyridin-4-yl)-2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

3-(2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)-2-methylphenol;

4-(2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)-2-methyloxazole;

4-(1H-indazol-4-yl)-2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-4-(2-(trifluoromethyl)pyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-4-(2-(2,2,2-trifluoroethoxy)pyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-(methoxymethyl)cyclopentyl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-ethoxypyridin-4-yl)-2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(4-fluoro-3-methoxyphenyl)-2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(4-fluorophenyl)-2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-(methoxymethyl)cyclopentyl)-4-(3-methoxyphenyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-fluoro-5-methoxyphenyl)-2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(3-chloro-phenyl)-2-(1-methoxymethyl-cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(3-(methoxymethyl)pentan-3-yl)-4-(1-methyl-1H-pyrazol-5-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(3-(methoxymethyl)pentan-3-yl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclopentyl-4-(2-ethylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-cyclopentyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)-N-methylpyridin-2-amine;

2-cyclopentyl-3-(1H-tetrazol-5-yl)-4-(2-(trifluoromethyl)pyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(1-methyl-1H-pyrazol-5-yl)-2-(3-methylpentan-3-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-ethylpyridin-4-yl)-2-isopropyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-isopropyl-3-(1H-tetrazol-5-yl)-4-(2-(2,2,2-trifluoroethoxy)pyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-ethoxypyridin-4-yl)-2-isopropyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-methoxycyclopentyl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-methoxycyclopentyl)-4-phenyl-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-methoxycyclopentyl)-4-(2-methoxypyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-chloropyridin-4-yl)-2-(1-methoxycyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-methoxycyclopentyl)-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

(1-(4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-yl)cyclopentyl)methanol;

(1-(4-phenyl-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinolin-2-yl)cyclopentyl)methanol;

(1-(4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-yl)cyclopentyl)methanol;

(1-(4-(3-chlorophenyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-yl)cyclopentyl)methanol;

(1-(4-(4-fluorophenyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-yl)cyclopentyl)methanol;

(S)-tert-butyl 2-(4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-yl)pyrrolidine-1-carboxylate;

(S)-4-phenyl-2-(pyrrolidin-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine 2,2,2-trifluoroacetate;

2-cyclopentyl-4-phenyl-3-(1H-tetrazol-5-yl)-7,8-dihydro-5H-pyrido[2,3-c]azepin-9(6H)-one;

2-(1-methoxy-2-methylpropan-2-yl)-6,6-dimethyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

6,6-dimethyl-4-(1-methyl-1H-pyrazol-5-yl)-2-tert-pentyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-methoxy-2-methylpropan-2-yl)-6,6-dimethyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-(methoxymethyl)cyclopentyl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

6,6-difluoro-2-(1-(methoxymethyl)cyclopentyl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

6,6-difluoro-2-(1-methoxymethyl-cyclohexyl)-4-phenyl-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydro-quinoline;

6,6-difluoro-2-(1-(methoxymethyl)cyclopentyl)-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(4-methyltetrahydro-2H-pyran-4-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

6,6-difluoro-2-(4-methyltetrahydro-2H-pyran-4-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-(methoxymethyl)cyclopentyl)-6-methyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-(methoxymethyl)cyclohexyl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

6,6-difluoro-2-(1-(methoxymethyl)cyclopentyl)-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-(methoxymethyl)cyclopentyl)-6,6-dimethyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(2-methyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

6,6-difluoro-2-(2-methyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

6,6-dimethyl-2-(2-methyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

4-(1-methyl-1H-pyrazol-5-yl)-2-(2-methyltetrahydrofuran-2-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

6,6-dimethyl-4-(1-methyl-1H-pyrazol-5-yl)-2-(2-methyltetrahydrofuran-2-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(R)-2-(2-methyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(S)-2-(2-methyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(R)-6,6-difluoro-2-(2-methyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(S)-6,6-difluoro-2-(2-methyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(R)-6,6-dimethyl-2-(2-methyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(S)-6,6-dimethyl-2-(2-methyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-(methoxymethyl)cyclopentyl)-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-(methoxymethyl)cyclohexyl)-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-(methoxymethyl)cyclohexyl)-6,6-dimethyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

6,6-difluoro-2-(1-(methoxymethyl)cyclohexyl)-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

6,6-difluoro-4-(1-methyl-1H-pyrazol-5-yl)-2-(2-methyltetrahydrofuran-2-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-(methoxymethyl)cyclohexyl)-4-(1-methyl-1H-pyrazol-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-6,6-dimethyl-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

6,6-difluoro-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(2-ethyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(2-ethyltetrahydrofuran-2-yl)-6,6-dimethyl-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(2-ethyltetrahydrofuran-2-yl)-6,6-difluoro-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(R)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(S)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(R)-6,6-difluoro-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(S)-6,6-difluoro-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(R)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-6,6-dimethyl-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(S)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-6,6-dimethyl-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(2-ethyltetrahydrofuran-2-yl)-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-(methoxymethyl)cyclopentyl)-4-(1-methyl-1H-pyrazol-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

4-(3-chlorophenyl)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

4-(3-chlorophenyl)-2-(2-methyltetrahydrofuran-2-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-4-(3-methoxyphenyl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

4-(4-fluoro-3-methoxyphenyl)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-(methylsulfonylmethyl)cyclopentyl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(R)-4-(4-fluoro-3-methoxyphenyl)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(S)-4-(4-fluoro-3-methoxyphenyl)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-(methoxymethyl)cyclopentyl)-4-(3-(methylsulfonyl)phenyl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-(methoxymethyl)cyclopentyl)-4-(3-methoxyphenyl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

4-(2-fluoro-5-methoxyphenyl)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

4-(2-fluoro-5-methoxyphenyl)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-(ethoxymethyl)cyclopentyl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(R)-4-(3-chlorophenyl)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-6,6-dimethyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(S)-4-(3-chlorophenyl)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-6,6-dimethyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(3,3-difluorocyclobutyl)-4-(1-methyl-1H-pyrazol-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1,5-dimethyl-1H-pyrazol-4-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-tert-butyl-4-(1-methyl-1H-pyrazol-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(3,3-difluorocyclobutyl)-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-sec-butyl-4-(1-methyl-1H-pyrazol-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-tert-butyl-6,6-difluoro-4-(2-methyl-pyridin-4-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydro-quinoline;

2-tert-butyl-6,6-difluoro-4-(1-methyl-1H-pyrazol-4-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydro-quinoline;

2-tert-butyl-6,6-difluoro-4-(2-methyl-2H-pyrazol-3-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydro-quinoline;

2-tert-butyl-4-phenyl-3-(1H-tetrazol-5-yl)-7,8-dihydro-5H-thiopyrano[4,3-b]pyridine;

2-tert-butyl-8,8-dimethyl-4-phenyl-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-tert-butyl-7,7-dimethyl-4-phenyl-3-(1H-tetrazol-5-yl)-6,7-dihydro-5H-cyclopenta[b]pyridine;

2-tert-butyl-8,8-dimethyl-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-tert-butyl-8,8-dimethyl-4-(1-methyl-1H-pyrazol-4-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-(methoxymethyl)cyclobutyl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-(methoxymethyl)cyclobutyl)-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-(methoxymethyl)cyclobutyl)-4-(1-methyl-1H-pyrazol-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(perfluoroethyl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-tert-butyl-8,8-dimethyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2,4-bis(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-isopropoxy-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-methoxy-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-ethoxy-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

(S)-4-phenyl-2-(tetrahydrofuran-3-yloxy)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile;

(R)-4-phenyl-2-(tetrahydrofuran-3-yloxy)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile;

2-ethoxy-4-(1-methyl-1H-pyrazol-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-isopropoxy-4-(1-methyl-1H-pyrazol-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-ethoxy-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(2-methoxyethoxy)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-phenyl-2-((tetrahydrofuran-2-yl)methoxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(3-fluoropropoxy)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(2,2-difluoroethoxy)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

(S)-4-phenyl-2-(tetrahydrofuran-3-yloxy)-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

4-(2-methylpyridin-4-yl)-2-(tetrahydro-2H-pyran-4-yloxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

(S)-4-(2-methylpyridin-4-yl)-2-(tetrahydrofuran-3-yloxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

(S)-4-(2-methylpyridin-4-yl)-2-(tetrahydrofuran-3-yloxy)-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(2-methoxyethoxy)-3-(1H-tetrazol-5-yl)-4-(4-(trifluoromethyl)phenyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(3-fluorophenyl)-2-(2-methoxyethoxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

(S)-4-(3-fluorophenyl)-2-(tetrahydrofuran-3-yloxy)-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

4-(3,5-difluorophenyl)-2-(2-methoxyethoxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

(S)-4-(3-fluorophenyl)-2-(tetrahydrofuran-3-yloxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

(S)-4-(3,5-difluorophenyl)-2-(tetrahydrofuran-3-yloxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-fluorophenyl)-2-((S)-tetrahydrofuran-3-yloxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-fluorophenyl)-2-(2-methoxyethoxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

(S)-2-(tetrahydrofuran-3-yloxy)-3-(1H-tetrazol-5-yl)-4-(thiophen-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(3-fluoropropoxy)-3-(1H-tetrazol-5-yl)-4-(thiophen-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

(S)-2-(tetrahydrofuran-3-yloxy)-3-(1H-tetrazol-5-yl)-4-(thiophen-3-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-phenyl-2-(tetrahydro-2H-pyran-4-yloxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-methylcyclopentyl)-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid;

4-(3-chlorophenyl)-2-(1-methylcyclopentyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid;

4-(1-methyl-1H-pyrazol-5-yl)-2-(1-methylcyclohexyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid;

2-(1-methylcyclohexyl)-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid;

2-cyclohexyl-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid;

2-(1-methylcyclohexyl)-4-(2-methylpyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid;

2-cyclohexyl-4-(2-methylpyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid;

2-cyclopentyl-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carboxylic acid;

2-(1-(methoxymethyl)cyclopentyl)-6-pentyl-4-phenyl-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

tert-butyl 2-methyl-2-(4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-yl)propanoate;

2-methyl-2-(4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-yl)propanoic acid;

and pharmaceutically acceptable salts thereof.

Further particular examples of compounds of formula (I) as described herein are selected from

6-methyl-4-(1-methyl-1H-pyrazol-5-yl)-2-(piperidin-1-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

4-(3-chlorophenyl)-N,N-diethyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine;

2-cyclopentyl-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-phenyl-2-(tetrahydrofuran-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-(methoxymethyl)cyclopentyl)-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclopentyl-6,6-difluoro-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-cyclopentyl-6-methyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-cyclopentyl-6,6-dimethyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

and pharmaceutically acceptable salts thereof.

Also further particular examples of compounds of formula (I) as described herein are selected from

2-((R)-2-methyl-tetrahydro-furan-2-yl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-methylcyclopentyl)-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-chloropyridin-4-yl)-2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

(R)-6,6-dimethyl-2-(2-methyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(R)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(S)-4-phenyl-2-(tetrahydrofuran-3-yloxy)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile;

2-(1-methylcyclohexyl)-4-(2-methylpyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid;

and pharmaceutically acceptable salts thereof.

Processes for the manufacture of compounds of formula (I) as described herein are an object of the invention.

The preparation of compounds of formula (I) of the present invention may be carried out in sequential or convergent synthetic routes. Syntheses of the invention are shown in the following general schemes. The skills required for carrying out the reaction and purification of the resulting products are known to those persons skilled in the art. In case a mixture of enantiomers or diastereoisomers is produced during a reaction, these enantiomers or diastereoisomers can be separated by methods described herein or known to the person skilled in the art such as e.g. chiral chromatography or crystallization. In case one of the starting materials or compounds of formula (I) contain one or more functional groups which are not stable or are reactive under the reaction conditions of one or more reaction steps, appropriate protecting groups can be introduced before the critical step applying methods well known in the art. Such protecting groups can be removed at a later stage of the synthesis using standard methods described in the literature. The substituents and indices used in the following description of the processes have the significance given herein.

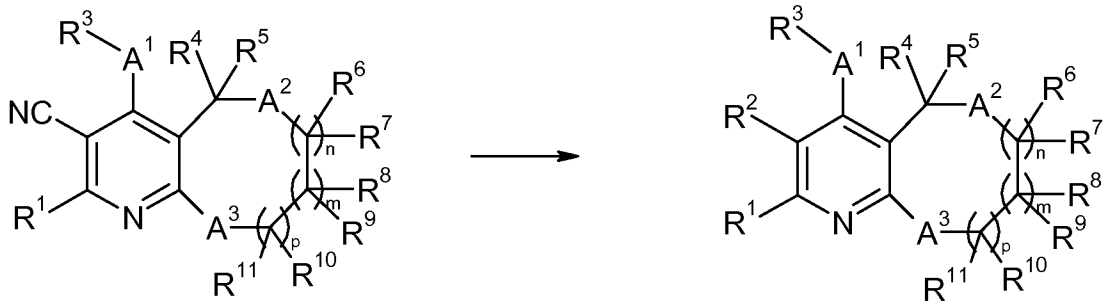
Abbreviations

The following abbreviations are used in the present text:

d = days, DCM = dichloromethane, DMA = N,N-dimethylacetamide, DMF = N,N-dimethylformamide, DMSO = dimethylsulfoxide, EtOAc = ethyl acetate, ESP = Electrospray Ionisation, positive ions, ESN = Electrospray Ionisation, negative ions, EtOH = ethanol, h = hours, HCl = hydrochloric acid, MeOH = methanol, min = minutes, NaOH = sodium hydroxide, Na_2SO_4 = sodium sulfate, OTf = CF_3-SO_2-O-, THF = tetrahydrofuran.

Compounds of formula (I), wherein R^2 is 5-tetrazolyl may be prepared as illustrated in scheme 1.

Scheme 1

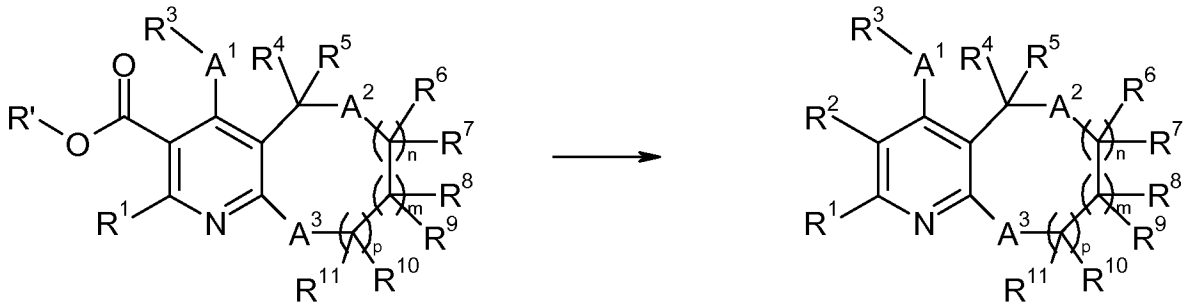


(II) (I) R^2 is tetrazolyl

Nitrile derivatives of formula (II) can be converted into formula (I) compounds, wherein R^2 is 5-tetrazolyl, by reaction with azide reagents M-N_3, wherein M represents sodium, trialkyltin or trialkylsilyl, optionally in presence of additives such as zinc salts or dibutyltin oxide. Typical conditions include sodium azide in the presence of zinc chloride in a solvent such as DMF at elevated temperature, trimethyltin azide in a solvent such as xylene at elevated temperature or trimethylsilyl azide in the presence of dibutyltin oxide in a solvent such as dioxane at elevated temperature.

Compounds of formula (I), wherein R^2 is –COOH may be prepared as illustrated in scheme 2.

Scheme 2



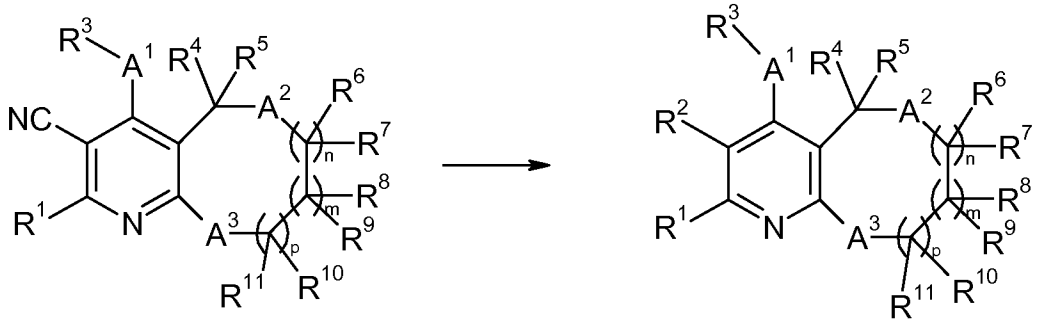
(III) R' is alkyl, e.g. Me, Et or t-Bu (I) R^2 is $-CO_2H$

Ester derivatives of formula (III) can be converted into compounds of formula (I), wherein R^2 is –COOH, by reaction with a metal hydroxide such as lithium, sodium or potassium hydroxide in solvent mixtures containing DMSO-water, ethanol-water, THF-methanol-water or methanol-water at elevated temperature. Alternatively, ester cleavage can also be accomplished by reaction with a nucleophile such as lithium iodide in pyridine at elevated temperatures. Ester derivatives of formula (III), wherein R' is tert-butyl can be converted into compounds of formula

(I), wherein R^2 is -COOH by reaction with an acid such as HCl in a solvent such as dioxane or with TFA in a solvent such as DCM. Other methods for cleavage of esters can be found in the literature.

Alternatively, compounds of formula (I), wherein R^2 is –COOH may be prepared as illustrated in scheme 3.

Scheme 3

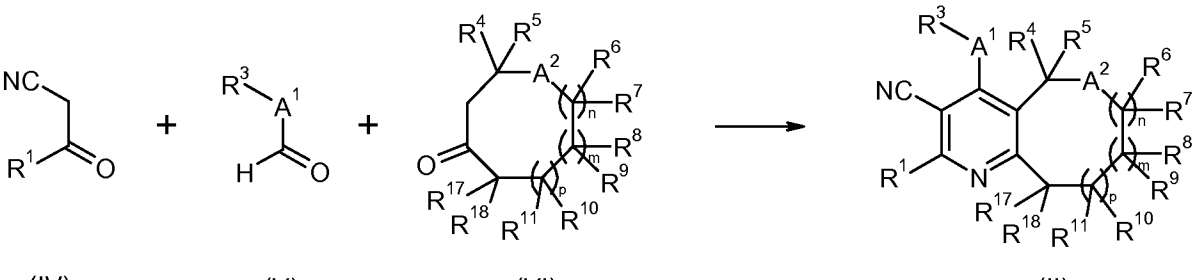


(II) (I) R^2 is $-CO_2H$

Nitrile derivatives of formula (II) can be treated with aqueous acid such as HCl or alternatively with an aqueous base such as potassium hydroxide at elevated temperature to obtain compounds of formula (I), wherein R^2 is –COOH. Nitriles of formula (II) can also be converted to compounds of formula (I), wherein R^2 is –COOH by conversion to the corresponding iminoether by addition of alcoholic solutions of acids such as HCl, HBr or the like at various temperatures, preferably ranging from 0 to 100 °C, followed by hydrolysis of the iminoether to the corresponding ester and hydrolysis of the ester as described above.

Nitrile intermediates of formula (II) wherein A^3 is $–CR^{17}R^{18}–$ can be obtained as illustrated in scheme 4.

Scheme 4

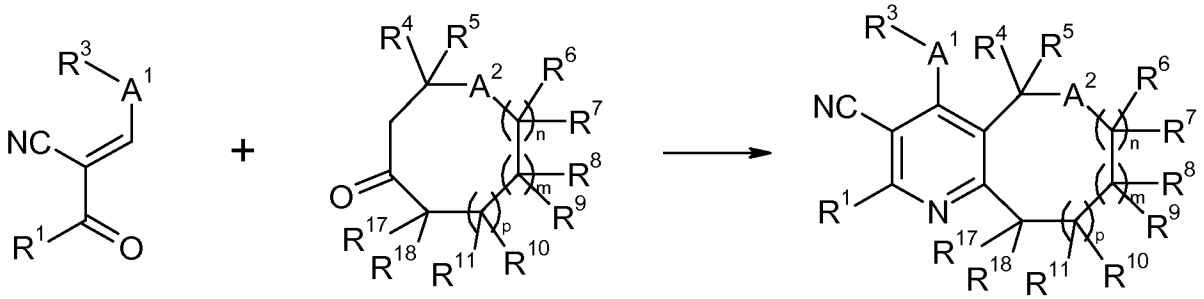


(IV) (V) (VI) (II)

Four component reaction of suitable β-keto nitriles (IV), aldehydes (V), cyclic ketones of formula (VI) and ammonium acetate in an inert solvent such as toluene at elevated temperature optionally with removal of water affords dihydropyridine compounds that can be oxidized to derivatives of formula (II) using oxidizing agents such as ceric ammonium nitrate.

An alternative preparation of intermediates of formula (II) wherein A^3 is $-CR^{17}R^{18}-$ is illustrated in scheme 5.

Scheme 5

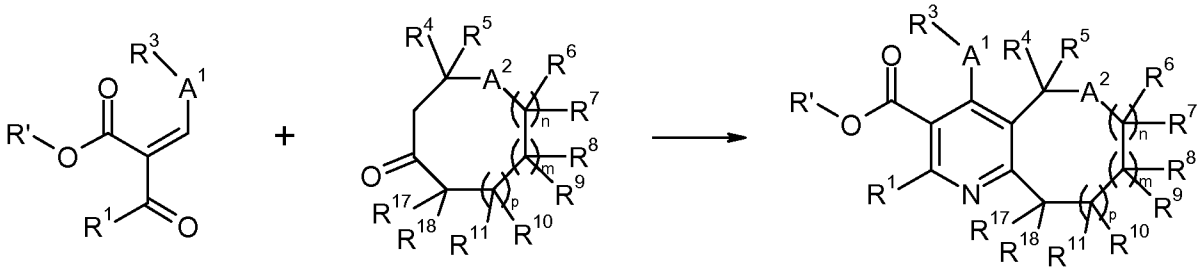


(VII) (VI) (II)

Three component reaction of α,β-unsaturated keto nitriles (VII), cyclic ketones of formula (VI) and ammonium acetate at elevated temperature under air atmosphere affords intermediates of formula (II). Compounds of formula (VII) can be prepared by Knoevenagel condensation using suitable β-keto nitriles (IV) and aldehydes (V). Typical conditions for this transformation include the reaction of compounds of formula (IV) and (V) in an alcoholic solvent such as ethanol or methanol, optionally in presence of L-proline at room temperature or the reaction of compounds of formula (IV) and (V) in presence of an amine such as piperidine in toluene as a solvent at reflux temperature optionally with removal of water.

Ester intermediates of formula (III) wherein A^3 is $-CR^{17}R^{18}-$ and R' is alkyl such as methyl, ethyl or tert-butyl can be obtained as illustrated in scheme 6.

Scheme 6

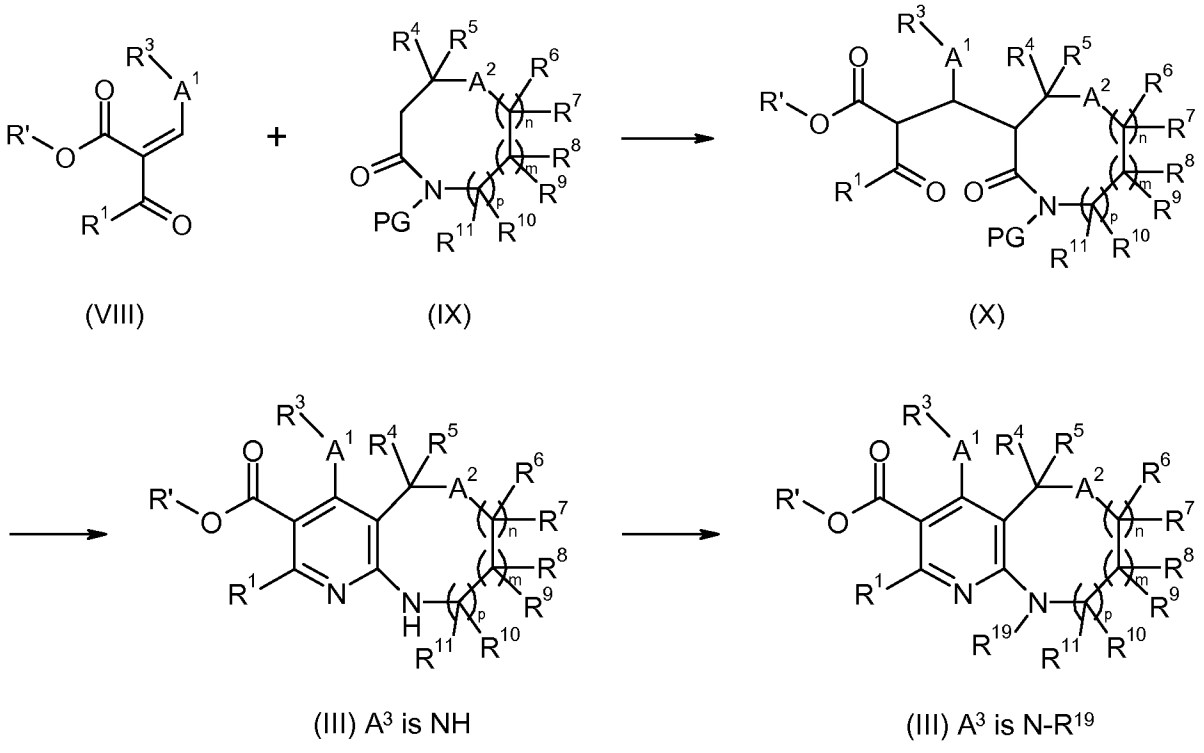


(VIII) R' is alkyl, e.g. Me, Et or t-Bu (VI) (III)

Michael addition of enolates derived from cyclic ketones of formula (VI) with α,β-unsaturated keto esters (VIII) and subsequent reaction with ammonium actetate and oxidation affords ester intermediates of formula (III). Enolate formation from ketones of formula (VI) can be accomplished with bases such as LDA, LiHMDS and NaHMDS in an inert solvent such as THF at low temperature. Cyclization of the resulting Michael adducts with ammonium acetate in presence of a catalytic amount of an acid such as p-toluenesulfonic acid in an alcoholic solvent such as ethanol at elevated temperature affords dihydropyridines that can be oxidized to derivatives of formula (III) using oxidizing agents such as DDQ.

Ester intermediates of formula (III), wherein A^3 is N-R^{19} and R' is alkyl such as methyl, ethyl or tert-butyl can be obtained as illustrated in scheme 7.

Scheme 7



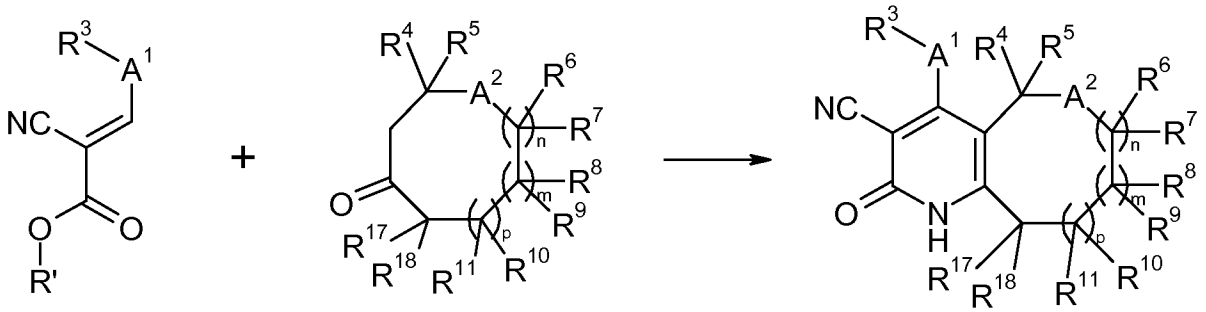
(VIII) (IX) (X)

(III) A^3 is NH (III) A^3 is N-R^{19}

Michael addition of enolates derived from lactams of formula (IX) with α,β-unsaturated keto esters (VIII) affords compounds of formula (X). The enolate formation can be accomplished by reacting lactams of formula (IX) with a base such as LDA, LiHMDS or NaHMDS in a solvent such as THF at low temperature. Conversion of compounds of formula (X) into formula (III) compounds wherein A^3 is NH requires stepwise reaction with phosphorus pentachloride, ammonium acetate and copper (I) acetate. Derivatives of formula (III), wherein A^3 is NH can be elaborated into compounds of formula (III), wherein A^3 is N-R^{19} and R^{19} represents alkyl, cycloalkyl and haloalkyl by reaction with an appropriate reagent R^{19}-X wherein X is Br or I in presence of a base such as sodium hydride. In a similar manner, compounds of formula (III), wherein A^3 is N-R^{19} and R^{19} represents alkylcarbonyl can be obtained by reaction with a suitable carboxylic acid anhydride in presence of a base such as triethylamine.

Alternatively to the preparations described in schemes 4 and 5, nitrile intermediates of formula (II) wherein A^3 is $-CR^{17}R^{18}-$ can be obtained as illustrated in scheme 8.

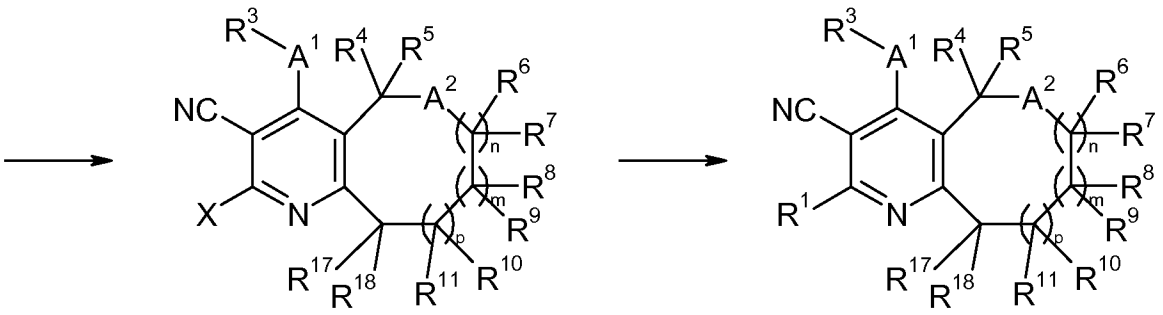
Scheme 8



(XI) R' is alkyl, e.g. Me or Et

(VI)

(XII)



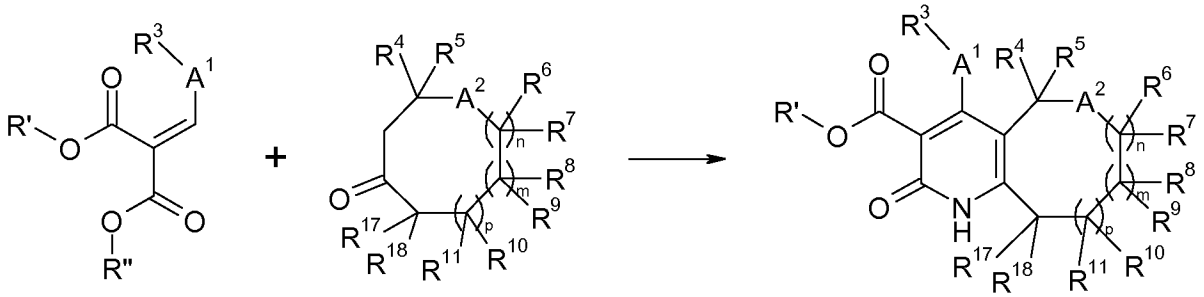
(XIII) X is Cl or OTf

(II)

Reaction of α,β-unsaturated ester nitriles (XI) with ketones of formula (VI) and ammonium acetate at elevated temperature under air atmosphere affords compounds of formula (XII). α,β-Unsaturated ester nitriles (XI) can be prepared by Knoevenagel condensation using alkyl cyanoacetates and aldehydes (V). Typical conditions for this transformation include the reaction of both components in an alcoholic solvent such as ethanol or methanol at room temperature or the reaction of both components in presence of an amine such as piperidine in toluene as a solvent at reflux temperature optionally with removal of water. Compounds of formula (XII) can be elaborated into derivatives of formula (II) in 2 steps. Reaction of compounds of formula (XII) with phosphorus oxychloride delivers pyridines of formula (XIII), wherein X is Cl. Alternatively, compounds of formula (XII) can be reacted with N-phenylbis(trifluoromethanesulphonimide) in presence of a base such as sodium hydride to obtain derivatives of formula (XIII), wherein X is OTf. Compounds of formula (XIII), wherein X is Cl or OTf can be reacted with alcohols in presence of a base such as sodium hydride to obtain compounds of formula (II), wherein R^1 represents alkoxy, haloalkoxy, cycloalkoxy or halocycloalkoxy. Compounds of formula (XIII), wherein X is Cl or OTf can also be reacted with amines or amides, optionally in presence of a base such as triethylamine, potassium carbonate or sodium hydride to obtain compounds of formula (II), wherein R^1 represents heterocycloalkyl, substituted heterocycloalkyl or substituted amino.

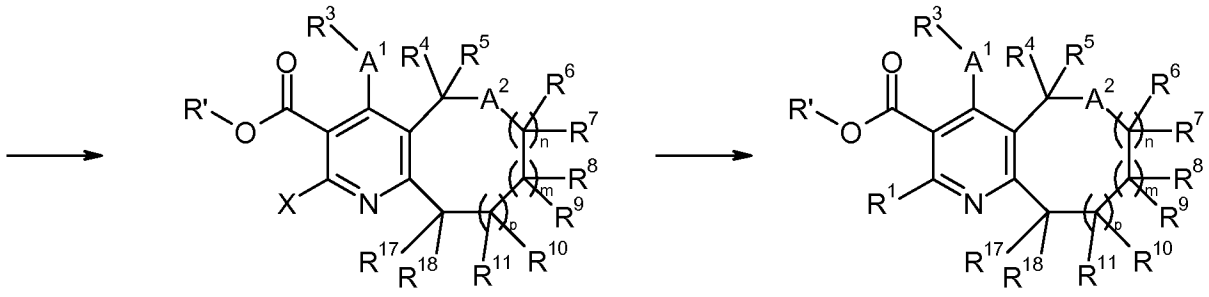
Alternatively to the preparations described in schemes 6 and 7, ester intermediates of formula (III) wherein A^3 is $-CR^{17}R^{18}-$ and R' is alkyl such as methyl, ethyl or tert-butyl can be obtained as illustrated in scheme 9.

Scheme 9



(XIV) (VI) (XV)

R' is alkyl,
e.g. Me, Et or t-Bu,
R" is alkyl,
e.g. Me, Et or t-Bu



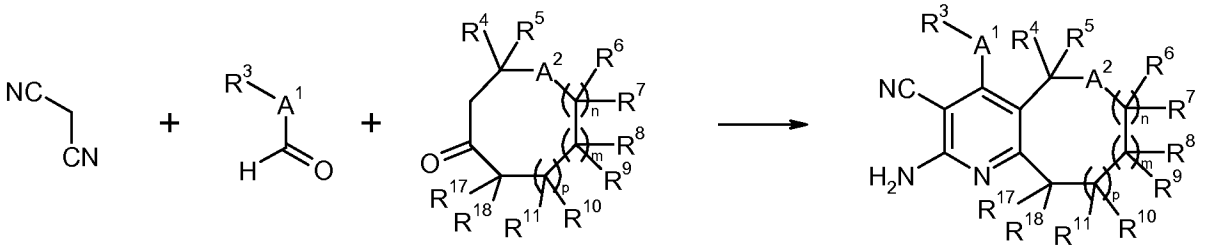
(XVI) X is Cl or OTf (III)

Pyridone derivatives of formula (XV) are accessible from α,β-unsaturated diesters (XIV) and ketones of formula (VI) in 3 steps. The Michael adducts that result from reaction of enolates derived from ketones of formula (VI) and α,β-unsaturated diesters (XIV) can be cyclized with ammonium acetate at elevated temperature. Final oxidation using an oxidizing agent such as $FeCl_3$ in refluxing propionic acid delivers pyridines of formula (XV). Compounds of formula (XV) can be elaborated into derivatives of formula (III) in 2 steps. Reaction of compounds of formula (XV) with phosphorus oxychloride delivers pyridines of formula (XVI), wherein X is Cl.

Alternatively, compounds of formula (XV) can be reacted with N-phenylbis(trifluoromethanesulphonimide) in presence of a base such as sodium hydride to obtain derivatives of formula (XVI), wherein X is OTf. Compounds of formula (XVI), wherein X is Cl or OTf can be reacted with alcohols in presence of a base such as sodium hydride to obtain compounds of formula (III), wherein R^1 represents alkoxy, haloalkoxy, cycloalkoxy or halocycloalkoxy. Compounds of formula (XVI), wherein X is Cl or OTf can also be reacted with amines or amides, optionally in presence of a base such as triethylamine, potassium carbonate or sodium hydride to obtain compounds of formula (III), wherein R^1 represents heterocycloalkyl, substituted heterocycloalkyl or substituted amino.

Nitrile intermediates of formula (II) wherein A^3 is $-CR^{17}R^{18}-$ and R^2 is $-NH_2$ can be obtained as illustrated in scheme 10.

Scheme 10

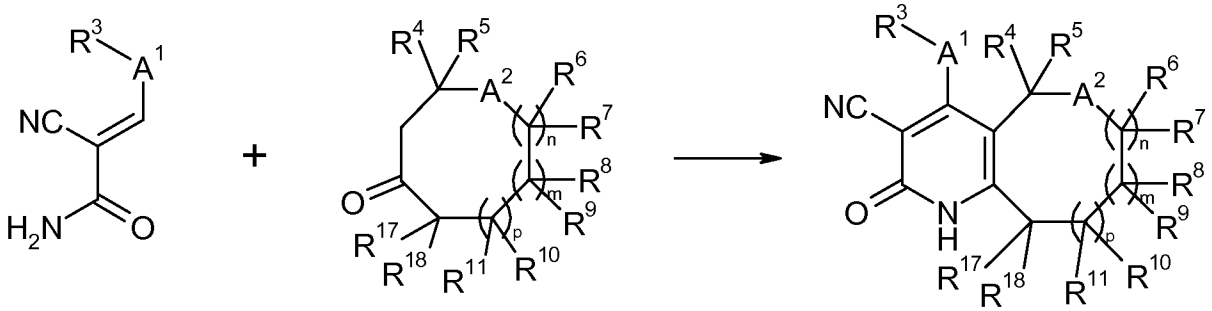


(XVII) (V) (VI) (II) R^1 is $-NH_2$

Four component reaction of malononitrile (XVII) with suitable aldehydes (V), cyclic ketones of formula (VI) and ammonium acetate in an inert solvent such as benzene at elevated temperature affords compounds of formula (II) wherein R^2 is $-NH_2$.

Alternatively to the preparation described in scheme 8, intermediates of formula (XII) wherein A^3 is $-CR^{17}R^{18}-$ can also be obtained as illustrated in scheme 11.

Scheme 11

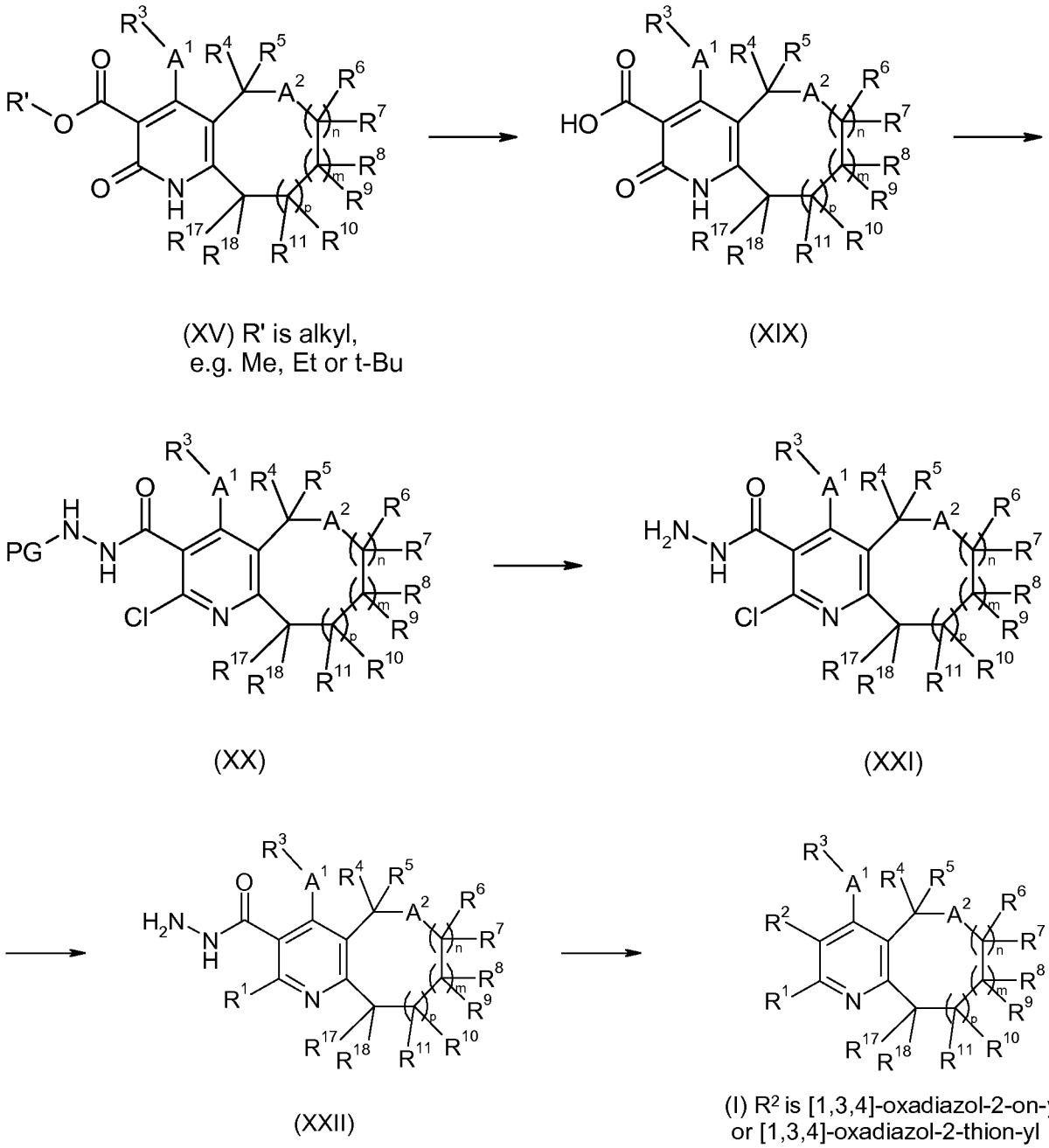


(XVIII) (VI) (XII)

α,β-Unsaturated nitrile amides (XVIII) can be reacted with ketones of formula (VI) in the presence of potassium tert-butoxide in a polar aprotic solvent such as DMSO at room temperature under air or oxygen atmosphere (R. Jain et. al., *Tetrahedron Lett.* **1995**, *36*, 3307) to obtain compounds of formula (XII).

Compounds of formula (I), wherein A^3 is $-CR^{17}R^{18}-$ and R^2 is [1,3,4]-oxadiazol-2-on-yl or [1,3,4]-oxadiazol-2-thion-yl may be prepared as described in scheme 12.

Scheme 12

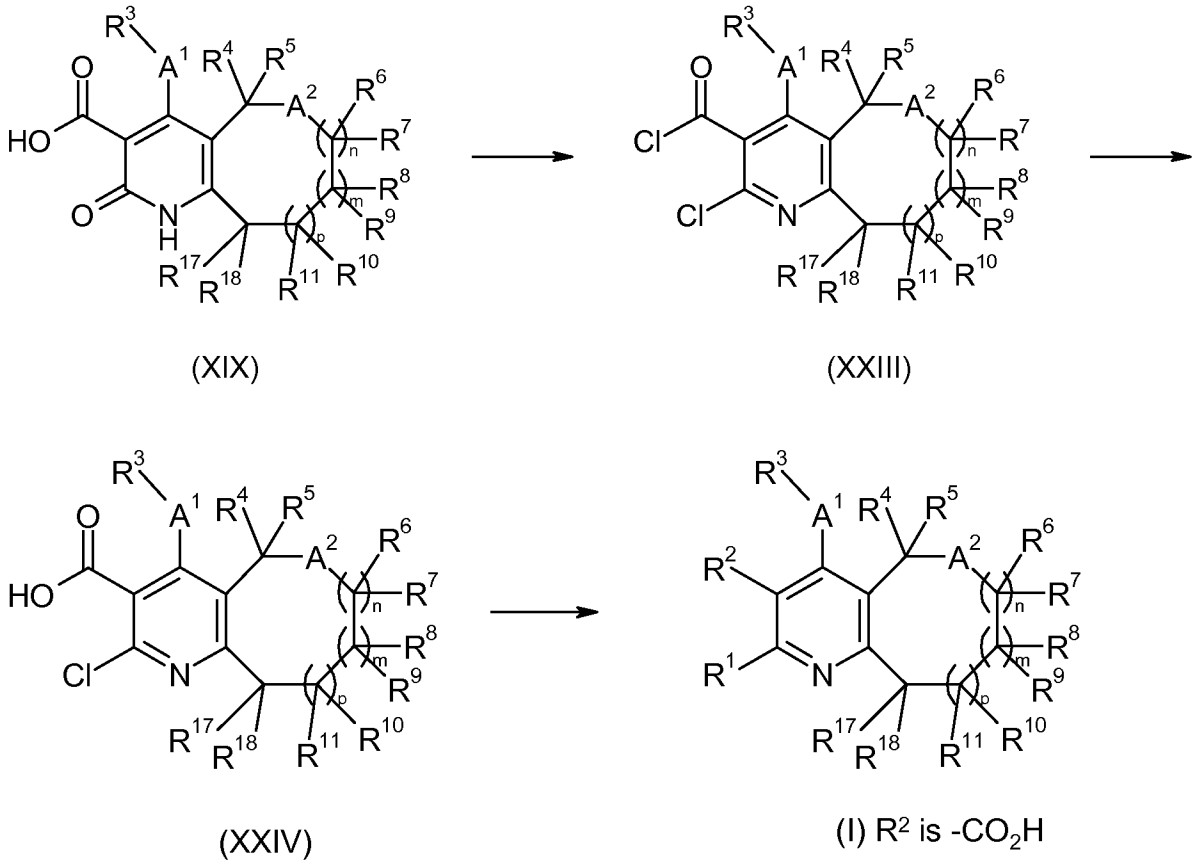


Derivatives of formula (XV) can be reacted with lithium, sodium or potassium hydroxide in a solvent such as methanol or ethanol at elevated temperatures to obtain carboxylic acids of formula (XIX). To elaborate compounds of formula (XIX) into derivatives of formula (XX), wherein PG is a protecting group they can be reacted first with phenylphosphonic dichloride and then with suitably protected hydrazine. If PG represents a 9-fluorenylmethoxycarbonyl (Fmoc) group and acyclic or cyclic secondary amines are introduced as R^1 substituents, cleavage of the protecting group and nucleophilic displacement can be performed stepwise via compounds of formula (XXI) or in one step to obtain compounds of formula (XXII). Compounds of formula

(XXII) can be reacted with N,N'-carbonyldiimidazole or 1,1'-thiocarbonyldiimidazole in presence of a base such as triethylamine and in a solvent such as THF to obtain compounds of formula (I), wherein R^2 is [1,3,4]-oxadiazol-2-on-yl or [1,3,4]-oxadiazol-2-thion-yl.

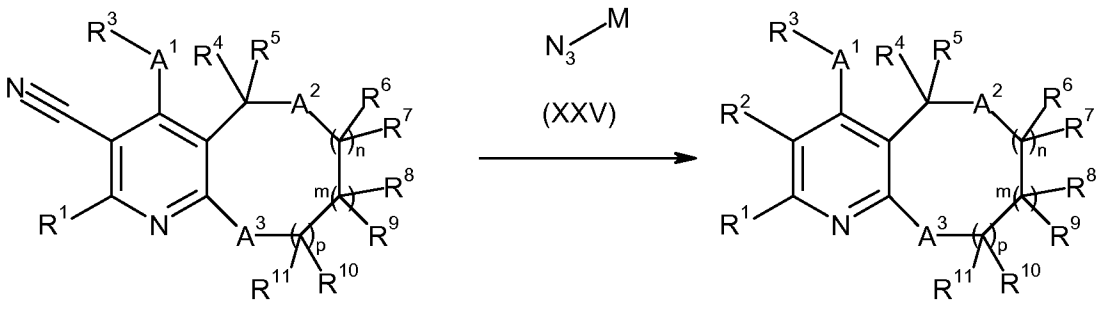
Compounds of formula (I) wherein A^3 is $-CR^{17}R^{18}-$ and R^2 is –COOH can also be prepared as illustrated in scheme 13.

Scheme 13



Reaction of derivatives of formula (XIX) with phenylphosphonic dichloride at elevated temperature affords dichloro intermediates of formula (XXIII). Derivatives of formula (XXIV) can be obtained by hydrolysis of the acid chloride moiety of (XXIII) to a carboxylic acid with water in a co-solvent such as THF at room temperature or elevated temperature. Derivatives of formula (XXIV) can be reacted with amines in the presence of copper powder, copper (I) bromide and potassium carbonate in a solvent such as DMA at elevated temperature to obtain compounds of formula (I), wherein R^1 represents heterocycloalkyl, substituted heterocycloalkyl or substituted amino.

Also an embodiment of the present invention is a process to prepare a compound of formula (I) as defined above comprising the reaction of a compound of formula (II) in the presence of a compound of formula (XXV), wherein M is sodium, trialkyltin, such as trimethyltin, or trialkylsilyl, such as trimethylsilyl, optionally in presence of additives such as zinc salts or dibutyltin oxide, in a solvent such as DMF, xylene or dioxane, at elevated temperature.



(II) (I)

Also an object of the present invention is a compound according to formula (I) as described herein for use as therapeutically active substance.

Likewise an object of the present invention is a pharmaceutical composition comprising a compound according to formula (I) as described herein and a therapeutically inert carrier.

In accordance with the invention, the compounds of formula (I) or their pharmaceutically acceptable salts and esters can be used for the treatment or prophylaxis of type 2 diabetes, metabolic syndrome, atherosclerosis, dyslipidemia, liver diseases, obesity, lipodystrophy, cancer, eye diseases, lung diseases, sarcoidosis, chronic renal diseases, chronic inflammatory and autoimmune inflammatory diseases, preeclampsia and polycystic ovary syndrome.

Particular liver diseases are liver diseases involving inflammation, steatosis and/or fibrosis, such non-alcoholic fatty liver disease, more particularly non-alcoholic steatohepatitis.

Particular lipodystrophy are genetic and iatrogenic lipodystrophy.

Particular eye diseases are eye diseases supported by endothelial proliferation and angiogenesis, particularly macular degeneration and retinopathy.

Particular lung diseases are asthma, bronchopulmonary dysplasia and chronic obstructive pulmonary disease.

Particular chronic renal diseases are vasculitis, focal segmental glomerulosclerosis, diabetic nephropathy, lupus nephritis, polycystic kidney disease and drug or toxin-induced chronic tubulointerstitial nephritis.

The present invention also relates to the use of a compound according to formula (I) as described herein for the treatment or prophylaxis of type 2 diabetes, metabolic syndrome, atherosclerosis, dyslipidemia, liver diseases, obesity, lipodystrophy, cancer, eye diseases, lung diseases, sarcoidosis, chronic renal diseases, chronic inflammatory and autoimmune inflammatory diseases, preeclampsia and polycystic ovary syndrome.

The present invention particularly relates to the use of a compound according to formula (I) as described herein for the treatment or prophylaxis of type 2 diabetes, atherosclerosis, cancer, chronic renal disease and non-alcoholic steatohepatitis.

The present invention also relates to the use of a compound according to formula (I) as described herein for the treatment or prophylaxis of non-alcoholic steatohepatitis.

A particular embodiment of the present invention is a compound according to formula (I) as described herein for the treatment or prophylaxis of type 2 diabetes, metabolic syndrome, atherosclerosis, dyslipidemia, liver diseases, obesity, lipodystrophy, cancer, eye diseases, lung diseases, sarcoidosis, chronic renal diseases, chronic inflammatory and autoimmune inflammatory diseases, preeclampsia and polycystic ovary syndrome.

Another particular embodiment of the present invention is a compound according to formula (I) as described herein for the treatment or prophylaxis of type 2 diabetes, atherosclerosis, cancer, chronic renal disease and non-alcoholic steatohepatitis.

Also a particular embodiment of the present invention is a compound according to formula (I) as described herein for the treatment or prophylaxis of non-alcoholic steatohepatitis.

The present invention also relates to the use of a compound according to formula (I) as described herein for the preparation of a medicament for the treatment or prophylaxis of type 2 diabetes, metabolic syndrome, atherosclerosis, dyslipidemia, liver diseases, obesity, lipodystrophy, cancer, eye diseases, lung diseases, sarcoidosis, chronic renal diseases, chronic inflammatory and autoimmune inflammatory diseases, preeclampsia and polycystic ovary syndrome.

The present invention particularly relates to the use of a compound according to formula (I) as described herein for the preparation of a medicament for the treatment or prophylaxis of type 2 diabetes, atherosclerosis, cancer, chronic renal disease and non-alcoholic steatohepatitis.

Also an embodiment of the present invention is the use of a compound according to formula (I) as described herein for the preparation of a medicament for the treatment or prophylaxis of non-alcoholic steatohepatitis.

Also an object of the invention is a method for the treatment or prophylaxis of type 2 diabetes, metabolic syndrome, atherosclerosis, dyslipidemia, liver diseases, obesity, lipodystrophy, cancer, eye diseases, lung diseases, sarcoidosis, chronic renal diseases, chronic inflammatory and autoimmune inflammatory diseases, preeclampsia and polycystic ovary syndrome, which method comprises administering an effective amount of a compound according to formula (I) as described herein.

Another object of the invention is a method for the treatment or prophylaxis of type 2 diabetes, atherosclerosis, cancer, chronic renal disease and non-alcoholic steatohepatitis, which method comprises administering an effective amount of a compound according to formula (I) as described herein.

Also an embodiment of the present invention is a method for the treatment or prophylaxis of non-alcoholic steatohepatitis, which method comprises administering an effective amount of a compound according to formula (I) as described herein.

Also an embodiment of the present invention is a method for the treatment or prophylaxis of lipodystrophy, which method comprises administering an effective amount of a compound according to formula (I) as described herein.

Also a particular embodiment of the present invention is a compound according to formula (I) as described herein, when manufactured according to any one of the described processes.

Assay procedures

Compounds were profiled for activity against human FABP4 (huFABP4) and/or human FABP5 (huFABP5) in Terbium (Tb) time resolved-fluorescence energy transfer (TR-FRET) assays monitoring the direct binding of Bodipy labeled fatty acid to His6 tagged FABP proteins (huFABP4 was expressed in house in E. coli and purified, huFABP5 was purchased from

Cayman Chemical Co., cat.no. 10010364), bound to Terbium labeled anti His6 tag antibody. Assay read-outs reflected energy transfer, upon binding of the ligand to the FABP protein, from the Terbium donor molecule to the acceptor Bodipy moiety. Final ligand concentration (125nM) approximated the Kd for each protein.

Stock DMSO solutions (1.8mM) of compounds were serially diluted 3-fold for ten concentrations with 100% DMSO (50μM to 0.003 μM final compound concentration). 1μl of these compound dilutions and 1μl of Bodipy labeled fatty acid 4.5μM in 100% DMSO (Bodipy FL C11, cat. no. D3862, Invitrogen) were sequentially pipetted in wells of 384-well black polypropylene plates (Thermo Matrix cat. no. 4344). FABP4 or FABP5 protein was then added (28μl of 64nM protein in 25mM Tris pH 7.5, 0.4mg/ml γ-globulin, 1mM DTT, 0.012% NP40, final protein concentration: 50nM). Assay blanks contained ligand, but no protein. Neutral controls contained ligand, but no compound. After adding the detection reagent (Tb antiHis6 antibody, Columbia Biosciences, TB-110, 6μl of a 24nM Ab solution in 25mM Tris pH 7.5, 0.4mg/ml γ-globulin, final Tb antiHis6 Ab concentration: 4nM), plates were spun one minute at 1000rpm. Following an incubation at room temperature with shaking for 30 minutes, plates were read using an Envision reader (Perkin Elmer, Extinction wavelength: 340nm, Emission: 490nm and 520nm, time delay: 100μs; time window: 200μs, 50 flashes).

Final assay conditions were: 50nM FABP protein, 125nM Bodipy labeled fatty acid, 0.009% (vol/vol) NP40, 5.5% (vol/vol)DMSO in a total final assay volume of 36μl. The assay was performed in triplicate.

The relative fluorescence units (RFU) ratio (520nm*10000/488nm) were used to calculate the percent inhibition: 100 – (RFU ratio compound –blank) / neutral control – blank) * 100. These percent inhibition values were then fit to dose response curves using a 4 parameter logistic model (Hill sigmoidal dose-response model). IC_{50}s reflected compound concentrations associated with 50% inhibition of protein activity compared to that of neutral controls.

Example	IC50 h-fabp4-ecoli-r µM	IC50 h-fabp5-ecoli-r µM
1	0.23	10.98
2	2.06	
3	0.06	0.95
4	0.42	1.36
5	0.07	0.75
6	0.22	0.73
7	0.01	0.61
8	0.03	1.38
9	0.11	33.73
10	0.33	8.68
11	0.96	
12	0.3	12.09
13	9.96	13.82
14	0.26	6.13
15	0.23	10.14
16	0.32	

Example	IC50 h-fabp4-ecoli-r µM	IC50 h-fabp5-ecoli-r µM
17	0.16	6.01
18	0.28	12.24
19	0.05	2.25
20	0.42	6.52
21	2.97	26.94
22	3.95	
23	0.33	1.83
24	0.02	0.07
25	0.06	0.19
26	0.01	0.13
27	0.11	0.17
28	0.02	0.12
29	0.04	0.27
30	0.03	0.38
31	0.02	0.19
32	0.04	0.25

Example	IC50 h-fabp4-ecoli-r µM	IC50 h-fabp5-ecoli-r µM
33	0.02	0.23
34	0.32	1.04
35	0.04	0.13
36	0.42	11.1
37	0.02	0.25
38	0.01	0.26
39	0.08	0.38
40	0.04	0.57
41	4.63	7.94
42	1.46	10.96
43	0.17	0.82
44	0.05	0.42
45	0.03	0.31
46	0.52	2.01
47	0.13	0.86
48	3.33	4.34
49	1.19	3.21

Example	IC50 h-fabp4-ecoli-r µM	IC50 h-fabp5-ecoli-r µM
50	0.07	0.28
51	0.18	0.43
52	0.25	2.16
53	0.09	1.51
54	4.17	10.34
55	0.05	1.09
56	0.04	0.24
57	0.04	0.12
58	0.03	0.7
59	0.07	0.97
60	0.04	0.77
61	0.14	5.36
62	0.03	0.13
63	0.03	0.78
64	0.23	
65	0.03	3.74
66	0.04	3.1

Example	IC50 h-fabp4-ecoli-r µM	IC50 h-fabp5-ecoli-r µM
67	0.01	0.52
68	0.11	1.24
69	0.02	0.26
70	0.12	0.63
71	0.31	10.53
72	1.41	46.17
73	3.46	
74	0.15	0.74
75	0.03	0.2
76	0.08	1.76
77	13.01	
78	0.04	1.32
79	0.18	2.13
80	0.04	0.22
81	0.06	1.75
82	0.004	0.167
83	0.086	0.18

Example	IC50 h-fabp4-ecoli-r µM	IC50 h-fabp5-ecoli-r µM
84	0.012	0.074
85	0.024	0.54
86	0.11	0.38
87	0.03	0.4
88	0.14	1.54
89	16.37	16.43
90	0.22	21.12
91	2.9833	7.6219
92	0.2621	6.5653
93	0.7122	4.2287
94	0.026	0.0996
95	0.9872	3.5918
96	0.86	4.71
97	0.28	1.81
98	0.08	7.53
99	2.78	11.46
100	0.29	0.97

Example	IC50 h-fabp4-ecoli-r µM	IC50 h-fabp5-ecoli-r µM
101	3.22	16.2
102	1.06	21.81
103	0.08	0.44
104	0.04	0.37
105	0.15	1.6
106	0.59	1.61
107	1.29	0.09
108	1.8	1.67
109	0.08	0.37
110	0.02	0.31
111	0.69	0.71
112	0.042	0.726
113	0.01	0.066
114	2.097	2.104
115	0.206	1.097
116	0.16	0.1
117	5.03	1.23

Example	IC50 h-fabp4-ecoli-r µM	IC50 h-fabp5-ecoli-r µM
118	0.06	0.2835
119	0.24	1.49
120	0.02	0.05
121	0.02	0.3
122	0.19	0.48
123	0.04	0.37
124	0.09	2.47
125	0.77	1.67
126	0.01	0.07
127	0.015	0.051
128	0.046	0.462
129	0.01	0.13
130	0.01	0.08
131	0.03	0.37
132	0.02	0.05
133	0.03	0.61
134	0.0591	2.4221

Example	IC50 h-fabp4-ecoli-r µM	IC50 h-fabp5-ecoli-r µM
135	0.0165	0.3187
136	0.0979	5.6834
137	0.043	2.3478
138	0.02	0.09
139	0.2	19.85
140	0.08	9.35
141	0.17	5.08
142	0.93	2.46
143	0.01	0.28
144	0.77	3.56
145	0.03	0.57
146	0.05	0.86
147	0.04	0.98
149	0.06	0.86
150	0.12	6.74
151	0.17	2.58
152	0.1	1.68

Example	IC50 h-fabp4-ecoli-r µM	IC50 h-fabp5-ecoli-r µM
153	0.09	1.04
154	0.01	0.09
155	0.02	0.14
156	0.02	0.06
157	0.02	0.17
158	0.01	0.09
159	0.01	0.2
160	0.04	0.16
161	0.02	0.17
162	0.02	0.13
163	0.02	0.13
164	0.02	0.09
165	0.02	0.18
166	0.01	0.04
167	0.02	0.04
168	0.02	0.05
169	0.24	0.26

Example	IC50 h-fabp4-ecoli-r µM	IC50 h-fabp5-ecoli-r µM
170	0.01	0.05
171	0.01	0.25
172	0.01	0.06
173	0.09	1.96
174	0.02	0.14
175	0.15	2.19
176	0.05	0.09
177	0.03	0.66
178	0.02	0.28
179	0.05	0.36
180	3.44	20.61
181	0.04	0.1
182	0.07	1.35
183	4.15	23.2
184	0.01	0.1
185	0.11	0.87
186	0.01	0.11

Example	IC50 h-fabp4-ecoli-r µM	IC50 h-fabp5-ecoli-r µM
187	0.02	0.12
188	0.02	0.1
189	0.02	0.12
190	0.02	0.11
191	0.09	4.19
192	0.02	0.19
193	0.01	0.1
194	0.02	0.04
195	0.11	1.29
196	0.05	0.64
197	0.02	0.77
198	1.04	16.16
199	0.08	3.08
200	0.02	0.04
201	0.02	0.06
202	0.03	0.21
203	0.04	0.27

Example	IC50 h-fabp4-ecoli-r µM	IC50 h-fabp5-ecoli-r µM
204	0.02	0.12
205	0.05	0.06
206	0.02	0.05
207	0.02	0.03
208	0.02	0.04
209	0.02	0.06
210	5.96	24.15
211	3.56	49.02
212	28.08	>50
213	0.08	2.29
214	0.03	0.14
215	0.03	0.48
216	0.02	0.18
217	0.03	1.01
218	0.02	1.13
219	0.04	0.26
220	0.02	0.44

Example	IC50 h-fabp4-ecoli-r µM	IC50 h-fabp5-ecoli-r µM
221	0.09	0.29
222	0.02	0.09
223	0.02	0.09
224	0.14	7.92
225	0.24	0.98
226	0.02	0.2
227	0.02	0.63
228	0.04	0.22
229	0.05	1.56
230	0.33	1.04
231	0.01	0.19
232	0.01	0.19
233	0.02	0.28
234	0.03	0.49
235	0.02	0.11
236	0.09	0.32
237	0.03	1.55

Example	IC50 h-fabp4-ecoli-r µM	IC50 h-fabp5-ecoli-r µM
238	0.04	0.9
239	0.12	0.64
240	0.04	3.14
241	0.08	5.84
242	0.03	0.61
243	0.11	7.11
244	0.16	0.58
245	0.1	2.35
246	0.02	0.15
247	0.03	0.18
248	0.03	0.39
249	0.02	0.75
250	0.12	1.22
251	0.05	1.81
252	0.28	10.78
253	0.08	0.54
254	0.58	2.64

Example	IC50 h-fabp4-ecoli-r µM	IC50 h-fabp5-ecoli-r µM
255	0.1	2.92
256	0.08	2.51
257	0.04	1.59
258	0.02	0.47
259	0.02	2.66
260	0.02	1.36
261	0.04	0.49
262	0.01	1.88
263	0.05	11.91
264	0.7	>50
265	0.02	0.49
266	0.03	2.68
267	3.72	>50
268	0.02	0.14
269	0.12	1.65
270	0.77	12.24
271	3.66	14.62

Example	IC50 h-fabp4-ecoli-r µM	IC50 h-fabp5-ecoli-r µM
272	6.6	32
273	0.02	1.57
274	0.17	1.4
275	0.49	1.31
276	0.02	0.1
277	0.2	4.04
278	0.04	1.46
279	0.02	0.29
280	0.02	0.03
281	0.02	0.05
282	0.03	0.07
283	0.01	0.27
284	0.03	0.72
285	0.02	1
286	2.75	12.4
287	0.01	0.18
288	0.02	0.08

Example	IC50 h-fabp4-ecoli-r µM	IC50 h-fabp5-ecoli-r µM
289	0.24	1.31
290	0.02	0.22
291	0.02	0.61
292	0.03	1.04
293	0.02	0.16
294	0.02	0.59
295	2.63	5.53
296	3.23	8.29
297	0.03	0.54
298	0.02	1.22
299	0.13	1.04
300	0.02	0.2
301	0.02	0.4
302	0.03	0.73
303	0.1	1.31
304	0.04	0.74
305	0.05	0.51

Example	IC50 h-fabp4-ecoli-r µM	IC50 h-fabp5-ecoli-r µM
306	6.61	8.77
307	0.14	2.89
308	0.1	1.18
309	0.1	2.12
310	0.08	0.64
311	0.15	0.83
312	0.07	0.29
313	0.03	1.32
314	0.02	0.46
315	0.02	0.39
316	0.02	0.76
317	0.1	0.51

Example	IC50 h-fabp4-ecoli-r µM	IC50 h-fabp5-ecoli-r µM
318	0.03	0.24
319	0.03	0.18
320	0.03	0.65
321	0.01	0.07
322	0.85	1.06
323	0.02	0.14
324	1.61	3.9
325	0.14	4.91
326	0.02	0.02
327	0.22	2.47
328	0.02	1.36

Compounds of formula (I) and their pharmaceutically acceptable salts or esters thereof as described herein have IC_{50} (FABP4 inhibition) values between 0.000001 µM and 1000 µM, particular compounds have IC_{50} values between 0.000005 µM and 500 µM, further particular compounds have IC_{50} values between 0.00005 µM and 5 µM.

Compounds of formula (I) and their pharmaceutically acceptable salts or esters thereof as described herein have IC_{50} (FABP5 inhibition) values between 0.000001 μM and 1000 μM, particular compounds have IC_{50} values between 0.000005 μM and 500 μM, further particular compounds have IC_{50} values between 0.00005 μM and 50 μM.

The compounds of formula (I) and their pharmaceutically acceptable salts can be used as medicaments (e.g. in the form of pharmaceutical preparations). The pharmaceutical preparations can be administered internally, such as orally (e.g. in the form of tablets, coated tablets, dragées, hard and soft gelatin capsules, solutions, emulsions or suspensions), nasally (e.g. in the form of nasal sprays) or rectally (e.g. in the form of suppositories). However, the administration can also be effected parentally, such as intramuscularly or intravenously (e.g. in the form of injection solutions).

The compounds of formula (I) and their pharmaceutically acceptable salts can be processed with pharmaceutically inert, inorganic or organic adjuvants for the production of tablets, coated tablets, dragées and hard gelatin capsules. Lactose, corn starch or derivatives thereof, talc, stearic acid or its salts etc. can be used, for example, as such adjuvants for tablets, dragées and hard gelatin capsules.

Suitable adjuvants for soft gelatin capsules are, for example, vegetable oils, waxes, fats, semi-solid substances and liquid polyols, etc.

Suitable adjuvants for the production of solutions and syrups are, for example, water, polyols, saccharose, invert sugar, glucose, etc.

Suitable adjuvants for injection solutions are, for example, water, alcohols, polyols, glycerol, vegetable oils, etc.

Suitable adjuvants for suppositories are, for example, natural or hardened oils, waxes, fats, semi-solid or liquid polyols, etc.

Moreover, the pharmaceutical preparations can contain preservatives, solubilizers, viscosity-increasing substances, stabilizers, wetting agents, emulsifiers, sweeteners, colorants, flavorants, salts for varying the osmotic pressure, buffers, masking agents or antioxidants. They can also contain still other therapeutically valuable substances.

The dosage can vary in wide limits and will, of course, be fitted to the individual requirements in each particular case. In general, in the case of oral administration a daily dosage of about 0.1 mg to 20 mg per kg body weight, preferably about 0.5 mg to 4 mg per kg body weight (e.g. about 300 mg per person), divided into preferably 1-3 individual doses, which can consist, for example, of the same amounts, should be appropriate. It will, however, be clear that the upper limit given herein can be exceeded when this is shown to be indicated.

In accordance with the invention, the compounds of formula (I) or their pharmaceutically acceptable salts and esters can be used for the treatment or prophylaxis of type 2 diabetes related microvascular complications (such as, but not limited to diabetic retinopathy, diabetic neuropathy and diabetic nephropathy), coronary artery disease, obesity and underlying inflammatory diseases, chronic inflammatory and autoimmune/inflammatory diseases

The invention is illustrated hereinafter by Examples, which have no limiting character.

In case the preparative examples are obtained as a mixture of enantiomers, the pure enantiomers can be separated by methods described herein or by methods known to the person skilled in the art, such as e.g. chiral chromatography or crystallization.

Examples

All examples and intermediates were prepared under argon atmosphere if not specified otherwise.

General Method A: A mixture of the ester (Intermediate E) (0.129 mmol, 1eq) and lithium iodide (10 eq) in pyridine (3 ml) is heated to 135 °C for 1-4 days. The pyridine is then removed, the remaining residue is diluted with water and the pH is adjusted to 2-3 by addition of 0.1N HCl. The mixture is extracted with ethyl acetate and the combined extracts are washed with water (acidified to pH 2-3 with 0.1N HCl) and brine, dried (Na_2SO_4) and evaporated. The remaining residue is purified by column chromatography.

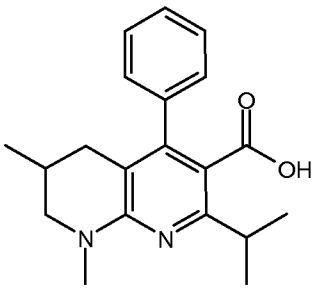
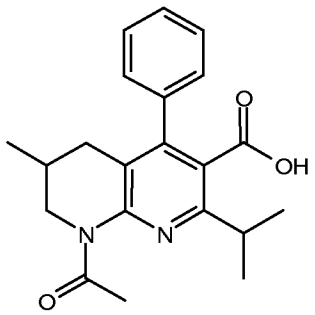
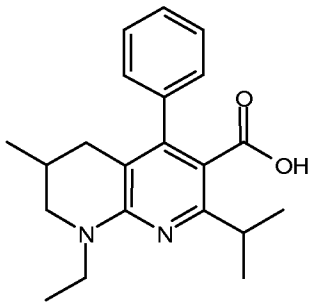
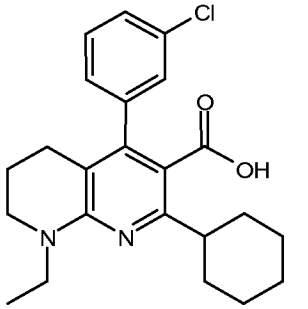
General Method B: To a solution of the ester (Intermediate E) (0.1 mmol, 1eq) in DMSO (3 ml) and water (0.1 ml) is added NaOH (2 eq) and the mixture is heated to 100 °C in a sealed tube for 1-4 days. If necessary, additional NaOH (1eq) and water (0.15 ml) is added during this time. The reaction mixture is then diluted with water and the pH is adjusted to 2-3 by addition of 0.1N HCl. The mixture is extracted with ethyl acetate and the combined extracts are washed with water (acidified to pH 2-3 with 0.1N HCl), dried (Na_2SO_4) and evaporated. The remaining residue is purified by column chromatography.

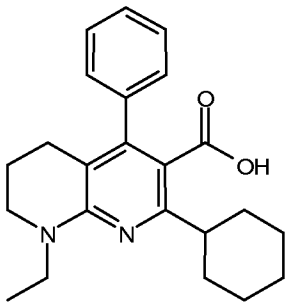
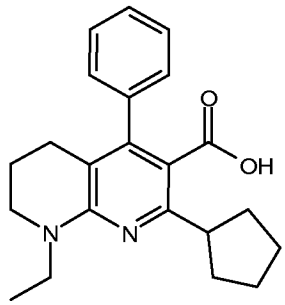
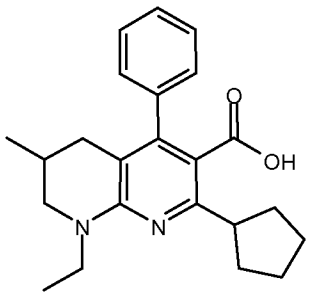
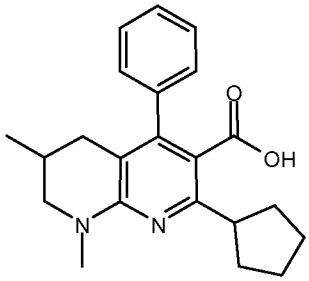
General Method C: A solution of the nitrile (Intermediate N) (0.336 mmol, 1 eq) and azidotrimethylstannane (3 eq) in xylene (3.5 ml) is heated to 120 °C for 1-7 days. The precipitate that forms is filtered off, washed with hot toluene and suspended in a mixture of ethyl acetate and 0.1N HCl. The suspension is stirred vigorously at room temperature until all solids are dissolved. The layers are separated and the aqueous layer is extracted with ethyl acetate. The combined organic layers are washed with water and brine (both acidified to pH 1 with HCl), dried (Na_2SO_4) and evaporated. The remaining residue is purified by column chromatography.

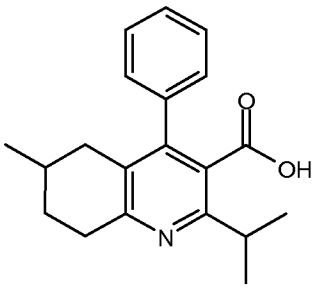
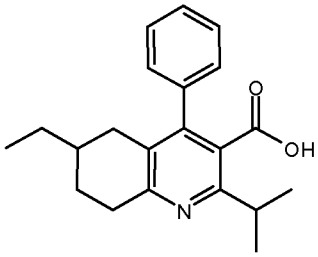
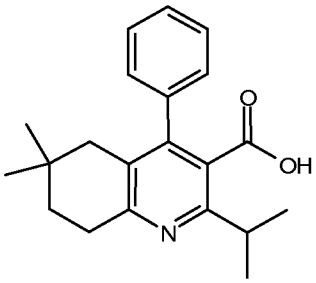
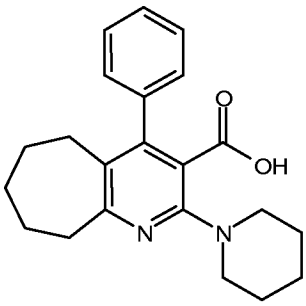
If no precipitate forms during the heating period, the reaction mixture is cooled to room temperature and ethyl acetate and 0.1N HCl are added. The mixture is stirred for 1.5 h, the layers are separated and the aqueous layer is extracted with ethyl acetate. The combined organic layers are washed with water and brine (both acidified to pH 1 with HCl), dried (Na_2SO_4) and evaporated. The remaining residue is purified by column chromatography.

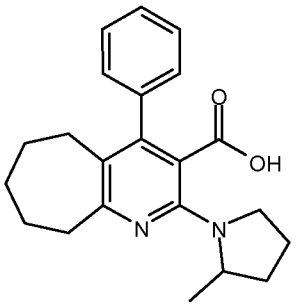
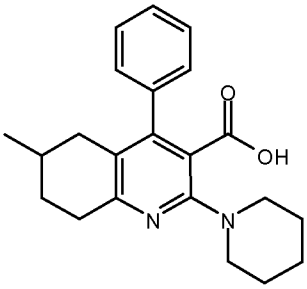
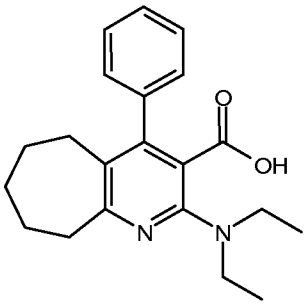
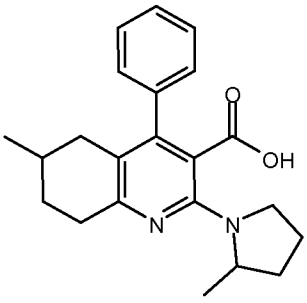
General Method D: A mixture of the nitrile (Intermediate N) (2.5 mmol, 1 eq), sodium azide (2.2 eq) and zinc chloride (0.5 eq) in DMF (5 ml) is refluxed for 3 days. After evaporation of the solvent the residue is stirred with EtOAc / water. The precipitate is filtered, stirred with 1N HCl /

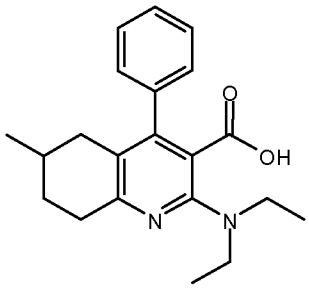
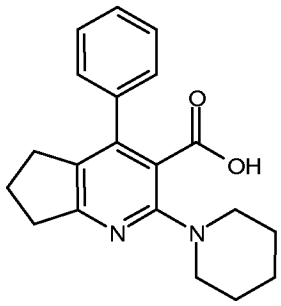
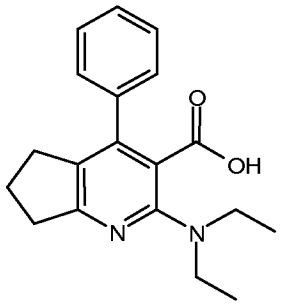
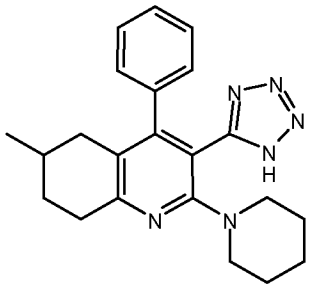
water and filtered. The obtained solid is triturated with ethanol and purified by column chromatography.

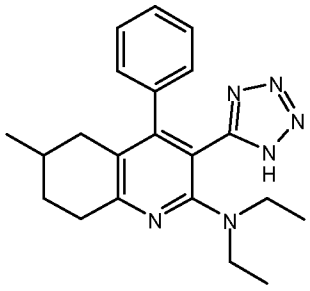
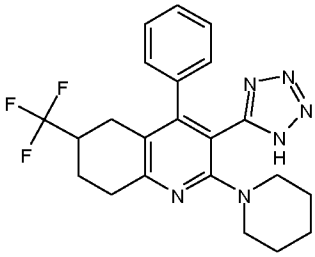
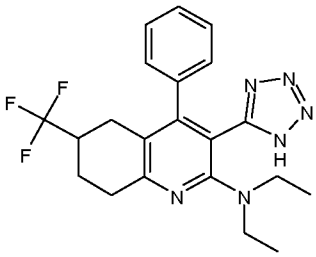
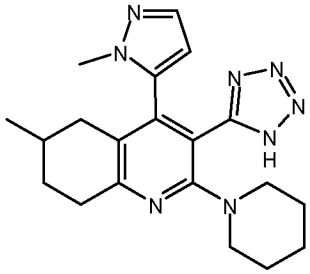
Ex.	Name	Structure	MS	Method	Starting Material
1	2-Isopropyl-6,8-dimethyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylic acid		ESP $[M+H]^+$: 325.3	A	E1
2	8-Acetyl-2-isopropyl-6-methyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylic acid		ESP $[M+H]^+$: 353.3	A	E2
3	8-Ethyl-2-isopropyl-6-methyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylic acid		ESP $[M+H]^+$: 339.3	A	E3
4	4-(3-Chlorophenyl)-2-cyclohexyl-8-ethyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylic acid		ESP $[M+H]^+$: 399.1	A	E4

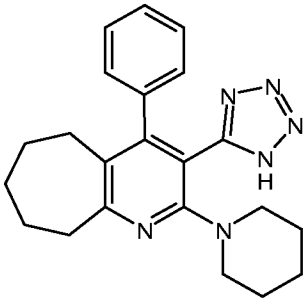
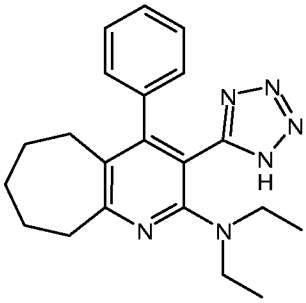
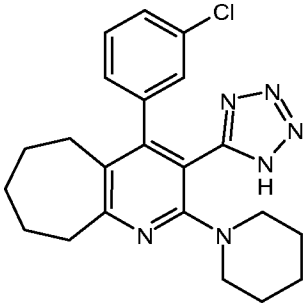
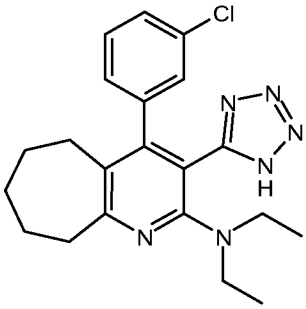
Ex.	Name	Structure	MS	Method	Starting Material
5	2-Cyclohexyl-8-ethyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylic acid		ESP $[M+H]^+$: 365.2	B	E5
6	2-Cyclopentyl-8-ethyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylic acid		ESP $[M+H]^+$: 351.4	A	E6
7	2-Cyclopentyl-8-ethyl-6-methyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylic acid		ESP $[M+H]^+$: 365.5	A	E7
8	2-Cyclopentyl-6,8-dimethyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylic acid		ESP $[M+H]^+$: 351.4	A	E8

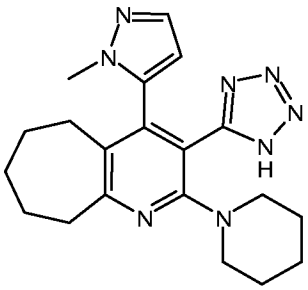
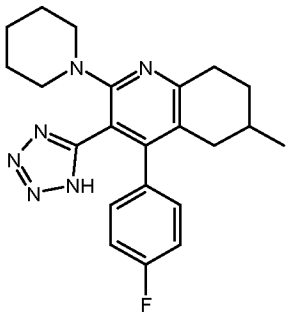
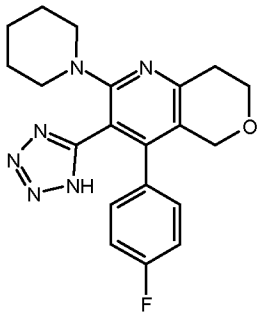
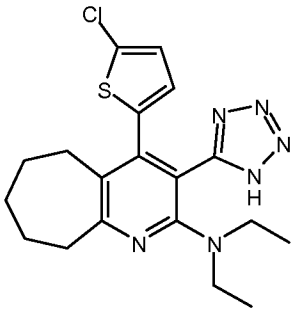
Ex.	Name	Structure	MS	Method	Starting Material
9	2-Isopropyl-6-methyl-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carboxylic acid		ESP $[M+H]^+$: 310.3	A	E9
10	6-Ethyl-2-isopropyl-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carboxylic acid		ESP $[M+H]^+$: 324.2	A	E10
11	2-Isopropyl-6,6-dimethyl-4-phenyl-5,6,7,8-tetrahydro-quinoline-3-carboxylic acid		ESN $[M-H]^-$: 322.3	A	E11
14	4-Phenyl-2-(piperidin-1-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid		ESN $[M-H]^-$: 349.4	A	E14

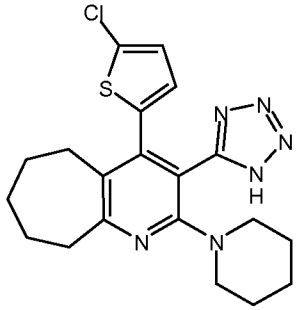
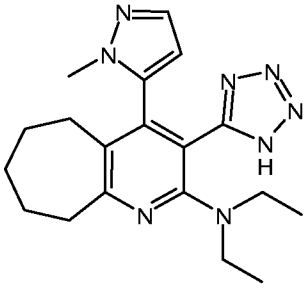
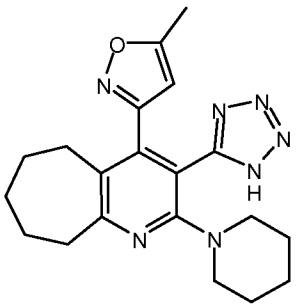
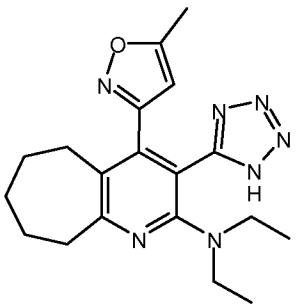
Ex.	Name	Structure	MS	Method	Starting Material
15	2-(2-Methylpyrrolidin-1-yl)-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid		ESN $[M-H]^-$: 349.4	A	E15
16	6-Methyl-4-phenyl-2-(piperidin-1-yl)-5,6,7,8-tetrahydroquinoline-3-carboxylic acid		ESN $[M-H]^-$: 349.4	A	E16
17	2-(Diethylamino)-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid		ESN $[M-H]^-$: 337.5	A	E17
18	6-Methyl-2-(2-methylpyrrolidin-1-yl)-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carboxylic acid		ESN $[M-H]^-$: 349.4	A	E18

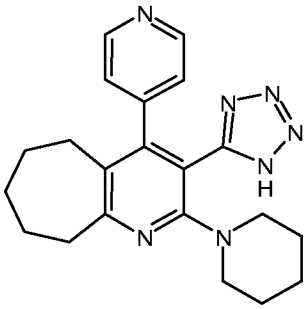
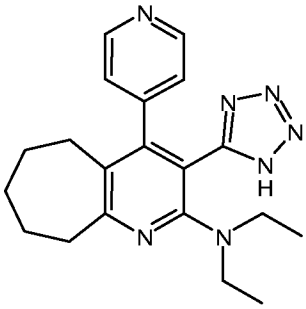
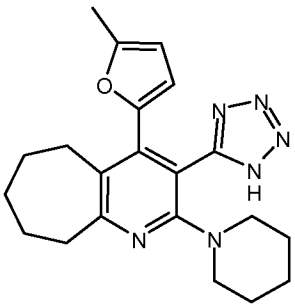
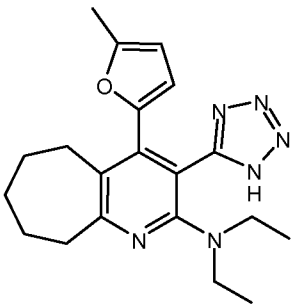
Ex.	Name	Structure	MS	Method	Starting Material
19	2-(Diethylamino)-6-methyl-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carboxylic acid		ESN $[M-H]^-$: 337.5	A	E19
21	4-Phenyl-2-(piperidin-1-yl)-6,7-dihydro-5H-cyclopenta[b]pyridine-3-carboxylic acid		ESN $[M-H]^-$: 321.3	A	E21
22	2-(Diethylamino)-4-phenyl-6,7-dihydro-5H-cyclopenta[b]pyridine-3-carboxylic acid		ESN $[M-H]^-$: 309.4	A	E22
25	6-Methyl-4-phenyl-2-(piperidin-1-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 375.2	C	N25

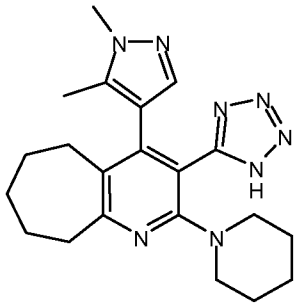
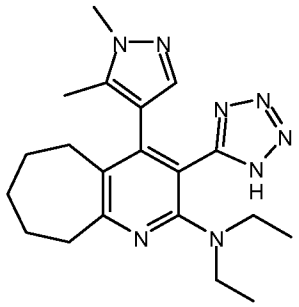
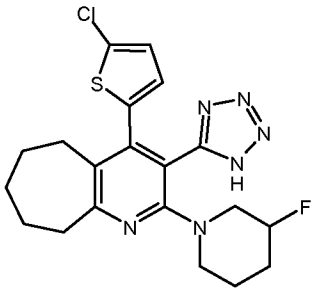
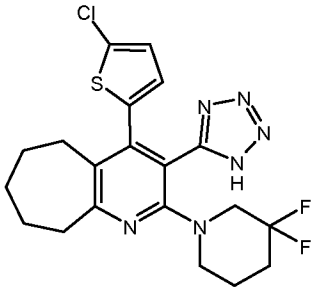
Ex.	Name	Structure	MS	Method	Starting Material
26	N,N-Diethyl-6-methyl-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinolin-2-amine		ESP $[M+H]^+$: 363.4	C	N26
27	4-Phenyl-2-(piperidin-1-yl)-3-(2H-tetrazol-5-yl)-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 429.5	C	N27
28	N,N-Diethyl-4-phenyl-3-(2H-tetrazol-5-yl)-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinolin-2-amine		ESP $[M+H]^+$: 417.5	C	N28
29	6-Methyl-4-(1-methyl-1H-pyrazol-5-yl)-2-(piperidin-1-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESN $[M-H]^-$: 377.5	C	N29

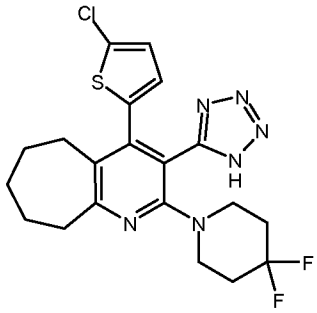
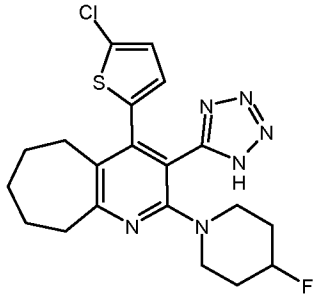
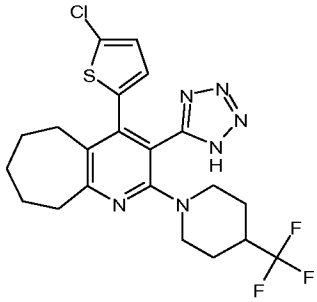
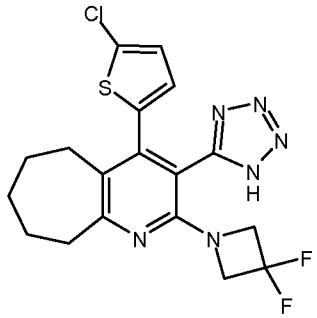
Ex.	Name	Structure	MS	Method	Starting Material
30	4-Phenyl-2-(piperidin-1-yl)-3-(2H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESN [M-H]⁻: 373.4	C	N30
31	N,N-Diethyl-4-phenyl-3-(2H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine		ESN [M-H]⁻: 361.1	C	N31
32	4-(3-Chlorophenyl)-2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESN [M-H]⁻: 407.6	C	N32
33	4-(3-Chlorophenyl)-N,N-diethyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine		ESN [M-H]⁻: 395.4	C	N33

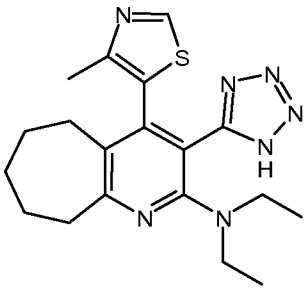
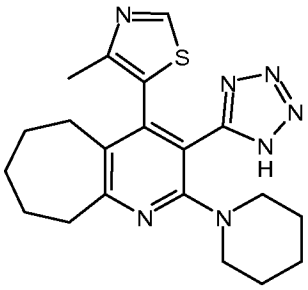
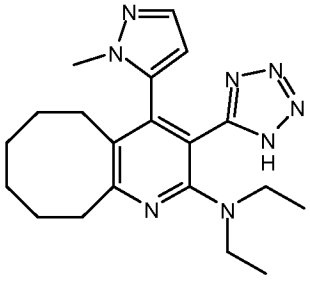
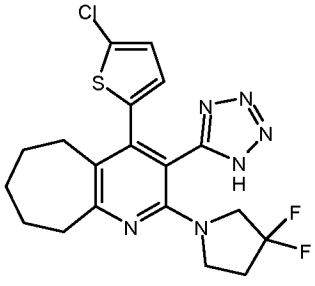
Ex.	Name	Structure	MS	Method	Starting Material
34	4-(1-Methyl-1H-pyrazol-5-yl)-2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESN $[M-H]^-$: 377.2	C	N34
35	4-(4-Fluorophenyl)-6-methyl-2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESN $[M-H]^-$: 391.5	C	N35
36	4-(4-Fluorophenyl)-2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-7,8-dihydro-5H-pyrano[4,3-b]pyridine		ESN $[M-H]^-$: 379.5	C	N36
38	4-(5-Chlorothiophen-2-yl)-N,N-diethyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine		ESP $[M+H]^+$: 403.5	C	N38

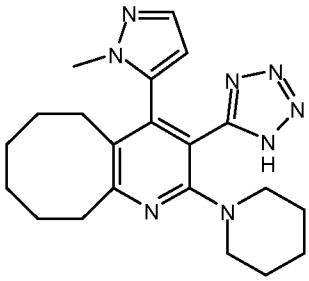
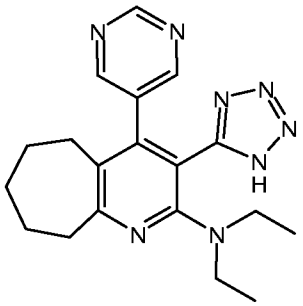
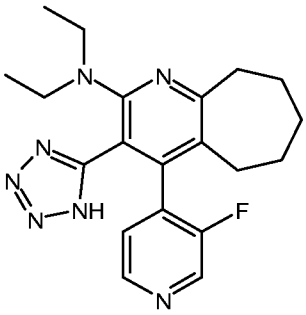
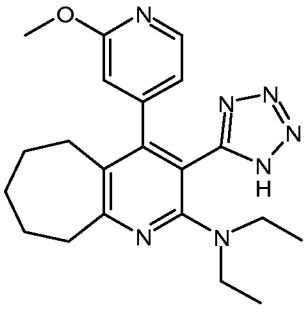
Ex.	Name	Structure	MS	Method	Starting Material
39	4-(5-Chlorothiophen-2-yl)-2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESN $[M-H]^-$: 413.5	C	N39
40	N,N-Diethyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine		ESN $[M-H]^-$: 365.6	C	N40
41	5-Methyl-3-(2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)isoxazole		ESP $[M+H]^+$: 380.5	C	N41
42	N,N-Diethyl-4-(5-methylisoxazol-3-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine		ESP $[M+H]^+$: 368.5	C	N42

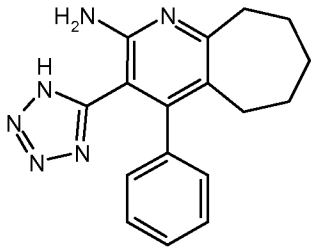
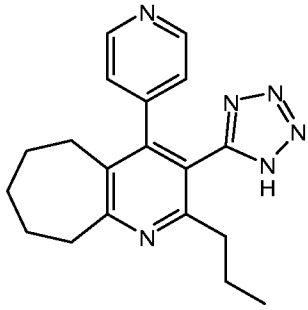
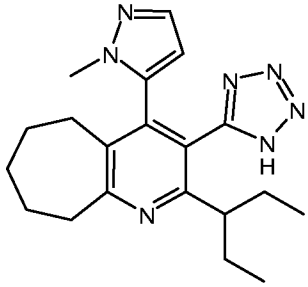
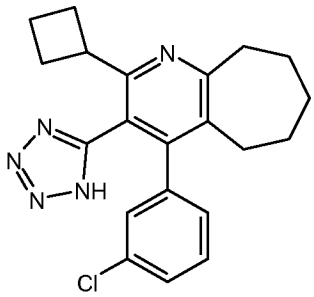
Ex.	Name	Structure	MS	Method	Starting Material
44	2-(Piperidin-1-yl)-4-(pyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 376.5	C	N44
45	N,N-Diethyl-4-(pyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine		ESP $[M+H]^+$: 364.6	C	N45
46	4-(5-Methylfuran-2-yl)-2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 379.4	C	N46
47	N,N-Diethyl-4-(5-methylfuran-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine		ESP $[M+H]^+$: 367.5	C	N47

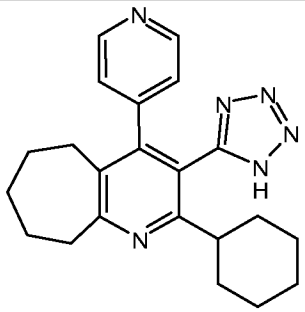
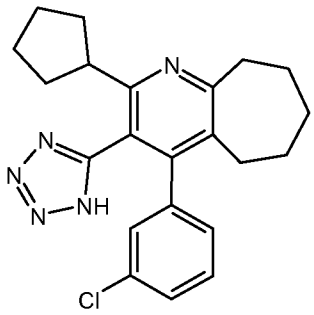
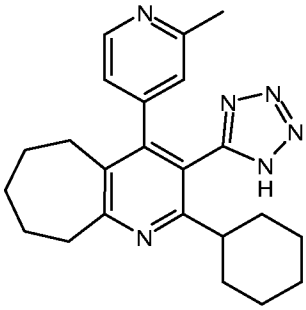
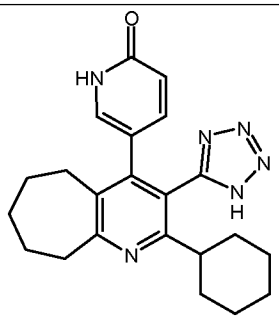
Ex.	Name	Structure	MS	Method	Starting Material
48	4-(1,5-Dimethyl-1H-pyrazol-4-yl)-2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 393.6	C	N48
49	4-(1,5-Dimethyl-1H-pyrazol-4-yl)-N,N-diethyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine		ESP $[M+H]^+$: 381.5	C	N49
50	4-(5-Chlorothiophen-2-yl)-2-(3-fluoropiperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 433.4	C	N50
51	4-(5-Chlorothiophen-2-yl)-2-(3,3-difluoropiperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 451.4	C	N51

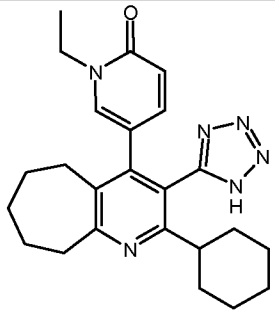
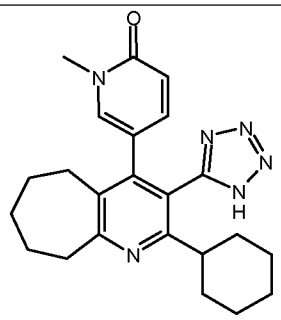
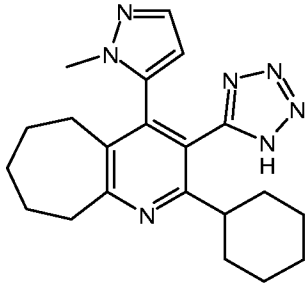
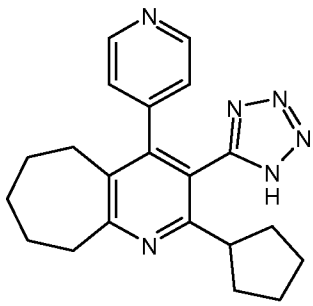
Ex.	Name	Structure	MS	Method	Starting Material
52	4-(5-Chlorothiophen-2-yl)-2-(4,4-difluoropiperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 451.4	C	N52
53	4-(5-Chlorothiophen-2-yl)-2-(4-fluoropiperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 433.4	C	N53
54	4-(5-Chlorothiophen-2-yl)-3-(1H-tetrazol-5-yl)-2-(4-(trifluoromethyl)piperidin-1-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 483.4	C	N54
55	4-(5-Chlorothiophen-2-yl)-2-(3,3-difluoroazetidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 423.5	C	N55

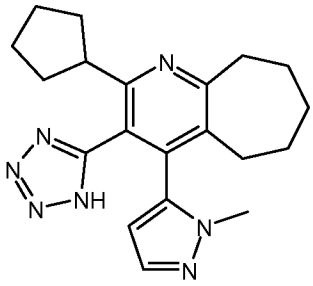
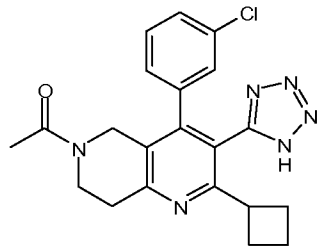
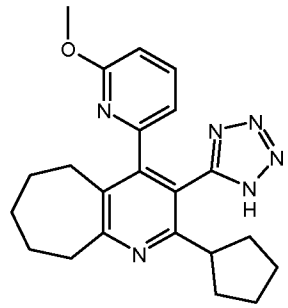
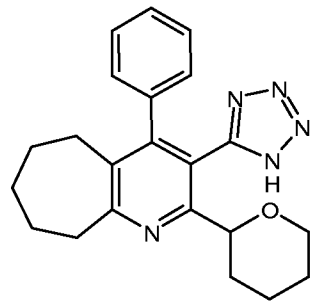
Ex.	Name	Structure	MS	Method	Starting Material
56	N,N-Diethyl-4-(4-methylthiazol-5-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine		ESP $[M+H]^+$: 384.4	C	N56
57	4-Methyl-5-(2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)thiazole		ESP $[M+H]^+$: 396.5	C	N57
58	N,N-Diethyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8,9,10-hexahydrocycloocta[b]pyridin-2-amine		ESP $[M+H]^+$: 381.5	C	N58
59	4-(5-Chlorothiophen-2-yl)-2-(3,3-difluoropyrrolidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 437.4	C	N59

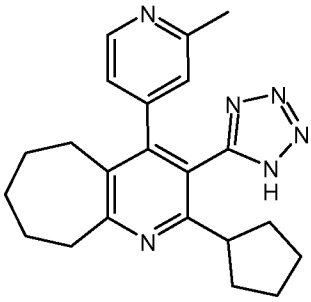
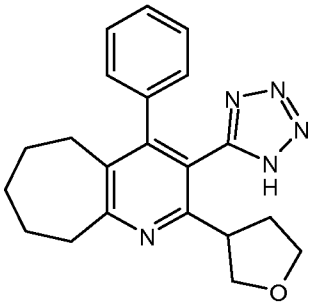
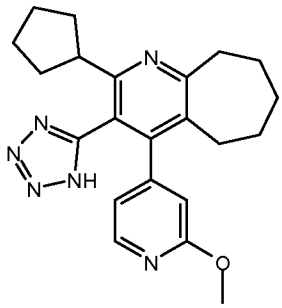
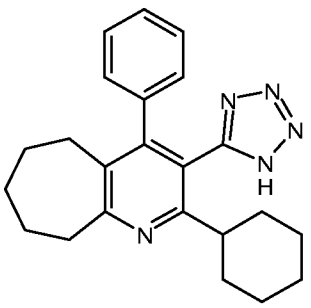
Ex.	Name	Structure	MS	Method	Starting Material
60	4-(1-Methyl-1H-pyrazol-5-yl)-2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8,9,10-hexahydrocycloocta[b]pyridine		ESP $[M+H]^+$: 393.5	C	N60
61	Diethyl-[4-pyrimidin-5-yl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-yl]-amine		ESP $[M+H]^+$: 365.4	C	N61
62	N,N-Diethyl-4-(3-fluoropyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine		ESP $[M+H]^+$: 382.5	C	N62
63	N,N-Diethyl-4-(2-methoxypyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine		ESP $[M+H]^+$: 394.5	C	N63

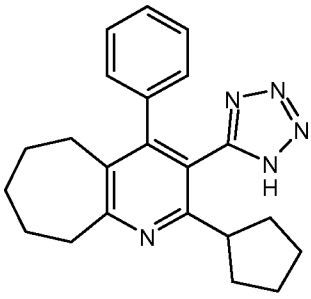
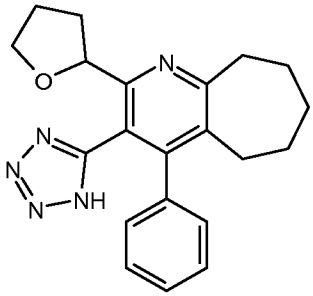
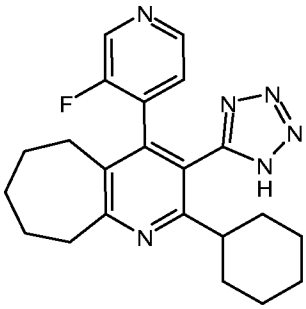
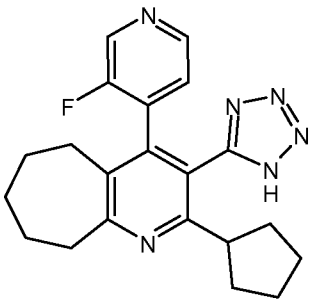
Ex.	Name	Structure	MS	Method	Starting Material
64	4-Phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine		ESP $[M+H]^+$: 307.5	D	N64
65	2-Propyl-4-(pyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 335.5	C	N65
66	4-(1-Methyl-1H-pyrazol-5-yl)-2-(pentan-3-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 366.5	C	N66
67	4-(3-Chlorophenyl)-2-cyclobutyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 380.5	C	N67

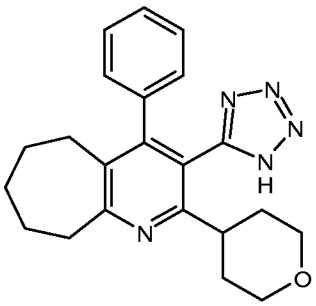
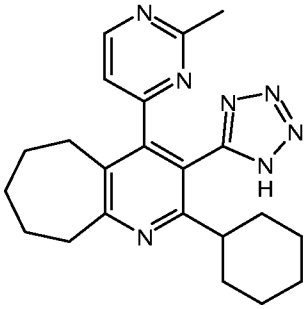
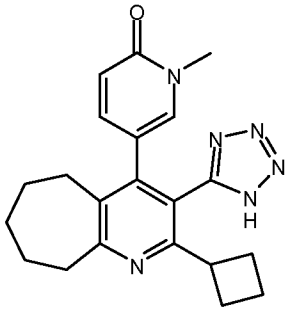
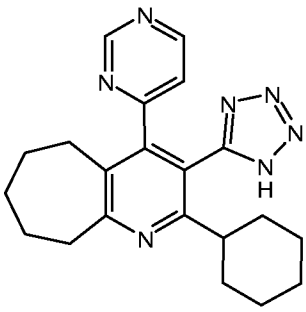
Ex.	Name	Structure	MS	Method	Starting Material
68	2-Cyclohexyl-4-pyridin-4-yl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 375.5	C	N68
69	4-(3-Chloro-phenyl)-2-cyclopentyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 394.4	C	N69
70	2-Cyclohexyl-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 389.5	C	N70
71	5-(2-Cyclohexyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)pyridin-2(1H)-one		ESP $[M+H]^+$: 391.5	C	N71

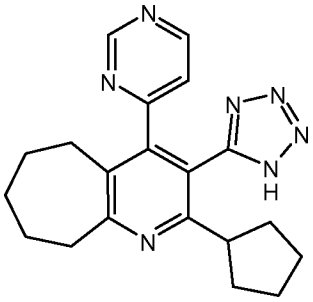
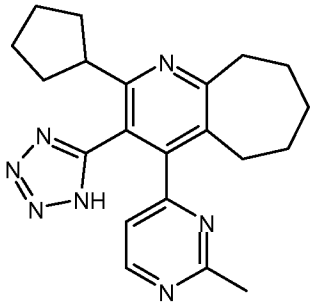
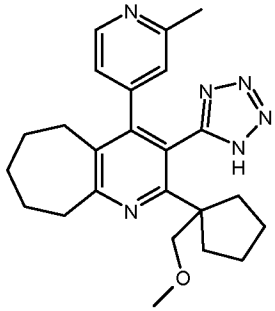
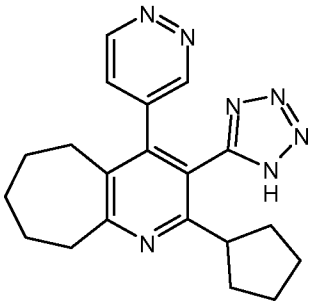
Ex.	Name	Structure	MS	Method	Starting Material
72	5-(2-Cyclohexyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)-1-ethylpyridin-2(1H)-one		ESP $[M+H]^+$: 419.5	C	N72
73	5-(2-Cyclohexyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)-1-methylpyridin-2(1H)-one		ESP $[M+H]^+$: 405.5	C	N73
74	2-Cyclohexyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 378.5	C	N74
75	2-Cyclopentyl-4-(pyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 361.5	C	N75

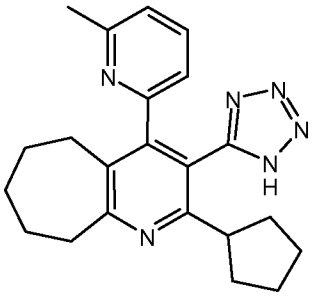
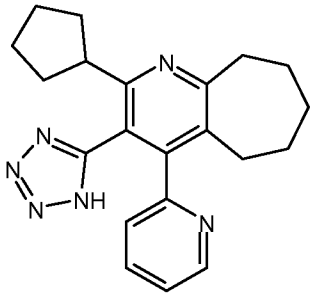
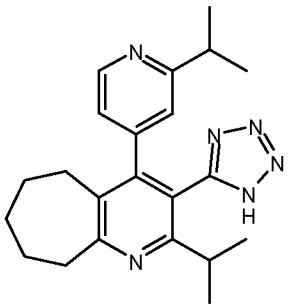
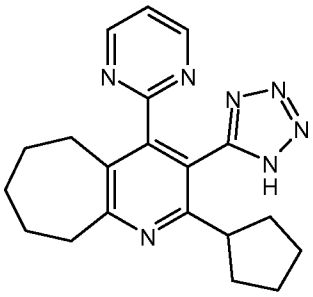
Ex.	Name	Structure	MS	Method	Starting Material
76	2-Cyclopentyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 364.5	C	N76
77	1-(4-(3-Chlorophenyl)-2-cyclobutyl-3-(1H-tetrazol-5-yl)-7,8-dihydro-1,6-naphthyridin-6(5H)-yl)ethanone		ESP $[M+H]^+$: 409.4	C	N77
78	2-Cyclopentyl-4-(6-methoxypyridin-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 391.5	C	N78
79	4-Phenyl-2-(tetrahydro-2H-pyran-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 376.5	C	N79

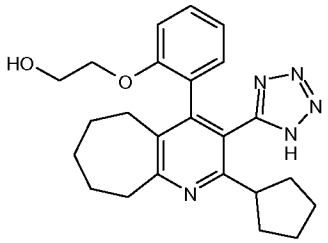
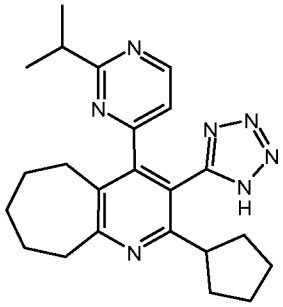
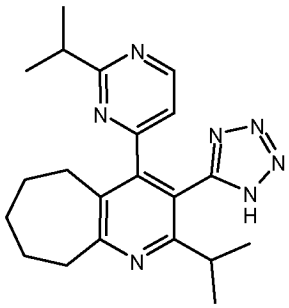
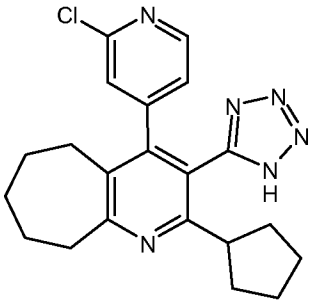
Ex.	Name	Structure	MS	Method	Starting Material
80	2-Cyclopentyl-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 375.5	C	N80
81	4-Phenyl-2-(tetrahydrofuran-3-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 362.5	C	N81
82	2-Cyclopentyl-4-(2-methoxypyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 391.5	C	N82
83	2-Cyclohexyl-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 374.6	C	N83

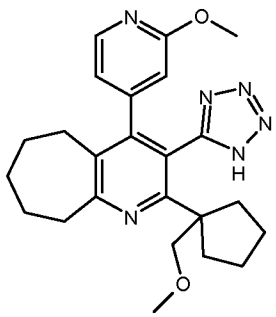
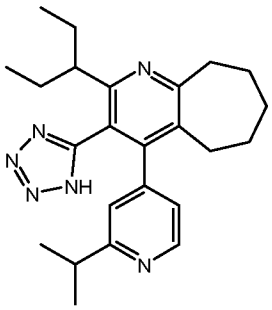
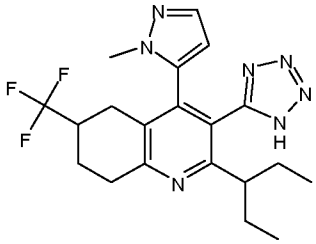
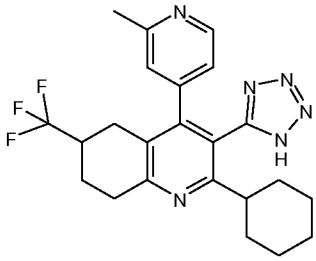
Ex.	Name	Structure	MS	Method	Starting Material
84	2-Cyclopentyl-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 360.6	C	N84
85	4-Phenyl-2-(tetrahydrofuran-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 362.5	C	N85
86	2-Cyclohexyl-4-(3-fluoropyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 393.5	C	N86
87	2-Cyclopentyl-4-(3-fluoropyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 379.5	C	N87

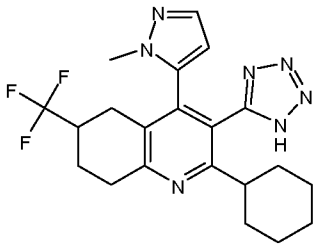
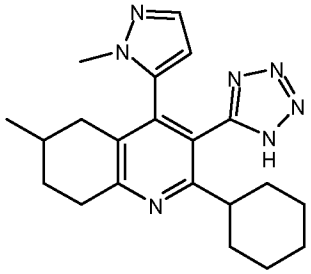
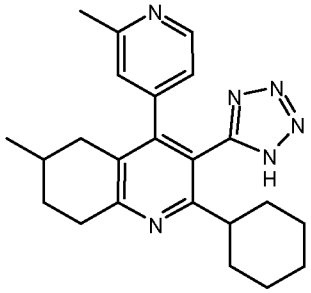
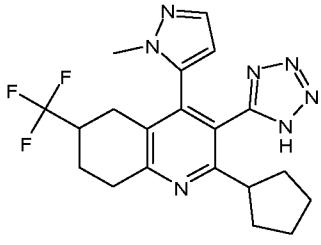
Ex.	Name	Structure	MS	Method	Starting Material
88	4-Phenyl-2-(tetrahydro-2H-pyran-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 376.5	C	N88
89	2-Cyclohexyl-4-(2-methylpyrimidin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 390.5	C	N89
90	5-(2-Cyclobutyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)-1-methylpyridin-2(1H)-one		ESP $[M+H]^+$: 377.5	C	N90
91	2-Cyclohexyl-4-(pyrimidin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 376.5	C	N91

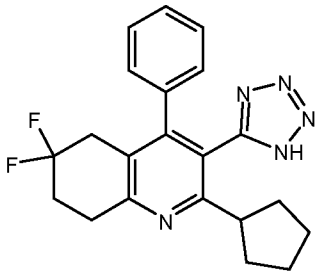
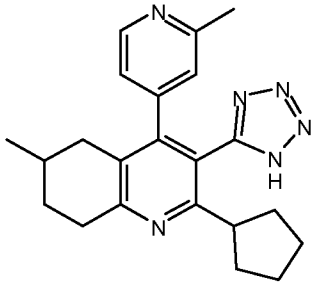
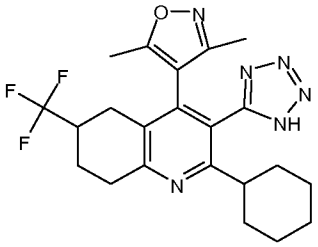
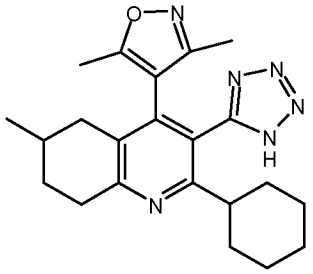
Ex.	Name	Structure	MS	Method	Starting Material
92	2-Cyclopentyl-4-(pyrimidin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 362.5	C	N92
93	2-Cyclopentyl-4-(2-methylpyrimidin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 376.5	C	N93
94	2-(1-(Methoxymethyl)cyclopentyl)-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 419.5	C	N94
95	2-Cyclopentyl-4-(pyridazin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 362.5	C	N95

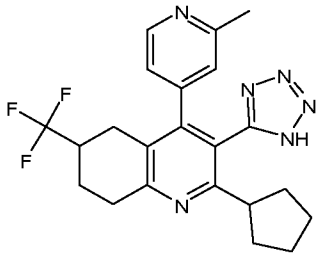
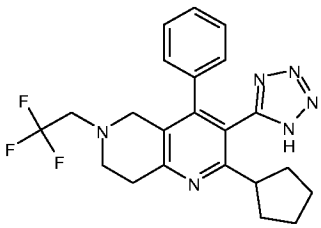
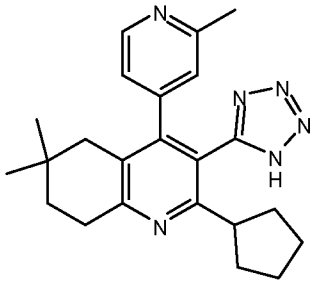
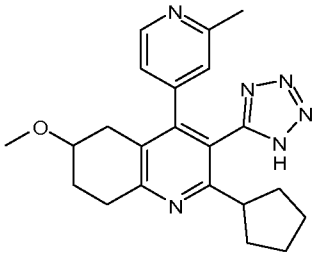
Ex.	Name	Structure	MS	Method	Starting Material
96	2-Cyclopentyl-4-(6-methylpyridin-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 375.5	C	N96
97	2-Cyclopentyl-4-(pyridin-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 361.5	C	N97
98	2-Isopropyl-4-(2-isopropylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 377.5	C	N98
99	2-Cyclopentyl-4-(pyrimidin-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 362.6	C	N99

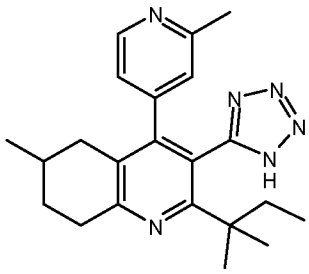
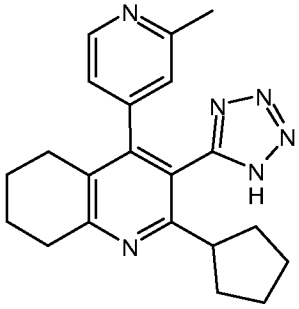
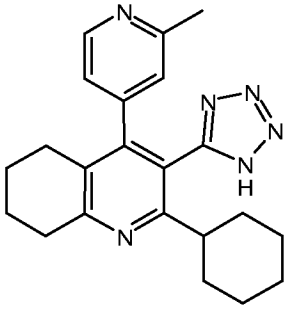
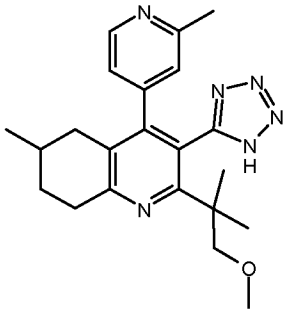
Ex.	Name	Structure	MS	Method	Starting Material
100	2-(2-(2-Cyclopentyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)phenoxy)ethanol		ESP $[M+H]^+$: 420.6	C	N100
101	2-Cyclopentyl-4-(2-isopropylpyrimidin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 404.6	C	N101
102	2-Isopropyl-4-(2-isopropylpyrimidin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 378.6	C	N102
103	4-(2-Chloropyridin-4-yl)-2-cyclopentyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 395.5	C	N103

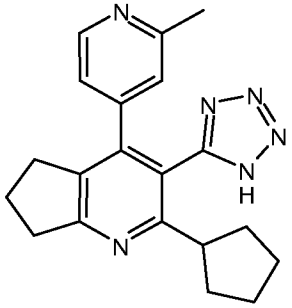
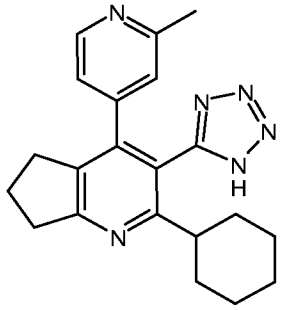
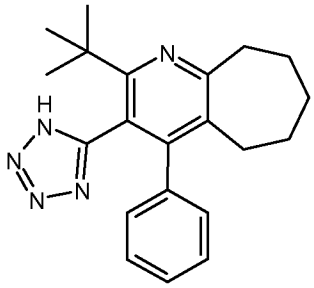
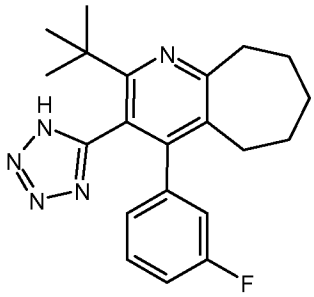
Ex.	Name	Structure	MS	Method	Starting Material
104	2-(1-(Methoxymethyl)cyclopentyl)-4-(2-methoxypyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 435.5	C	N104
105	4-(2-Isopropylpyridin-4-yl)-2-(pentan-3-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 405.6	C	N105
106	4-(1-Methyl-1H-pyrazol-5-yl)-2-(pentan-3-yl)-3-(2H-tetrazol-5-yl)-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 420.5	C	N106
107	2-Cyclohexyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 443.5	C	N107

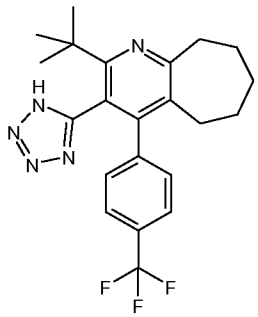
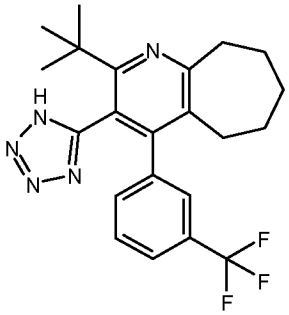
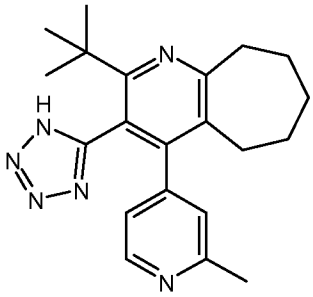
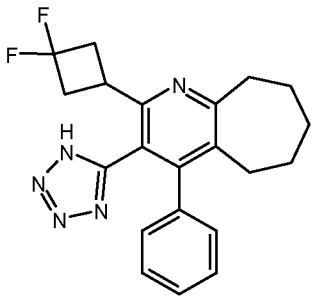
Ex.	Name	Structure	MS	Method	Starting Material
108	2-Cyclohexyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 432.5	C	N108
109	2-Cyclohexyl-6-methyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 378.5	C	N109
110	2-Cyclohexyl-6-methyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 389.5	C	N110
111	2-Cyclopentyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 418.5	C	N111

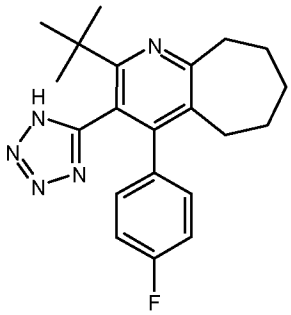
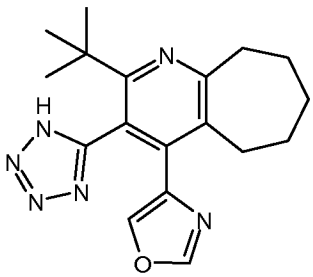
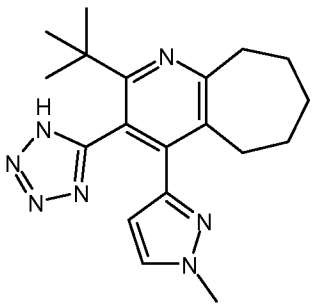
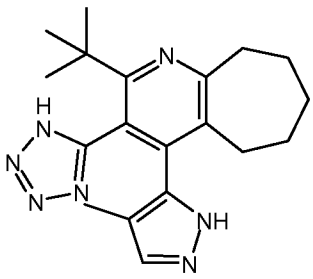
Ex.	Name	Structure	MS	Method	Starting Material
112	2-Cyclopentyl-6,6-difluoro-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 382.4	C	N112
113	2-Cyclopentyl-6-methyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 375.5	C	N113
114	4-(2-Cyclohexyl-6-methyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinolin-4-yl)-3,5-dimethylisoxazole		ESP $[M+H]^+$: 447.6	C	N114
115	4-(2-Cyclohexyl-6-methyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinolin-4-yl)-3,5-dimethylisoxazole		ESP $[M+H]^+$: 393.6	C	N115

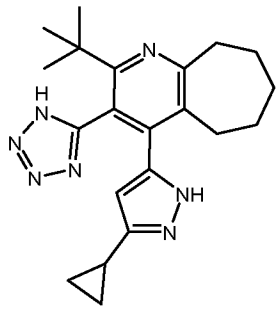
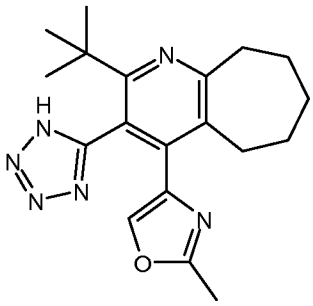
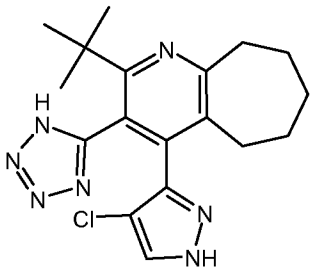
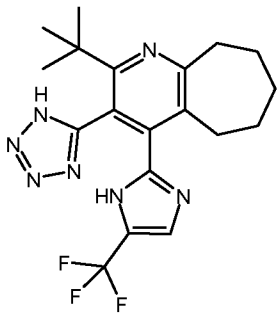
Ex.	Name	Structure	MS	Method	Starting Material
116	2-Cyclopentyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 429.5	C	N116
117	2-Cyclopentyl-4-phenyl-3-(2H-tetrazol-5-yl)-6-(2,2,2-trifluoroethyl)-5,6,7,8-tetrahydro-1,6-naphthyridine		ESP $[M+H]^+$: 429.4	C	N117
118	2-Cyclopentyl-6,6-dimethyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 389.6	C	N118
119	2-Cyclopentyl-6-methoxy-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 391.5	C	N119

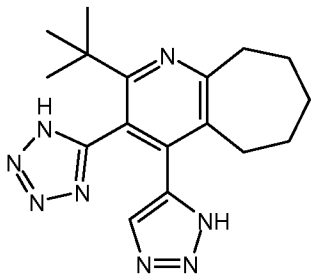
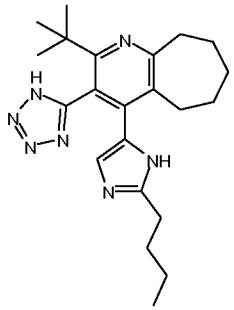
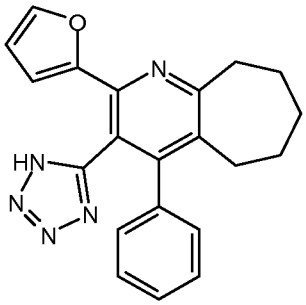
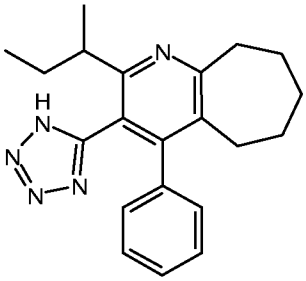
Ex.	Name	Structure	MS	Method	Starting Material
120	6-Methyl-4-(2-methylpyridin-4-yl)-2-tert-pentyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 377.6	C	N120
121	2-Cyclopentyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 361.6	C	N121
122	2-Cyclohexyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESN $[M-H]^-$: 373.4	C	N122
123	2-(1-Methoxy-2-methylpropan-2-yl)-6-methyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 393.6	C	N123

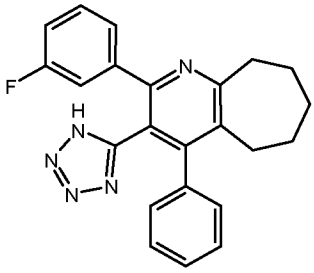
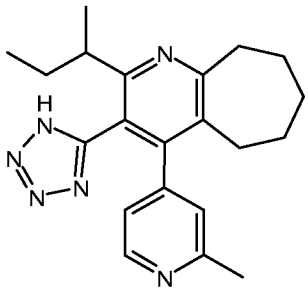
Ex.	Name	Structure	MS	Method	Starting Material
124	2-Cyclopentyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-6,7-dihydro-5H-cyclopenta[b]pyridine		ESN [M-H]-: 345.5	C	N124
125	2-Cyclohexyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-6,7-dihydro-5H-cyclopenta[b]pyridine		ESP $[M+H]^+$: 361.5	C	N125
126	2-tert-Butyl-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 348.2	D	N126
127	2-tert-Butyl-4-(3-fluorophenyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 366.5	C	N127

Ex.	Name	Structure	MS	Method	Starting Material
128	2-tert-Butyl-3-(1H-tetrazol-5-yl)-4-(4-(trifluoromethyl)phenyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 416.5	C	N128
129	2-tert-Butyl-3-(1H-tetrazol-5-yl)-4-(3-(trifluoromethyl)phenyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 416.4	C	N129
130	2-tert-Butyl-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 363.4	C	N130
131	2-(3,3-Difluorocyclobutyl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESN $[M-H]^-$: 380.2	C	N131

Ex.	Name	Structure	MS	Method	Starting Material
132	2-tert-Butyl-4-(4-fluoro-phenyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 366.5	C	N132
133	4-(2-tert-Butyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)oxazole		ESP $[M+H]^+$: 339.5	C	N133
134	2-tert-Butyl-4-(1-methyl-1H-pyrazol-3-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 352.5	C	N134
135	2-tert-Butyl-4-(4-methyl-1H-pyrazol-5-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 352.5	C	N135

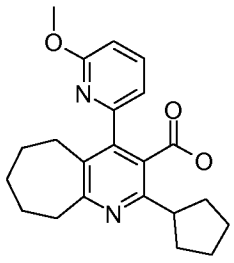
Ex.	Name	Structure	MS	Method	Starting Material
136	2-tert-Butyl-4-(3-cyclopropyl-1H-pyrazol-5-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 378.6	C	N136
137	4-(2-tert-Butyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)-2-methyloxazole		ESP $[M+H]^+$: 353.5	C	N137
138	2-tert-Butyl-4-(4-chloro-1H-pyrazol-3-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESN $[M-H]^-$: 370.5	C	N138
139	2-tert-Butyl-3-(1H-tetrazol-5-yl)-4-(4-(trifluoromethyl)-1H-imidazol-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 406.2	C	N139

Ex.	Name	Structure	MS	Method	Starting Material
140	2-tert-Butyl-3-(1H-tetrazol-5-yl)-4-(1H-1,2,3-triazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 339.2	C	N140
141	2-tert-Butyl-4-(2-butyl-1H-imidazol-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 394.6	C	N141
142	2-Furan-2-yl-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 358.4	C	N142
143	2-sec-Butyl-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 348.5	C	N143

Ex.	Name	Structure	MS	Method	Starting Material
144	2-(3-Fluorophenyl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 386.5	C	N144
145	2-sec-Butyl-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 363.2	C	N145

Example 12

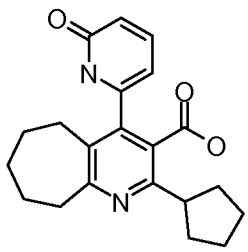
2-Cyclopentyl-4-(6-methoxypyridin-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid



Intermediate N78 (471 mg) and aqueous HCl 37 % (2.67 g) were combined with dioxane (20.0 ml) and stirred at 100 °C for 1 h. After cooling to room temperature, the mixture was diluted with water and extracted with EtOAc. The organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude material was purified by column chromatography (gradient of DCM / MeOH 100:0 => 80:20) to give the title compound (47 mg) as a colorless amorphous solid. MS (ESN): m/z = 365.4 $[M-H]^-$.

Example 13

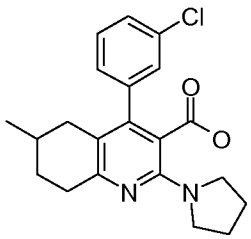
2-Cyclopentyl-4-(6-oxo-1,6-dihydropyridin-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid



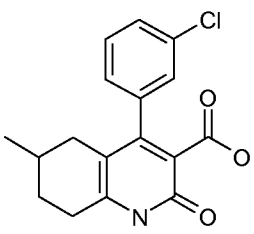
In the synthesis of Example 12, there was also obtained the title compound (114 mg) as a light yellow solid. MS (ESP): m/z = 353.4 $[M+H]^+$.

Example 20

4-(3-Chlorophenyl)-6-methyl-2-(pyrrolidin-1-yl)-5,6,7,8-tetrahydroquinoline-3-carboxylic acid



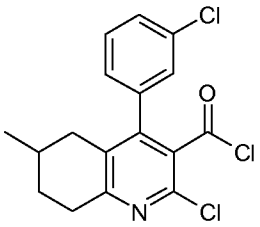
Step 1: 4-(3-Chlorophenyl)-6-methyl-2-oxo-1,2,5,6,7,8-hexahydroquinoline-3-carboxylic acid



A solution of lithium hydroxide (104 mg) in water (4.0 ml) was added at room temperature to a solution of Intermediate P20 (500 mg) in EtOH (9.3 ml) and THF (2.7 ml). After the addition the

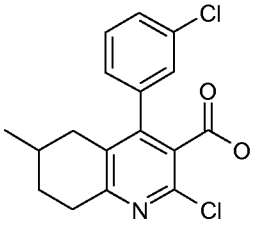
solution was stirred at 90 °C for 4 h. The organic solvents were removed in vacuo, the residue was diluted with 15 mL of aqueous 1 M NaOH and extracted with dichloromethane. The aqueous layer was acidified with aqueous 1 M HCl to pH1 and extracted with DCM and with EtOAc. The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo to give the title compound (452 mg) as an off-white solid. MS (ESP): m/z = 318.1 $[M+H]^+$.

Step 2: 2-Chloro-4-(3-chloro-phenyl)-6-methyl-5,6,7,8-tetrahydro-quinoline-3-carbonyl chloride



A suspension of the product of step 1 (440 mg) in phenylphosphonic dichloride (863 mg) was stirred at 135 °C for 3 h. After cooling to room temperature, the mixture was diluted with water (10 ml) and extracted with DCM. The organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude material was purified by column chromatography (gradient of DCM / MeOH 100:0 => 90:10) to give the title compound (271 mg) as an off-white solid. MS (ESP): m/z = 356.0 $[M+H]^+$.

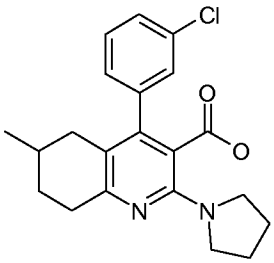
Step 3: 2-Chloro-4-(3-chlorophenyl)-6-methyl-5,6,7,8-tetrahydroquinoline-3-carboxylic acid



A solution of the product of step 2 (138 mg) in THF (1 ml) and water (1.00 ml) was stirred for 6 days at room temperature, for 5 h at 50 °C and for 11 h at 60 °C. The reaction mixture was poured into water (10 ml) / aqueous 1 M NaOH (1 ml) and extracted with diethyl ether.

The aqueous layer was acidified to pH 1 with aqueous 2 M HCl and back-extracted with EtOAc. The organic layers (EtOAc) were combined, dried over $MgSO_4$ and concentrated in vacuo to give the title compound (114 mg) as an off-white solid. MS (ESN): m/z = 336.1 $[M-H]^-$.

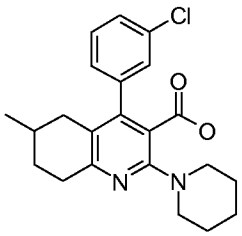
Step 4: 4-(3-Chlorophenyl)-6-methyl-2-(pyrrolidin-1-yl)-5,6,7,8-tetrahydroquinoline-3-carboxylic acid



A suspension of the product of step 3 (50 mg), potassium carbonate (24.7 mg), copper powder (0.56 mg), copper (I) bromide (1.1 mg) and pyrrolidine (18.0 mg) in DMA (0.2 ml) was stirred at 150 °C for 4 h. The reaction mixture was allowed to cool to room temperature overnight. The reaction mixture was poured into EtOAc (10 ml) and water (10 ml) and acidified to pH 3 with saturated aqueous citric acid solution. The mixture was extracted with EtOAc. The organic layers were combined, dried over $MgSO_4$ and concentrated in vacuo. The crude material was purified by preparative TLC (silica gel, 2.0 mm, DCM / MeOH 9:1) to give the title compound (14 mg) as an off-white solid. MS (ESN): m/z = 369.1 $[M-H]^-$.

Example 23

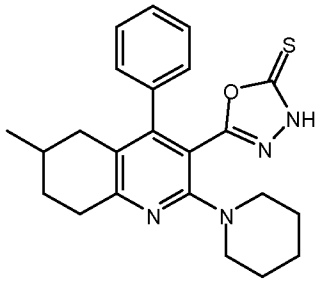
4-(3-Chlorophenyl)-6-methyl-2-(piperidin-1-yl)-5,6,7,8-tetrahydroquinoline-3-carboxylic acid



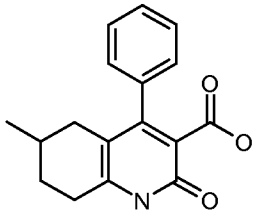
In analogy to Example 20, step 4, 2-chloro-4-(3-chlorophenyl)-6-methyl-5,6,7,8-tetrahydroquinoline-3-carboxylic acid (Example 20, step 3) was converted to the title compound by reaction with piperidine in the presence of potassium carbonate, copper powder, copper (I) bromide and DMA. Off-white solid. MS (ESN): m/z = 383.4 $[M-H]^-$.

Example 24

5-(6-Methyl-4-phenyl-2-(piperidin-1-yl)-5,6,7,8-tetrahydroquinolin-3-yl)-1,3,4-oxadiazole-2(3H)-thione

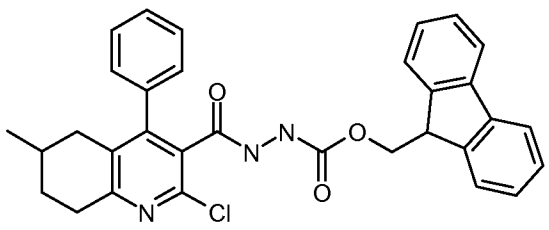


Step 1: 6-Methyl-2-oxo-4-phenyl-1,2,5,6,7,8-hexahydro-quinoline-3-carboxylic acid



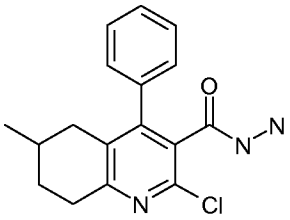
To a solution of intermediate P16 (660 mg, 2.12 mmol) in a solvent mixture of EtOH (6.6 ml), THF (2.64 ml) and water (6.6 ml) was added lithium hydroxide (152 mg, 6.36 mmol) and the reaction mixture was heated to reflux for 2d. The organic solvents were removed and the pH of the remaining water layer was adjusted to 14. The water layer was washed 3 times with diethyl ether, then acidified to pH1 with 1N HCl and extracted with ethyl acetate. The combined ethyl acetate layers were washed with water and brine, dried (Na_2SO_4) and evaporated to obtain the title compound as white solid (550 mg). MS (ESP): m/z = 284.2 $[M+H]^+$.

Step 2: N'-(2-Chloro-6-methyl-4-phenyl-5,6,7,8-tetrahydro-quinoline-3-carbonyl)-hydrazinecarboxylic acid 9H-fluoren-9-ylmethyl ester



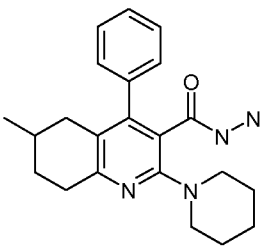
A mixture of 6-methyl-2-oxo-4-phenyl-1,2,5,6,7,8-hexahydro-quinoline-3-carboxylic acid (170 mg, 600 µmol) and phenylphosphonic dichloride (351 mg, 253 µl, 1.8 mmol) was heated to 135 °C under argon for 6h. The reaction mixture was then concentrated and the remaining residue was purified by silica column chromatography (50g silica gel, DCM). The fractions containing the desired 2-chloro-6-methyl-4-phenyl-5,6,7,8-tetrahydro-quinoline-3-carbonyl chloride intermediate were combined, evaporated and dissolved in DCM (4 ml). (9H-Fluoren-9-yl)methyl hydrazinecarboxylate (183 mg, 720 µmol) was added and the reaction mixture was stirred at room temperature for 20 h. Water was added and the mixture was extracted with ethyl acetate. The combined extracts were washed with water and brine, dried (Na_2SO_4) and evaporated to obtain the title compound (308 mg) as a white solid. MS (ESP): m/z = 538.4 $[M+H]^+$.

Step 3: 2-Chloro-6-methyl-4-phenyl-5,6,7,8-tetrahydro-quinoline-3-carboxylic acid hydrazide



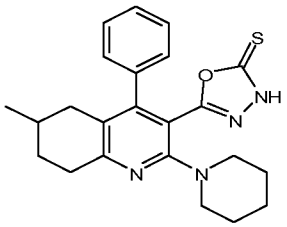
To a solution of N'-(2-chloro-6-methyl-4-phenyl-5,6,7,8-tetrahydro-quinoline-3-carbonyl)-hydrazinecarboxylic acid 9H-fluoren-9-ylmethyl ester (170 mg, 253 µmol) in DMF (2.25 ml) was added piperidine (215 mg, 250 µl, 2.53 mmol) and the reaction mixture was stirred at room temperature for 2 h. Water was added and the mixture was extracted with ethyl acetate. The combined extracts were washed with water and brine, dried (Na_2SO_4) and evaporated. The remaining residue was purified by silica column chromatography (20 g silica gel, DCM/EtOAc 1:1) to obtain the title compound (71 mg) as a light yellow solid. MS (ESP): m/z = 316.2 $[M+H]^+$.

Step 4: 6-Methyl-4-phenyl-2-piperidin-1-yl-5,6,7,8-tetrahydro-quinoline-3-carboxylic acid hydrazide



2-Chloro-6-methyl-4-phenyl-5,6,7,8-tetrahydro-quinoline-3-carboxylic acid hydrazide (70 mg, 222 µmol), piperidine (189 mg, 219 µl, 2.22 mmol) and triethylamine (67.3 mg, 92.7 µl, 665 µmol) were dissolved in DMF (1 ml) and the reaction mixture was heated to 120 °C for 24 h. Water was added and the mixture was extracted with EtOAc. The combined extracts were washed with brine, dried (Na_2SO_4) and evaporated. The remaining residue was purified by silica column chromatography (10 g silica gel, DCM/EtOAc 2:1) to obtain the title compound (45 mg) as a white solid. MS (ESP): m/z = 365.3 $[M+H]^+$.

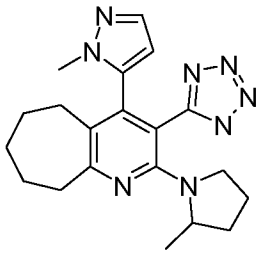
Step 5: 5-(6-Methyl-4-phenyl-2-(piperidin-1-yl)-5,6,7,8-tetrahydroquinolin-3-yl)-1,3,4-oxadiazole-2(3H)-thione



6-Methyl-4-phenyl-2-piperidin-1-yl-5,6,7,8-tetrahydro-quinoline-3-carboxylic acid hydrazide (43 mg, 94.4 µmol) and 1,1'-thiocarbonyldiimidazole (23.5 mg, 132 µmol) were dissolved in THF (1.1 ml). Then triethylamine (15.3 mg, 21.0 µl, 151 µmol) was added and the reaction mixture was stirred at room temperature for 16 h. Water was added and the mixture was extracted with ethyl acetate. The combined extracts were washed with water and brine, dried (Na_2SO_4) and evaporated. The remaining residue was purified by silica column chromatography (5 g silica gel, DCM/methanol 95:5). The fractions containing the desired 6-methyl-4-phenyl-2-piperidin-1-yl-5,6,7,8-tetrahydro-quinoline-3-carboxylic acid N'-(imidazole-1-carbothioyl)-hydrazide intermediate were combined, evaporated and dissolved in THF (1.1 ml). Triethylamine (15.3 mg, 21.0 µl, 151 µmol) was added and the reaction mixture was heated in a sealed tube to 50 °C for 4 d. Water was added and the mixture was extracted with ethyl acetate. The combined extracts were washed with brine, dried (Na_2SO_4) and evaporated. The remaining residue was purified by silica column chromatography (5 g silica gel, DCM/ethyl acetate 9:1) to obtain the title compound (13 mg) as white solid. MS (ESN): m/z = 405.4 $[M-H]^-$.

Examples 37 and 43

4-(1-Methyl-1H-pyrazol-5-yl)-2-(2-methylpyrrolidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine (diastereomeric racemates)



Using General Method C, Intermediate N37 was converted to the tetrazole. The two diastereomeric racemates (caused by atropisomerism) could be separated by preparative HPLC (reverse phase chromatography, column: Gemini Axia C18 5u 110A 5 micron 100 x 30 mm, Solvent A: water + 0.01% formic acid, Solvent B: acetonitrile, Method: gradient 30% to 95 % B).

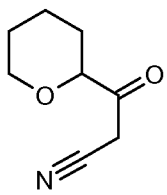
First-eluting isomer (Example 37): Off-white amorphous solid. MS (ESP): m/z = 379.2 $[M+H]^+$.

Second-eluting isomer (Example 43): Colorless amorphous solid. MS (ESP): m/z = 379.2 $[M+H]^+$.

Synthesis of Intermediates

Intermediate B79

3-Oxo-3-(tetrahydro-2H-pyran-2-yl)propanenitrile

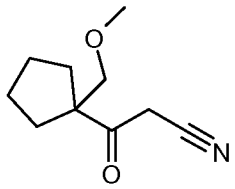


To a suspension of sodium hydride (55 % in mineral oil, 969 mg) in THF (4.79 ml) was added at 70 °C dropwise a solution of methyl tetrahydro-2H-pyran-2-carboxylate (3 g) and acetonitrile (994 mg) in THF (1.96 ml). The mixture was heated to 75 °C and stirred for 2 h. EtOAc was added and acidified with 1 M HCl under stirring (exothermic).The mixture was extracted with EtOAc. The organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude material was purified by column chromatography (gradient of n-heptane / EtOAc 1:0

=> 2:3) to give the title compound (2.42 g) as a light brown liquid. MS (ESP): m/z = 152.2 $[M+H]^+$.

Intermediate B94

3-(1-(Methoxymethyl)cyclopentyl)-3-oxopropanenitrile



In analogy to the synthesis of Intermediate B79, methyl 1-(methoxymethyl)cyclopentanecarboxylate (CAS# 220875-97-8) was converted to the title compound by a reaction with sodium hydride and acetonitrile in THF. Light yellow liquid. MS (ESN): m/z = 180.2 $[M-H]^-$.

Intermediates K (via Knoevenagel condensation)

General Method E: A solution of the beta-ketoester or beta-ketonitrile or dialkylmalonate (3.5 mmol, 1 eq), the aldehyde (1.1 eq), piperidine (0.15 eq) and acetic acid (0.15 eq) in 2-propanol (10 ml) is stirred at room temperature overnight. Most of the 2-propanol is removed by evaporation. The mixture is diluted with $Na_2S_2O_5$ (20% g/g sol.) and extracted with DCM. The organic layers are washed with $Na_2S_2O_5$ (20% g/g sol.), sat. aqueous $NaHCO_3$ solution and water, dried over Na_2SO_4 and evaporated. The products are obtained as cis/trans mixtures and are used in the next step without further purification.

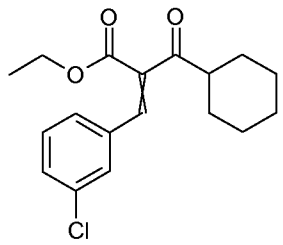
General Method F: A solution of the aldehyde (4.5 mmol, 1 eq), the beta-ketoester or beta-ketonitrile or dialkylmalonate or methyl cyanoacetate (1.1 eq) and piperidine (0.02 eq) in toluene (8.4 ml) is heated to reflux using a Dean-Stark trap for 1-2 h. The reaction mixture is concentrated and the product can be purified by crystallization or chromatography or can be used in the next step without further purification.

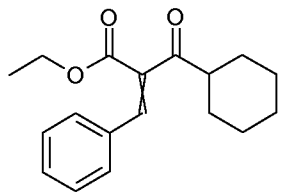
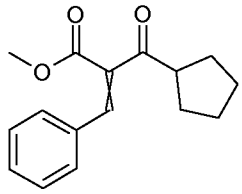
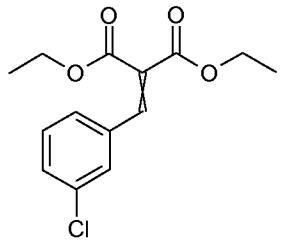
General Method G: To a suspension of 2-cyanoacetamide (1.1 eq) in methanol (10 ml) and water (3 ml) are added the aldehyde (40 mmol, 1 eq) and piperidine (0.2 eq). The mixture is stirred for 1-2 h. 1M HCl (9 ml) and water (10 ml) are added. The precipitate is collected by

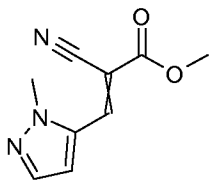
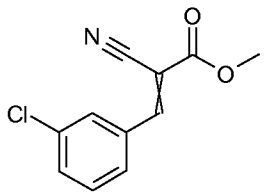
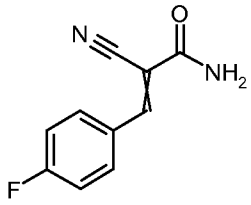
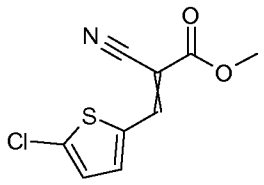
filtration, washed with water and ethyl acetate and dried. The product can be further purified by crystallization or can be used in the next step without further purification.

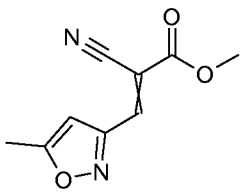
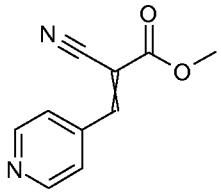
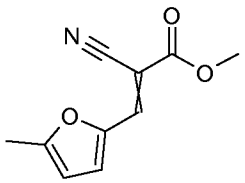
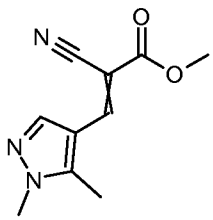
General Method H: The aldehyde (7.75 mmol, 1 eq), methyl cyanoacetate or a beta-ketonitrile (1 eq) and methanol (5.3 ml) are combined and stirred for 1-4 days. If the product precipitates, it can be collected by filtration. If the product does not precipitate, it can be purified by evaporation of the solvent and either crystallization or chromatography or can be used in the next step without further purification.

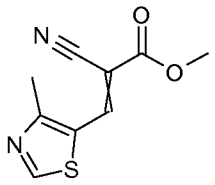
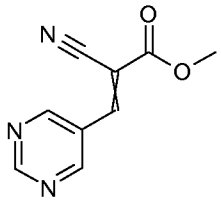
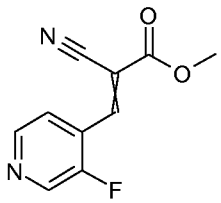
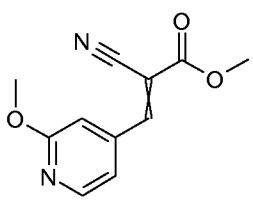
General Method I: The aldehyde (4.4 mmol, 1 eq), the beta-ketonitrile (1 eq) and L-proline (0.2 eq) are combined with ethanol or methanol (6.5 ml) and stirred for 1-4 days. If the product precipitates, it can be collected by filtration. If the product does not precipitate, it can be purified by evaporation of the solvent and either crystallization or chromatography or can be used in the next step without further purification.

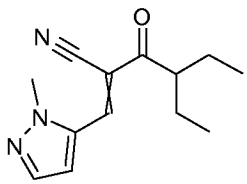
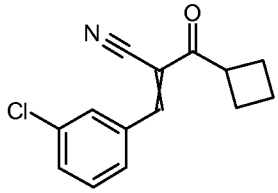
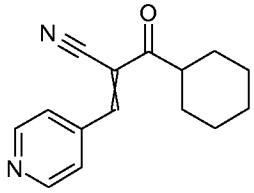
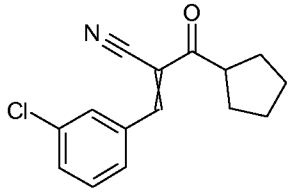
Intermediate	Name and Structure	MS	Method	Reagents
K4	Ethyl 3-(3-chlorophenyl)-2-(cyclohexanecarbonyl)acrylate 	ESP $[M+H]^+$: 321.1	E	3-Chlorobenzaldehyde, 3-cyclohexyl-3-oxo-propionic acid ethyl ester (CAS# 15971-92-3)

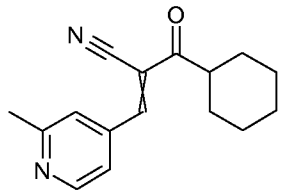
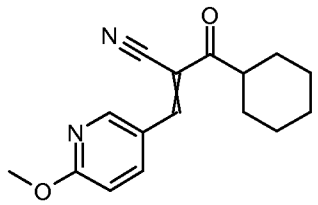
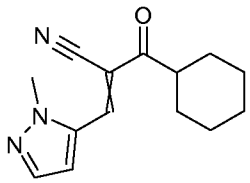
Interm ediate	Name and Structure	MS	Method	Reagents
K5	2-Cyclohexanecarbonyl-3-phenyl-acrylic acid ethyl ester 	ESP $[M+H]^+$: 287.0	E	Benzaldehyde, 3-cyclohexyl-3-oxo-propionic acid ethyl ester (CAS# 15971-92-3)
K6	2-Cyclopentanecarbonyl-3-phenyl-acrylic acid methyl ester 	ESP $[M+H]^+$: 259.1	E	Benzaldehyde, methyl 3-cyclopentyl-3-oxopropanoate (CAS# 64670-14-0)
K20	Diethyl 2-(3-chlorobenzylidene)malonate 		E	3-Chlorobenzaldehyde, diethylmalonate

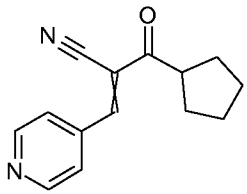
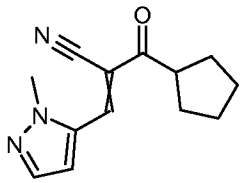
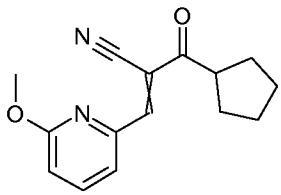
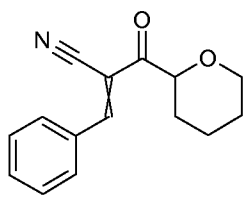
Intermediate	Name and Structure	MS	Method	Reagents
K29	Methyl 2-cyano-3-(1-methyl-1H-pyrazol-5-yl)acrylate 	ESP $[M+H]^+$: 192.3	F	1-Methyl-1H-pyrazole-5-carbaldehyde, methyl cyanoacetate
K32	Methyl 3-(3-chlorophenyl)-2-cyanoacrylate 	ESP $[M+NH_4]^+$: 238.9	F	3-Chlorobenzaldehyde, methyl cyanoacetate
K35	2-Cyano-3-(4-fluorophenyl)acrylamide 		G	4-Fluorobenzaldehyde, 2-cyanoacetamide
K38	Methyl 3-(5-chlorothiophen-2-yl)-2-cyanoacrylate 	ESP $[M+H]^+$: 228.3	F	5-Chlorothiophene-2-carbaldehyde, methyl cyanoacetate

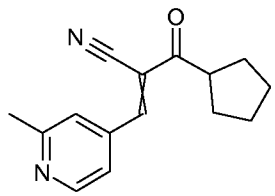
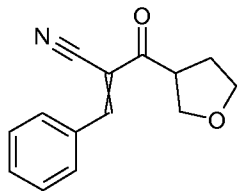
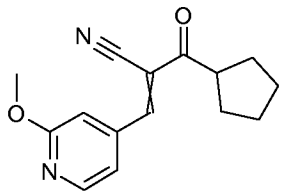
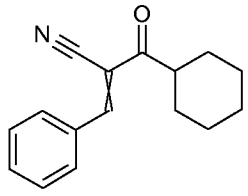
Intermediate	Name and Structure	MS	Method	Reagents
K41	Methyl 2-cyano-3-(5-methylisoxazol-3-yl)acrylate 	ESP $[M+H]^+$: 191.3	F	5-Methylisoxazole-3-carbaldehyde, methyl cyanoacetate
K44	Methyl 2-cyano-3-(pyridin-4-yl)acrylate 	ESP $[M+H]^+$: 189.1	F	Isonicotinaldehyde, methyl cyanoacetate
K46	Methyl 2-cyano-3-(5-methylfuran-2-yl)acrylate 	ESP $[M+H]^+$: 192.3	F	5-Methylfuran-2-carbaldehyde, methyl cyanoacetate
K48	Methyl 2-cyano-3-(1,5-dimethyl-1H-pyrazol-4-yl)acrylate 	ESP $[M+H]^+$: 206.4	F	1,5-Dimethyl-1H-pyrazole-4-carbaldehyde, methyl cyanoacetate

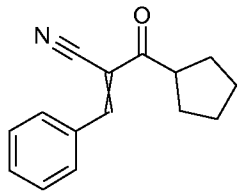
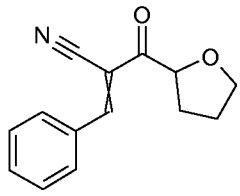
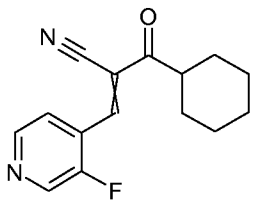
Intermediate	Name and Structure	MS	Method	Reagents
K56	Methyl 2-cyano-3-(4-methylthiazol-5-yl)acrylate 		F	4-Methylthiazole-5-carbaldehyde, methyl cyanoacetate
K61	Cyano-3-pyrimidin-5-yl-acrylic acid methyl ester 	ESP $[M+H]^+$: 190.3	F	Pyrimidine-5-carbaldehyde, methyl cyanoacetate
K62	Methyl 2-cyano-3-(3-fluoropyridin-4-yl)acrylate 	ESP $[M+H]^+$: 207.3	H	3-Fluoroisonicotinaldehyde, methyl cyanoacetate
K63	Methyl 2-cyano-3-(2-methoxypyridin-4-yl)acrylate 		H	2-Methoxyisonicotinaldehyde, methyl cyanoacetate

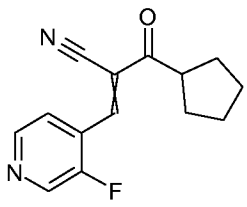
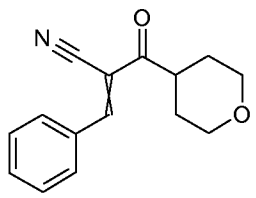
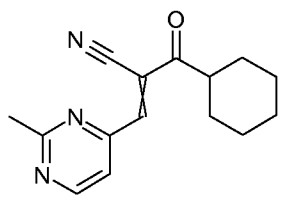
Intermediate	Name and Structure	MS	Method	Reagents
K66	4-Ethyl-2-((1-methyl-1H-pyrazol-5-yl)methylene)-3-oxohexanenitrile 		F	1-Methyl-1H-pyrazole-5-carbaldehyde, 4-ethyl-3-oxo-hexanenitrile (CAS# 42124-67-4)
K67	3-(3-Chloro-phenyl)-2-cyclobutanecarbonyl-acrylonitrile 		F	3-Chlorobenzaldehyde β-Cyclobutyl-β-oxopropionitrile (CAS# 118431-89-3)
K68	2-Cyclohexanecarbonyl-3-pyridin-4-yl-acrylonitrile 		F	Isonicotinaldehyde, 3-cyclohexyl-3-oxo-propanenitrile (CAS# 62455-70-3)
K69	3-(3-Chlorophenyl)-2-(cyclopentanecarbonyl)acrylonitrile 	ESP $[M+H]^+$: 260.3	F	3-Chlorobenzaldehyde, 3-cyclopentyl-3-oxopropanenitrile (CAS# 95882-33-0)

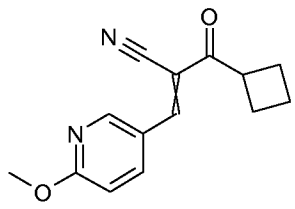
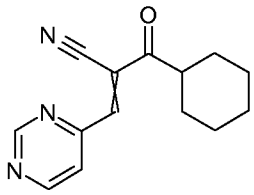
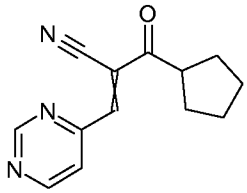
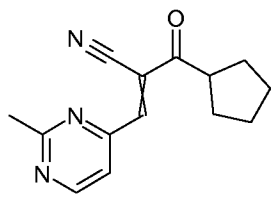
Intermediate	Name and Structure	MS	Method	Reagents
K70	2-Cyclohexanecarbonyl-3-(2-methyl-pyridin-4-yl)-acrylonitrile 		I	2-Methylisonicotinaldehyde, 3-cyclohexyl-3-oxo-propanenitrile (CAS# 62455-70-3)
K71	2-(Cyclohexanecarbonyl)-3-(6-methoxypyridin-3-yl)acrylonitrile 	ESP $[M+H]^+$: 271.4	F	6-Methoxynicotinaldehyde, 3-cyclohexyl-3-oxo-propanenitrile (CAS# 62455-70-3)
K74	2-Cyclohexanecarbonyl-3-(2-methyl-2H-pyrazol-3-yl)-acrylonitrile 	ESP $[M+H]^+$: 244.4	F	1-Methyl-1H-pyrazole-5-carbaldehyde, 3-cyclohexyl-3-oxo-propanenitrile (CAS# 62455-70-3)

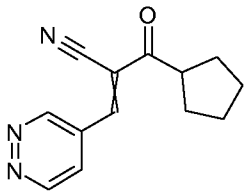
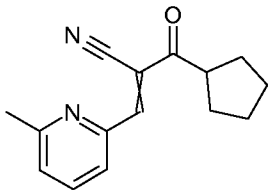
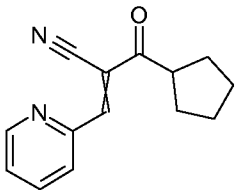
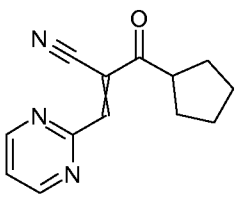
Intermediate	Name and Structure	MS	Method	Reagents
K75	2-Cyclopentanecarbonyl-3-pyridin-4-yl-acrylonitrile 	ESP $[M+H]^+$: 227.4	H	Isonicotinaldehyde, 3-cyclopentyl-3-oxopropanenitrile (CAS# 95882-33-0)
K76	2-Cyclopentanecarbonyl-3-(2-methyl-2H-pyrazol-3-yl)-acrylonitrile 	ESP $[M+H]^+$: 230.4	F	1-Methyl-1H-pyrazole-5-carbaldehyde, 3-cyclopentyl-3-oxopropanenitrile (CAS# 95882-33-0)
K78	2-(Cyclopentanecarbonyl)-3-(6-methoxypyridin-2-yl)acrylonitrile 	ESP $[M+H]^+$: 257.4	F	6-Methoxypicolinaldehyde, 3-cyclopentyl-3-oxopropanenitrile (CAS# 95882-33-0)
K79	3-Phenyl-2-(tetrahydro-2H-pyran-2-carbonyl)acrylonitrile 	ESP $[M+H]^+$: 242.3	F	Benzaldehyde, Intermediate B79

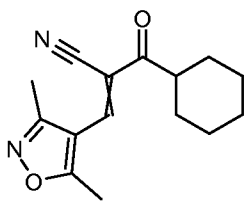
Intermediate	Name and Structure	MS	Method	Reagents
K80	2-Cyclopentanecarbonyl-3-(2-methyl-pyridin-4-yl)-acrylonitrile 	ESP $[M+H]^+$: 241.4	I	2-Methylisonicotinaldehyde, 3-cyclopentyl-3-oxopropanenitrile (CAS# 95882-33-0)
K81	3-Phenyl-2-(tetrahydrofuran-3-carbonyl)acrylonitrile 	ESP $[M+H]^+$: 228.4	F	Benzaldehyde, 3-oxo-3-(tetrahydrofuran-3-yl)propanenitrile (CAS# 1186610-03-6)
K82	2-Cyclopentanecarbonyl-3-(2-methoxy-pyridin-4-yl)-acrylonitrile 		H	2-Methoxyisonicotinaldehyde, 3-cyclopentyl-3-oxopropanenitrile (CAS# 95882-33-0)
K83	2-(Cyclohexanecarbonyl)-3-phenylacrylonitrile 	ESP $[M+H]^+$: 240.3	F	Benzaldehyde, 3-cyclohexyl-3-oxo-propanenitrile (CAS# 62455-70-3)

Intermediate	Name and Structure	MS	Method	Reagents
K84	2-(cyclopentanecarbonyl)-3-phenylacrylonitrile 	ESP $[M+H]^+$: 226.1	F	Benzaldehyde, 3-cyclopentyl-3-oxopropanenitrile (CAS# 95882-33-0)
K85	3-Phenyl-2-(tetrahydro-furan-2-carbonyl)-acrylonitrile 	ESP $[M+H]^+$: 228.3	H	Benzaldehyde, 3-oxo-3-(tetrahydro-furan-2-yl)-propionitrile (CAS# 1092282-15-9)
K86	2-Cyclohexanecarbonyl-3-(3-fluoro-pyridin-4-yl)-acrylonitrile 	ESP $[M+H]^+$: 259.4	H	3-Fluoroisonicotinaldehyde, 3-cyclohexyl-3-oxo-propanenitrile (CAS# 62455-70-3)

Intermediate	Name and Structure	MS	Method	Reagents
K87	2-Cyclopentanecarbonyl-3-(3-fluoro-pyridin-4-yl)-acrylonitrile 	ESP $[M+H]^+$: 245.4	H	3-Fluoroisonicotinaldehyde, 3-cyclopentyl-3-oxopropanenitrile (CAS# 95882-33-0)
K88	3-Phenyl-2-(tetrahydro-2H-pyran-4-carbonyl)acrylonitrile 	ESP $[M+H]^+$: 242.4	I	Benzaldehyde, 3-oxo-3-(tetrahydro-2H-pyran-4-yl)propanenitrile (CAS# 1010798-64-7)
K89	2-Cyclohexanecarbonyl-3-(2-methyl-pyrimidin-4-yl)-acrylonitrile 	ESP $[M+H]^+$: 256.4	H	2-Methylpyrimidine-4-carbaldehyde, 3-cyclohexyl-3-oxo-propanenitrile (CAS# 62455-70-3)

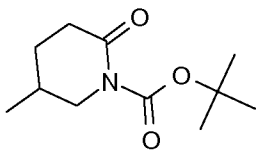
Intermediate	Name and Structure	MS	Method	Reagents
K90	2-(Cyclobutanecarbonyl)-3-(6-methoxypyridin-3-yl)acrylonitrile 	ESP $[M+H]^+$: 243.4	I	6-Methoxynicotinaldehyde, β-Cyclobutyl-β-oxopropionitrile (CAS# 118431-89-3)
K91	2-Cyclohexanecarbonyl-3-pyrimidin-4-yl-acrylonitrile 	ESP $[M+H]^+$: 242.4	H	Pyrimidine-4-carbaldehyde, 3-cyclohexyl-3-oxo-propanenitrile (CAS# 62455-70-3)
K92	2-Cyclopentanecarbonyl-3-pyrimidin-4-yl-acrylonitrile 	ESP $[M+H]^+$: 228.4	H	Pyrimidine-4-carbaldehyde, 3-cyclopentyl-3-oxopropanenitrile (CAS# 95882-33-0)
K93	2-Cyclopentanecarbonyl-3-(2-methyl-pyrimidin-4-yl)-acrylonitrile 		H	2-Methylpyrimidine-4-carbaldehyde, 3-cyclopentyl-3-oxopropanenitrile (CAS# 95882-33-0)

Intermediate	Name and Structure	MS	Method	Reagents
K95	2-Cyclopentanecarbonyl-3-pyridazin-4-yl-acrylonitrile 		H	Pyridazine-4-carbaldehyde, 3-cyclopentyl-3-oxopropanenitrile (CAS# 95882-33-0)
K96	2-Cyclopentanecarbonyl-3-(6-methyl-pyridin-2-yl)-acrylonitrile 	ESP $[M+H]^+$: 241.4	H	6-Methylpicolinaldehyde, 3-cyclopentyl-3-oxopropanenitrile (CAS# 95882-33-0)
K97	2-Cyclopentanecarbonyl-3-pyridin-2-yl-acrylonitrile 		H	Picolinaldehyde, 3-cyclopentyl-3-oxopropanenitrile (CAS# 95882-33-0)
K99	2-Cyclopentanecarbonyl-3-pyrimidin-2-yl-acrylonitrile 	ESP $[M+H]^+$: 228.4	I	Pyrimidine-2-carbaldehyde, 3-cyclopentyl-3-oxopropanenitrile (CAS# 95882-33-0)

Intermediate	Name and Structure	MS	Method	Reagents
K114	2-(Cyclohexanecarbonyl)-3-(3,5-dimethylisoxazol-4-yl)acrylonitrile 	ESN $[M-H]^-$: 257.4	F	3,5-Dimethylisoxazole-4-carbaldehyde, 3-cyclohexyl-3-oxo-propanenitrile (CAS# 62455-70-3)

Intermediate L

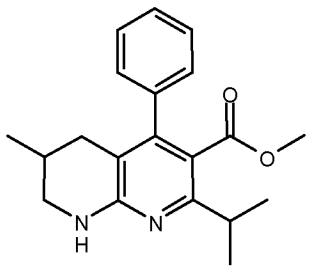
5-Methyl-2-oxo-piperidine-1-carboxylic acid tert-butyl ester

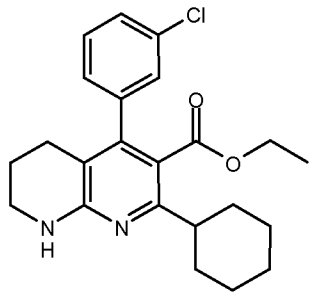
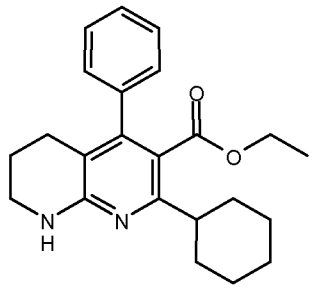
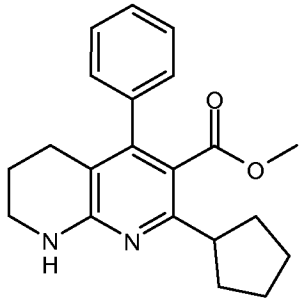


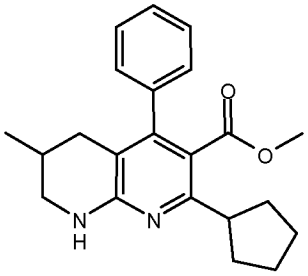
Triethylamine (447 mg, 616 µl, 4.42 mmol), 4-dimethylaminopyridine (54.0 mg, 0.442 mmol) and di-tert-butyl-dicarbonate (1.45 g, 6.63 mmol) were added to a solution of 5-methylpiperidin-2-one (CAS# 3298-16-6) (500 mg, 4.42 mmol) in dry DCM (10 ml) at room temperature and the solution was stirred for 5 h. All volatiles were removed and the remaining oil was purified by silica column chromatography (50 g silica gel, n-hexane/diethyl ether 1:3) to obtain the title compound (717 mg) as yellow oil. MS (ESP): m/z = 214.2 $[M+H]^+$.

General Method M: Lithium bis(trimethylsilyl)amide (1M solution in THF, 1.1 eq) is added to a solution of N-protected lactam (1 eq) in THF (1 ml / mmol) at -30°C and the mixture is stirred for 25 minutes. The mixture is then transferred into a precooled (-20 °C) solution of Knoevenagel condensation products of beta-keto esters and aldehydes (1 eq) in dry THF (1.5 ml / mmol) and the reaction mixture is stirred at -20 °C for 1.5 h. Then saturated NH_4Cl solution is

added and the mixture is extracted with ethyl acetate. The combined extracts are dried (Na_2SO_4) and evaporated. The remaining residue is dissolved in 1,2-dichloroethane (4 ml / mmol), phosphorus pentachloride (1.2 eq) is added and the reaction mixture is heated to 65 °C for 2.5 h. After cooling to 0 °C, ammonia in methanol (2M solution, 6 eq) is added and the precipitating solid is filtered off. The filtrate is concentrated, methanol (5 ml / mmol) and ammonium acetate (4 eq) are added and the mixture is heated to 60 °C for 4 h. Then copper (I) acetate (1.05 eq) is added and the reaction mixture is heated to reflux overnight, cooled to room temperature and filtered. The filtrate is concentrated, Na_2CO_3 solution (pH 10) is added and the mixture is extracted with ethyl acetate. The combined extracts are washed with Na_2CO_3 solution (pH 10), dried (Na_2SO_4) and evaporated and the remaining residue is purified by column chromatography.

Intermediate	Name and Structure	MS	Method	Reagents
AP1	Methyl 2-isopropyl-6-methyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylate 	ESP $[M+H]^+$: 325.3	M	Methyl 4-methyl-3-oxo-2-(phenylmethylene)pentanoate (CAS# 912998-81-3), intermediate L

Intermediate	Name and Structure	MS	Method	Reagents
AP4	Ethyl 4-(3-chlorophenyl)-2-cyclohexyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylate 	ESP $[M+H]^+$: 399.1	M	Intermediate K4, 2-oxopiperidine-1-carboxylic acid tert-butyl ester (CAS# 85908-96-9)
AP5	Ethyl 2-cyclohexyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylate 	ESP $[M+H]^+$: 365.2	M	Intermediate K5, 2-oxopiperidine-1-carboxylic acid tert-butyl ester (CAS# 85908-96-9)
AP6	Methyl 2-cyclopentyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylate 	ESP $[M+H]^+$: 337.3	M	Intermediate K6, 2-oxopiperidine-1-carboxylic acid tert-butyl ester (CAS# 85908-96-9)

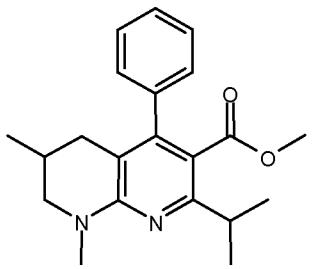
Intermediate	Name and Structure	MS	Method	Reagents
AP7	Methyl 2-cyclopentyl-6-methyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylate 	ESP $[M+H]^+$: 351.5	M	Intermediate K6, Intermediate L

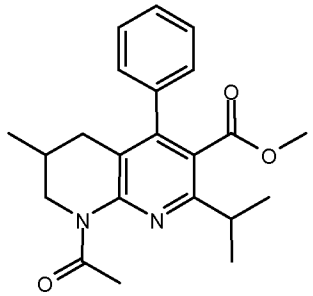
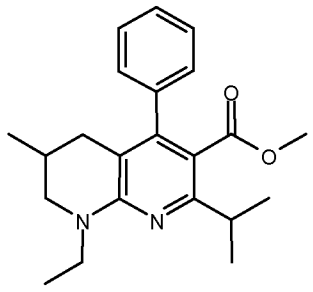
General Method N: To a solution of intermediate (AP) (1 eq) in dry DMF (7 ml / mmol) is added carefully sodium hydride (55% in mineral oil, 1.1 eq) at 0°C and the resulting mixture is stirred for 45 minutes. Then a solution of an alkyl iodide (1.1 eq) in dry DMF (6 ml / mmol) is added, the mixture is allowed to warm to room temperature and is stirred overnight. The reaction mixture is then carefully diluted with water and the pH adjusted to 10 by addition of saturated Na_2CO_3 solution. The mixture is extracted with ethyl acetate and the combined organic layers are washed with Na_2CO_3 solution (pH 10), dried (Na_2SO_4) and evaporated. The remaining residue is purified by silica column chromatography.

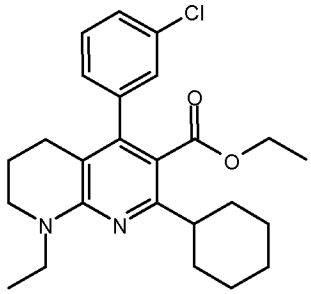
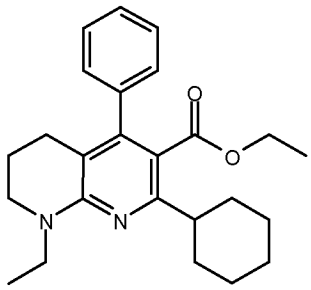
General Method O: A mixture of intermediate (AP) (1 eq), triethylamine (3 eq) and a carboxylic acid anhydride (2 eq) in dry DCM (9 ml / mmol) is stirred in a sealed tube at 50°C for 2 d. The solvent is removed and the remaining residue is purified by silica column chromatography.

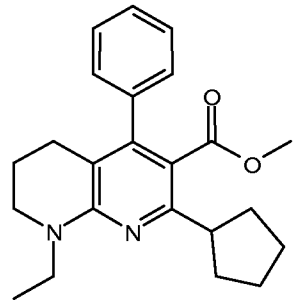
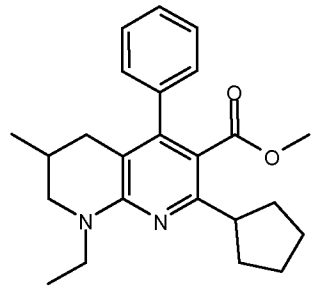
General Method P: A solution of a cyclic ketone (0.85 eq) in THF (0.3 ml / mmol) is added dropwise to a solution of NaHMDS (1M solution in THF, 1 eq) in THF (0.5 ml / mmol) at -78°C. The mixture is allowed to warm to 0°C and is maintained at this temperature for 15 minutes before it is cooled again to -78°C. A pre-cooled solution of Knoevenagel condensation products of beta-keto esters and aldehydes (1 eq) in THF (0.5 ml / mmol) is added quickly and the

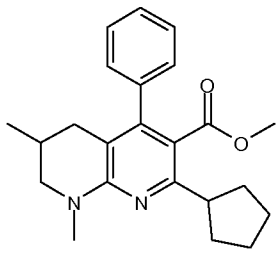
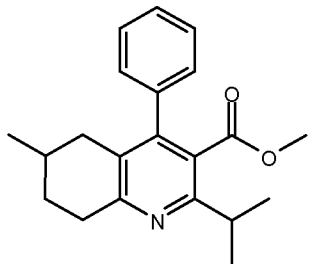
reaction mixture is stirred at -78°C for 4 h. Then a solution of acetic acid (4.3 eq) in THF (0.1 ml / mmol) is added, the mixture is warmed to room temperature, diluted with water and extracted with ethyl acetate. The combined extracts are washed with water and brine, dried (Na_2SO_4) and evaporated. The remaining residue is dissolved in ethanol (2.5 ml / mmol), ammonium acetate (12.5 eq) and p-toluenesulfonic acid monohydrate (0.05 eq) are added and the mixture is heated to reflux for 1.5 d. The reaction mixture is then concentrated and DCM is added. The white precipitate is filtered off and the filtrate is evaporated. The remaining residue is dissolved in DCM (2.5 ml / mmol), 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (0.95 eq) is added at room temperature and the reaction mixture is stirred for 2 to 2.5 h. Then saturated $NaHCO_3$ solution is added and the mixture is extracted with DCM. The combined organic layers are washed with saturated $NaHCO_3$ solution twice, dried (Na_2SO_4) and evaporated. The remaining residue is purified by silica column chromatography.

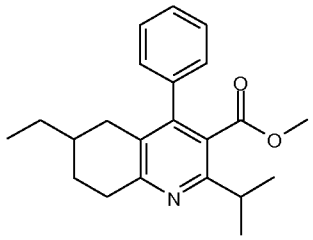
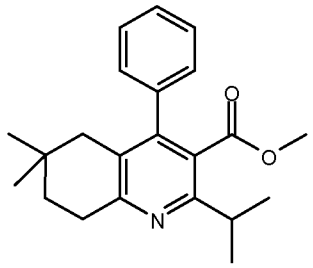
Intermediate	Name and Structure	MS	Method	Reagents
E1	Methyl 2-isopropyl-6,8-dimethyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylate 	ESP $[M+H]^+$: 339.3	N	Intermediate AP1, methyl iodide

Intermediate	Name and Structure	MS	Method	Reagents
E2	Methyl 8-acetyl-2-isopropyl-6-methyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylate 	ESP $[M+H]^+$: 367.1	O	Intermediate AP1, acetic anhydride
E3	Methyl 8-ethyl-2-isopropyl-6-methyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylate 	ESP $[M+H]^+$: 353.3	N	Intermediate AP1, ethyl iodide

Intermediate	Name and Structure	MS	Method	Reagents
E4	Ethyl 4-(3-chlorophenyl)-2-cyclohexyl-8-ethyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylate 	ESP $[M+H]^+$: 427.5	N	Intermediate AP4, ethyl iodide
E5	Ethyl 2-cyclohexyl-8-ethyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylate 	ESP $[M+H]^+$: 393.2	N	Intermediate AP5, ethyl iodide

Intermediate	Name and Structure	MS	Method	Reagents
E6	Methyl 2-cyclopentyl-8-ethyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylate 	ESP $[M+H]^+$: 365.2	N	Intermediate AP6, ethyl iodide
E7	Methyl 2-cyclopentyl-8-ethyl-6-methyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylate 	ESP $[M+H]^+$: 379.5	N	Intermediate AP7, ethyl iodide

Intermediate	Name and Structure	MS	Method	Reagents
E8	Methyl 2-cyclopentyl-6,8-dimethyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylate 	ESP $[M+H]^+$: 365.5	N	Intermediate AP7, methyl iodide
E9	Methyl 2-isopropyl-6-methyl-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carboxylate 	ESP $[M+H]^+$: 324.2	P	Methyl 4-methyl-3-oxo-2-(phenylmethylene)pentanoate (CAS# 912998-81-3), 4-methyl-cyclohexanone

Intermediate	Name and Structure	MS	Method	Reagents
E10	Methyl 6-ethyl-2-isopropyl-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carboxylate 	ESP $[M+H]^+$: 338.3	P	Methyl 4-methyl-3-oxo-2-(phenylmethylene)pentanoate (CAS# 912998-81-3), 4-ethyl-cyclohexanone
E11	2-Isopropyl-6,6-dimethyl-4-phenyl-5,6,7,8-tetrahydro-quinoline-3-carboxylic acid methyl ester 	ESP $[M+H]^+$: 338.2	P	Methyl 4-methyl-3-oxo-2-(phenylmethylene)pentanoate (CAS# 912998-81-3), 4,4-dimethyl-cyclohexanone

Intermediates P

General Method Q:

Step 1: A solution of the ketone (4.46 mmol, 0.85 eq) in THF (3 ml) is added dropwise at -78 °C to a solution of LiHMDS (1M in THF, 5.24 mmol, 1 eq) in THF (3 ml). The solution is stirred for 1 h at -78 °C. A pre-cooled solution of the Knoevenagel adduct (Intermediate K, 5.24 mmol, 1 eq) in THF (3 ml) is added quickly via a double-tip needle at a temperature below -67 °C. The

solution is stirred at -78 °C for 5 h and then quenched by adding a solution of acetic acid (4.3 eq) in THF (1.5 ml). The mixture is allowed to warm to room temperature, diluted with water and extracted with ethyl acetate. The organic layers are combined, washed with water and brine, dried over $MgSO_4$ and concentrated in vacuo. The product can be purified by flash chromatography.

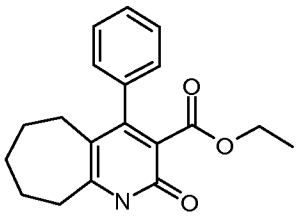
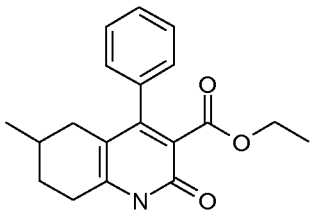
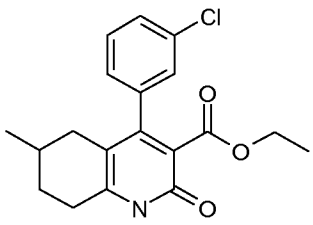
Step 2: The product of step 1 (1.21 mmol) is combined with ammonium acetate (10 eq) and heated to 120 °C under air for 4-10 h while stirring. After cooling to room temperature, the mixture is extracted with ethyl acetate. The organic layers are combined, washed with water and brine, dried over $MgSO_4$ and concentrated in vacuo.

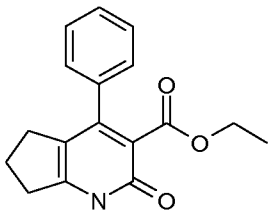
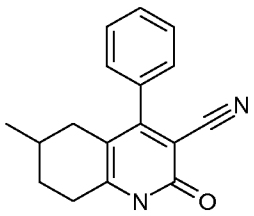
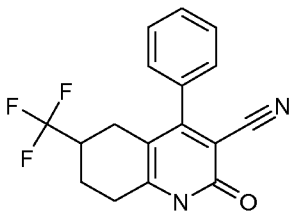
Step 3: The product of step 2 (1.18 mmol) is combined with $FeCl_3$ (3 eq) and propionic acid (5.5 ml) and heated to reflux for 1 h. The mixture is allowed to cool to room temperature, diluted with 1 M HCl and extracted with DCM. The organic layers are combined, washed with saturated aqueous $NaHCO_3$ solution and brine, dried over $MgSO_4$ and concentrated in vacuo. The product can be purified by flash chromatography to give the pyridone (Intermediate P).

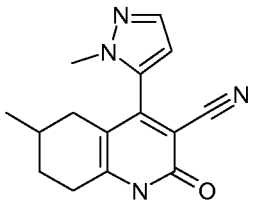
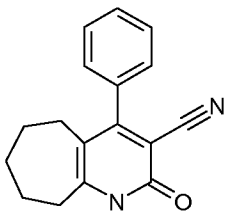
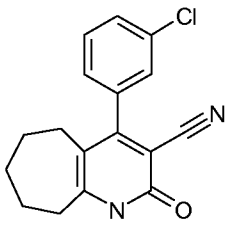
General Method R:

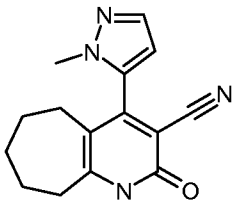
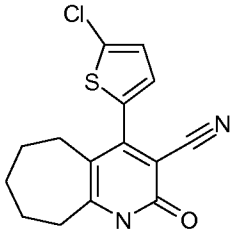
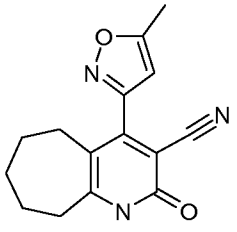
A mixture of the ketone (1 eq), the Knoevenagel adduct (Intermediate K, 1 to 2 eq, see table) and ammonium acetate (10 eq) is stirred at 170 °C under air for 5-10 h. After cooling to room temperature, the mixture is diluted with water and extracted with ethyl acetate. The organic layers are combined, washed with water and brine, dried over $MgSO_4$ and concentrated in vacuo. The product can be purified by flash chromatography or crystallization.

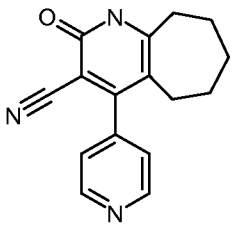
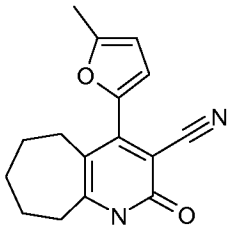
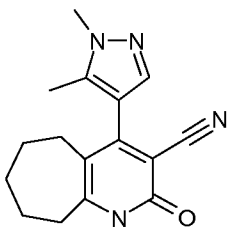
Intermediate	Name and Structure	MS	Method	Reagents

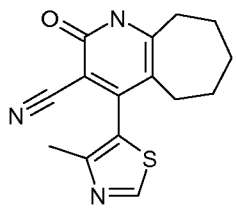
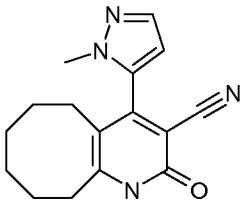
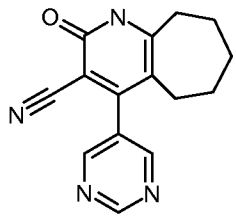
Intermediate	Name and Structure	MS	Method	Reagents
P14	Ethyl 2-oxo-4-phenyl-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carboxylate 	ESP $[M+H]^+$: 312.1	Q	Benzylidene malonic acid diethyl ester (CAS# 5292-53-5), cycloheptanone
P16	Ethyl 6-methyl-2-oxo-4-phenyl-1,2,5,6,7,8-hexahydroquinoline-3-carboxylate 	ESP $[M+H]^+$: 312.3	Q	Benzylidene malonic acid diethyl ester (CAS# 5292-53-5), 4-methylcyclohexanone
P20	Ethyl 4-(3-chlorophenyl)-6-methyl-2-oxo-1,2,5,6,7,8-hexahydroquinoline-3-carboxylate 	ESN $[M-H]^-$: 344.0	Q	Intermediate K20, 4-methylcyclohexanone

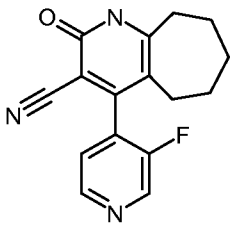
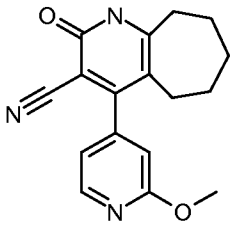
Intermediate	Name and Structure	MS	Method	Reagents
P21	Ethyl 2-oxo-4-phenyl-2,5,6,7-tetrahydro-1H-cyclopenta[b]pyridine-3-carboxylate 	ESN [M-H]$^-$: 282.0	Q	Benzylidene malonic acid diethyl ester (CAS# 5292-53-5), cyclopentanone
P25	6-Methyl-2-oxo-4-phenyl-1,2,5,6,7,8-hexahydroquinoline-3-carbonitrile 	ESN [M-H]$^-$: 262.9	R	2-Cyano-3-phenylpropenoic acid ethyl ester (CAS# 2025-40-3, 2 eq), 4-methylcyclohexanone
P27	2-Oxo-4-phenyl-6-(trifluoromethyl)-1,2,5,6,7,8-hexahydroquinoline-3-carbonitrile 	ESP [M+H]$^+$: 319.3	R	2-Cyano-3-phenylpropenoic acid ethyl ester (CAS# 2025-40-3, 2 eq), 4-(trifluoromethyl)-cyclohexanone

Intermediate	Name and Structure	MS	Method	Reagents
P29	6-Methyl-4-(1-methyl-1H-pyrazol-5-yl)-2-oxo-1,2,5,6,7,8-hexahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 269.0	R	Intermediate K29 (1.2 eq), 4-methylcyclohexanone
P30	2-Oxo-4-phenyl-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 265.0	R	2-Cyano-3-phenylpropenoic acid ethyl ester (CAS# 2025-40-3, 1.2 eq), cycloheptanone
P32	4-(3-Chloro-phenyl)-2-oxo-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 299.4	R	Intermediate K32 (1.2 eq), cycloheptanone

Intermediate	Name and Structure	MS	Method	Reagents
P34	4-(1-Methyl-1H-pyrazol-5-yl)-2-oxo-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 269.2	R	Intermediate K29 (1.2 eq), cycloheptanone
P38	4-(5-Chlorothiophen-2-yl)-2-oxo-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 305.1	R	Intermediate K38 (1.2 eq), cycloheptanone
P41	4-(5-Methyl-isoxazol-3-yl)-2-oxo-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 270.3	R	Intermediate K41 (1.2 eq), cycloheptanone

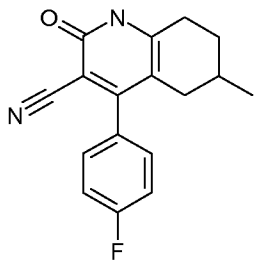
Intermediate	Name and Structure	MS	Method	Reagents
P44	2-Oxo-4-(pyridin-4-yl)-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 266.1	R	Intermediate K44 (1.2 eq), cycloheptanone
P46	4-(5-Methylfuran-2-yl)-2-oxo-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 269.3	R	Intermediate K46 (1.2 eq), cycloheptanone
P48	4-(1,5-Dimethyl-1H-pyrazol-4-yl)-2-oxo-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 283.4	R	Intermediate K48 (1.2 eq), cycloheptanone

Intermediate	Name and Structure	MS	Method	Reagents
P56	4-(4-Methylthiazol-5-yl)-2-oxo-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 286.3	R	Intermediate K56 (1.2 eq), cycloheptanone
P58	4-(2-Methyl-2H-pyrazol-3-yl)-2-oxo-1,2,5,6,7,8,9,10-octahydro-cycloocta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 283.4	R	Intermediate K29 (1.2 eq), cyclooctanone
P61	2-Oxo-4-pyrimidin-5-yl-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 267.4	R	Intermediate K61 (1.2 eq), cycloheptanone

Intermediate	Name and Structure	MS	Method	Reagents
P62	4-(3-Fluoropyridin-4-yl)-2-oxo-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 284.3	R	Intermediate K62 (1.2 eq), cycloheptanone
P63	4-(2-Methoxy-pyridin-4-yl)-2-oxo-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 296.4	R	Intermediate K63 (1.2 eq), cycloheptanone

Intermediate P35

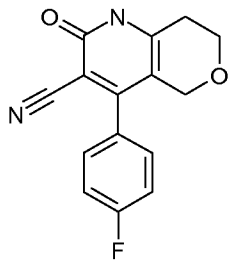
4-(4-Fluoro-phenyl)-6-methyl-2-oxo-1,2,5,6,7,8-hexahydro-quinoline-3-carbonitrile



To a solution of 2-cyano-3-(4-fluorophenyl)acrylamide (Intermediate K35, 2 g) in DMSO (21.0 ml) were added 4-methylcyclohexanone (1.18 g) and potassium tert-butoxide (1.18 g) at room temperature under air with exclusion of moisture. After stirring for 30 min, MS indicated formation of the Michael adduct. Potassium tert-butoxide (3.54 g) was added and stirring was continued at room temperature for 3 h. Water (80 ml) was added and the mixture was cooled in an ice bath. Slowly the mixture was acidified with 25 % HCl. The precipitate was collected by filtration, washed with water and dried. The crude material was purified by flash chromatography (SiO_2, 0% to 100% EtOAc in n-heptane) to afford the title compound (1.02 g), sufficiently pure to be used in the next step without further purification as an off-white solid. MS (ESP): m/z = 283.3 $[M+H]^+$.

Intermediate P36

4-(4-Fluoro-phenyl)-2-oxo-1,5,7,8-tetrahydro-2H-pyrano[4,3-b]pyridine-3-carbonitrile



In analogy to the synthesis of Intermediate P35, the title compound was synthesized starting from 2-cyano-3-(4-fluorophenyl)acrylamide (Intermediate K35) and dihydro-2H-pyran-4(3H)-one. MS (ESP): m/z = 271.0 $[M+H]^+$.

Intermediates E/N

General Method S:

Step 1: A solution of the pyridone (Intermediate P, 0.51 mmol, 1 eq) in dry DMA (2.73 ml) is added dropwise to a suspension of sodium hydride (55% in mineral oil, 1.3 eq) in dry DMA (0.91 ml). The mixture is stirred for 45 min. A solution of N-phenylbis(trifluoromethanesulfonimide) (1.3 eq) in DMA (2.73 ml) is added dropwise, then the reaction is stirred at room temperature overnight. The reaction is quenched with saturated

aqueous NH_4Cl solution and extracted with ethyl acetate. The organic layers are combined, washed with water and brine, dried over $MgSO_4$ and concentrated in vacuo. The product can be purified by flash chromatography.

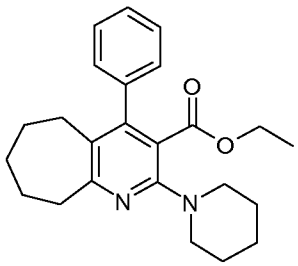
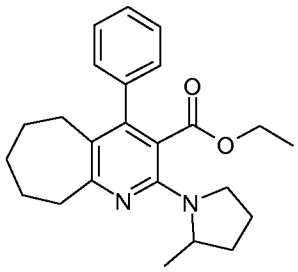
Step 2: A suspension of the triflate obtained in step 1 (0.31 mmol, 1 eq), a primary or secondary amine (4 eq) and potassium carbonate (2 eq) in THF (4.7 ml) is heated to 70 °C for 1-10 h. After cooling to room temperature, the mixture is diluted with water and extracted with ethyl acetate. The organic layers are combined, washed with water and brine, dried over $MgSO_4$ and concentrated in vacuo. The product can be purified by flash chromatography.

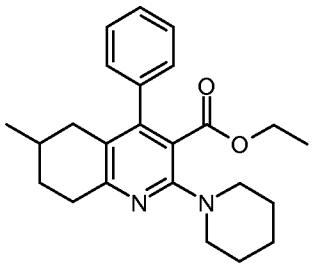
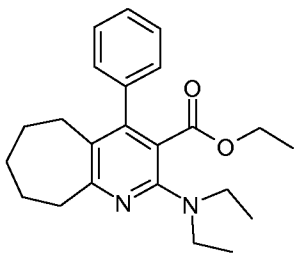
General Method T:

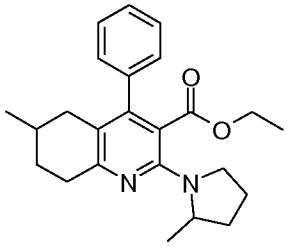
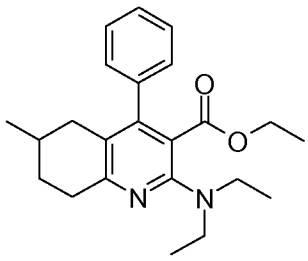
Step 1: A mixture of the pyridone (Intermediate P, 3.0 mmol, 1 eq) and phosphorus oxychloride (30 eq) is stirred at reflux for 2-20 h. After cooling to room temperature the mixture is slowly and carefully diluted with water, neutralized with 2 M aqueous NaOH and extracted with DCM. The organic layers are combined, washed with water and brine, dried over $MgSO_4$ and concentrated in vacuo. The product can be purified by flash chromatography.

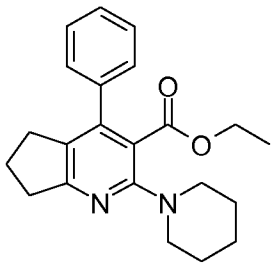
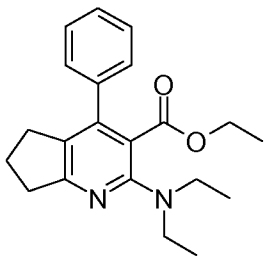
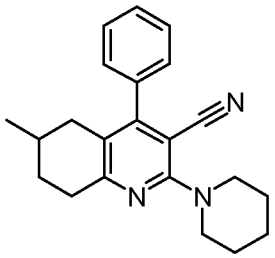
Step 2: A solution of the 2-chloropyridine obtained in step 1 (0.35 mmol, 1 eq), a primary or secondary amine (2 eq) and triethylamine (3 eq) in DMF (1.5 ml) is heated to 120 °C for 1-20 h. If the reaction does not reach completion, more of the primary or secondary amine and triethylamine can be added. After cooling to room temperature, the mixture is diluted with water and extracted with ethyl acetate. The organic layers are combined, washed with water and brine, dried over $MgSO_4$ and concentrated in vacuo. The product can be purified by flash chromatography.

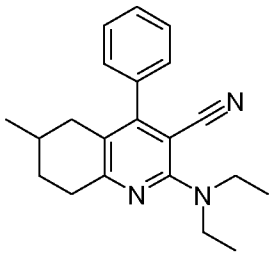
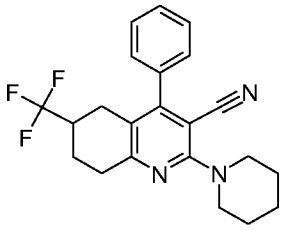
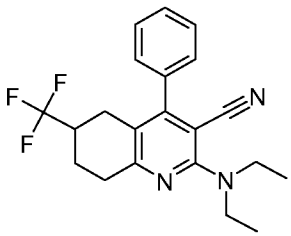
Intermediate	Name and Structure	MS	Method	Reagents

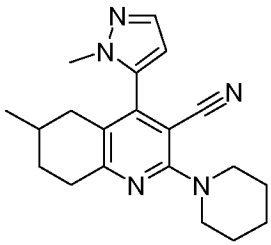
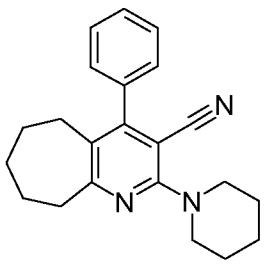
Intermediate	Name and Structure	MS	Method	Reagents
E14	Ethyl 4-phenyl-2-(piperidin-1-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylate 	ESP $[M+H]^+$: 379.5	S	Intermediate P14, piperidine
E15	Ethyl 2-(2-methylpyrrolidin-1-yl)-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylate 	ESP $[M+H]^+$: 379.5	S	Intermediate P14, 2-methylpyrrolidine

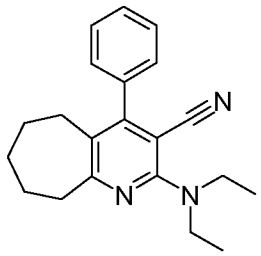
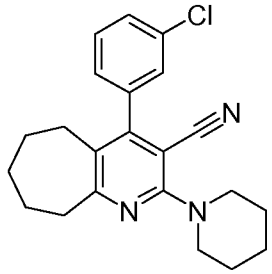
Interm ediate	Name and Structure	MS	Method	Reagents
E16	Ethyl 6-methyl-4-phenyl-2-(piperidin-1-yl)-5,6,7,8-tetrahydroquinoline-3-carboxylate 	ESP $[M+H]^+$: 379.5	S	Intermediate P16, piperidine
E17	Ethyl 2-(diethylamino)-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylate 	ESP $[M+H]^+$: 367.3	S	Intermediate P14, diethylamine

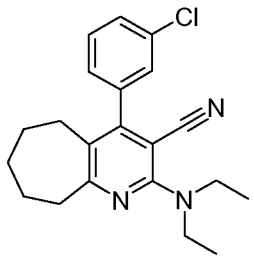
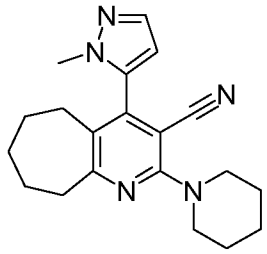
Intermediate	Name and Structure	MS	Method	Reagents
E18	Ethyl 6-methyl-2-(2-methylpyrrolidin-1-yl)-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carboxylate 	ESP $[M+H]^+$: 379.4	S	Intermediate P16, 2-methylpyrrolidine
E19	Ethyl 2-(diethylamino)-6-methyl-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carboxylate 	ESP $[M+H]^+$: 367.1	S	Intermediate P16, diethylamine

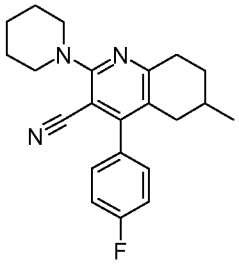
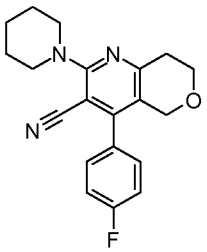
Intermediate	Name and Structure	MS	Method	Reagents
E21	Ethyl 4-phenyl-2-(piperidin-1-yl)-6,7-dihydro-5H-cyclopenta[b]pyridine-3-carboxylate 	ESP $[M+H]^+$: 351.3	S	Intermediate P21, piperidine
E22	Ethyl 2-(diethylamino)-4-phenyl-6,7-dihydro-5H-cyclopenta[b]pyridine-3-carboxylate 	ESP $[M+H]^+$: 339.4	S	Intermediate P21, diethylamine
N25	6-Methyl-4-phenyl-2-(piperidin-1-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 332.2	T	Intermediate P25, piperidine

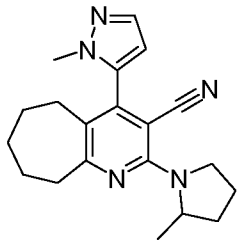
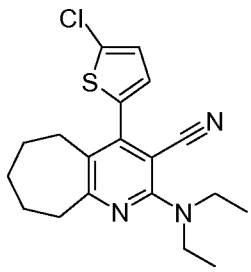
Intermediate	Name and Structure	MS	Method	Reagents
N26	2-(Diethylamino)-6-methyl-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 320.3	T	Intermediate P25, diethylamine
N27	4-Phenyl-2-(piperidin-1-yl)-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 386.5	S	Intermediate P27, piperidine
N28	2-(Diethylamino)-4-phenyl-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 374.6	S	Intermediate P27, diethylamine

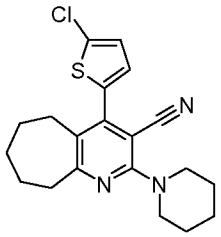
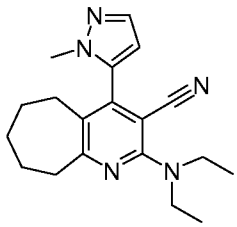
Intermediate	Name and Structure	MS	Method	Reagents
N29	6-Methyl-4-(1-methyl-1H-pyrazol-5-yl)-2-(piperidin-1-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 336.4	S	Intermediate P29, piperidine
N30	4-Phenyl-2-(piperidin-1-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 332.3	S	Intermediate P30, piperidine

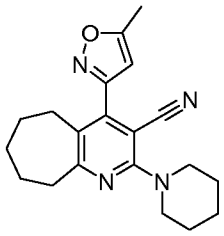
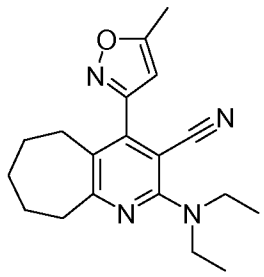
Interm ediate	Name and Structure	MS	Method	Reagents
N31	2-(Diethylamino)-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 320.1	S	Intermediate P30, diethylamine
N32	4-(3-Chlorophenyl)-2-(piperidin-1-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 366.1	S	Intermediate P32, piperidine

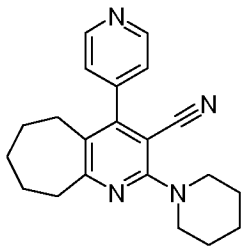
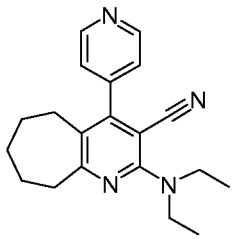
Intermediate	Name and Structure	MS	Method	Reagents
N33	4-(3-Chlorophenyl)-2-(diethylamino)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 354.3	S	Intermediate P32, diethylamine
N34	4-(1-Methyl-1H-pyrazol-5-yl)-2-(piperidin-1-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 336.2	S	Intermediate P34, piperidine

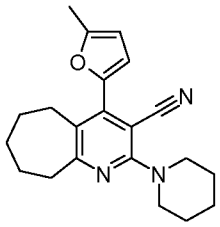
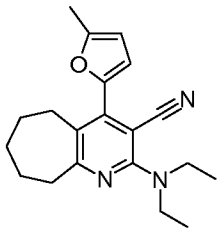
Intermediate	Name and Structure	MS	Method	Reagents
N35	4-(4-Fluorophenyl)-6-methyl-2-(piperidin-1-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 350.3	T	Intermediate P35, piperidine
N36	4-(4-Fluorophenyl)-2-(piperidin-1-yl)-7,8-dihydro-5H-pyrano[4,3-b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 338.4	T	Intermediate P36, piperidine

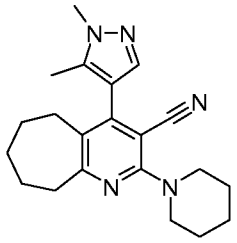
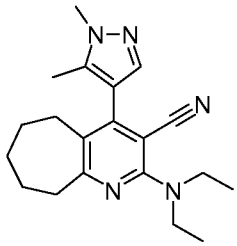
Intermediate	Name and Structure	MS	Method	Reagents
N37	4-(1-Methyl-1H-pyrazol-5-yl)-2-(2-methylpyrrolidin-1-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 336.2	S	Intermediate P34, 2-methylpyrrolidine
N38	4-(5-Chlorothiophen-2-yl)-2-(diethylamino)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 360.2	S	Intermediate P38, diethylamine

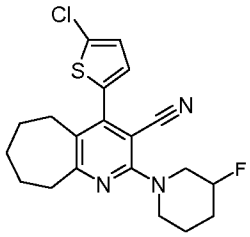
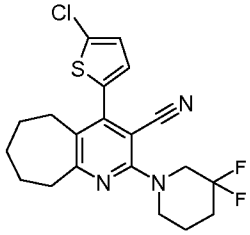
Intermediate	Name and Structure	MS	Method	Reagents
N39	4-(5-Chlorothiophen-2-yl)-2-(piperidin-1-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 372.2	S	Intermediate P38, piperidine
N40	2-(Diethylamino)-4-(1-methyl-1H-pyrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 324.4	S	Intermediate P34, diethylamine

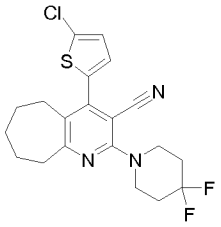
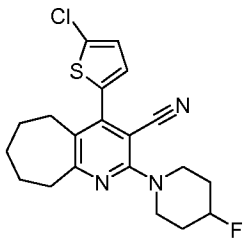
Intermediate	Name and Structure	MS	Method	Reagents
N41	4-(5-Methylisoxazol-3-yl)-2-(piperidin-1-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 337.5	S	Intermediate P41, piperidine
N42	2-(Diethylamino)-4-(5-methylisoxazol-3-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 325.5	S	Intermediate P41, diethylamine

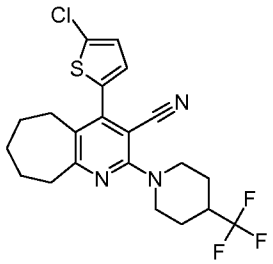
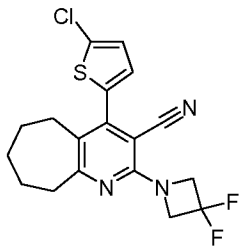
Interm ediate	Name and Structure	MS	Method	Reagents
N44	2-(Piperidin-1-yl)-4-(pyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 333.4	S	Intermediate P44, piperidine
N45	2-(Diethylamino)-4-(pyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 321.3	S	Intermediate P44, diethylamine

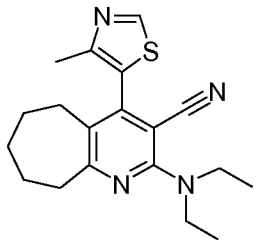
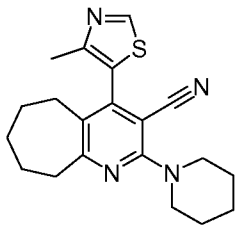
Intermediate	Name and Structure	MS	Method	Reagents
N46	4-(5-Methylfuran-2-yl)-2-(piperidin-1-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 336.5	S	Intermediate P46, piperidine
N47	2-(Diethylamino)-4-(5-methylfuran-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 324.5	S	Intermediate P46, diethylamine

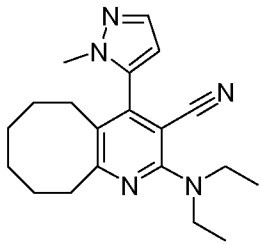
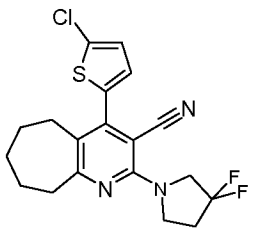
Intermediate	Name and Structure	MS	Method	Reagents
N48	4-(1,5-Dimethyl-1H-pyrazol-4-yl)-2-(piperidin-1-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 350.5	S	Intermediate P48, piperidine
N49	2-(Diethylamino)-4-(1,5-dimethyl-1H-pyrazol-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 338.5	S	Intermediate P48, diethylamine

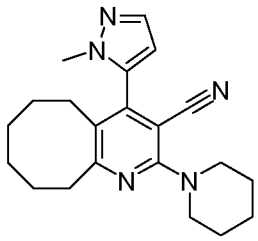
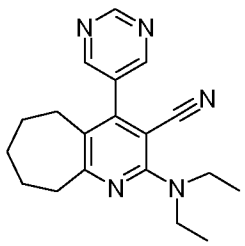
Intermediate	Name and Structure	MS	Method	Reagents
N50	4-(5-Chloro-thiophen-2-yl)-2-(3-fluoro-piperidin-1-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 390.4	S	Intermediate P38, 3-fluoropiperidine
N51	4-(5-Chloro-thiophen-2-yl)-2-(3,3-difluoro-piperidin-1-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 408.4	S	Intermediate P38, 3,3-difluoropiperidine

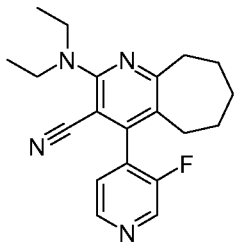
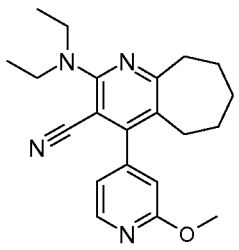
Intermediate	Name and Structure	MS	Method	Reagents
N52	4-(5-Chlorothiophen-2-yl)-2-(4,4-difluoropiperidin-1-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 		S	Intermediate P38, 4,4-difluoropiperidine
N53	4-(5-Chlorothiophen-2-yl)-2-(4-fluoropiperidin-1-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 390.3	S	Intermediate P38, 4-fluoropiperidine

Intermediate	Name and Structure	MS	Method	Reagents
N54	4-(5-Chloro-thiophen-2-yl)-2-(4-trifluoromethyl-piperidin-1-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 		S	Intermediate P38, 4-(trifluoromethyl)piperidine
N55	4-(5-Chlorothiophen-2-yl)-2-(3,3-difluoroazetidin-1-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 380.3	S	Intermediate P38, 3,3-difluoroazetidine

Intermediate	Name and Structure	MS	Method	Reagents
N56	2-(Diethylamino)-4-(4-methylthiazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 341.4	S	Intermediate P56, diethylamine
N57	4-(4-Methylthiazol-5-yl)-2-(piperidin-1-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 353.4	S	Intermediate P56, piperidine

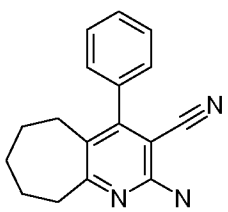
Intermediate	Name and Structure	MS	Method	Reagents
N58	2-(Diethylamino)-4-(1-methyl-1H-pyrazol-5-yl)-5,6,7,8,9,10-hexahydrocycloocta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 338.5	S	Intermediate P58, diethylamine
N59	4-(5-Chloro-thiophen-2-yl)-2-(3,3-difluoro-pyrrolidin-1-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 		S	Intermediate P38, 3,3-difluoropyrrolidine

Intermediate	Name and Structure	MS	Method	Reagents
N60	4-(1-Methyl-1H-pyrazol-5-yl)-2-(piperidin-1-yl)-5,6,7,8,9,10-hexahydrocycloocta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 350.5	S	Intermediate P58, piperidine
N61	2-(Diethylamino)-4-(pyrimidin-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 322.4	S	Intermediate P61, diethylamine

Intermediate	Name and Structure	MS	Method	Reagents
N62	2-(Diethylamino)-4-(3-fluoropyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 339.4	S	Intermediate P62, diethylamine
N63	2-Diethylamino-4-(2-methoxy-pyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 351.5	S	Intermediate P63, diethylamine

Intermediate N64

2-Amino-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile

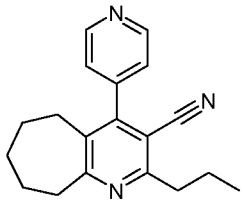


Prepared according to: Kambe, Satoshi; Saito, Koji; Sakurai, Akio; Midorikawa, Hiroshi

Synthesis **1980**, *5*, 366-8.

Intermediate N65

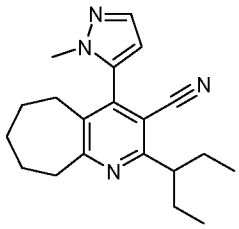
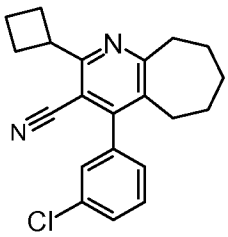
2-Propyl-4-pyridin-4-yl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile

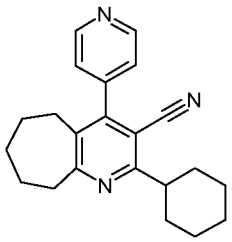
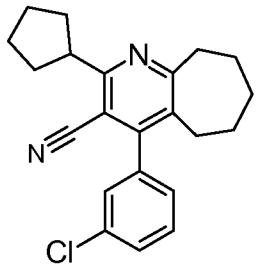
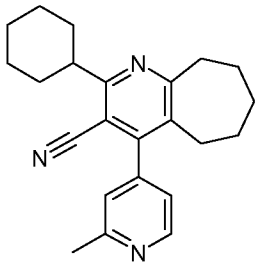


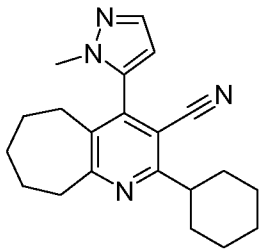
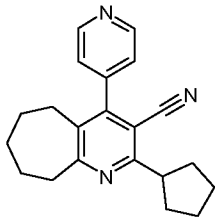
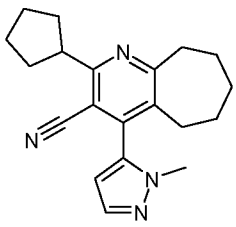
Intermediate P44 was converted to 3-cyano-4-(pyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-yl trifluoromethanesulfonate using General Method S, step 1. 3-Cyano-4-(pyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-yl trifluoromethanesulfonate (1096 mg), n-propylboronic acid (727 mg) and potassium phosphate tribasic (1.79 g) were combined with toluene (34.4 ml), molsieves (4 Å) were added and the mixture was stirred at room temperature for 5 min. (1,3-Diisopropylimidazol-2-ylidene)(3-chloropyridyl)palladium(II) dichloride (PEPPSI) (150 mg) was added and the reaction mixture was heated to 100°C for 52 h. (1,3-Diisopropylimidazol-2-ylidene)(3-chloropyridyl)palladium(II) dichloride (150 mg) was added and stirring at 100 °C was continued for 24 h. The reaction mixture was filtered with EtOAc and water through glass fiber paper, then it was extracted with EtOAc, the organic phases were washed with water and brine, dried over $MgSO_4$ and concentrated in vacuo. The crude material was purified by flash chromatography (silica gel, 50 g, 5% to 60% EtOAc in n-heptane) to give the title compound (156 mg) as an off-white solid. MS (ESP): m/z = 292.4 $[M+H]^+$.

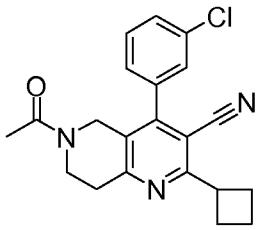
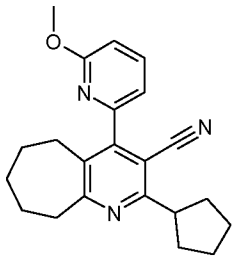
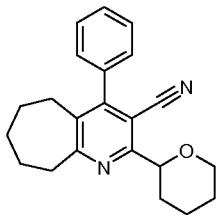
General Method U: The Knoevenagel condensation product (Intermediate K, 1.1 mmol, 1.2 eq), ketone (1 eq) and ammonium acetate (10 eq) is combined and heated to 170 °C for 2.5 h in an open flask. The reaction mixture is cooled to room temperature, diluted with water and extracted 3 times with EtOAc. Combined organic phases are re-extracted with water and brine and dried over $MgSO_4$. Evaporation of the solvent is followed by either crystallization or purification by chromatography or using it as such in the next step without further purification.

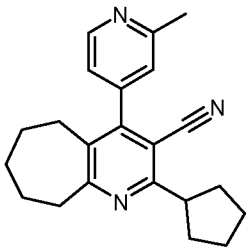
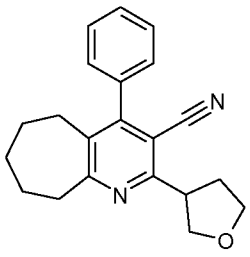
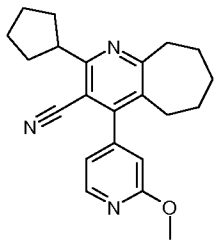
General Method V: A suspension of aldehyde (2.8 mmol, 1 eq), ketone (1 eq), ketonitrile (1 eq), ammonium acetate (5 eq) and toluene (9 ml) is refluxed for 50 min. The reaction mixture is cooled to room temperature, diluted with water and extracted 3 times with EtOAc. The combined organic phases are evaporated and the dihydropyridine-intermediate is dissolved in acetone (14 ml). At room temperature a suspension of ceric ammonium nitrate (3.1 g, 2 eq) in water (2 ml) is slowly added and the yellow reaction mixture is stirred for 30 min. After evaporation of the solvents the residue is extracted with water / EtOAc (3x). The combined organic phases are concentrated and purified by crystallization or chromatography.

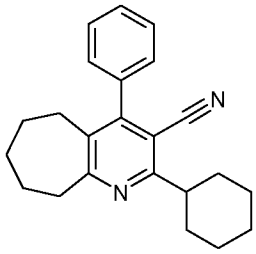
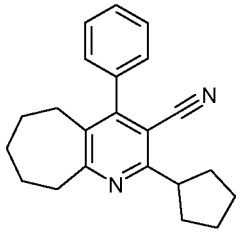
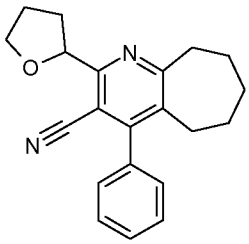
Intermediate	Name and Structure	MS	Method	Reagents
N66	4-(1-Methyl-1H-pyrazol-5-yl)-2-(pentan-3-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 323.2	U	Intermediate K66, cycloheptanone
N67	4-(3-Chlorophenyl)-2-cyclobutyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 337.1	U	Intermediate K67, cycloheptanone

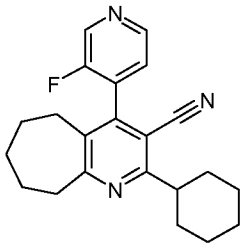
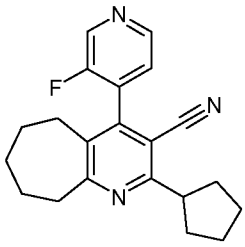
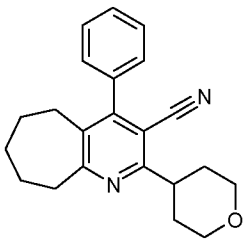
Intermediate	Name and Structure	MS	Method	Reagents
N68	2-Cyclohexyl-4-(pyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 332.5	U	Intermediate K68, cycloheptanone
N69	4-(3-Chlorophenyl)-2-cyclopentyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 351.4	U	Intermediate K69, cycloheptanone
N70	2-Cyclohexyl-4-(2-methylpyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 346.5	U	Intermediate K70, cycloheptanone

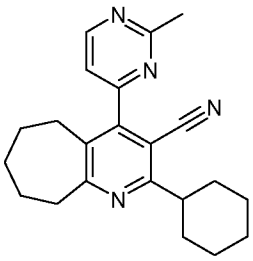
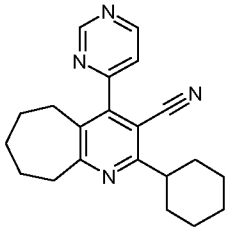
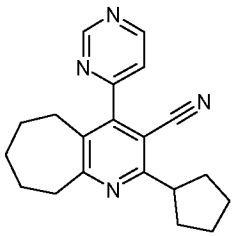
Intermediate	Name and Structure	MS	Method	Reagents
N74	2-Cyclohexyl-4-(1-methyl-1H-pyrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 335.5	U	Intermediate K74, cycloheptanone
N75	2-Cyclopentyl-4-pyridin-4-yl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 318.4	U	Intermediate K75, cycloheptanone
N76	2-Cyclopentyl-4-(1-methyl-1H-pyrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 321.4	U	Intermediate K76, cycloheptanone

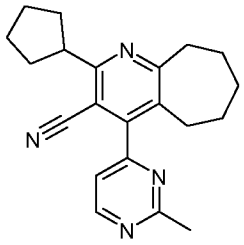
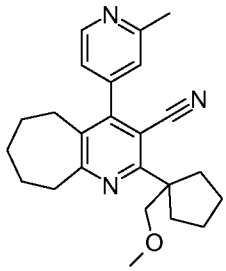
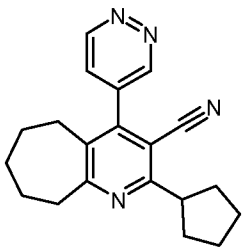
Intermediate	Name and Structure	MS	Method	Reagents
N77	6-Acetyl-4-(3-chlorophenyl)-2-cyclobutyl-5,6,7,8-tetrahydro-[1,6]naphthyridin-3-carbonitrile 	ESP $[M+H]^+$: 366.4	U	Intermediate K67, 1-acetylpiperidin-4-one
N78	2-Cyclopentyl-4-(6-methoxypyridin-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 348.5	U	Intermediate K78, cycloheptanone
N79	4-Phenyl-2-(tetrahydro-2H-pyran-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 333.4	U	Intermediate K79, cycloheptanone

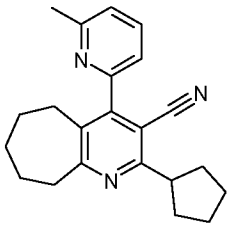
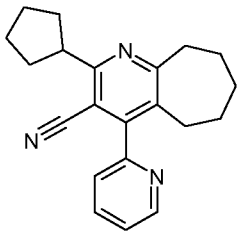
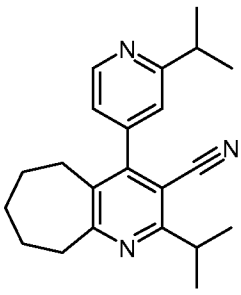
Intermediate	Name and Structure	MS	Method	Reagents
N80	2-Cyclopentyl-4-(2-methylpyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 332.5	U	Intermediate K80, cycloheptanone
N81	4-Phenyl-2-(tetrahydrofuran-3-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 319.4	U	Intermediate K81, cycloheptanone
N82	2-Cyclopentyl-4-(2-methoxy-pyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 348.5	U	Intermediate K82, cycloheptanone

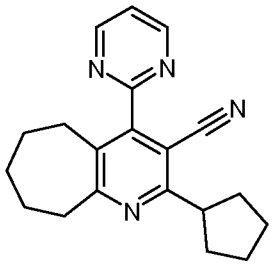
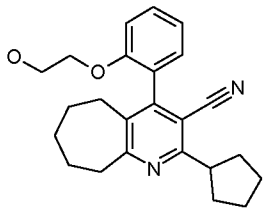
Intermediate	Name and Structure	MS	Method	Reagents
N83	2-Cyclopentyl-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 331.5	U	Intermediate K83, cycloheptanone
N84	2-Cyclopentyl-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 317.4	U	Intermediate K84, cycloheptanone
N85	4-Phenyl-2-(tetrahydrofuran-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 319.4	U	Intermediate K85, cycloheptanone

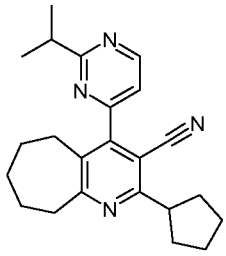
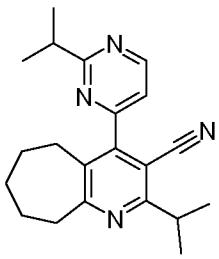
Intermediate	Name and Structure	MS	Method	Reagents
N86	2-Cyclohexyl-4-(3-fluoropyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 350.5	U	Intermediate K86, cycloheptanone
N87	2-Cyclopentyl-4-(3-fluoropyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 336.5	U	Intermediate K87, cycloheptanone
N88	4-Phenyl-2-(tetrahydro-2H-pyran-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 333.5	U	Intermediate K88, cycloheptanone

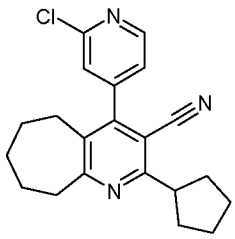
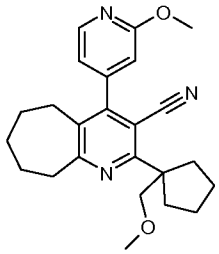
Intermediate	Name and Structure	MS	Method	Reagents
N89	2-Cyclohexyl-4-(2-methylpyrimidin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 347.5	U	Intermediate K89, cycloheptanone
N91	2-Cyclohexyl-4-(pyrimidin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 333.5	U	Intermediate K91, cycloheptanone
N92	2-Cyclopentyl-4-(pyrimidin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 319.5	U	Intermediate K92, cycloheptanone

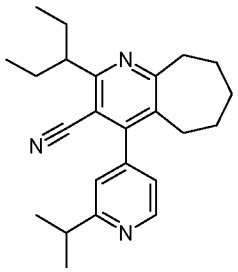
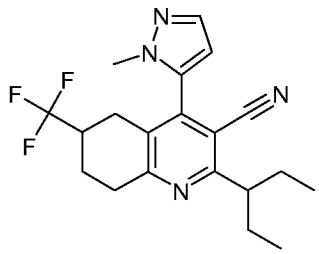
Intermediate	Name and Structure	MS	Method	Reagents
N93	2-Cyclopentyl-4-(2-methylpyrimidin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 333.5	U	Intermediate K93, cycloheptanone
N94	2-(1-(Methoxymethyl)cyclopentyl)-4-(2-methylpyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 376.5	V	Intermediate B94, cycloheptanone, 2-methylisonicotinaldehyde
N95	2-Cyclopentyl-4-(pyridazin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 319.5	U	Intermediate K95, cycloheptanone

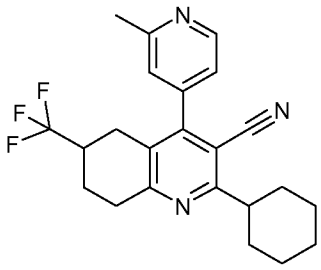
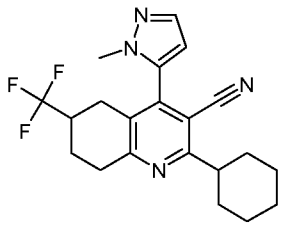
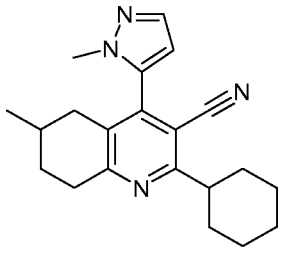
Intermediate	Name and Structure	MS	Method	Reagents
N96	2-Cyclopentyl-4-(6-methylpyridin-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 332.5	U	Intermediate K96, cycloheptanone
N97	2-Cyclopentyl-4-(pyridin-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 318.5	U	Intermediate K97, cycloheptanone
N98	2-Isopropyl-4-(2-isopropylpyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 334.5	V	4-Methyl-3-oxopentanenitrile (CAS# 29509-06-6), cycloheptanone, 2-isopropylisonicotinaldehyde

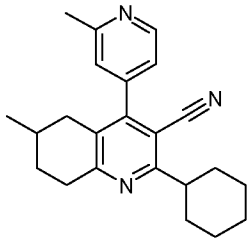
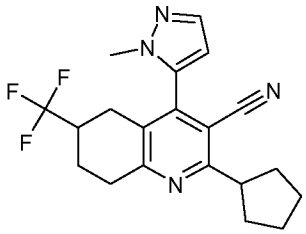
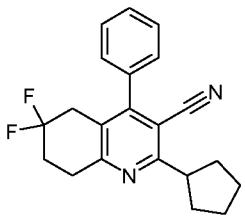
Intermediate	Name and Structure	MS	Method	Reagents
N99	2-Cyclopentyl-4-(pyrimidin-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$:	U	Intermediate K99, cycloheptanone
N100	2-Cyclopentyl-4-(2-(2-hydroxyethoxy)phenyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 377.5	V	3-Cyclopentyl-3-oxopropanenitrile (CAS# 95882-33-0), cycloheptanone, 2-(2-hydroxyethoxy)benzaldehyde

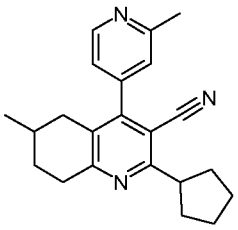
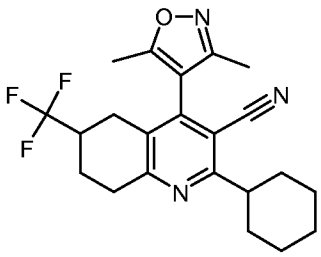
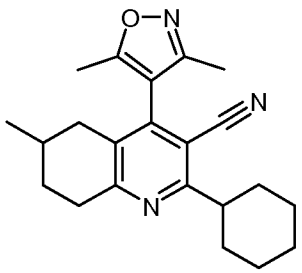
Intermediate	Name and Structure	MS	Method	Reagents
N101	2-Cyclopentyl-4-(2-isopropylpyrimidin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 361.6	V	3-Cyclopentyl-3-oxopropanenitrile (CAS# 95882-33-0), cycloheptanone, 2-isopropyl-pyrimidine-4-carbaldehyde
N102	2-Isopropyl-4-(2-isopropylpyrimidin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 335.5	V	4-Methyl-3-oxopentanenitrile (CAS# 29509-06-6), cycloheptanone, 2-isopropyl-pyrimidine-4-carbaldehyde

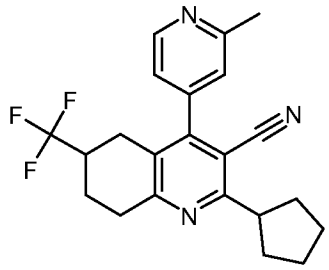
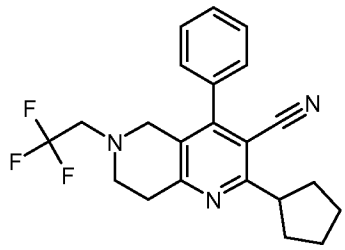
Intermediate	Name and Structure	MS	Method	Reagents
N103	4-(2-Chloropyridin-4-yl)-2-cyclopentyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 352.5	V	3-Cyclopentyl-3-oxopropanenitrile (CAS# 95882-33-0), cycloheptanone, 2-chloropyridine-4-carbaldehyde
N104	2-(1-(Methoxymethyl)cyclopentyl)-4-(2-methoxypyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 392.5	V	Intermediate B94, cycloheptanone, 2-methoxypyridine-4-carbaldehyde

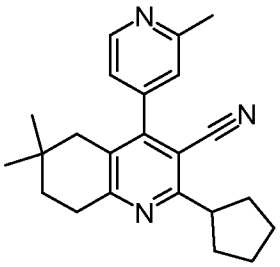
Intermediate	Name and Structure	MS	Method	Reagents
N105	4-(2-Isopropylpyridin-4-yl)-2-(pentan-3-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 362.6	V	4-Ethyl-3-oxo-hexanenitrile (CAS# 42124-67-4), cycloheptanone, 2-isopropylpyridine-4-carbaldehyde
N106	4-(1-Methyl-1H-pyrazol-5-yl)-2-(pentan-3-yl)-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 377.2	U	Intermediate K66, 4-trifluoromethyl-cyclohexanone

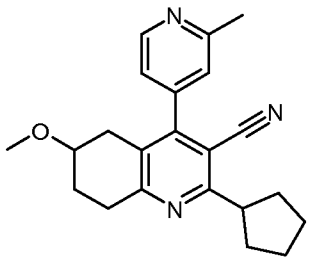
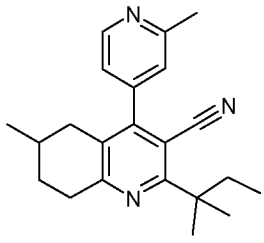
Intermediate	Name and Structure	MS	Method	Reagents
N107	2-Cyclohexyl-4-(2-methylpyridin-4-yl)-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 400.5	U	Intermediate K70, 4-trifluoromethyl-cyclohexanone
N108	2-Cyclohexyl-4-(1-methyl-1H-pyrazol-5-yl)-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 389.4	U	Intermediate K74, 4-trifluoromethyl-cyclohexanone
N109	2-Cyclohexyl-6-methyl-4-(1-methyl-1H-pyrazol-5-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 335.5	U	Intermediate K74, 4-methyl-cyclohexanone

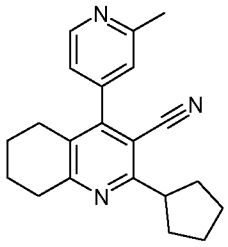
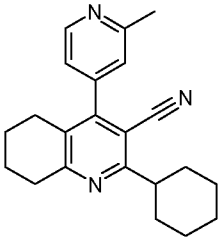
Intermediate	Name and Structure	MS	Method	Reagents
N110	2-Cyclohexyl-6-methyl-4-(2-methylpyridin-4-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 346.5	U	Intermediate K70, 4-methyl-cyclohexanone
N111	2-Cyclopentyl-4-(1-methyl-1H-pyrazol-5-yl)-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 375.4	U	Intermediate K76, 4-trifluoromethyl-cyclohexanone
N112	2-Cyclopentyl-6,6-difluoro-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 339.4	U	Intermediate K84, 4,4-difluoro-cyclohexanone

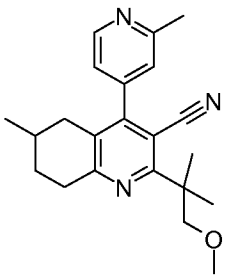
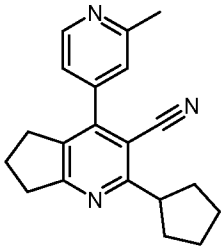
Intermediate	Name and Structure	MS	Method	Reagents
N113	2-Cyclopentyl-6-methyl-4-(2-methylpyridin-4-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 332.5	U	Intermediate K80, 4-methyl-cyclohexanone
N114	2-Cyclohexyl-4-(3,5-dimethylisoxazol-4-yl)-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 404.5	U	Intermediate K114, 4-trifluoromethyl-cyclohexanone
N115	2-Cyclohexyl-4-(3,5-dimethylisoxazol-4-yl)-6-methyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 350.5	U	Intermediate K114, 4-methyl-cyclohexanone

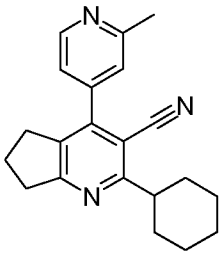
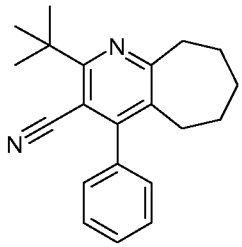
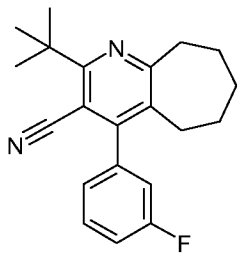
Intermediate	Name and Structure	MS	Method	Reagents
N116	2-Cyclopentyl-4-(2-methylpyridin-4-yl)-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 386.6	U	Intermediate K80, 4-trifluoromethyl-cyclohexanone
N117	2-Cyclopentyl-4-phenyl-6-(2,2,2-trifluoroethyl)-5,6,7,8-tetrahydro-1,6-naphthyridine-3-carbonitrile 	ESP $[M+H]^+$: 386.5	U	Intermediate K84, 1-(2,2,2-trifluoroethyl)-piperidin-4-one

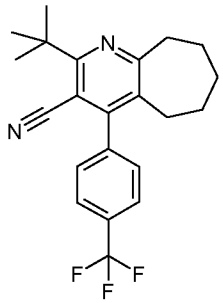
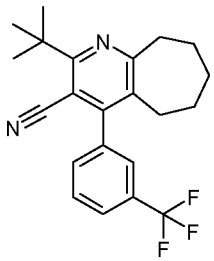
Intermediate	Name and Structure	MS	Method	Reagents
N118	2-Cyclopentyl-6,6-dimethyl-4-(2-methylpyridin-4-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 346.5	V	3-Cyclopentyl-3-oxopropanenitrile (CAS# 95882-33-0), 4,4-dimethyl-cyclohexanone, 2-methyl-pyridine-4-carbaldehyde

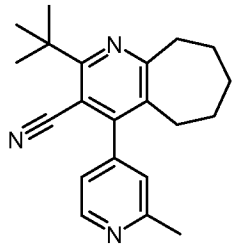
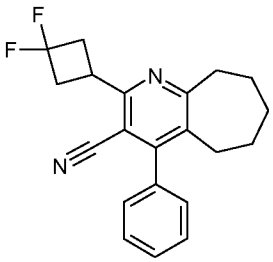
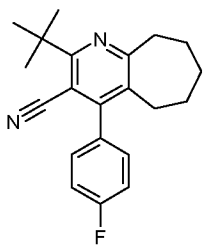
Intermediate	Name and Structure	MS	Method	Reagents
N119	2-Cyclopentyl-6-methoxy-4-(2-methylpyridin-4-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 348.5	V	3-Cyclopentyl-3-oxopropanenitrile (CAS# 95882-33-0), 4-methoxy-cyclohexanone, 2-methyl-pyridine-4-carbaldehyde
N120	6-Methyl-4-(2-methylpyridin-4-yl)-2-tert-pentyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 334.5	V	4,4-Dimethyl-3-oxohexanenitrile (CAS# 876299-62-6), 4-methyl-cyclohexanone , 2-methyl-pyridine-4-carbaldehyde

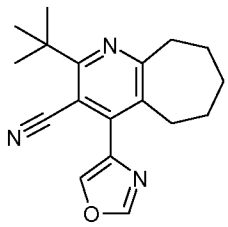
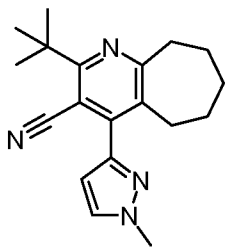
Intermediate	Name and Structure	MS	Method	Reagents
N121	2-Cyclopentyl-4-(2-methylpyridin-4-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 318.5	V	3-Cyclopentyl-3-oxopropanenitrile (CAS# 95882-33-0), cyclohexanone , 2-methyl-pyridine-4-carbaldehyde
N122	2-Cyclohexyl-4-(2-methylpyridin-4-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 332.6	V	3-Cyclohexyl-3-oxo-propanenitrile (CAS# 62455-70-3), cyclohexanone , 2-methyl-pyridine-4-carbaldehyde

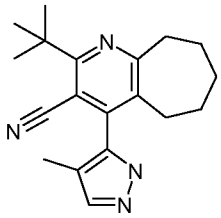
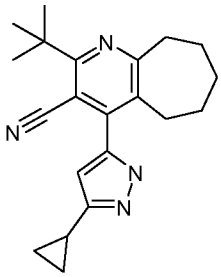
Intermediate	Name and Structure	MS	Method	Reagents
N123	2-(1-Methoxy-2-methylpropan-2-yl)-6-methyl-4-(2-methylpyridin-4-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 350.6	V	5-Methoxy-4,4-dimethyl-3-oxopentanenitrile (CAS# 90087-79-9), 4-methyl-cyclohexanone, 2-methyl-pyridine-4-carbaldehyde
N124	2-Cyclopentyl-4-(2-methylpyridin-4-yl)-6,7-dihydro-5H-cyclopenta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 304.6	V	3-Cyclopentyl-3-oxopropanenitrile (CAS# 95882-33-0), cyclopentanone , 2-methyl-pyridine-4-carbaldehyde

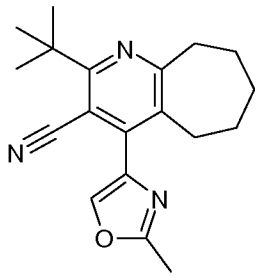
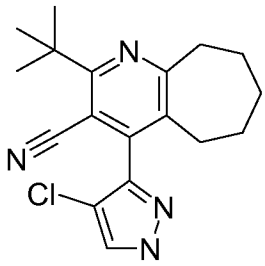
Intermediate	Name and Structure	MS	Method	Reagents
N125	2-Cyclohexyl-4-(2-methylpyridin-4-yl)-6,7-dihydro-5H-cyclopenta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 318.1	V	3-Cyclohexyl-3-oxo-propanenitrile (CAS# 62455-70-3), cyclopentanone , 2-methyl-pyridine-4-carbaldehyde
N126	2-tert-Butyl-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 305.4	V	4,4-Dimethyl-3-oxo-pentanenitrile (CAS# 59997-51-2), cycloheptanone, benzaldehyde
N127	2-tert-Butyl-4-(3-fluorophenyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 323.5	V	4,4-Dimethyl-3-oxo-pentanenitrile (CAS# 59997-51-2), cycloheptanone, 3-fluoro-benzaldehyde

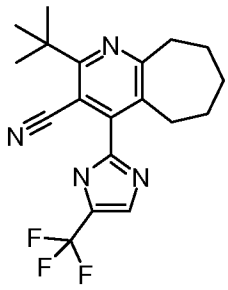
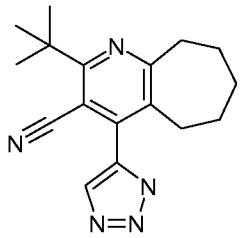
Intermediate	Name and Structure	MS	Method	Reagents
N128	2-tert-Butyl-4-(4-(trifluoromethyl)phenyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 373.5	V	4,4-Dimethyl-3-oxo-pentanenitrile (CAS# 59997-51-2), cycloheptanone, 4-trifluoromethyl-benzaldehyde
N129	2-tert-Butyl-4-(3-(trifluoromethyl)phenyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 373.5	V	4,4-Dimethyl-3-oxo-pentanenitrile (CAS# 59997-51-2), cycloheptanone, 3-trifluoromethyl-benzaldehyde

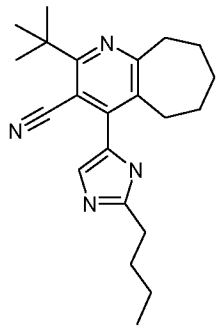
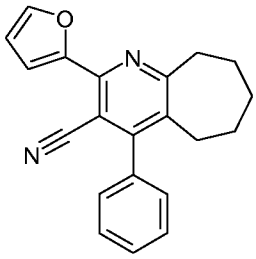
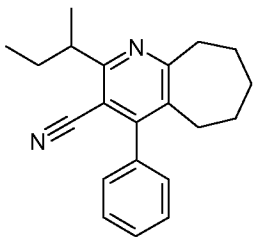
Interm ediate	Name and Structure	MS	Method	Reagents
N130	2-tert-Butyl-4-(2-methylpyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 320.5	V	4,4-Dimethyl-3-oxo-pentanenitrile (CAS# 59997-51-2), cycloheptanone, 2-methyl-pyridine-4-carbaldehyde
N131	2-(3,3-Difluorocyclobutyl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine 	ESN $[M-H]^-$: 380.1	V	3-(3,3-Difluoro-cyclobutyl)-3-oxo-propionitrile (CAS# 1234616-26-2), cycloheptanone, benzaldehyde
N132	2-tert-Butyl-4-(4-fluoro-phenyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 323.4	V	4,4-Dimethyl-3-oxo-pentanenitrile (CAS# 59997-51-2), cycloheptanone, 4-fluoro-benzaldehyde

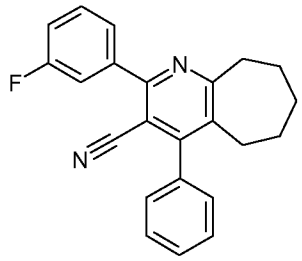
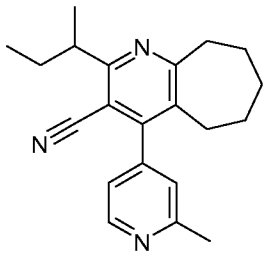
Intermediate	Name and Structure	MS	Method	Reagents
N133	2-tert-Butyl-4-(oxazol-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 296.4	V	4,4-Dimethyl-3-oxo-pentanenitrile (CAS# 59997-51-2), cycloheptanone, oxazole-4-carbaldehyde
N134	2-tert-Butyl-4-(1-methyl-1H-pyrazol-3-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 309.5	V	4,4-Dimethyl-3-oxo-pentanenitrile (CAS# 59997-51-2), cycloheptanone, 1-methyl-1H-pyrazole-3-carbaldehyde

Intermediate	Name and Structure	MS	Method	Reagents
N135	2-tert-Butyl-4-(4-methyl-1H-pyrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 309.4	V	4,4-Dimethyl-3-oxo-pentanenitrile (CAS# 59997-51-2), cycloheptanone, 4-methyl-2H-pyrazole-3-carbaldehyde
N136	2-tert-Butyl-4-(3-cyclopropyl-1H-pyrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 335.5	V	4,4-Dimethyl-3-oxo-pentanenitrile (CAS# 59997-51-2), cycloheptanone, 5-cyclopropyl-2H-pyrazole-3-carbaldehyde

Intermediate	Name and Structure	MS	Method	Reagents
N137	2-tert-Butyl-4-(2-methyloxazol-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 310.4	V	4,4-Dimethyl-3-oxo-pentanenitrile (CAS# 59997-51-2), cycloheptanone, 2-methyl-oxazole-4-carbaldehyde
N138	2-tert-Butyl-4-(4-chloro-1H-pyrazol-3-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 329.4	V	4,4-Dimethyl-3-oxo-pentanenitrile (CAS# 59997-51-2), cycloheptanone, 4-chloro-1H-pyrazole-3-carbaldehyde

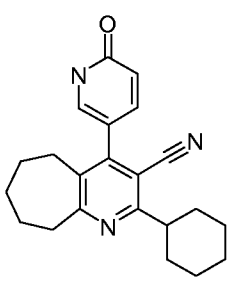
Intermediate	Name and Structure	MS	Method	Reagents
N139	2-tert-Butyl-4-(4-(trifluoromethyl)-1H-imidazol-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 363.5	V	4,4-Dimethyl-3-oxo-pentanenitrile (CAS# 59997-51-2), cycloheptanone, 5-trifluoromethyl-1H-imidazole-2-carbaldehyde
N140	2-tert-Butyl-4-(1H-1,2,3-triazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 296.4	V	4,4-Dimethyl-3-oxo-pentanenitrile (CAS# 59997-51-2), cycloheptanone, 3H-[1,2,3]triazole-4-carbaldehyde

Intermediate	Name and Structure	MS	Method	Reagents
N141	2-tert-Butyl-4-(2-butyl-1H-imidazol-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 351.5	V	4,4-Dimethyl-3-oxo-pentanenitrile (CAS# 59997-51-2), cycloheptanone, 2-butyl-3H-imidazole-4-carbaldehyde
N142	2-Furan-2-yl-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 315.4	V	2-Furoylacetonitrile (CAS# 31909-58-7), cycloheptanone, benzaldehyde
N143	2-sec-Butyl-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 305.5	V	4-Methyl-3-oxohexanenitrile (CAS# 42124-66-3), cycloheptanone, benzaldehyde

Intermediate	Name and Structure	MS	Method	Reagents
N144	2-(3-Fluorophenyl)-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 343.4	V	3-Fluorobenzoylacetonitrile (CAS# 21667-61-8), cycloheptanone, benzaldehyde
N145	2-sec-Butyl-4-(2-methylpyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 320.5	V	4-Methyl-3-oxohexanenitrile (CAS# 42124-66-3), cycloheptanone, 2-methyl-pyridine-4-carbaldehyde

Intermediate N71

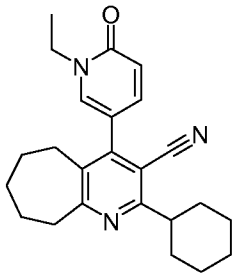
2-Cyclohexyl-4-(6-oxo-1,6-dihydropyridin-3-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile



Using General Method R, Intermediate K71 was reacted with cycloheptanone and ammonium acetate to give 2-cyclohexyl-4-(6-methoxypyridin-3-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile. 2-Cyclohexyl-4-(6-methoxypyridin-3-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile (1.162 g) and aqueous HCl 37% (6.34 g) were combined with dioxane (47.5 ml) and stirred at 100 °C for 1 h. After cooling to room temperature, the mixture was diluted with water and extracted with EtOAc. The organic layers were concentrated in vacuo. The crude material was suspended in a small amount of EtOAc. The product was collected by filtration, washed with EtOAc and dried to give the title compound (1.12 g) as a colorless solid. MS (ESP): m/z = 348.5 $[M+H]^+$.

Intermediate N72

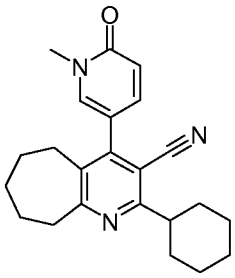
2-Cyclohexyl-4-(1-ethyl-6-oxo-1,6-dihydropyridin-3-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile



A suspension of Intermediate N71 (250 mg), potassium carbonate (109 mg) and ethyl iodide (118 mg) in DMA (4.13 ml) was stirred at room temperature for 3 days. The mixture was diluted with water and extracted with EtOAc. The organic layers were washed with water and brine, dried over $MgSO_4$ and concentrated in vacuo. The crude material was purified by flash chromatography (silica gel, 0% to 10% MeOH in DCM) to give the title compound (184 mg) as colorless foam. MS (ESP): m/z = 376.5 $[M+H]^+$.

Intermediate N73

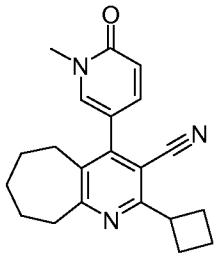
2-Cyclohexyl-4-(1-methyl-6-oxo-1,6-dihydropyridin-3-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile



In analogy to the synthesis of Intermediate N72, Intermediate N71 was converted to the title compound by reaction with methyl iodide in the presence of potassium carbonate. Colorless foam. MS (ESP): m/z = 362.5 $[M+H]^+$.

Intermediate N90

2-Cyclobutyl-4-(1-methyl-6-oxo-1,6-dihydropyridin-3-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile



Using General Method R, Intermediate K90 was reacted with cycloheptanone and ammonium acetate to give 2-cyclobutyl-4-(6-methoxypyridin-3-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile. This compound was converted to 2-cyclobutyl-4-(6-oxo-1,6-dihydropyridin-3-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile by reaction with HCl in dioxane in analogy to the synthesis of Intermediate N71. This compound was converted to the title compound by reaction with methyl iodide in the presence of potassium carbonate in analogy to the synthesis of Intermediate N72. Off-white amorphous solid. MS (ESP): m/z = 334.3 $[M+H]^+$.

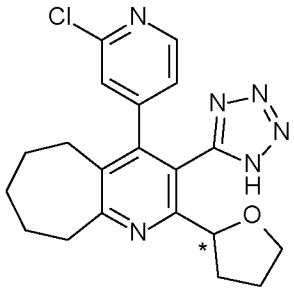
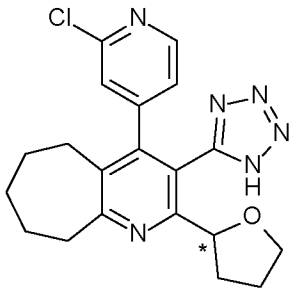
General Method W: Conversion of a methoxymethyl to a hydroxymethyl group

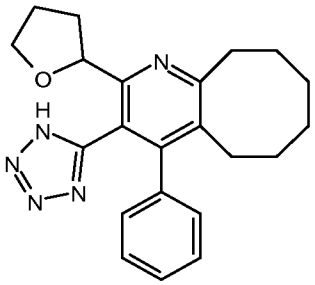
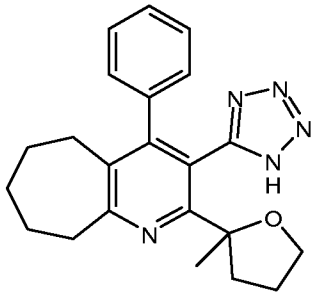
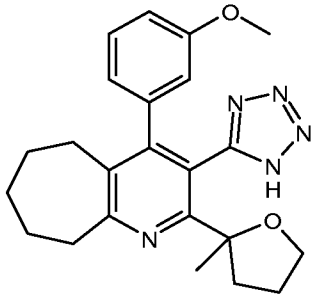
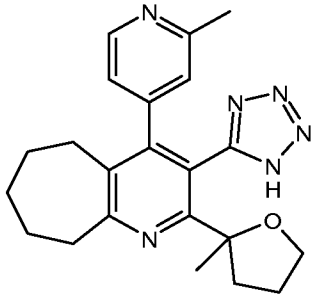
The methoxymethyl compound (1 equivalent) is combined with 48% aqueous HBr (29.0 equivalents) and stirred at 100 °C for 1-3 h. After cooling to room temperature, the product is collected by filtration, washed with water and dried. If desired, the product can be further

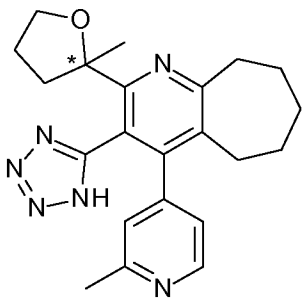
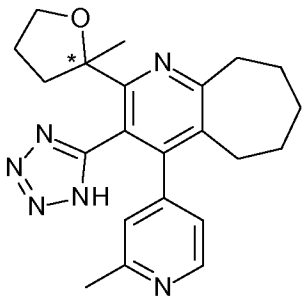
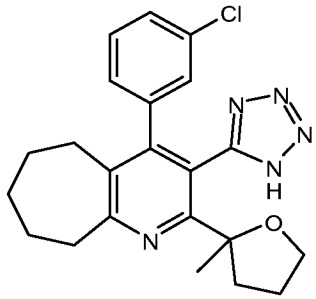
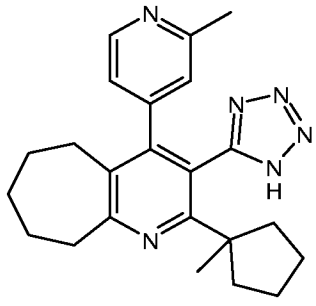
purified by chromatography. Alternatively, the product can be obtained by extraction using e.g. EtOAc.

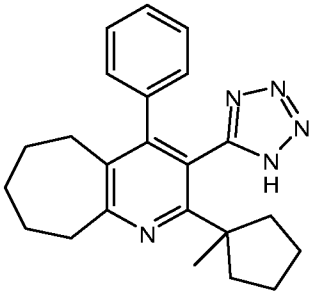
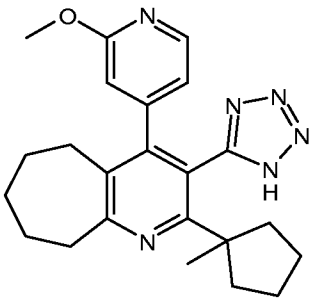
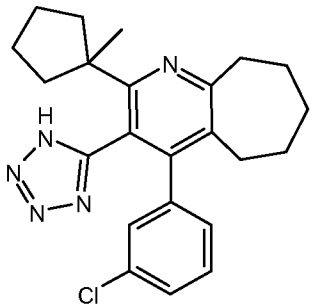
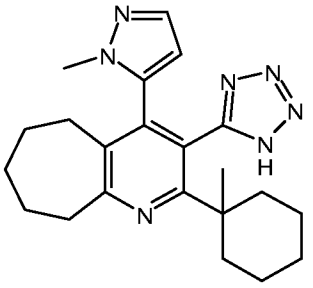
General Method Z: Conversion of a nitrile to a carboxylic acid

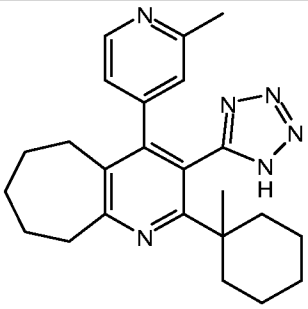
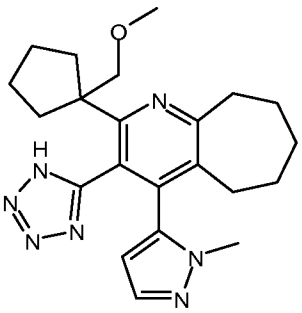
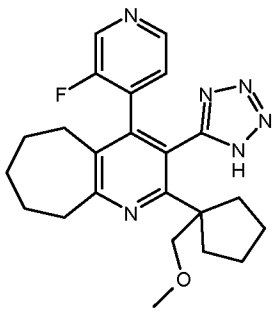
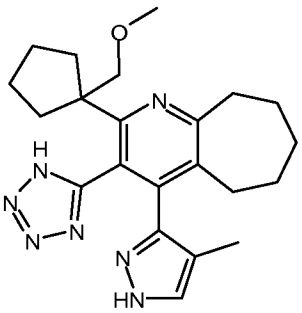
The nitrile (1 equivalent) and sulfuric acid (50% in water, 24 equivalents) are combined. The reaction mixture is heated to 145 °C (temperature of heating block) and stirred for 3 h. After cooling to room temperature, the mixture is placed in an ice bath and cooled to 5 -10 °C. A solution of sodium nitrite (1.8 equivalents) in water is slowly added under the surface of the reaction mixture and then heated up to 50 °C. The reaction mixture is stirred over night at 50 °C, and cooled down to room temperature. Water is added and stirred for 30 min. The reaction mixture is poured into 1 M aqueous NaOH and extracted with diethyl ether. The aqueous layer is acidified to pH 1 with HCl and extracted with EtOAc. The combined organic layers are dried over $MgSO_4$, evaporated and dried. The product can be purified by chromatography.

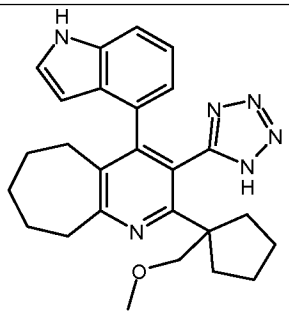
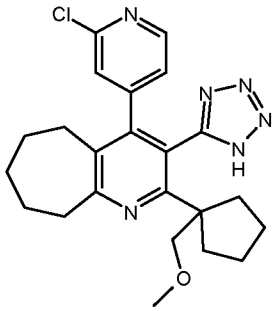
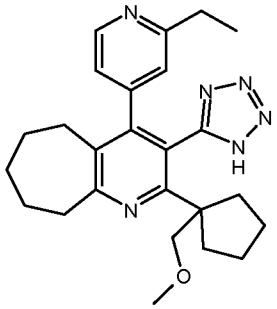
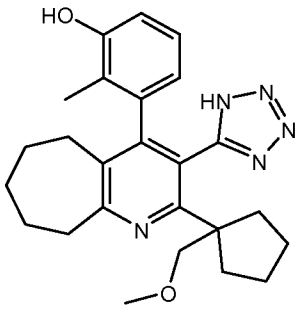
Ex.	Name	Structure	MS	Method	Starting Material
149	4-(2-Chloropyridin-4-yl)-2-(tetrahydrofuran-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 397.6	C	N149
150	4-(2-Chloropyridin-4-yl)-2-(tetrahydrofuran-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 397.6	C	N150

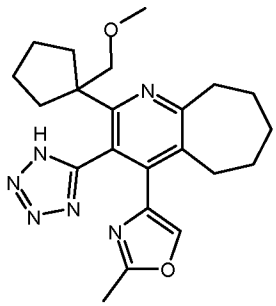
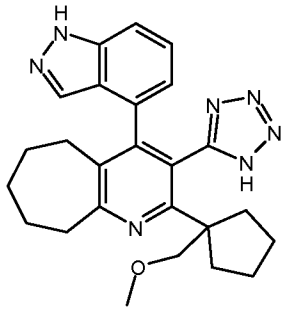
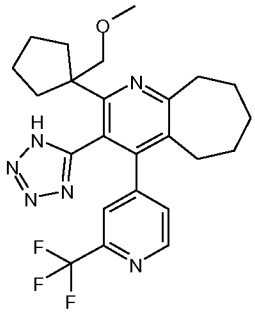
Ex.	Name	Structure	MS	Method	Starting Material
151	4-Phenyl-2-(tetrahydrofuran-2-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8,9,10-hexahydrocycloocta[b]pyridine		ESP $[M+H]^+$: 376.6	C	N151
154	2-(2-Methyltetrahydrofuran-2-yl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 376.6	C	N154
157	4-(3-Methoxyphenyl)-2-(2-methyltetrahydrofuran-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 406.6	C	N157
160	4-(2-Methylpyridin-4-yl)-2-(2-methyltetrahydrofuran-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 391.6	C	N160

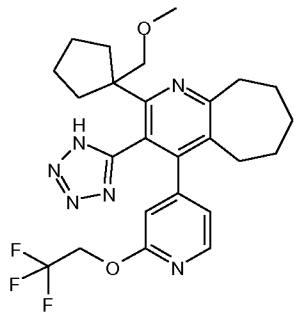
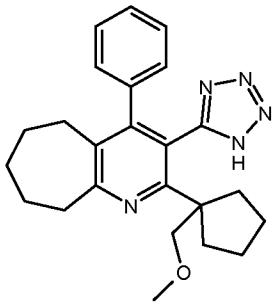
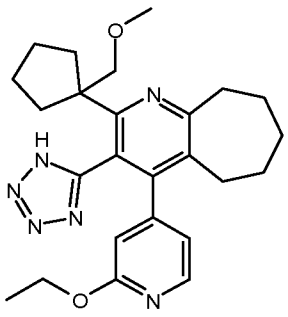
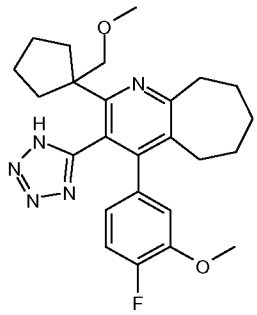
Ex.	Name	Structure	MS	Method	Starting Material
161	2-[2-Methyloxolan-2-yl]-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 391.5	C	N161
162	2-[2-Methyloxolan-2-yl]-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 391.5	C	N162
163	4-(3-Chlorophenyl)-2-(2-methyltetrahydrofuran-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 410.5	C	N163
166	2-(1-Methylcyclopentyl)-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 389.6	C	N166

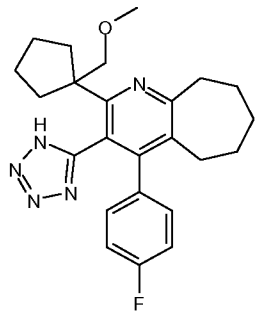
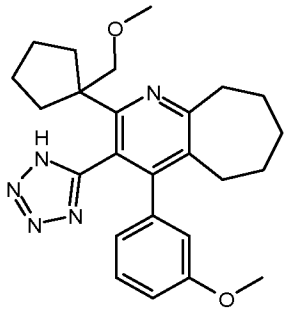
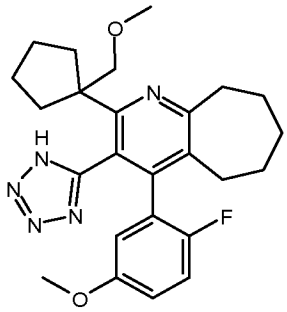
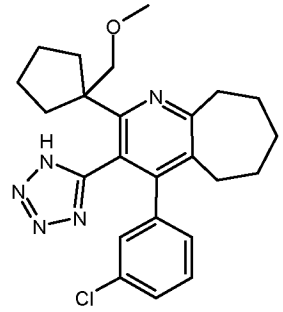
Ex.	Name	Structure	MS	Method	Starting Material
167	2-(1-Methylcyclopentyl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 374.7	C	N167
168	4-(2-Methoxypyridin-4-yl)-2-(1-methylcyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 405.7	C	N168
170	4-(3-Chloro-phenyl)-2-(1-methyl-cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 408.5	C	N170
171	4-(1-Methyl-1H-pyrazol-5-yl)-2-(1-methylcyclohexyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 392.6	C	N171

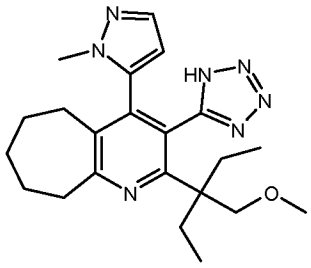
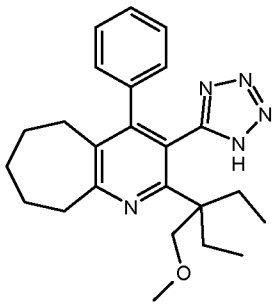
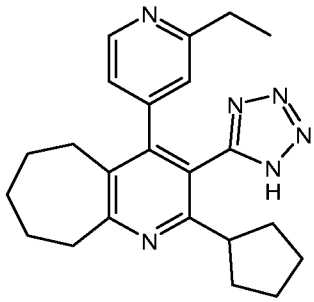
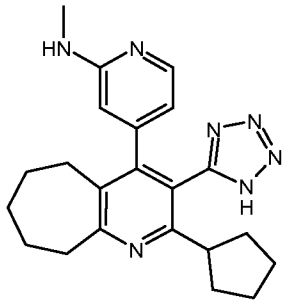
Ex.	Name	Structure	MS	Method	Starting Material
172	2-(1-Methylcyclohexyl)-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 403.6	C	N172
173	2-(1-Methoxymethyl-cyclopentyl)-4-(2-methyl-2H-pyrazol-3-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 408.6	C	N173
174	4-(3-Fluoropyridin-4-yl)-2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 423.5	C	N174
175	2-(1-(Methoxymethyl)cyclopentyl)-4-(4-methyl-1H-pyrazol-3-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 408.6	C	N175

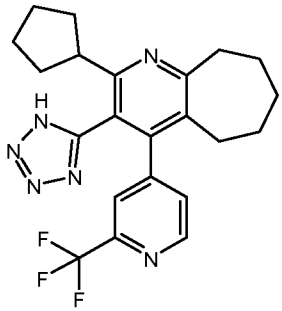
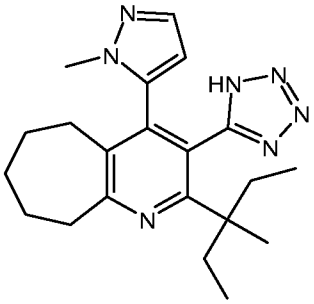
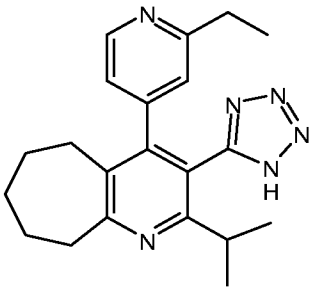
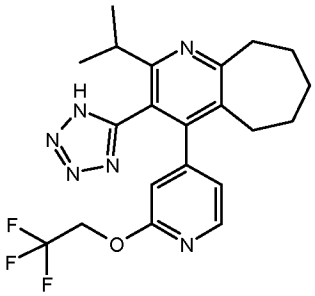
Ex.	Name	Structure	MS	Method	Starting Material
176	4-(1H-Indol-4-yl)-2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 443.7	C	N176
177	4-(2-Chloropyridin-4-yl)-2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 439.5	C	N177
178	4-(2-Ethylpyridin-4-yl)-2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 433.6	C	N178
179	3-(2-(1-(Methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)-2-methylphenol		ESP $[M+H]^+$: 434.7	C	N179

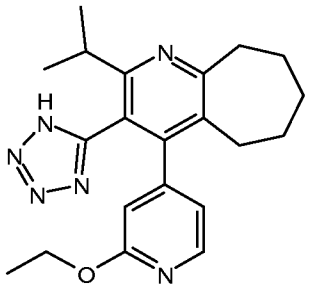
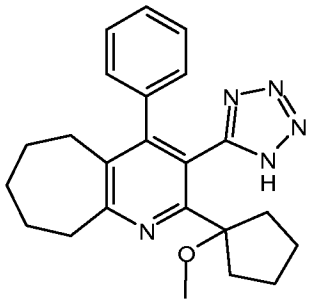
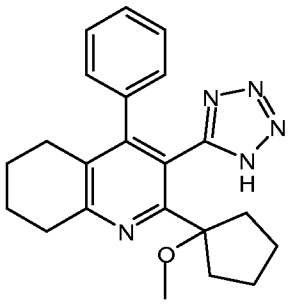
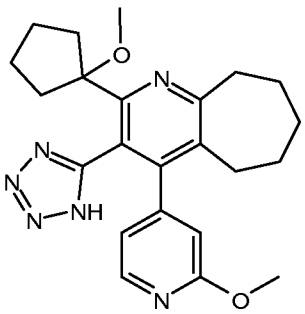
Ex.	Name	Structure	MS	Method	Starting Material
180	4-(2-(1-(Methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)-2-methyloxazole		ESP $[M+H]^+$: 409.6	C	N180
181	4-(1H-Indazol-4-yl)-2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 444.7	C	N181
182	2-(1-(Methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-4-(2-(trifluoromethyl)pyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 473.6	C	N182

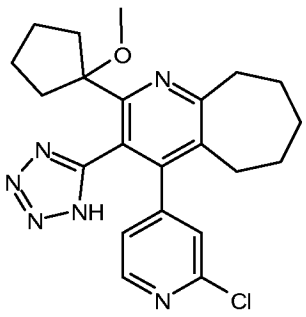
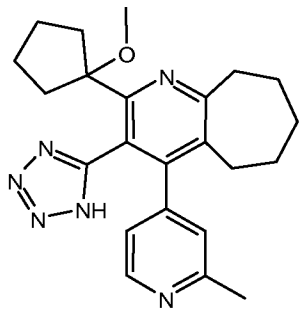
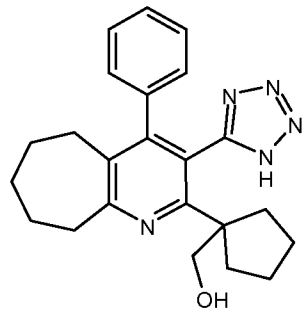
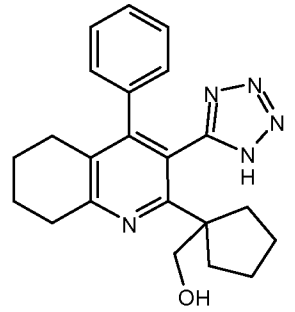
Ex.	Name	Structure	MS	Method	Starting Material
183	2-(1-(Methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-4-(2-(2,2,2-trifluoroethoxy)pyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 503.6	C	N183
184	2-(1-(Methoxymethyl)cyclopentyl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 404.6	C	N184
185	4-(2-Ethoxypyridin-4-yl)-2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 449.6	C	N185
186	4-(4-Fluoro-3-methoxyphenyl)-2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 452.6	C	N186

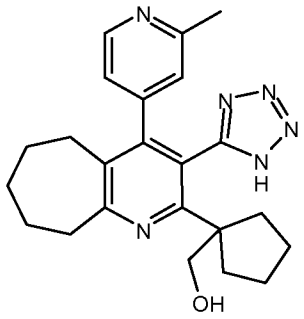
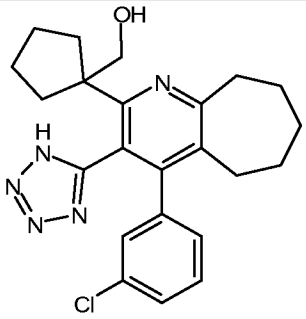
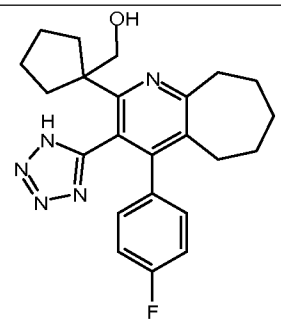
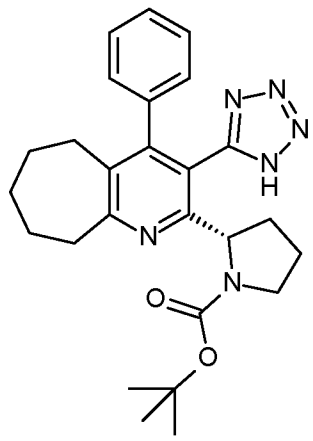
Ex.	Name	Structure	MS	Method	Starting Material
187	4-(4-Fluorophenyl)-2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 422.6	C	N187
188	2-(1-(Methoxymethyl)cyclopentyl)-4-(3-methoxyphenyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 434.6	C	N188
189	4-(2-Fluoro-5-methoxyphenyl)-2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 452.6	C	N189
190	4-(3-Chloro-phenyl)-2-(1-methoxymethyl-cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 438.6	C	N190

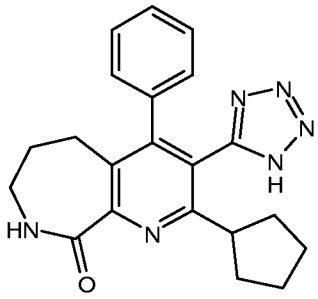
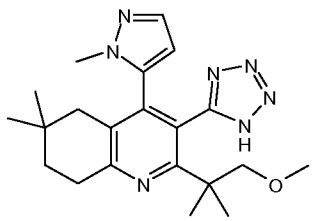
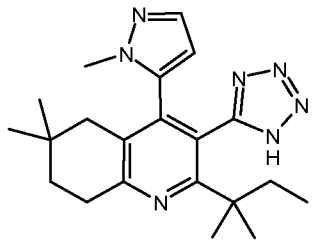
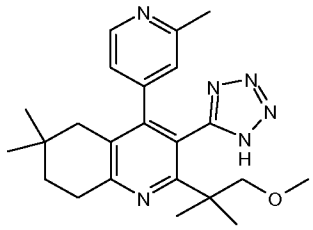
Ex.	Name	Structure	MS	Method	Starting Material
191	2-(3-(Methoxymethyl)pentan-3-yl)-4-(1-methyl-1H-pyrazol-5-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 410.7	C	N191
192	2-(3-(Methoxymethyl)pentan-3-yl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 406.7	C	N192
193	2-Cyclopentyl-4-(2-ethylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 389.6	C	N193
194	4-(2-Cyclopentyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)-N-methylpyridin-2-amine		ESP $[M+H]^+$: 390.7	C	N194

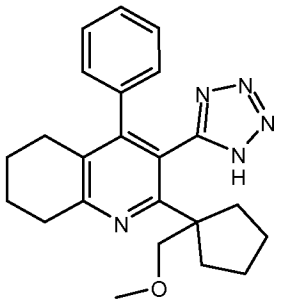
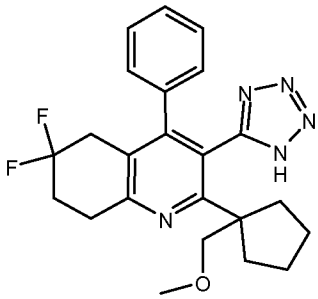
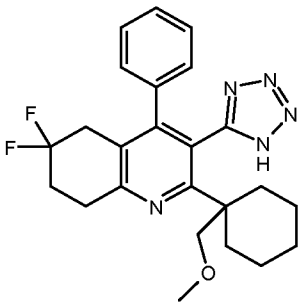
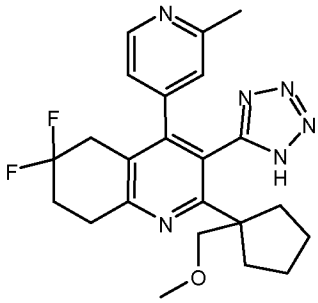
Ex.	Name	Structure	MS	Method	Starting Material
195	2-Cyclopentyl-3-(1H-tetrazol-5-yl)-4-(2-(trifluoromethyl)pyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 429.5	C	N195
196	4-(1-Methyl-1H-pyrazol-5-yl)-2-(3-methylpentan-3-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 380.7	C	N196
197	4-(2-Ethylpyridin-4-yl)-2-isopropyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 363.6	C	N197
198	2-Isopropyl-3-(1H-tetrazol-5-yl)-4-(2-(2,2,2-trifluoroethoxy)pyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 333.6	C	N198

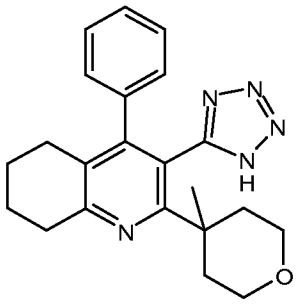
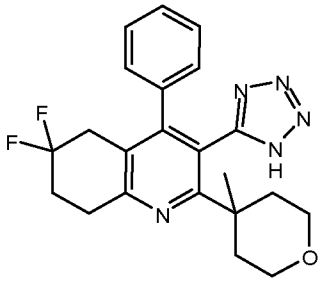
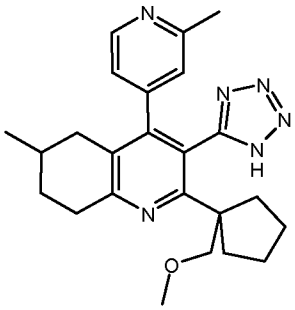
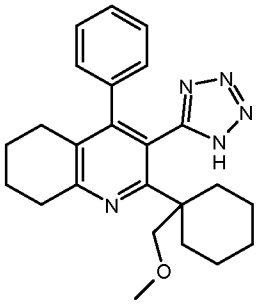
Ex.	Name	Structure	MS	Method	Starting Material
199	4-(2-Ethoxypyridin-4-yl)-2-isopropyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 379.6	C	N199
200	2-(1-Methoxycyclopentyl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 390.7	C	N200
201	2-(1-Methoxycyclopentyl)-4-phenyl-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 376.7	C	N201
202	2-(1-Methoxycyclopentyl)-4-(2-methoxypyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 421.6	C	N202

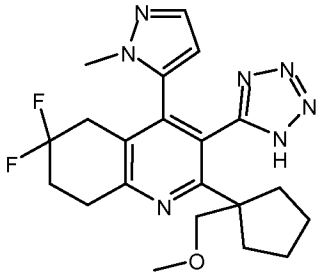
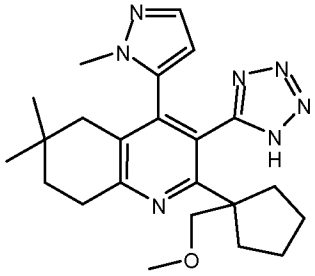
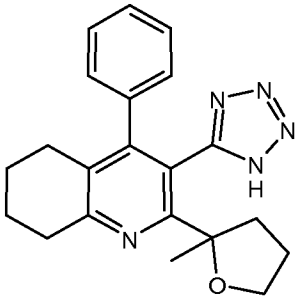
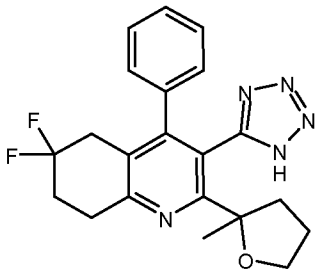
Ex.	Name	Structure	MS	Method	Starting Material
203	4-(2-Chloropyridin-4-yl)-2-(1-methoxycyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 425.6	C	N203
204	2-(1-Methoxycyclopentyl)-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 405.5	C	N204
205	(1-(4-Phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-yl)cyclopentyl)methanol		ESP $[M+H]^+$: 390.6	C	N205
206	(1-(4-Phenyl-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinolin-2-yl)cyclopentyl)methanol		ESP $[M+H]^+$: 376.6	W	Ex. 216

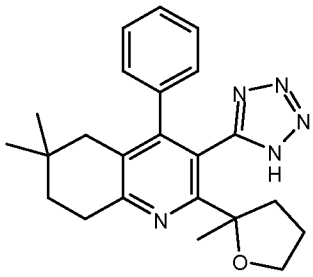
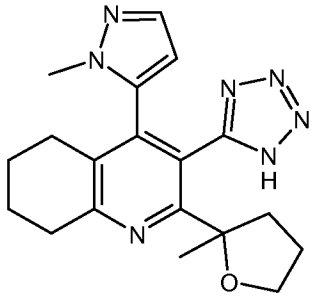
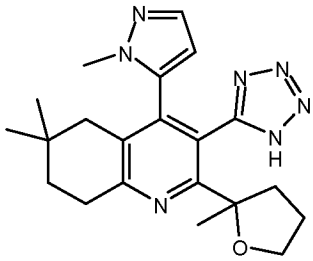
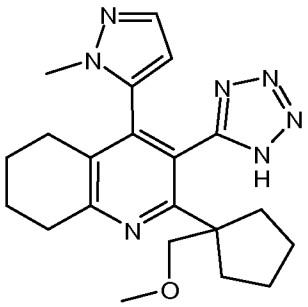
Ex.	Name	Structure	MS	Method	Starting Material
207	(1-(4-(2-Methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-yl)cyclopentyl)methanol		ESP $[M+H]^+$: 405.6	W	Ex. 94
208	(1-(4-(3-Chlorophenyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-yl)cyclopentyl)methanol		ESP $[M+H]^+$: 424.5	W	Ex. 190
209	(1-(4-(4-Fluorophenyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-yl)cyclopentyl)methanol		ESP $[M+H]^+$: 408.6	W	Ex. 187
210	(S)-tert-Butyl 2-(4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-yl)pyrrolidine-1-carboxylate		ESP $[M+H]^+$: 461.7	C	N210

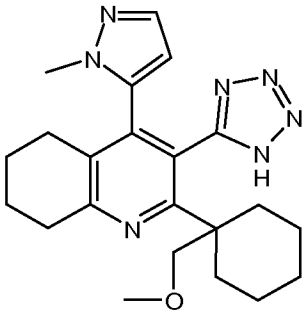
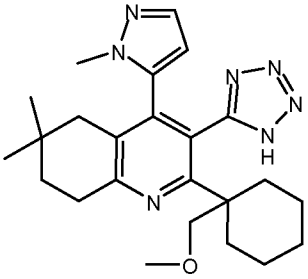
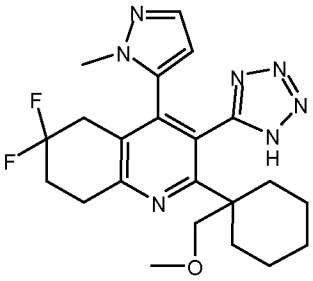
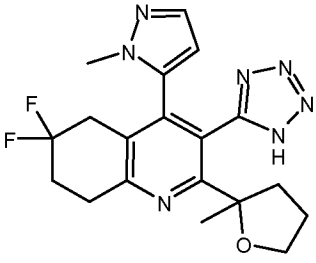
Ex.	Name	Structure	MS	Method	Starting Material
212	2-Cyclopentyl-4-phenyl-3-(1H-tetrazol-5-yl)-7,8-dihydro-5H-pyrido[2,3-c]azepin-9(6H)-one		ESP $[M+H]^+$: 375.6	C	N212
213	2-(1-Methoxy-2-methylpropan-2-yl)-6,6-dimethyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 396.6	C	N213
214	6,6-Dimethyl-4-(1-methyl-1H-pyrazol-5-yl)-2-tert-pentyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 380.6	C	N214
215	2-(1-Methoxy-2-methylpropan-2-yl)-6,6-dimethyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 407.6	C	N215

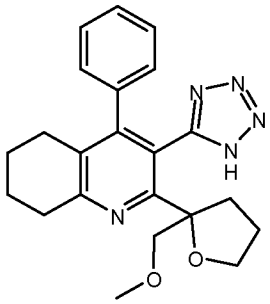
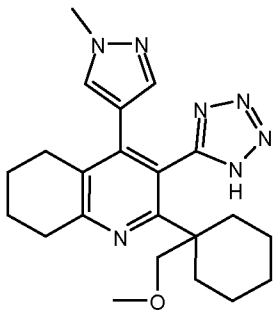
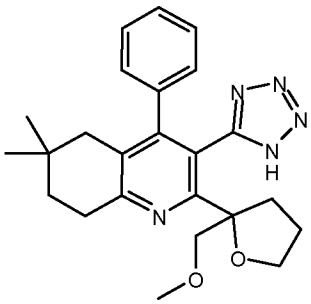
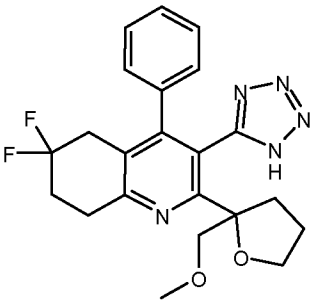
Ex.	Name	Structure	MS	Method	Starting Material
216	2-(1-(Methoxymethyl)cyclopentyl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 390.6	C	N216
217	6,6-Difluoro-2-(1-(methoxymethyl)cyclopentyl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 426.5	C	N217
218	6,6-Difluoro-2-(1-methoxymethyl-cyclohexyl)-4-phenyl-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydro-quinoline		ESP $[M+H]^+$: 440.7	C	N218
219	6,6-Difluoro-2-(1-(methoxymethyl)cyclopentyl)-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 441.7	C	N219

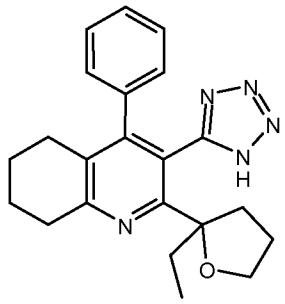
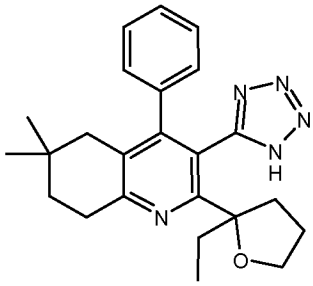
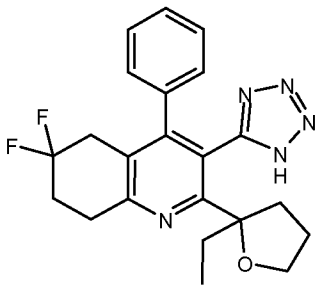
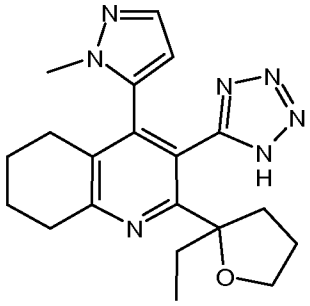
Ex.	Name	Structure	MS	Method	Starting Material
220	2-(4-Methyltetrahydro-2H-pyran-4-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 376.6	C	N220
221	6,6-Difluoro-2-(4-methyltetrahydro-2H-pyran-4-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 412.6	C	N221
222	2-(1-(Methoxymethyl)cyclopentyl)-6-methyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 419.6	C	N222
223	2-(1-(Methoxymethyl)cyclohexyl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 404.6	C	N223

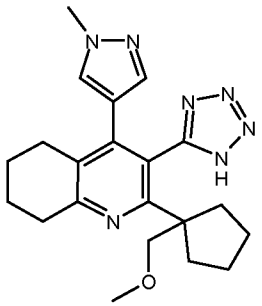
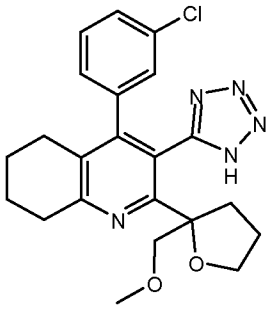
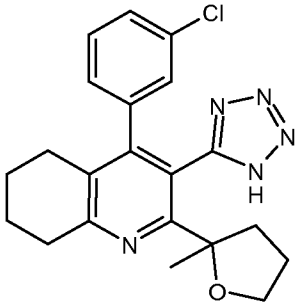
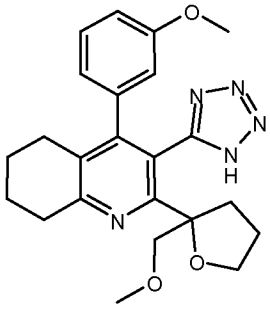
Ex.	Name	Structure	MS	Method	Starting Material
224	6,6-Difluoro-2-(1-(methoxymethyl)cyclopentyl)-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 430.6	C	N224
225	2-(1-(Methoxymethyl)cyclopentyl)-6,6-dimethyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 422.6	C	N225
226	2-(2-Methyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 362.6	C	N226
227	6,6-Difluoro-2-(2-methyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 398.6	C	N227

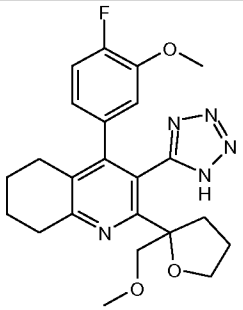
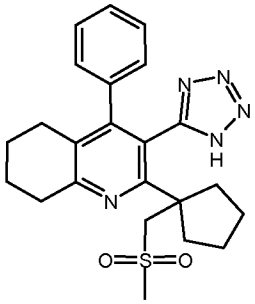
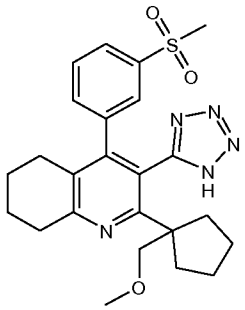
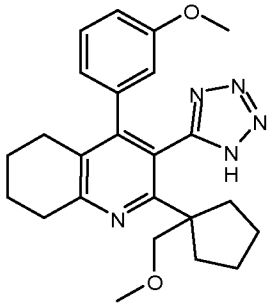
Ex.	Name	Structure	MS	Method	Starting Material
228	6,6-Dimethyl-2-(2-methyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 390.7	C	N228
229	4-(1-Methyl-1H-pyrazol-5-yl)-2-(2-methyltetrahydrofuran-2-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 366.6	C	N229
230	6,6-Dimethyl-4-(1-methyl-1H-pyrazol-5-yl)-2-(2-methyltetrahydrofuran-2-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 394.6	C	N230
237	2-(1-(Methoxymethyl)cyclopentyl)-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 394.7	C	N237

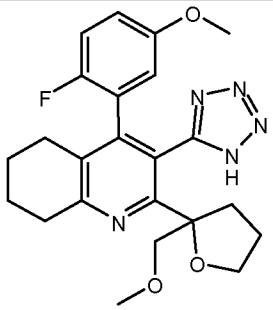
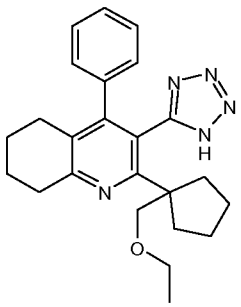
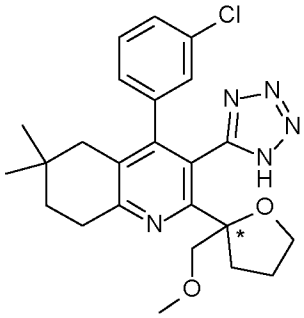
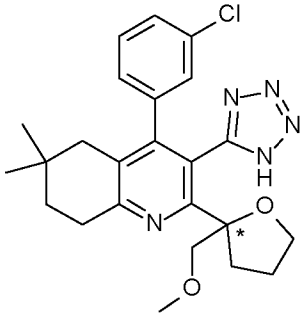
Ex.	Name	Structure	MS	Method	Starting Material
238	2-(1-(Methoxymethyl)cyclohexyl)-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 408.7	C	N238
239	2-(1-(Methoxymethyl)cyclohexyl)-6,6-dimethyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 436.8	C	N239
240	6,6-Difluoro-2-(1-(methoxymethyl)cyclohexyl)-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 444.6	C	N240
241	6,6-Difluoro-4-(1-methyl-1H-pyrazol-5-yl)-2-(2-methyltetrahydrofuran-2-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 402.7	C	N241

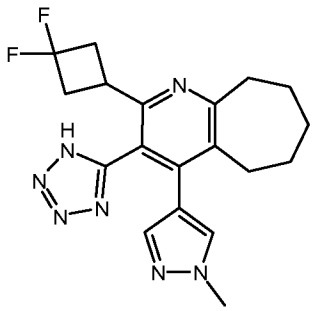
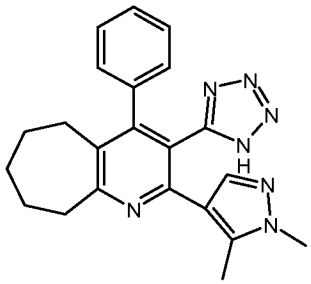
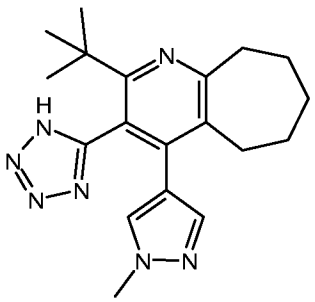
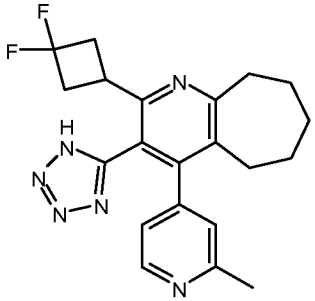
Ex.	Name	Structure	MS	Method	Starting Material
242	2-(2-(Methoxymethyl)tetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 392.7	C	N242
243	2-(1-(Methoxymethyl)cyclohexyl)-4-(1-methyl-1H-pyrazol-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 408.6	C	N243
244	2-(2-(Methoxymethyl)tetrahydrofuran-2-yl)-6,6-dimethyl-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 420.6	C	N244
245	6,6-Difluoro-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 428.6	C	N245

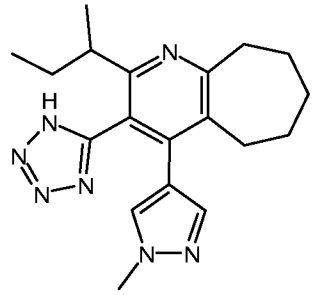
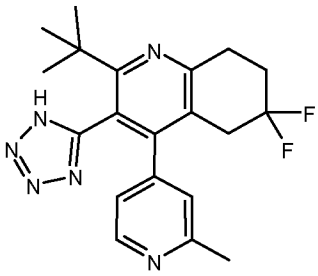
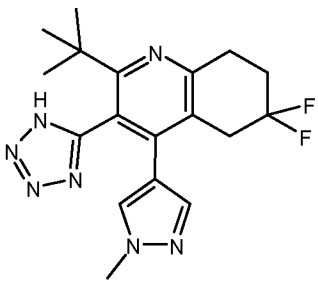
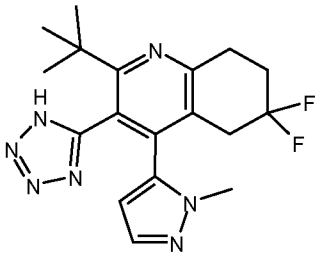
Ex.	Name	Structure	MS	Method	Starting Material
246	2-(2-Ethyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 376.5	C	N246
247	2-(2-Ethyltetrahydrofuran-2-yl)-6,6-dimethyl-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 404.6	C	N247
248	2-(2-Ethyltetrahydrofuran-2-yl)-6,6-difluoro-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 412.5	C	N248
255	2-(2-Ethyltetrahydrofuran-2-yl)-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 380.6	C	N255

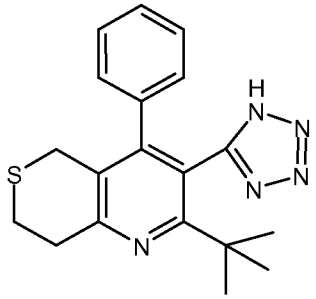
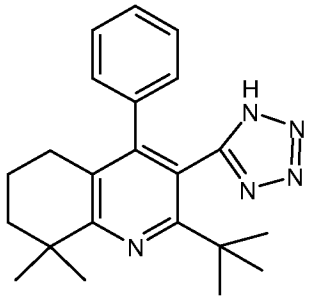
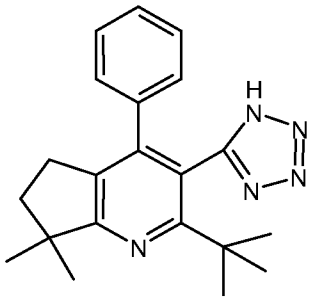
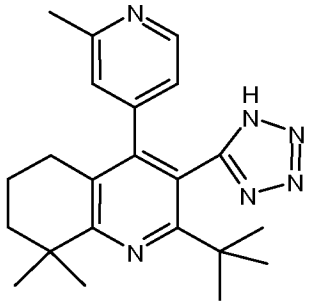
Ex.	Name	Structure	MS	Method	Starting Material
256	2-(1-(Methoxymethyl)cyclopentyl)-4-(1-methyl-1H-pyrazol-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 394.6	C	N256
257	4-(3-Chlorophenyl)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 426.5	C	N257
258	4-(3-Chlorophenyl)-2-(2-methyltetrahydrofuran-2-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 396.5	C	N258
259	2-(2-(Methoxymethyl)tetrahydrofuran-2-yl)-4-(3-methoxyphenyl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 422.5	C	N259

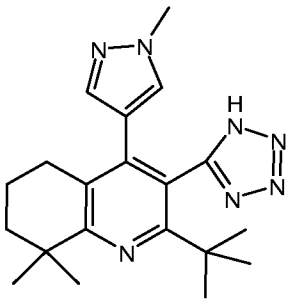
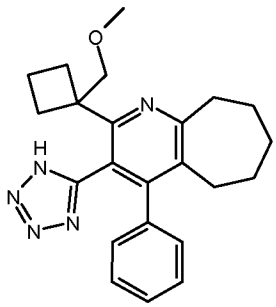
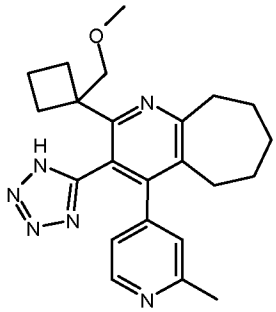
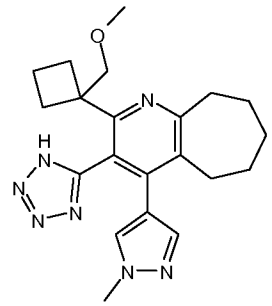
Ex.	Name	Structure	MS	Method	Starting Material
260	4-(4-Fluoro-3-methoxyphenyl)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 440.5	C	N260
261	2-(1-(Methylsulfonylmethyl)cyclopentyl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 438.5	C	N261
264	2-(1-(Methoxymethyl)cyclopentyl)-4-(3-(methylsulfonyl)phenyl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 468.5	C	N264
265	2-(1-(Methoxymethyl)cyclopentyl)-4-(3-methoxyphenyl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 420.6	C	N265

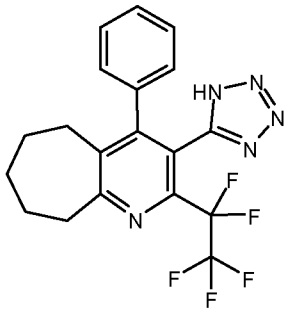
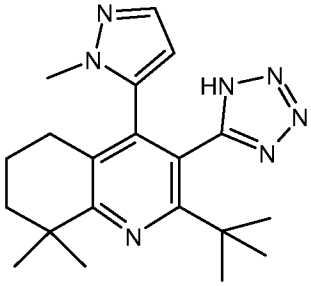
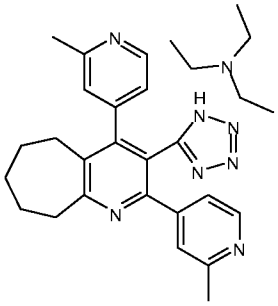
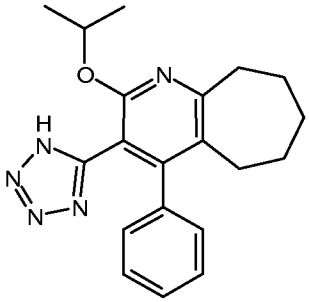
Ex.	Name	Structure	MS	Method	Starting Material
266	4-(2-Fluoro-5-methoxyphenyl)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 440.5	C	N266
268	2-(1-(Ethoxymethyl)cyclopentyl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 404.6	C	N268
269	4-(3-Chlorophenyl)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-6,6-dimethyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 454.5	C	N269
270	4-(3-Chlorophenyl)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-6,6-dimethyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 454.5	C	N270

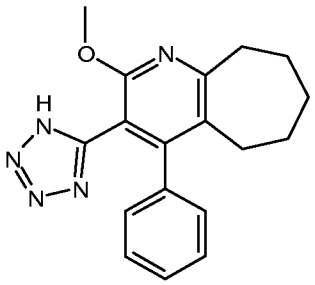
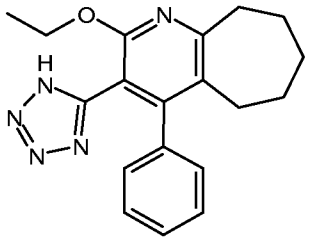
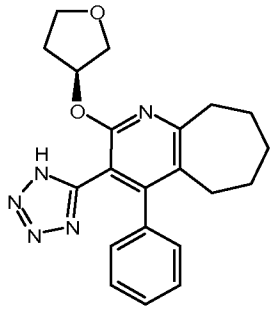
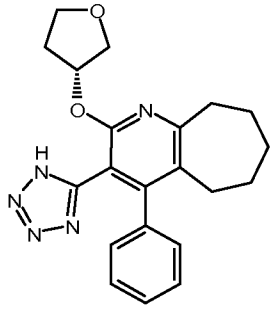
Ex.	Name	Structure	MS	Method	Starting Material
271	2-(3,3-Difluorocyclobutyl)-4-(1-methyl-1H-pyrazol-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 386.5	C	N271
272	2-(1,5-Dimethyl-1H-pyrazol-4-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESN $[M-H]^-$: 384.6	C	N272
273	2-tert-Butyl-4-(1-methyl-1H-pyrazol-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 352.5	C	N273
274	2-(3,3-Difluorocyclobutyl)-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 397.5	C	N274

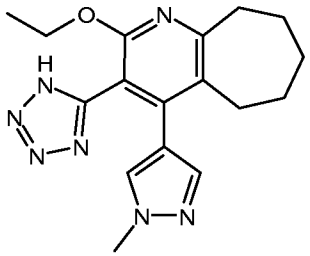
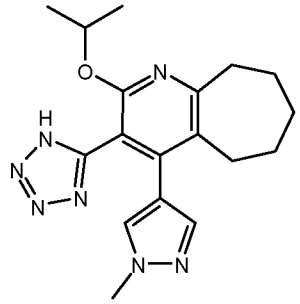
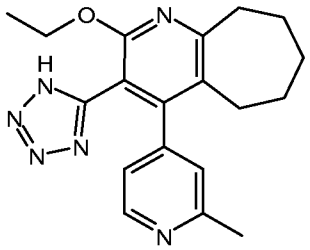
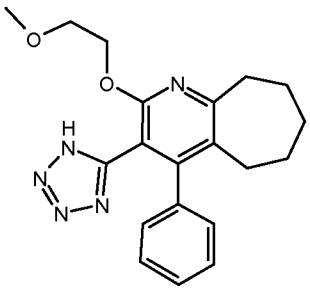
Ex.	Name	Structure	MS	Method	Starting Material
275	2-sec-Butyl-4-(1-methyl-1H-pyrazol-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 352.6	C	N275
276	2-tert-Butyl-6,6-difluoro-4-(2-methyl-pyridin-4-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydro-quinoline		ESP $[M+H]^+$: 385.5	C	N276
277	2-tert-Butyl-6,6-difluoro-4-(1-methyl-1H-pyrazol-4-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydro-quinoline		ESP $[M+H]^+$: 374.5	C	N277
278	2-tert-Butyl-6,6-difluoro-4-(2-methyl-2H-pyrazol-3-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydro-quinoline		ESP $[M+H]^+$: 374.5	C	N278

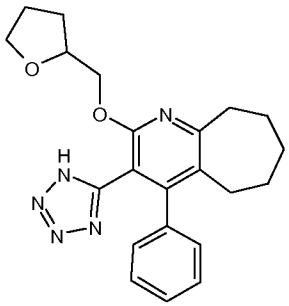
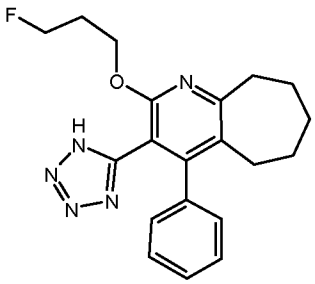
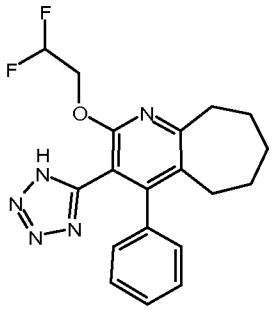
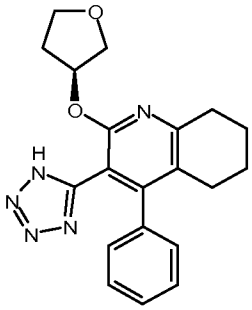
Ex.	Name	Structure	MS	Method	Starting Material
279	2-tert-Butyl-4-phenyl-3-(1H-tetrazol-5-yl)-7,8-dihydro-5H-thiopyrano[4,3-b]pyridine		ESP $[M+H]^+$: 352.6	C	N279
280	2-tert-Butyl-8,8-dimethyl-4-phenyl-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 362.6	C	N280
281	2-tert-Butyl-7,7-dimethyl-4-phenyl-3-(1H-tetrazol-5-yl)-6,7-dihydro-5H-cyclopenta[b]pyridine		ESP $[M+H]^+$: 348.6	C	N281
282	2-tert-Butyl-8,8-dimethyl-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 377.6	C	N282

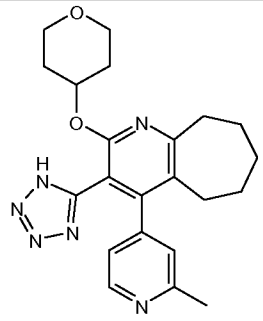
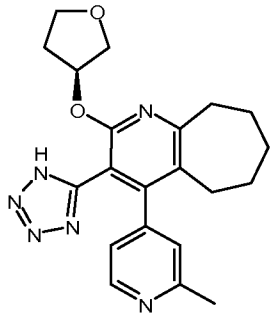
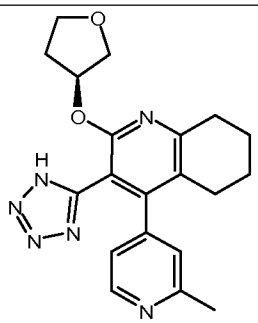
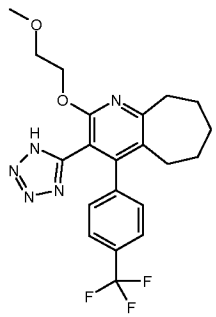
Ex.	Name	Structure	MS	Method	Starting Material
283	2-tert-Butyl-8,8-dimethyl-4-(1-methyl-1H-pyrazol-4-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 366.2	C	N283
284	2-(1-(Methoxymethyl)cyclobutyl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESN $[M-H]^-$: 388.6	C	N284
285	2-(1-(Methoxymethyl)cyclobutyl)-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 405.2	C	N285
286	2-(1-(Methoxymethyl)cyclobutyl)-4-(1-methyl-1H-pyrazol-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 394.6	C	N286

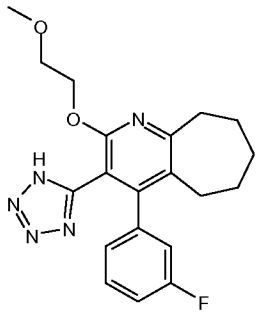
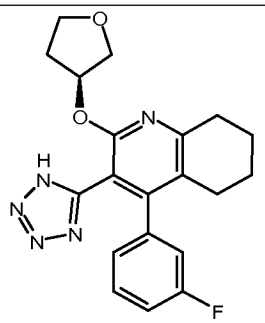
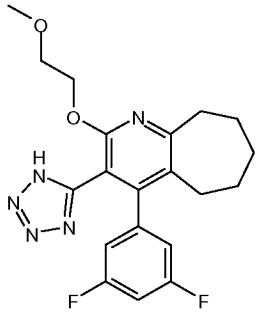
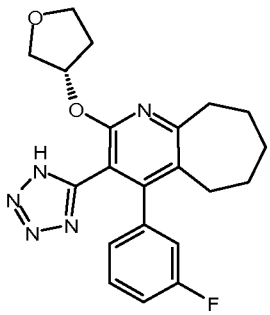
Ex.	Name	Structure	MS	Method	Starting Material
287	2-(Perfluoroethyl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESN [M-H]$^-$: 408.7	C	N287
288	2-tert-Butyl-8,8-dimethyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESN [M-H]$^-$: 364.8	C	N288
289	2,4-Bis(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine triethylamine sal		ESP [M+H]$^+$: 398.6	C	N289
290	2-Isopropoxy-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESN [M-H]$^-$: 348.5	C	N290

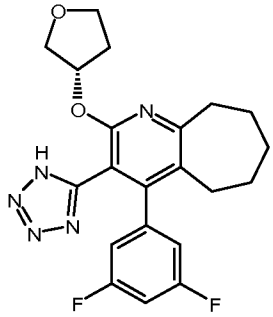
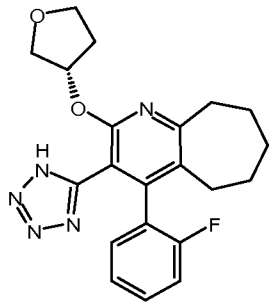
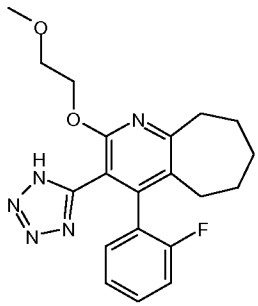
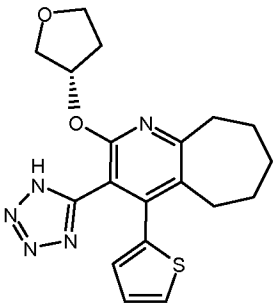
Ex.	Name	Structure	MS	Method	Starting Material
291	2-Methoxy-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 322.4	C	N291
292	2-Ethoxy-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 336.5	C	N292
293	(S)-4-Phenyl-2-(tetrahydrofuran-3-yloxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 378.6	C	N293
294	(R)-4-Phenyl-2-(tetrahydrofuran-3-yloxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 378.5	C	N294

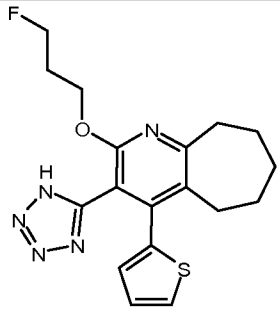
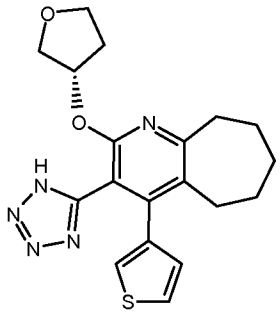
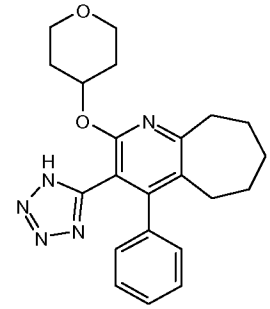
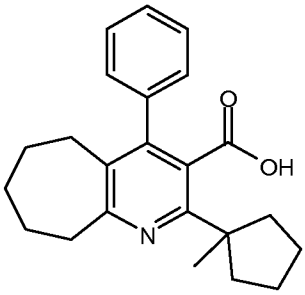
Ex.	Name	Structure	MS	Method	Starting Material
295	2-Ethoxy-4-(1-methyl-1H-pyrazol-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 340.5	C	N295
296	2-Isopropoxy-4-(1-methyl-1H-pyrazol-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 354.6	C	N296
297	2-Ethoxy-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 351.5	C	N297
298	2-(2-Methoxyethoxy)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 366.5	C	N298

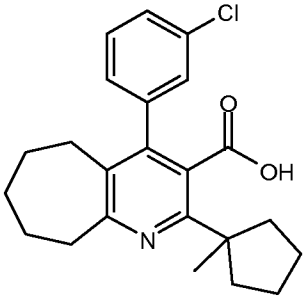
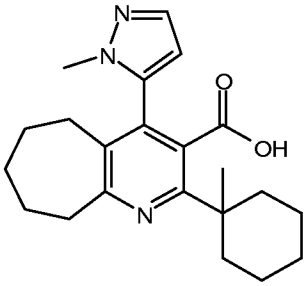
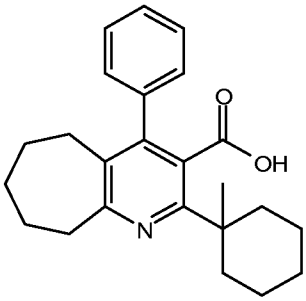
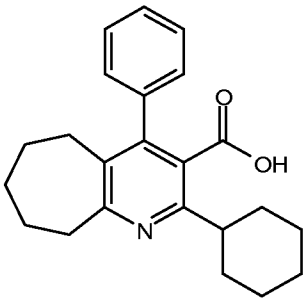
Ex.	Name	Structure	MS	Method	Starting Material
299	4-Phenyl-2-((tetrahydrofuran-2-yl)methoxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 392.5	C	N299
300	2-(3-Fluoropropoxy)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 368.5	C	N300
301	2-(2,2-Difluoroethoxy)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 372.5	C	N301
302	(S)-4-Phenyl-2-(tetrahydrofuran-3-yloxy)-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 364.5	C	N302

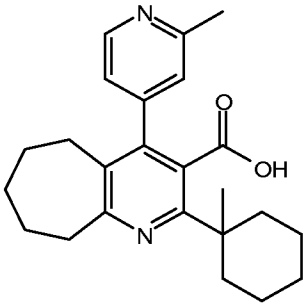
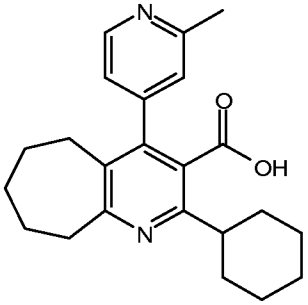
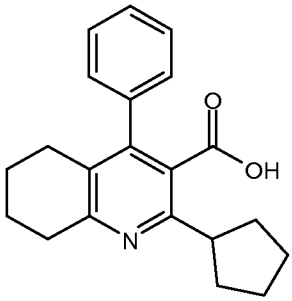
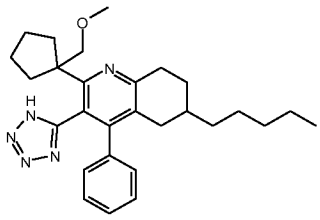
Ex.	Name	Structure	MS	Method	Starting Material
303	4-(2-Methylpyridin-4-yl)-2-(tetrahydro-2H-pyran-4-yloxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 407.5	C	N303
304	(S)-4-(2-Methylpyridin-4-yl)-2-(tetrahydrofuran-3-yloxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 393.5	C	N304
305	(S)-4-(2-Methylpyridin-4-yl)-2-(tetrahydrofuran-3-yloxy)-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 379.5	C	N305
306	2-(2-Methoxyethoxy)-3-(1H-tetrazol-5-yl)-4-(4-(trifluoromethyl)phenyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 434.5	C	N306

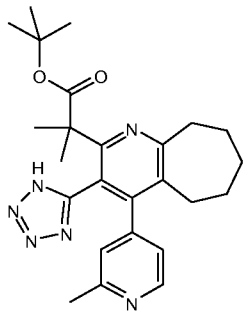
Ex.	Name	Structure	MS	Method	Starting Material
307	4-(3-Fluorophenyl)-2-(2-methoxyethoxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 384.5	C	N307
308	(S)-4-(3-Fluorophenyl)-2-(tetrahydrofuran-3-yloxy)-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESN $[M-H]^-$: 380.5	C	N308
309	4-(3,5-Difluorophenyl)-2-(2-methoxyethoxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 402.5	C	N309
310	(S)-4-(3-Fluorophenyl)-2-(tetrahydrofuran-3-yloxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 396.5	C	N310

Ex.	Name	Structure	MS	Method	Starting Material
311	(S)-4-(3,5-Difluorophenyl)-2-(tetrahydrofuran-3-yloxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 414.5	C	N311
312	4-(2-Fluorophenyl)-2-((S)-tetrahydrofuran-3-yloxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 396.5	C	N312
313	4-(2-Fluorophenyl)-2-(2-methoxyethoxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 384.4	C	N313
314	(S)-2-(Tetrahydrofuran-3-yloxy)-3-(1H-tetrazol-5-yl)-4-(thiophen-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 384.4	C	N314

Ex.	Name	Structure	MS	Method	Starting Material
315	2-(3-Fluoropropoxy)-3-(1H-tetrazol-5-yl)-4-(thiophen-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 374.4	C	N315
316	(S)-2-(Tetrahydrofuran-3-yloxy)-3-(1H-tetrazol-5-yl)-4-(thiophen-3-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 384.4	C	N316
317	4-Phenyl-2-(tetrahydro-2H-pyran-4-yloxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 392.5	C	N317
318	2-(1-Methylcyclopentyl)-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid		ESP $[M+H]^+$: 350.6	Z	N167

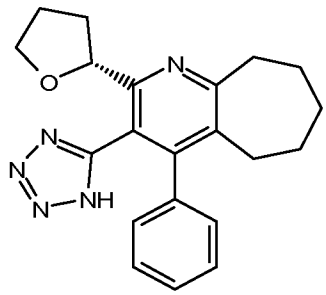
Ex.	Name	Structure	MS	Method	Starting Material
319	4-(3-Chlorophenyl)-2-(1-methylcyclopentyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid		ESP $[M+H]^+$: 384.5	Z	N170
320	4-(1-Methyl-1H-pyrazol-5-yl)-2-(1-methylcyclohexyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid		ESP $[M+H]^+$: 368.6	Z	N171
321	2-(1-Methylcyclohexyl)-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid		ESP $[M+H]^+$: 364.6	Z	N321
322	2-Cyclohexyl-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid		ESP $[M+H]^+$: 350.6	Z	from impurity in N321

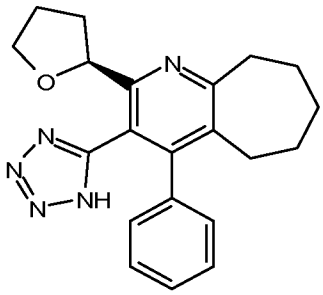
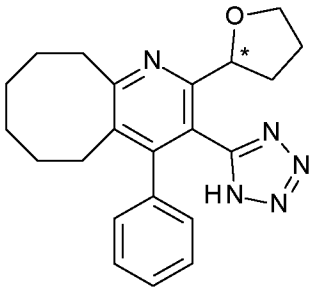
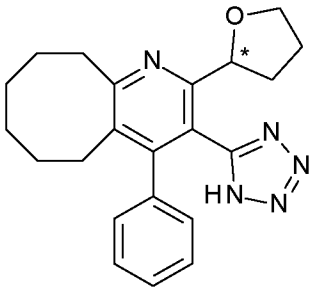
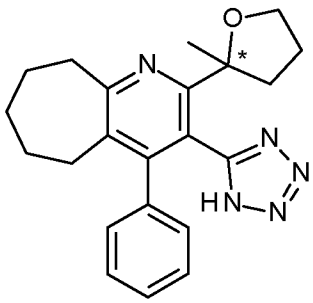
Ex.	Name	Structure	MS	Method	Starting Material
323	2-(1-Methylcyclohexyl)-4-(2-methylpyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid		ESP $[M+H]^+$: 379.5	Z	N172
324	2-Cyclohexyl-4-(2-methylpyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid		ESP $[M+H]^+$: 365.5	Z	from impurity in N172
325	2-Cyclopentyl-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carboxylic acid		ESP $[M+H]^+$: 322.6	A	E325
326	2-(1-(Methoxymethyl)cyclopentyl)-6-pentyl-4-phenyl-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 460.7	C	N326

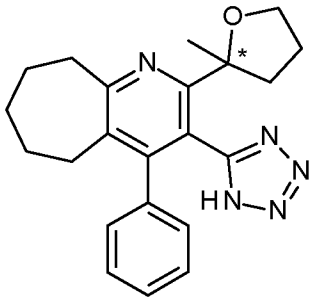
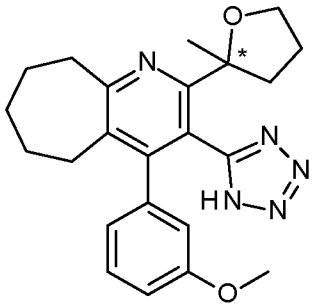
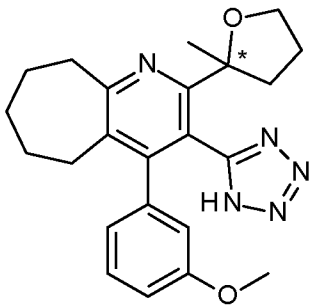
Ex.	Name	Structure	MS	Method	Starting Material
327	tert-Butyl 2-methyl-2-(4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-yl)propanoate		ESP $[M+H]^+$: 449.4	C	N327

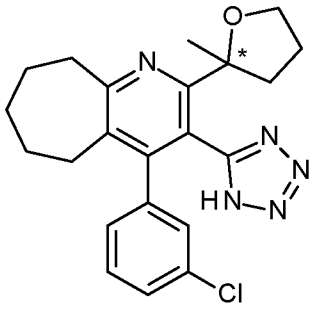
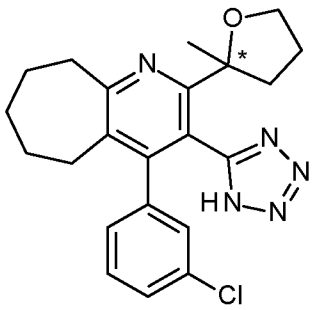
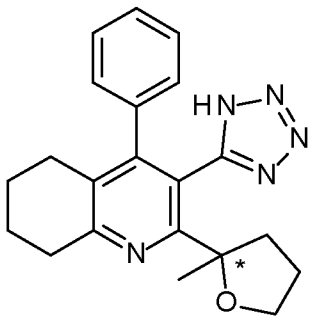
General Method X: Tetrazole compounds containing stereogenic centers and/or axis can be separated by preparative HPLC using one of the following conditions.

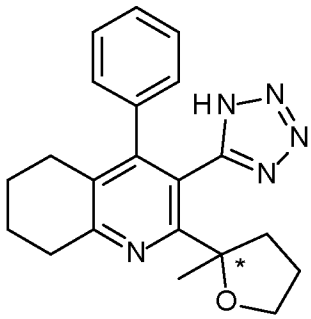
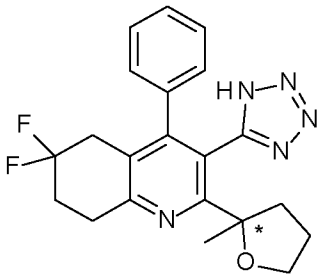
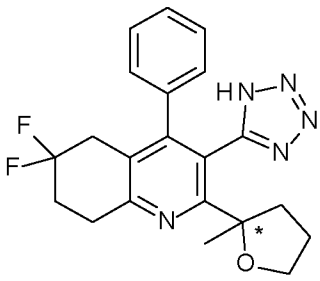
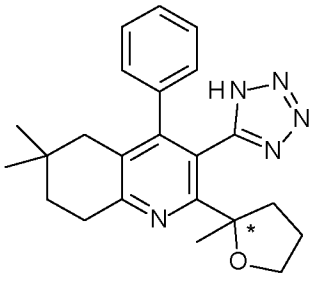
X1: Reprosil Chiral NR, 15% iPrOH in heptane
X2: Chiralpak AD-H, 10% EtOH in heptane
X3: Chiralpak AD, 10% iPrOH in heptane
X4: Chiralpak AD, 10% EtOH in heptane
X5: Chiralpak AD, 5% EtOH in heptane
X6: Chiralpak AD, 15% iPrOH in heptane

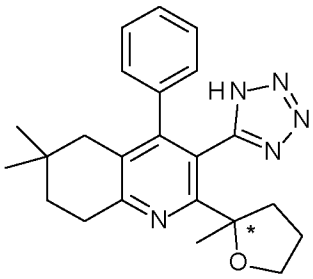
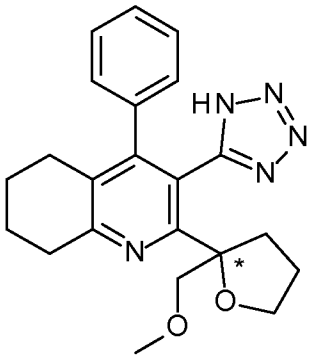
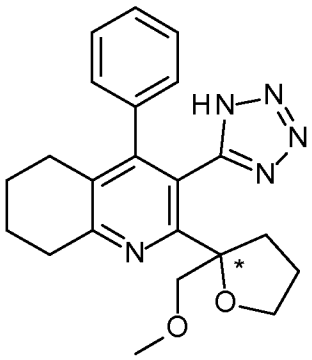
Ex.	Name	Structure	MS	Method	Starting Material
146	4-Phenyl-2-(R)-tetrahydro-furan-2-yl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 362.5	X1 1.Peak	Ex.85

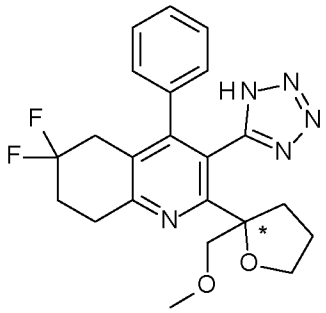
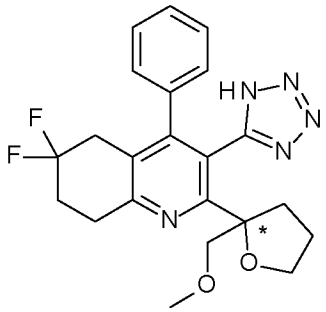
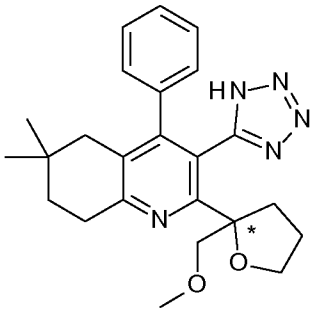
Ex.	Name	Structure	MS	Method	Starting Material
147	4-Phenyl-2-(S)-tetrahydro-furan-2-yl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 362.5	X1 2.Peak	Ex.85
152	4-Phenyl-2-(tetrahydrofuran-2-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8,9,10-hexahydrocycloocta[b]pyridine		ESP $[M+H]^+$: 376.6	X2 1.Peak	Ex.151
153	4-Phenyl-2-(tetrahydrofuran-2-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8,9,10-hexahydrocycloocta[b]pyridine		ESP $[M+H]^+$: 376.6	X2 2.Peak	Ex.151
155	2-(2-Methyl-tetrahydro-furan-2-yl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 376.5	X3 1.Peak	Ex. 154

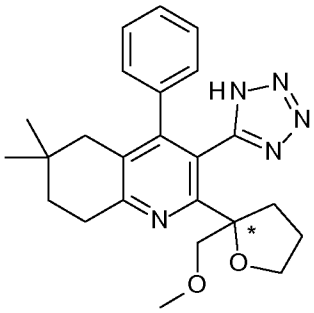
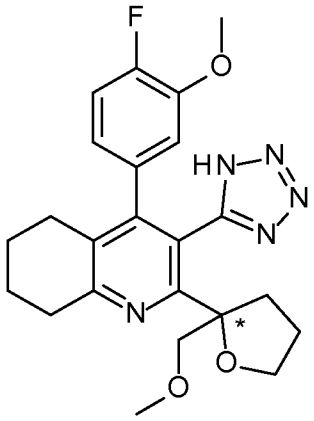
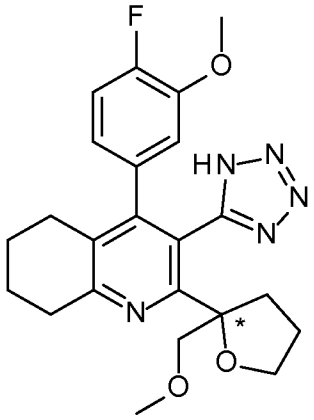
Ex.	Name	Structure	MS	Method	Starting Material
156	2-(2-Methyl-tetrahydro-furan-2-yl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 376.6	X3 2.Peak	Ex. 154
158	4-(3-Methoxy-phenyl)-2-(2-methyl-tetrahydro-furan-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 406.6	X4 1.Peak	Ex. 157
159	4-(3-Methoxy-phenyl)-2-(2-methyl-tetrahydro-furan-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 406.6	X4 2.Peak	Ex. 157

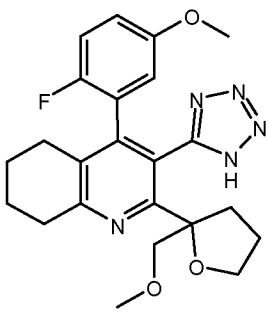
Ex.	Name	Structure	MS	Method	Starting Material
164	4-(3-Chloro-phenyl)-2-(2-methyl-tetrahydro-furan-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 410.5	X5 1.Peak	Ex. 163
165	4-(3-Chloro-phenyl)-2-(2-methyl-tetrahydro-furan-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine		ESP $[M+H]^+$: 410.5	X5 2.Peak	Ex. 163
231	2-(2-Methyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 362.7	X3 1. Peak	Ex. 226

Ex.	Name	Structure	MS	Method	Starting Material
232	2-(2-Methyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 362.7	X3 2. Peak	Ex. 226
233	6,6-Difluoro-2-(2-methyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 398.7	X3 1. Peak	Ex. 227
234	6,6-Difluoro-2-(2-methyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 398.7	X3 2. Peak	Ex. 227
235	6,6-Dimethyl-2-(2-methyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 390.7	X3 1. Peak	Ex. 228

Ex.	Name	Structure	MS	Method	Starting Material
236	6,6-Dimethyl-2-(2-methyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 390.7	X3 2. Peak	Ex. 228
249	2-(2-(Methoxymethyl)tetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 392.6	X3 1. Peak	Ex. 242
250	(S)-2-(2-(Methoxymethyl)tetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 392.6	X3 2. Peak	Ex. 242

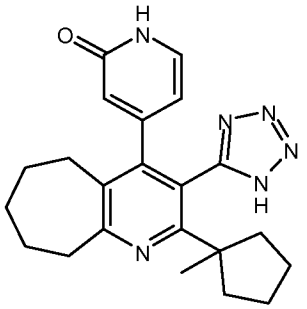
Ex.	Name	Structure	MS	Method	Starting Material
251	6,6-Difluoro-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 428.5	X3 1. Peak	Ex. 245
252	6,6-Difluoro-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 428.5	X3 2. Peak	Ex. 245
253	2-(2-(Methoxymethyl)tetrahydrofuran-2-yl)-6,6-dimethyl-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 420.6	X3 1. Peak	Ex. 244

Ex.	Name	Structure	MS	Method	Starting Material
254	2-(2-(Methoxymethyl)tetrahydrofuran-2-yl)-6,6-dimethyl-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 420.6	X3 2. Peak	Ex. 244
262	4-(4-Fluoro-3-methoxyphenyl)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 440.5	X6 1. Peak	Ex. 260
263	4-(4-Fluoro-3-methoxyphenyl)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 440.5	X6 2. Peak	Ex. 260

Ex.	Name	Structure	MS	Method	Starting Material
267	4-(2-Fluoro-5-methoxyphenyl)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline		ESP $[M+H]^+$: 440.5	X3 1. Peak (absolute configuration not assigned)	Ex. 266

Example 169

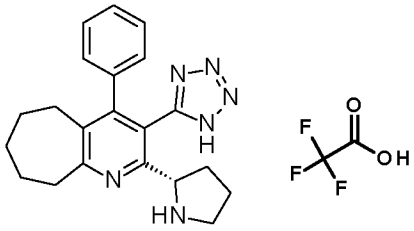
4-(2-(1-Methylcyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)pyridin-2(1H)-one



4-(2-Methoxypyridin-4-yl)-2-(1-methylcyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine (Example 168, 68.9 mg) was mixed with hydrobromic acid, 33% in acetic acid (1.42 g) and the suspension was stirred at 70 °C for 18 h. The reaction mixture was evaporated, twice evaporated with water und purified by preparative HPLC to give the title compound (26 mg) as a colorless solid. MS (ESP) = 391.7 $[M+H]^+$

Example 211

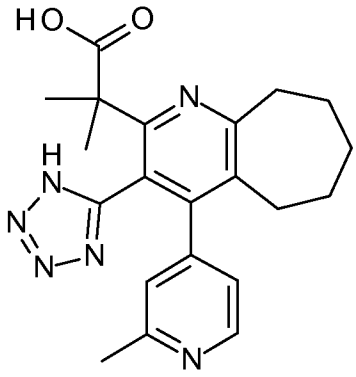
(S)-4-Phenyl-2-(pyrrolidin-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine 2,2,2-trifluoroacetate



(S)-tert-Butyl 2-(4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-yl)pyrrolidine-1-carboxylate (Example 210, 140 mg) was dissolved in DCM (2 ml). After addition of TFA (1.48 g) the reaction mixture was stirred for 1h at rt. The solvent was evaporated and the product was purified by preparative HPLC to give the title compound (55 mg) as an off-white solid. MS (ESP): m/z = 361.6 $[M+H]^+$.

Example 328

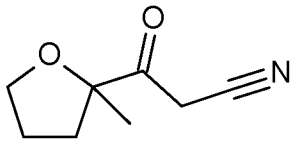
2-Methyl-2-(4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-yl)propanoic acid



tert-Butyl 2-methyl-2-(4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-yl)propanoate (Example 327, 28 mg) was dissolved in DCM (3 ml). After addition of TFA (7.12 mg) the reaction mixture was stirred for 27h at rt. The solvent was evaporated and the product was purified by preparative HPLC to afford the title compound (8 mg) as a white solid. MS (ESP): m/z = 393.5 $[M+H]^+$.

Intermediate B154

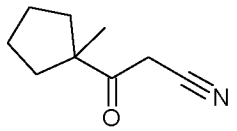
3-(2-Methyltetrahydrofuran-2-yl)-3-oxo-propanenitrile



In analogy to the synthesis of Intermediate B79, methyl 2-methyltetrahydrofuran-2-carboxylate (CAS# 1218915-91-3) was converted to the title compound by reaction with sodium hydride and acetonitrile in THF. Colorless liquid. MS (ESP): m/z = 154.2 $[M+H]^+$.

Intermediate B166

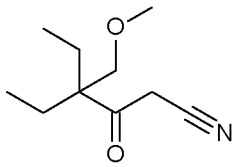
3-(1-Methylcyclopentyl)-3-oxopropanenitrile



In analogy to the synthesis of Intermediate B79, methyl 1-methylcyclopentanecarboxylate (CAS# 4630-83-5) was converted to the title compound by reaction with sodium hydride and acetonitrile in THF. Yellow oil. MS (ESN): m/z = 150.3 $[M-H]^-$.

Intermediate B191

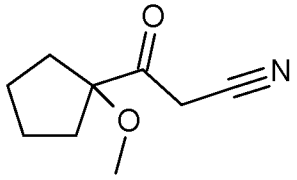
4-Ethyl-4-(methoxymethyl)-3-oxohexanenitrile



In analogy to the synthesis of Intermediate B218, ethyl 2-ethylbutanoate (CAS# 2983-38-2) was reacted with lithium diisopropylamide and chloromethyl methyl ether to obtain ethyl 2-ethyl-2-(methoxymethyl)butanoate which was converted to the title compound by reaction with sodium hydride and acetonitrile in THF. Light yellow liquid. MS (ESP): m/z = 189.3 $[M+H]^+$.

Intermediate B200

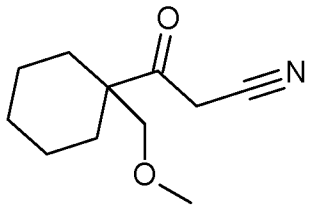
3-(1-Methoxycyclopentyl)-3-oxopropanenitrile



In analogy to the synthesis of Intermediate B79, methyl 1-methoxycyclopentanecarboxylate (CAS# 17860-29-6) was converted to the title compound by reaction with sodium hydride and acetonitrile in THF. Light yellow liquid. MS (ESN): m/z = 166.3 $[M-H]^-$.

Intermediate B218

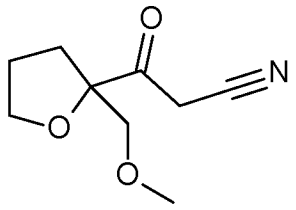
3-(1-(Methoxymethyl)cyclohexyl)-3-oxopropanenitrile



To a solution of diisopropylamine (3.66 g, 5.15 ml, 36.1 mmol) in THF (50 ml) under Argon was slowly added n-butyllithium (1.6 M in n-hexane, 22.5 ml, 36.0 mmol) at -78 °C and the mixture was stirred for 30 minutes. Then a solution of methyl cyclohexanecarboxylate (5 g, 35.2 mmol) in THF (25 ml) was added dropwise. The mixture was allowed to warm to -40 °C and stirred for 30 minutes at this temperature. Then a solution of chloromethyl methyl ether (2.83 g, 35.2 mmol) in THF (12.5 ml) was added dropwise. After the addition was completed, the reaction mixture was allowed to warm to rt. Water was added and the mixture was extracted with EtOAc. The combined organic extracts were washed with water and brine, dried with Na_2SO_4 and evaporated to give methyl 1-(methoxymethyl)cyclohexanecarboxylate as a light yellow oil which was converted to the title compound in analogy to the synthesis of Intermediate B79 by reaction with sodium hydride and acetonitrile in THF. Light yellow oil. MS (ESP): m/z = 196.5 $[M+H]^+$.

Intermediate B242

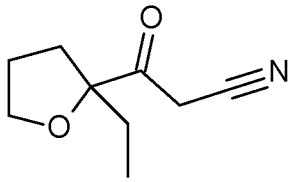
3-(2-(Methoxymethyl)tetrahydrofuran-2-yl)-3-oxopropanenitrile



In analogy to the synthesis of Intermediate B218, methyl tetrahydrofuran-2-carboxylate (CAS# 37443-42-8) was reacted with lithium diisopropylamide and chloromethyl methyl ether to obtain methyl 2-(methoxymethyl)tetrahydrofuran-2-carboxylate which was converted to the title compound by reaction with sodium hydride and acetonitrile in THF. Light yellow oil. MS (ESN): m/z = 182.3 $[M-H]^-$.

Intermediate B246

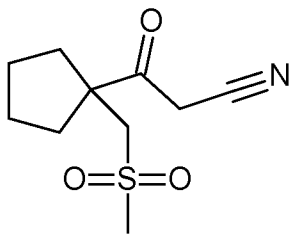
3-(2-Ethyltetrahydrofuran-2-yl)-3-oxopropanenitrile



In analogy to the synthesis of Intermediate B218, methyl tetrahydrofuran-2-carboxylate (CAS# 37443-42-8) was reacted with lithium diisopropylamide and iodoethane to obtain methyl 2-ethyltetrahydrofuran-2-carboxylate which was converted to the title compound by reaction with sodium hydride and acetonitrile in THF. Light yellow oil. MS (ESN): m/z = 166.4 $[M-H]^-$.

Intermediate B261

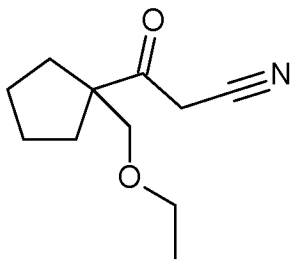
3-(1-(Methylsulfonylmethyl)cyclopentyl)-3-oxopropanenitrile



In analogy to the synthesis of Intermediate B218, methyl cyclopentanecarboxylate was reacted with lithium diisopropylamide and (chloromethyl)(methyl)sulfane to obtain methyl 1-(methylthiomethyl)cyclopentanecarboxylate which was converted to 3-(1-(methylthiomethyl)cyclopentyl)-3-oxopropanenitrile by reaction with sodium hydride and acetonitrile in THF. The 3-(1-(methylthiomethyl)cyclopentyl)-3-oxopropanenitrile (210 mg, 1.06 mmol) was then dissolved in dichloromethane (10 ml) and m-chloroperbenzoic acid (656 mg, 2.66 mmol) was added in one portion and the mixture was stirred at room temperature overnight. The resulting white suspension was diluted with water and extracted with DCM. The organic extracts were washed with Na_2SO_3 (15% g/g solution) and sat. aqueous $NaHCO_3$ solution, dried with Na_2SO_4 (containing solid Na_2SO_3) and evaporated to obtain the title compound as white solid. MS (ESN): m/z = 228.3 $[M-H]^-$.

Intermediate B268

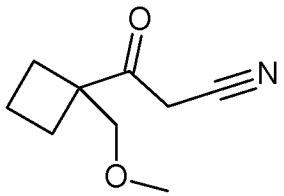
3-[1-(Ethoxymethyl)cyclopentyl]-3-oxo-propanenitrile



In analogy to the synthesis of Intermediate B79, methyl 1-(ethoxymethyl)cyclopentanecarboxylate (CAS# 1360569-15-8) was converted to the title compound by reaction with sodium hydride and acetonitrile in THF. Yellow liquid. MS (ESN): m/z = 194.3 $[M-H]^-$.

Intermediate B284

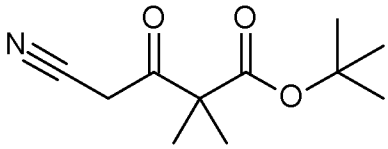
3-(1-(Methoxymethyl)cyclobutyl)-3-oxopropanenitrile



In analogy to the synthesis of Intermediate B218, methyl cyclobutanecarboxylate (CAS# 765-85-5) was reacted with lithium diisopropylamide and chloromethyl methyl ether to obtain methyl 1-(methoxymethyl)cyclobutanecarboxylate which was converted to the title compound by reaction with sodium hydride and acetonitrile in THF. Yellow liquid. MS (ESN): m/z = 166.3 $[M-H]^-$.

Intermediate B327

tert-Butyl 4-cyano-2,2-dimethyl-3-oxobutanoate



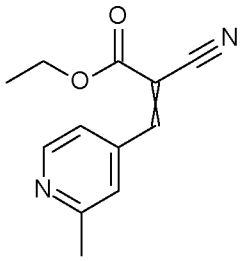
A solution of acetonitrile (0.60 g, 14.6 mmol) in THF (29 ml) was cooled in a dry ice bath. n-BuLi (9 ml of a 1.6 M solution in hexane, 14.4 mmol) was added dropwise and stirring was continued for 30 min. Then a solution of 1-tert-butyl 3-methyl 2,2-dimethylmalonate (CAS# 85293-46-5) (1.5 g, 7.3 mmol) in THF (7 ml) was added slowly. The mixture was stirred for 2 h at -78 °C. Acetic acid (2.4 ml, excess) was added and the reaction mixture was allowed to reach rt. After extractive workup (AcOEt / sat. aq. Seignette salt solution) the organic phase was dried (Na_2SO_4) and concentrated to furnish a light orange liquid (1.4 g) which was used in the next step without further purification.

Additional Intermediates K (via Knoevenagel condensation)

General Method Z2: Knoevenagel products by reaction of alkyl cyanoacetate with aldehyde and NH_4OAc at rt

A mixture of the aldehyde (1 eq), alkyl 2-cyanoacetate (1eq), ammonium acetate (1.5 eq) and an alcohol (typically ethanol) is stirred at rt for 1 h. After extractive workup (AcOEt / H_2O) the

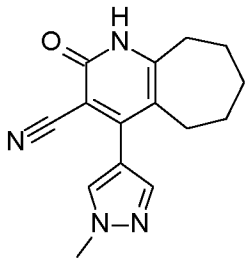
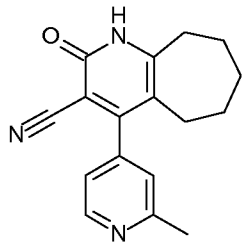
organic phase is dried (Na_2SO_4), filtered and concentrated to dryness to obtain the title compound as a solid which can be used as such. If necessary, it can be further purified by chromatography and/or recrystallization.

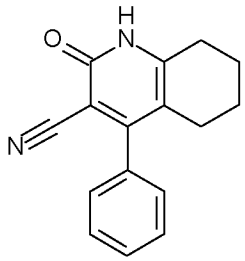
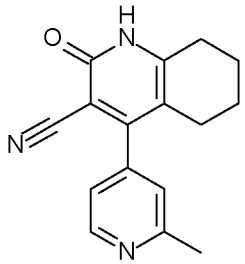
Intermediate	Name and Structure	MS	Method	Reagents
K297	Ethyl 2-cyano-3-(2-methylpyridin-4-yl)acrylate 	ESP $[M+H]^+$: 217.5	Z2	2-Methylisonicotinaldehyde, ethyl 2-cyanoacetate

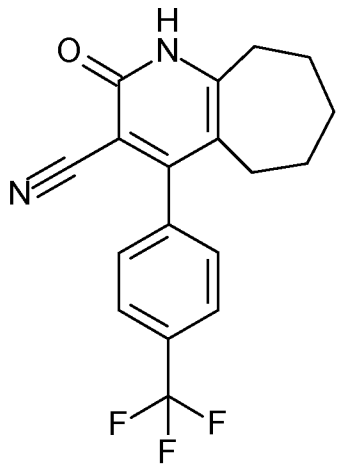
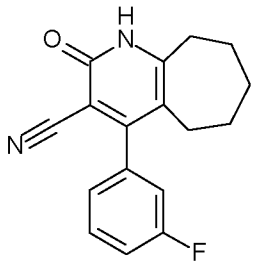
Additional Intermediates P (Pyridones)

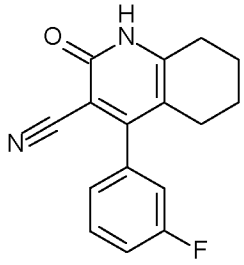
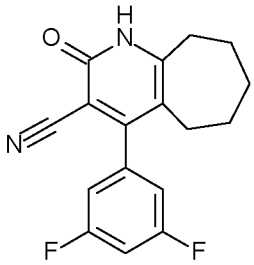
General Method Z1: pyridones from ketones, Knoevenagel adducts, NH_4OAc (78 °C) followed by reaction with ceric ammonium nitrate

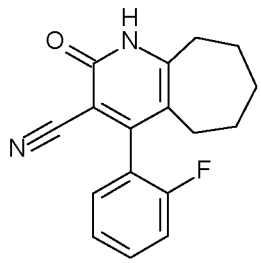
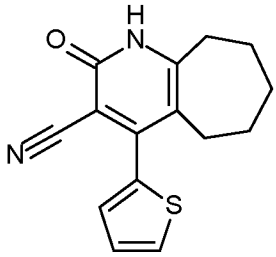
A mixture of the ketone (1 eq), the Knoevenagel adduct (Intermediate K, 1 eq), ammonium acetate (3 eq) and an alcohol (typically ethanol) is refluxed for 2 to 12 h. The suspension is cooled in an ice bath and filtered to obtain precipitate 1. The mother liquor is concentrated, dissolved in acetone / water (1 / 1) and cooled in an ice bath. Ceric ammonium nitrate (1eq) is added and stirring is continued for 20 min to 2 h at rt. The reaction mixture is filtered to obtain precipitate 2. The combined solids are dried and can be used as such. If necessary, the raw product can be further purified by chromatography and/or crystallization to obtain a pure specimen of the title compound.

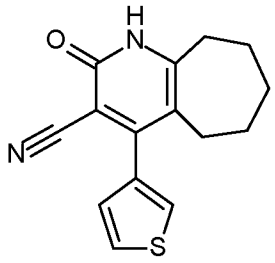
Intermediate	Name and Structure	MS	Method	Reagents
P295	4-(1-Methyl-1H-pyrazol-4-yl)-2-oxo-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 269.5	Z1	Ethyl 2-cyano-3-(1-methyl-1H-pyrazol-4-yl)acrylate, (CAS# 1005866-02-3), cycloheptanone
P297	4-(2-Methylpyridin-4-yl)-2-oxo-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 280.5	Z1	Ethyl 2-cyano-3-(2-methylpyridin-4-yl)acrylate (Intermediate K297), cycloheptanone

Intermediate	Name and Structure	MS	Method	Reagents
P302	2-Oxo-4-phenyl-1,2,5,6,7,8-hexahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 251.5	Z1	Ethyl 2-cyano-3-phenylacrylate (CAS# 2025-40-3), cyclohexanone
P305	4-(2-Methylpyridin-4-yl)-2-oxo-1,2,5,6,7,8-hexahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 266.5	Z1	Ethyl 2-cyano-3-(2-methylpyridin-4-yl)acrylate (Intermediate K297), cyclohexanone

Intermediate	Name and Structure	MS	Method	Reagents
P306	2-Oxo-4-(4-(trifluoromethyl)phenyl)-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile 	ESN [M-H]: 331.4	Z1	Ethyl 2-cyano-3-(4-(trifluoromethyl)phenyl)acrylate (CAS# 149550-21-0), cycloheptanone
P307	4-(3-Fluorophenyl)-2-oxo-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 283.4	Z1	Ethyl 2-cyano-3-(3-fluorophenyl)acrylate (CAS# 19310-52-2), cycloheptanone

Intermediate	Name and Structure	MS	Method	Reagents
P308	4-(3-Fluorophenyl)-2-oxo-1,2,5,6,7,8-hexahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 269.3	Z1	Ethyl 2-cyano-3-(3-fluorophenyl)acrylate (CAS# 19310-52-2), cyclohexanone
P309	4-(3,5-Difluorophenyl)-2-oxo-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 301.4	Z1	Ethyl 2-cyano-3-(3,5-difluorophenyl)acrylate (CAS# 623572-49-6), cycloheptanone

Intermediate	Name and Structure	MS	Method	Reagents
P312	4-(2-Fluorophenyl)-2-oxo-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 283.3	Z1	Ethyl 2-cyano-3-(2-fluorophenyl)acrylate (CAS# 84186-23-2), cycloheptanone
P314	2-Oxo-4-(thiophen-2-yl)-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile 	ESN $[M-H]^-$: 269.4	Z1	Ethyl 2-cyano-3-(thiophen-2-yl)acrylate (CAS#31330-51-5), cycloheptanone

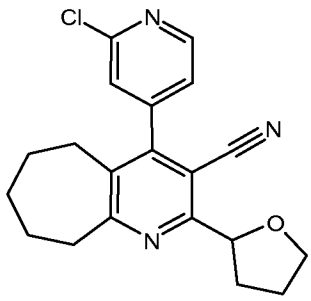
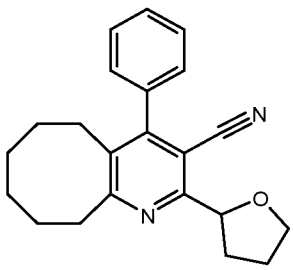
Intermediate	Name and Structure	MS	Method	Reagents
P316	2-Oxo-4-(thiophen-3-yl)-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 271.4	Z1	Ethyl 2-cyano-3-(thiophen-3-yl)acrylate (CAS#117106-47-5), cycloheptanone

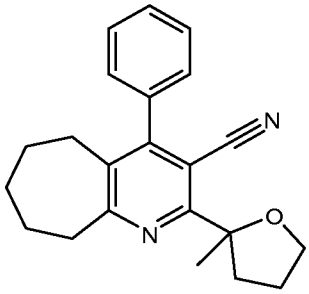
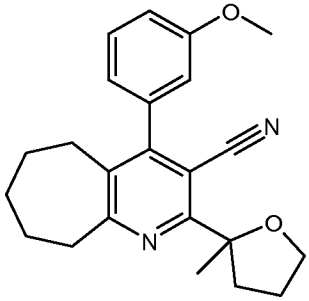
Additional Intermediates E/N

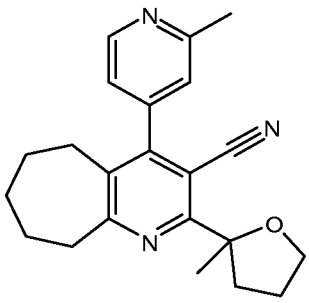
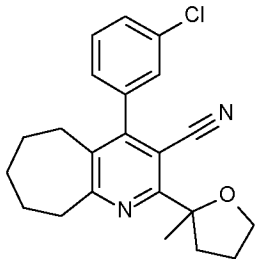
General Method Y: Conversion of pyridones into 2-alkoxypyridines via 2-chloropyridines

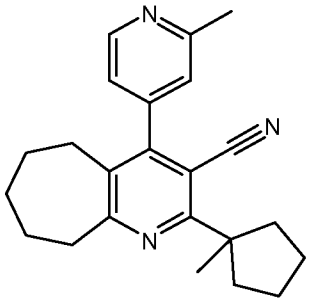
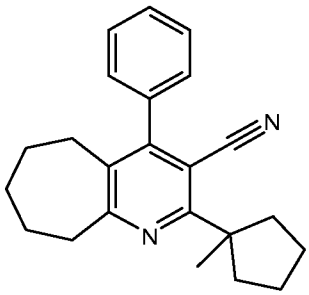
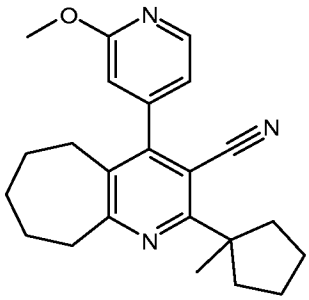
Step 1: To a suspension of pyridone (Intermediate P, 54.1 mmol) in phosphorous oxychloride (377 mmol, 7 eq) is slowly added DMF (23.1 mmol, 0.43 eq). After the exothermic reaction has ceased the mixture is heated to 105 °C for 4 h. All volatiles are evaporated and the oily residue is slowly poured onto water. The suspension is stirred for 1 h, filtered, washed with water and dried to obtain the 2-chloropyridine as a brown solid. The compound can be used as such or further purified by chromatography.

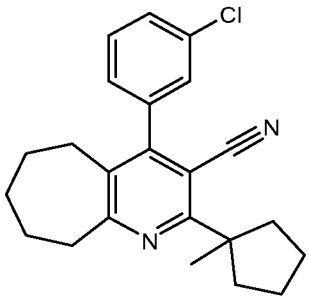
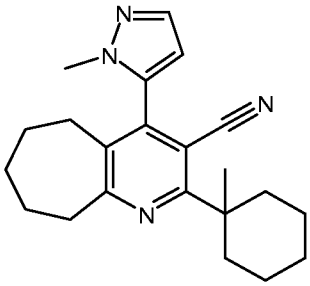
Step 2: The respective alcohol (4.2 mmol, 4 eq) is dissolved in THF (2 ml). Sodium hydride (4eq of a 55% dispersion in mineral oil) is added. The mixture is stirred at room temperature for 1 h followed by addition of a suspension of the chloropyridine obtained in step 1 (1.1 mmol,1 eq) in THF (3ml). The reaction mixture is stirred at rt for 3 h. Extractive workup (water / sat aq. sodium bicarbonate solution) followed by chromatography affords the target compound.

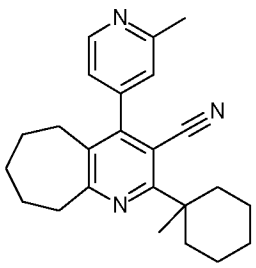
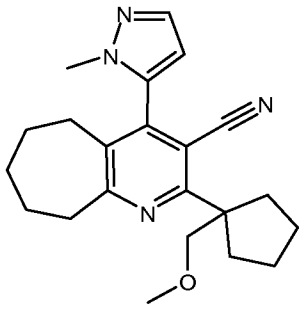
Intermediate	Name and Structure	MS	Method	Reagents
N149R	4-(2-Chloropyridin-4-yl)-2-(tetrahydrofuran-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 354.6	V	Intermediate B85, 2-chloroisonicotinaldehyde, cycloheptanone
N151	4-Phenyl-2-(tetrahydrofuran-2-yl)-5,6,7,8,9,10-hexahydrocycloocta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 333.5	V	Intermediate B85, benzaldehyde, cyclooctanone

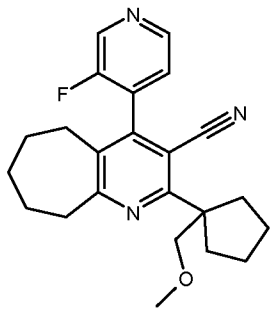
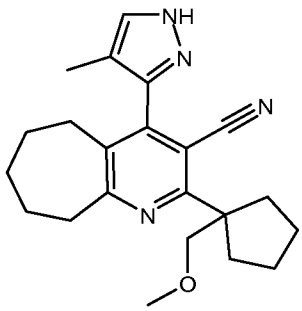
Intermediate	Name and Structure	MS	Method	Reagents
N154	2-(2-Methyltetrahydrofuran-2-yl)-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 333.6	V	Intermediate B154, benzaldehyde, cycloheptanone
N157	4-(3-Methoxyphenyl)-2-(2-methyltetrahydrofuran-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 363.5	V	Intermediate B154, 3-methoxybenzaldehyde, cycloheptanone

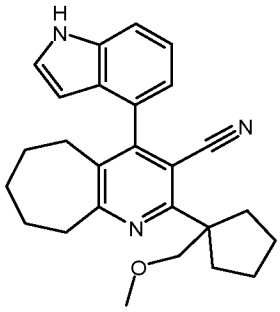
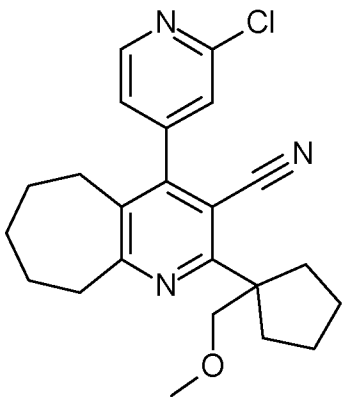
Intermediate	Name and Structure	MS	Method	Reagents
N160	4-(2-Methylpyridin-4-yl)-2-(2-methyltetrahydrofuran-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 348.5	V	Intermediate B154, 2-methylisonicotinaldehyde, cycloheptanone
N163	4-(3-Chlorophenyl)-2-(2-methyltetrahydrofuran-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 367.5	V	Intermediate B154, 3-chlorobenzaldehyde, cycloheptanone

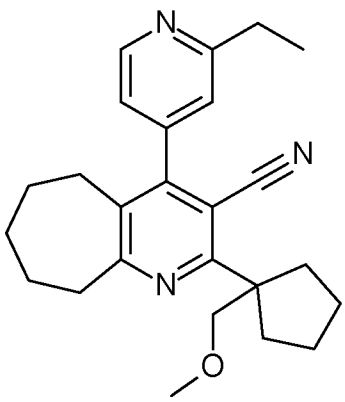
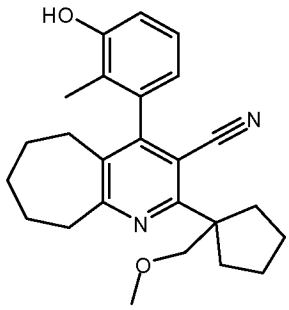
Intermediate	Name and Structure	MS	Method	Reagents
N166	2-(1-Methylcyclopentyl)-4-(2-methylpyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 346.5	V	Intermediate B166, 2-methylisonicotinaldehyde, cycloheptanone
N167	2-(1-Methylcyclopentyl)-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+NH_4]^+$: 349.6	V	Intermediate B166, benzaldehyde, cycloheptanone
N168	4-(2-Methoxypyridin-4-yl)-2-(1-methylcyclopentyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 362.7	V	Intermediate B166, 2-methoxyisonicotinaldehyde, cycloheptanone

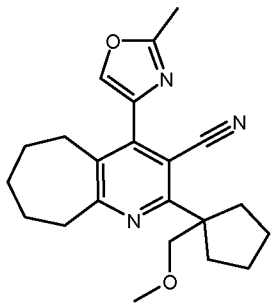
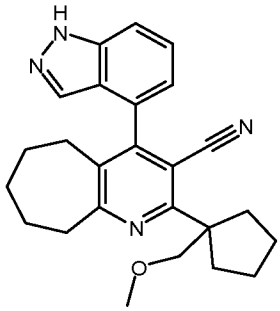
Intermediate	Name and Structure	MS	Method	Reagents
N170	4-(3-Chlorophenyl)-2-(1-methylcyclopentyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 		V	Intermediate B166, 3-chlorobenzaldehyde, cycloheptanone
N171	4-(1-Methyl-1H-pyrazol-5-yl)-2-(1-methylcyclohexyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 349.6	V	3-(1-Methylcyclohexyl)-3-oxopropanenitrile (CAS# 95882-32-9), 1-methyl-1H-pyrazole-5-carbaldehyde, cycloheptanone

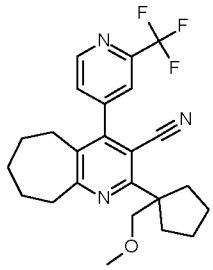
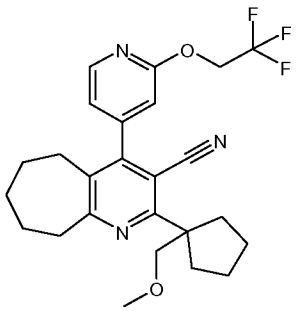
Intermediate	Name and Structure	MS	Method	Reagents
N172	2-(1-Methylcyclohexyl)-4-(2-methyl-4-pyridyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile, contains traces of 2-Cyclohexyl-4-(2-methyl-4-pyridyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 360.5	V	3-(1-Methylcyclohexyl)-3-oxopropanenitrile (CAS# 95882-32-9), 2-methylisonicotinaldehyde, cycloheptanone
N173	2-(1-(Methoxymethyl)cyclopentyl)-4-(1-methyl-1H-pyrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 365.6	V	Intermediate B94, 1-methyl-1H-pyrazole-5-carbaldehyde , cycloheptanone

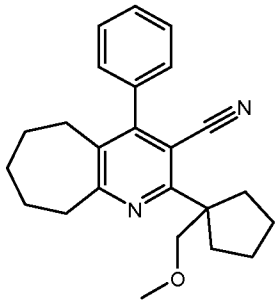
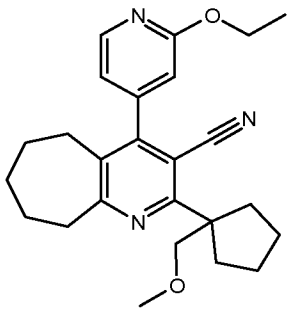
Intermediate	Name and Structure	MS	Method	Reagents
N174	4-(3-Fluoropyridin-4-yl)-2-(1-(methoxymethyl)cyclopentyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 380.5	V	Intermediate B94, 3-fluoroisonicotinaldehyde, cycloheptanone
N175	2-(1-(Methoxymethyl)cyclopentyl)-4-(4-methyl-1H-pyrazol-3-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 365.6	V	Intermediate B94, 4-methyl-1H-pyrazole-5-carbaldehyde, cycloheptanone

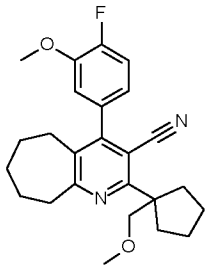
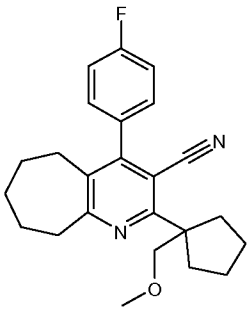
Intermediate	Name and Structure	MS	Method	Reagents
N176	4-(1H-Indol-4-yl)-2-(1-(methoxymethyl)cyclopentyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 400.7	V	Intermediate B94, 1H-indole-4-carbaldehyde, cycloheptanone
N177	4-(2-Chloro-4-pyridyl)-2-[1-(methoxymethyl)cyclopentyl]-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 396.5	V	Intermediate B94, 2-chloroisonicotinaldehyde, cycloheptanone

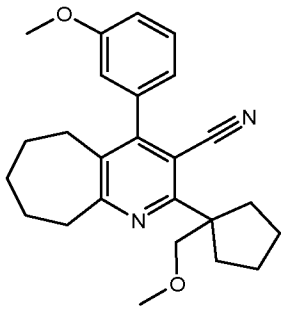
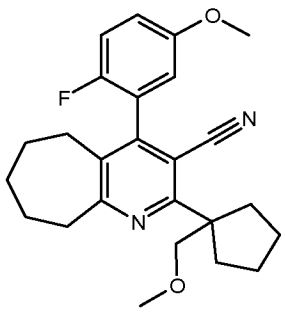
Interme diate	Name and Structure	MS	Method	Reagents
N178	4-(2-Ethyl-4-pyridyl)-2-[1-(methoxymethyl)cyclopentyl]-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 390.6	V	Intermediate B94, 2-ethylisonicotinaldehyde, cycloheptanone
N179	4-(3-Hydroxy-2-methylphenyl)-2-(1-(methoxymethyl)cyclopentyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 391.7	V	Intermediate B94, 3-hydroxy-2-methylbenzaldehyde, cycloheptanone

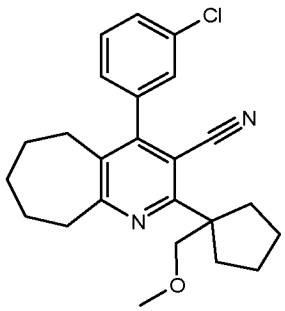
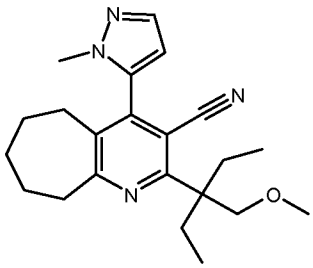
Interme diate	Name and Structure	MS	Method	Reagents
N180	2-(1-(Methoxymethyl)cyclopentyl)-4-(2-methyloxazol-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 366.6	V	Intermediate B94, 2-methyloxazole-4-carbaldehyde, cycloheptanone
N181	4-(1H-Indazol-4-yl)-2-(1-(methoxymethyl)cyclopentyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 401.7	V	Intermediate B94, 1H-indazole-4-carbaldehyde, cycloheptanone

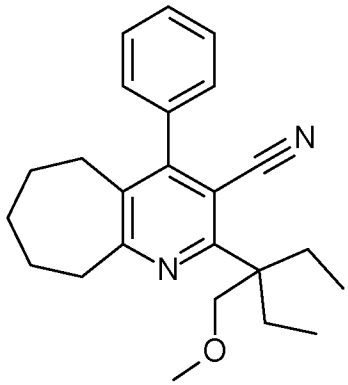
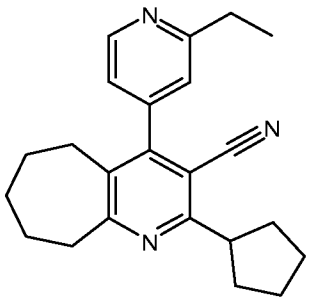
Intermediate	Name and Structure	MS	Method	Reagents
N182	2-[1-(Methoxymethyl)cyclopentyl]-4-[2-(trifluoromethyl)-4-pyridyl]-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 		V	Intermediate B94, 2-(trifluoromethyl)isonicotinaldehyde, cycloheptanone
N183	2-(1-(Methoxymethyl)cyclopentyl)-4-(2-(2,2,2-trifluoroethoxy)pyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 460.6	V	Intermediate B94, 2-(2,2,2-trifluoroethoxy)isonicotinaldehyde, cycloheptanone

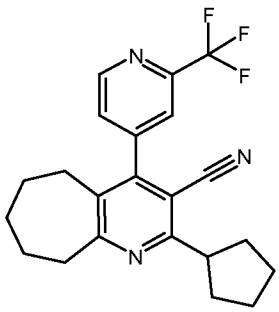
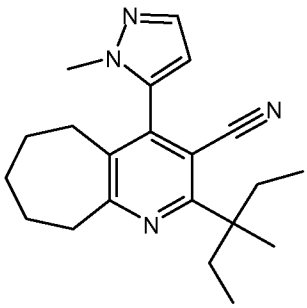
Intermediate	Name and Structure	MS	Method	Reagents
N184	2-(1-(Methoxymethyl)cyclopentyl)-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 361.6	V	Intermediate B94, benzaldehyde, cycloheptanone
N185	4-(2-Ethoxypyridin-4-yl)-2-(1-(methoxymethyl)cyclopentyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 406.6	V	Intermediate B94, 2-ethoxyisonicotinaldehyde, cycloheptanone

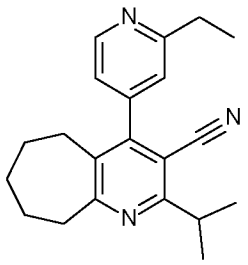
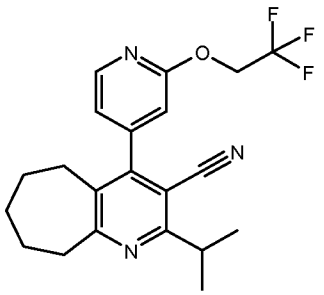
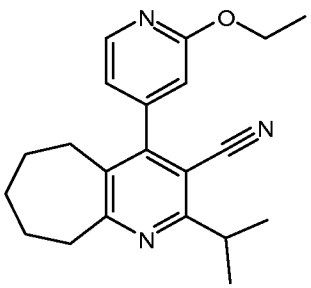
Intermediate	Name and Structure	MS	Method	Reagents
N186	4-(4-Fluoro-3-methoxy-phenyl)-2-[1-(methoxymethyl)cyclopentyl]-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 409.6	V	Intermediate B94, 4-fluoro-3-methoxybenzaldehyde, cycloheptanone
N187	4-(4-Fluorophenyl)-2-(1-(methoxymethyl)cyclopentyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 379.6	V	Intermediate B94, 4-fluorobenzaldehyde, cycloheptanone

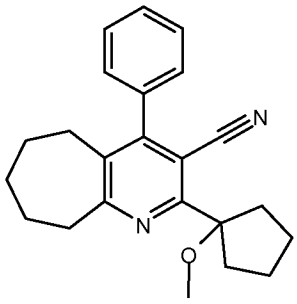
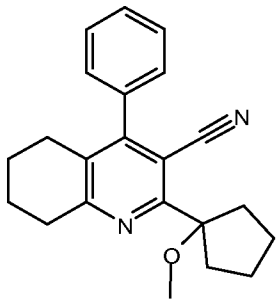
Intermediate	Name and Structure	MS	Method	Reagents
N188	2-(1-(Methoxymethyl)cyclopentyl)-4-(3-methoxyphenyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 391.6	V	Intermediate B94, 3-methoxybenzaldehyde, cycloheptanone
N189	4-(2-Fluoro-5-methoxyphenyl)-2-(1-(methoxymethyl)cyclopentyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 409.6	V	Intermediate B94, 2-fluoro-5-methoxybenzaldehyde, cycloheptanone

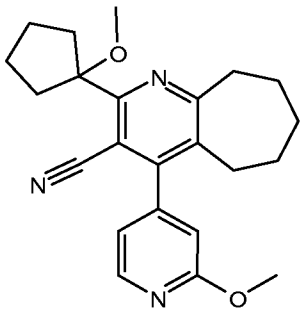
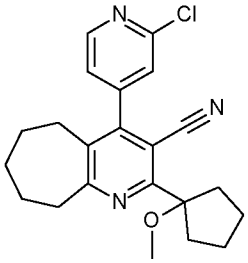
Intermediate	Name and Structure	MS	Method	Reagents
N190	4-(3-Chlorophenyl)-2-(1-(methoxymethyl)cyclopentyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 		V	Intermediate B94, 3-chlorobenzaldehyde, cycloheptanone
N191	2-(3-(Methoxymethyl)pentan-3-yl)-4-(1-methyl-1H-pyrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 367.6	V	Intermediate B191, 1-methyl-1H-pyrazole-5-carbaldehyde, cycloheptanone

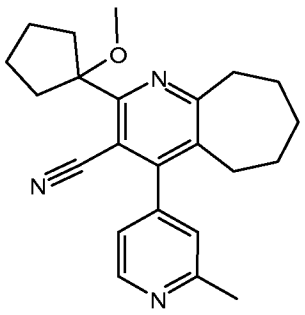
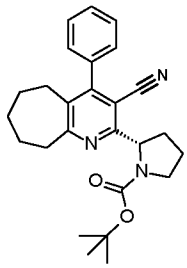
Intermediate	Name and Structure	MS	Method	Reagents
N192	2-[1-Ethyl-1-(methoxymethyl)propyl]-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 		V	Intermediate B191, benzaldehyde, cycloheptanone
N193	2-Cyclopentyl-4-(2-ethylpyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 346.5	V	3-Cyclopentyl-3-oxopropanenitrile(CAS# 95882-33-0), 2-ethylisonicotinaldehyde, cycloheptanone

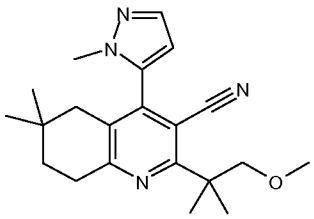
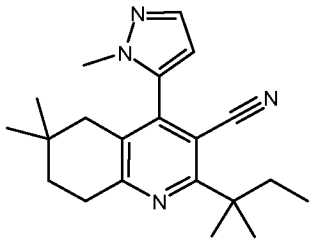
Intermediate	Name and Structure	MS	Method	Reagents
N195	2-Cyclopentyl-4-(2-(trifluoromethyl)pyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 386.5	V	3-Cyclopentyl-3-oxopropanenitrile(CAS# 95882-33-0), 2-(trifluoromethyl)isonicotinaldehyde, cycloheptanone
N196	4-(1-Methyl-1H-pyrazol-5-yl)-2-(3-methylpentan-3-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 337.7	V	4-Ethyl-4-methyl-3-oxohexanenitrile (CAS#87539-07-9), 1-methyl-1H-pyrazole-5-carbaldehyde, cycloheptanone

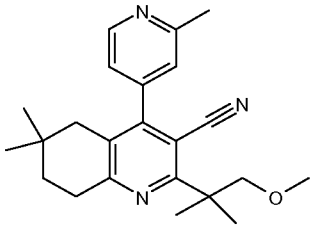
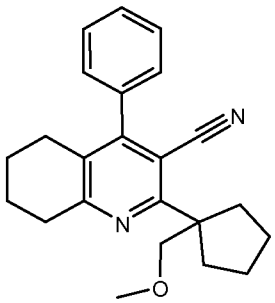
Intermediate	Name and Structure	MS	Method	Reagents
N197	4-(2-Ethyl-4-pyridyl)-2-isopropyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 320.5	V	4-Methyl-3-oxopentanenitrile(CAS# 29509-06-6), 2-ethylisonicotinaldehyde, cycloheptanone
N198	2-Isopropyl-4-(2-(2,2,2-trifluoroethoxy)pyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 390.5	V	4-Methyl-3-oxopentanenitrile(CAS# 29509-06-6), 2-(2,2,2-trifluoroethoxy)isonicotinaldehyde, cycloheptanone
N199	4-(2-Ethoxypyridin-4-yl)-2-isopropyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 336.6	V	4-Methyl-3-oxopentanenitrile(CAS# 29509-06-6), 2-ethoxyisonicotinaldehyde, cycloheptanone

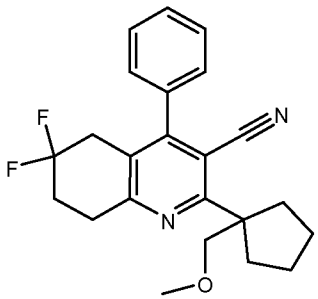
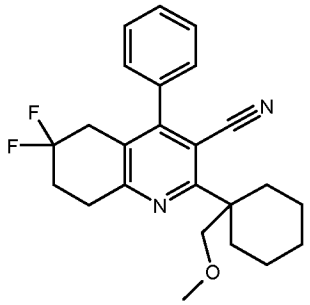
Intermediate	Name and Structure	MS	Method	Reagents
N200	2-(1-Methoxycyclopentyl)-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 347.7	V	Intermediate B200, benzaldehyde, cycloheptanone
N201	2-(1-Methoxycyclopentyl)-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 333.6	V	Intermediate B200, benzaldehyde, cyclohexanone

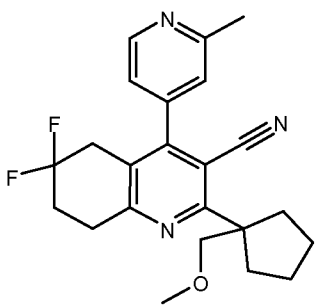
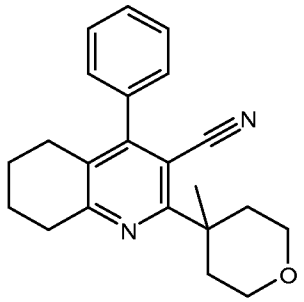
Intermediate	Name and Structure	MS	Method	Reagents
N202	2-(1-Methoxycyclopentyl)-4-(2-methoxypyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 378.5	V	Intermediate B200, 2-methoxyisonicotinaldehyde, cycloheptanone
N203	4-(2-Chloro-4-pyridyl)-2-(1-methoxycyclopentyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 382.5	V	Intermediate B200, 2-chloroisonicotinaldehyde, cycloheptanone

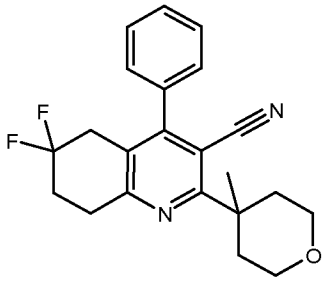
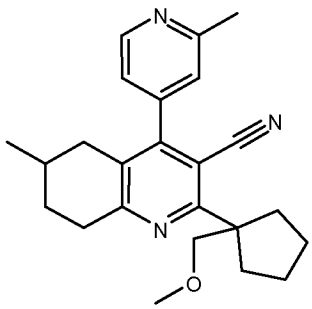
Intermediate	Name and Structure	MS	Method	Reagents
N204	2-(1-Methoxycyclopentyl)-4-(2-methylpyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 362.5	V	Intermediate B200, 2-methylisonicotinaldehyde, cycloheptanone
N210	(S)-tert-Butyl 2-(3-cyano-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-yl)pyrrolidine-1-carboxylate 	ESP $[M+H]^+$: 418.7	V	(S)-tert-Butyl 2-(2-cyanoacetyl)pyrrolidine-1-carboxylate (CAS# 173690-69-2), benzaldehyde, cycloheptanone

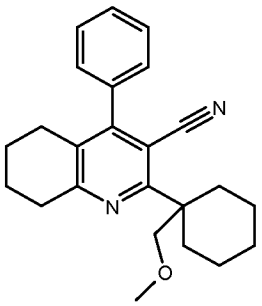
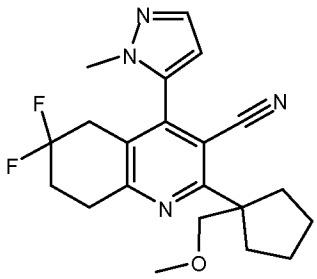
Intermediate	Name and Structure	MS	Method	Reagents
N213	2-(1-Methoxy-2-methylpropan-2-yl)-6,6-dimethyl-4-(1-methyl-1H-pyrazol-5-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 353.5	V	5-Methoxy-4,4-dimethyl-3-oxopentanenitrile (CAS# 90087-79-9), 1-methyl-1H-pyrazole-5-carbaldehyde, 4,4-dimethylcyclohexanone
N214	6,6-Dimethyl-4-(1-methyl-1H-pyrazol-5-yl)-2-tert-pentyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 337.5	V	4,4-Dimethyl-3-oxohexanenitrile (CAS# 876299-62-6), 1-methyl-1H-pyrazole-5-carbaldehyde, 4,4-dimethylcyclohexanone

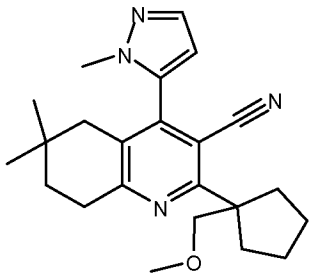
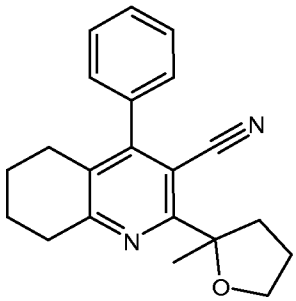
Intermediate	Name and Structure	MS	Method	Reagents
N215	2-(1-Methoxy-2-methylpropan-2-yl)-6,6-dimethyl-4-(2-methylpyridin-4-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 364.6	V	5-Methoxy-4,4-dimethyl-3-oxopentanenitrile (CAS# 90087-79-9), 2-methylpyridine-4-carbaldehyde, 4,4-dimethylcyclohexanone
N216	2-(1-(Methoxymethyl)cyclopentyl)-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 347.6	V	Intermediate B94, benzaldehyde, cyclohexanone

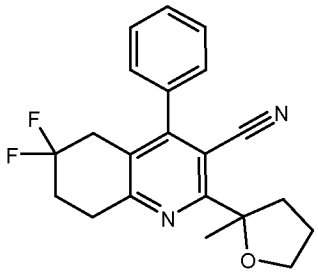
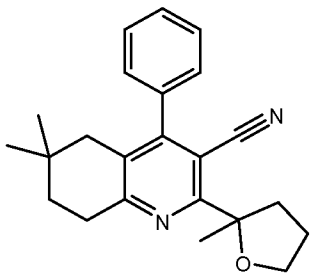
Intermediate	Name and Structure	MS	Method	Reagents
N217	6,6-Difluoro-2-(1-(methoxymethyl)cyclopentyl)-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 383.6	V	Intermediate B94, benzaldehyde, 4,4-difluorocyclohexanone
N218	6,6-Difluoro-2-(1-(methoxymethyl)cyclohexyl)-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 397.6	V	Intermediate B218, benzaldehyde, 4,4-difluorocyclohexanone

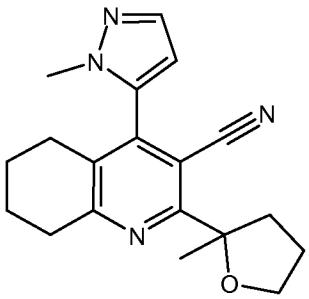
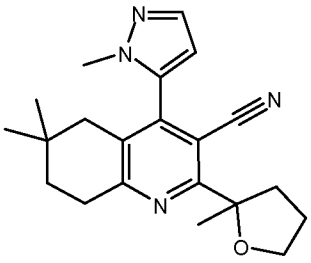
Intermediate	Name and Structure	MS	Method	Reagents
N219	6,6-Difluoro-2-(1-(methoxymethyl)cyclopentyl)-4-(2-methylpyridin-4-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 398.5	V	Intermediate B94, 2-methylpyridine-4-carbaldehyde, 4,4-difluorocyclohexanone
N220	2-(4-Methyltetrahydro-2H-pyran-4-yl)-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 333.5	V	Intermediate B220, benzaldehyde, cyclohexanone

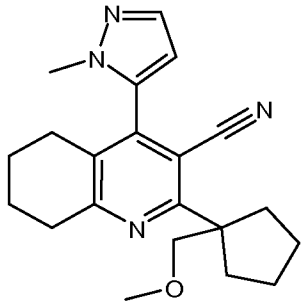
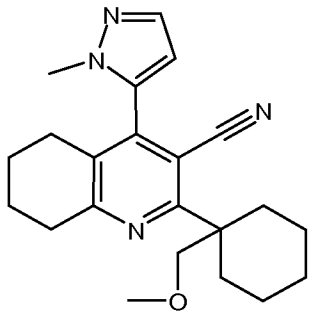
Intermediate	Name and Structure	MS	Method	Reagents
N221	6,6-Difluoro-2-(4-methyltetrahydro-2H-pyran-4-yl)-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 369.5	V	Intermediate B220, benzaldehyde, 4,4-difluorocyclohexanone
N222	2-(1-(Methoxymethyl)cyclopentyl)-6-methyl-4-(2-methylpyridin-4-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 376.5	V	Intermediate B94, 2-methylpyridine-4-carbaldehyde, 4-methylcyclohexanone

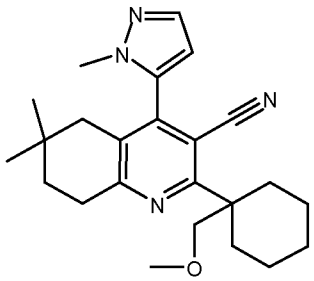
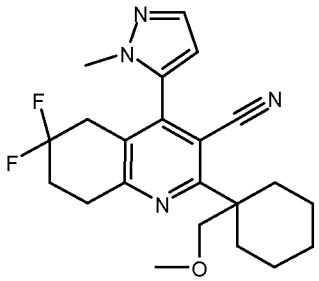
Intermediate	Name and Structure	MS	Method	Reagents
N223	2-(1-(Methoxymethyl)cyclohexyl)-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 361.7	V	Intermediate B218, benzaldehyde, cyclohexanone
N224	6,6-Difluoro-2-(1-(methoxymethyl)cyclopentyl)-4-(1-methyl-1H-pyrazol-5-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 387.6	V	Intermediate B94, 1-methyl-1H-pyrazole-5-carbaldehyde, 4,4-difluorocyclohexanone

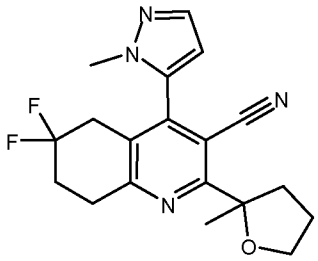
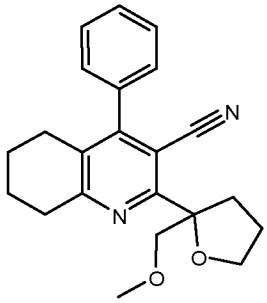
Intermediate	Name and Structure	MS	Method	Reagents
N225	2-(1-(Methoxymethyl)cyclopentyl)-6,6-dimethyl-4-(1-methyl-1H-pyrazol-5-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 379.6	V	Intermediate B94, 1-methyl-1H-pyrazole-5-carbaldehyde, 4,4-dimethylcyclohexanone
N226	2-(2-Methyltetrahydrofuran-2-yl)-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 319.5	V	Intermediate B154, benzaldehyde, cyclohexanone

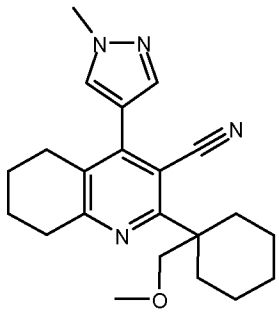
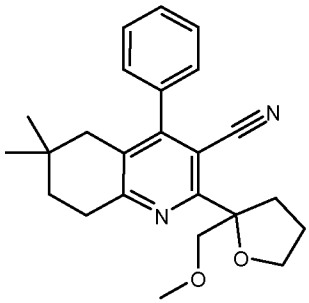
Intermediate	Name and Structure	MS	Method	Reagents
N227	6,6-Difluoro-2-(2-methyltetrahydrofuran-2-yl)-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 355.5	V	Intermediate B154, benzaldehyde, 4,4-difluorocyclohexanone
N228	6,6-Dimethyl-2-(2-methyltetrahydrofuran-2-yl)-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 347.6	V	Intermediate B154, benzaldehyde, 4,4-dimethylcyclohexanone

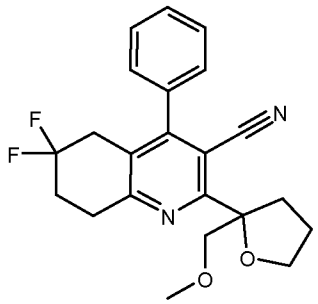
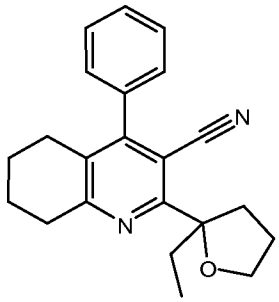
Intermediate	Name and Structure	MS	Method	Reagents
N229	4-(1-Methyl-1H-pyrazol-5-yl)-2-(2-methyltetrahydrofuran-2-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 323.6	V	Intermediate B154, 1-methyl-1H-pyrazole-5-carbaldehyde, cyclohexanone
N230	6,6-Dimethyl-4-(1-methyl-1H-pyrazol-5-yl)-2-(2-methyltetrahydrofuran-2-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 351.6	V	Intermediate B154, 1-methyl-1H-pyrazole-5-carbaldehyde, 4,4-dimethylcyclohexanone

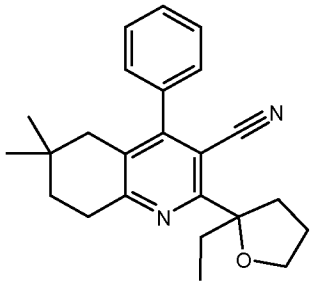
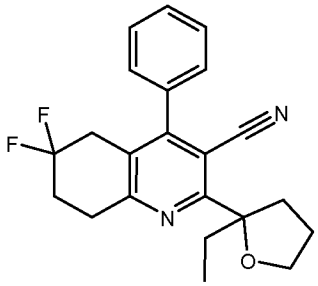
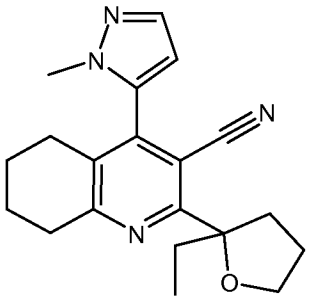
Intermediate	Name and Structure	MS	Method	Reagents
N237	2-(1-(Methoxymethyl)cyclopentyl)-4-(1-methyl-1H-pyrazol-5-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 351.7	V	Intermediate B94, 1-methyl-1H-pyrazole-5-carbaldehyde, cyclohexanone
N238	2-(1-(Methoxymethyl)cyclohexyl)-4-(1-methyl-1H-pyrazol-5-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 365.6	V	Intermediate B218, 1-methyl-1H-pyrazole-5-carbaldehyde, cyclohexanone

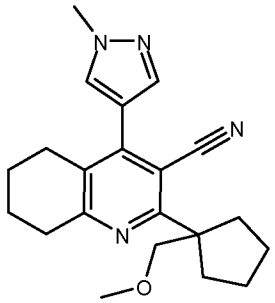
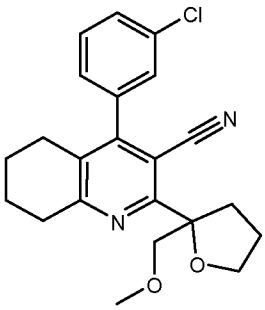
Intermediate	Name and Structure	MS	Method	Reagents
N239	2-(1-(Methoxymethyl)cyclohexyl)-6,6-dimethyl-4-(1-methyl-1H-pyrazol-5-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 393.7	V	Intermediate B218, 1-methyl-1H-pyrazole-5-carbaldehyde, 4,4-dimethylcyclohexanone
N240	6,6-Difluoro-2-(1-(methoxymethyl)cyclohexyl)-4-(1-methyl-1H-pyrazol-5-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 401.6	V	Intermediate B218, 1-methyl-1H-pyrazole-5-carbaldehyde, 4,4-difluorocyclohexanone

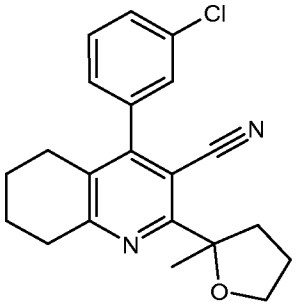
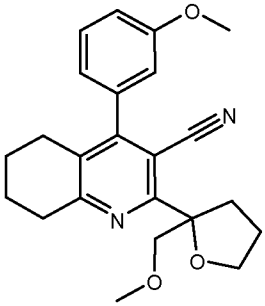
Intermediate	Name and Structure	MS	Method	Reagents
N241	6,6-Difluoro-4-(1-methyl-1H-pyrazol-5-yl)-2-(2-methyltetrahydrofuran-2-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 359.5	V	Intermediate B154, 1-methyl-1H-pyrazole-5-carbaldehyde, 4,4-difluorocyclohexanone
N242	2-(2-(Methoxymethyl)tetrahydrofuran-2-yl)-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 349.5	V	Intermediate B242, benzaldehyde, cyclohexanone

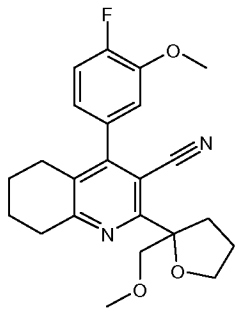
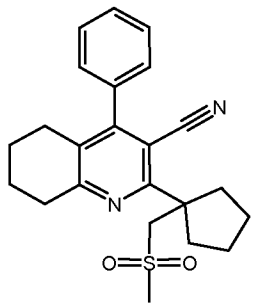
Intermediate	Name and Structure	MS	Method	Reagents
N243	2-(1-(Methoxymethyl)cyclohexyl)-4-(1-methyl-1H-pyrazol-4-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 365.7	V	Intermediate B218, 1-methyl-1H-pyrazole-4-carbaldehyde, cyclohexanone
N244	2-(2-(Methoxymethyl)tetrahydrofuran-2-yl)-6,6-dimethyl-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 377.7	V	Intermediate B242, benzaldehyde, 4,4-dimethylcyclohexanone

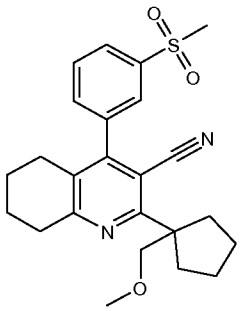
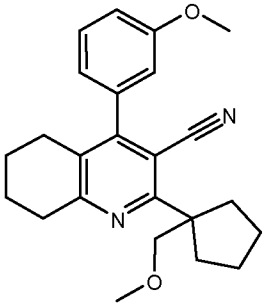
Intermediate	Name and Structure	MS	Method	Reagents
N245	6,6-Difluoro-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 385.5	V	Intermediate B242, benzaldehyde, 4,4-difluorocyclohexanone
N246	2-(2-Ethyltetrahydrofuran-2-yl)-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 333.6	V	Intermediate B246, benzaldehyde, cyclohexanone

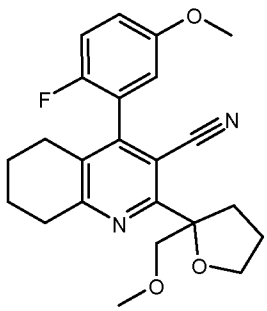
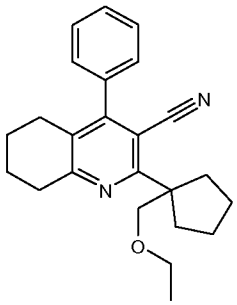
Intermediate	Name and Structure	MS	Method	Reagents
N247	2-(2-Ethyltetrahydrofuran-2-yl)-6,6-dimethyl-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 361.6	V	Intermediate B246, benzaldehyde, 4,4-dimethylcyclohexanone
N248	2-(2-Ethyltetrahydrofuran-2-yl)-6,6-difluoro-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 369.6	V	Intermediate B246, benzaldehyde, 4,4-difluorocyclohexanone
N255	2-(2-Ethyltetrahydrofuran-2-yl)-4-(1-methyl-1H-pyrazol-5-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 337.6	V	Intermediate B246, 1-methyl-1H-pyrazole-5-carbaldehyde, cyclohexanone

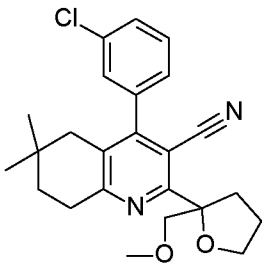
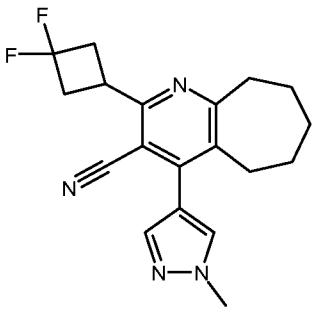
Intermediate	Name and Structure	MS	Method	Reagents
N256	2-(1-(Methoxymethyl)cyclopentyl)-4-(1-methyl-1H-pyrazol-4-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 351.6	V	Intermediate B94, 1-methyl-1H-pyrazole-4-carbaldehyde, cyclohexanone
N257	4-(3-Chlorophenyl)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 383.5	V	Intermediate B242, 3-chlorobenzaldehyde, cyclohexanone

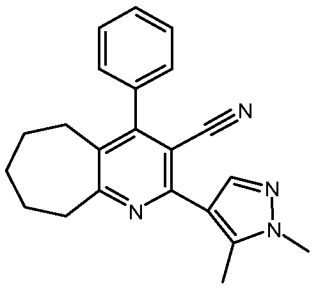
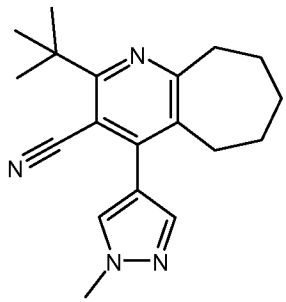
Intermediate	Name and Structure	MS	Method	Reagents
N258	4-(3-Chlorophenyl)-2-(2-methyltetrahydrofuran-2-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 353.5	V	Intermediate B154, 3-chlorobenzaldehyde, cyclohexanone
N259	2-(2-(Methoxymethyl)tetrahydrofuran-2-yl)-4-(3-methoxyphenyl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 379.5	V	Intermediate B242, 3-methoxybenzaldehyde, cyclohexanone

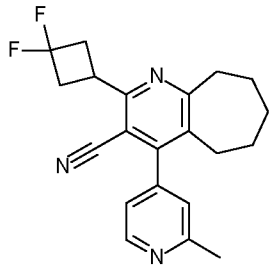
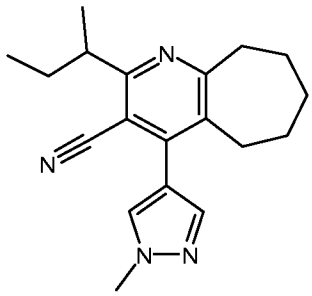
Intermediate	Name and Structure	MS	Method	Reagents
N260	4-(4-Fluoro-3-methoxyphenyl)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 397.5	V	Intermediate B242, 4-fluoro-3-methoxybenzaldehyde, cyclohexanone
N261	2-(1-(Methylsulfonylmethyl)cyclopentyl)-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 395.5	V	Intermediate B261, benzaldehyde, cyclohexanone

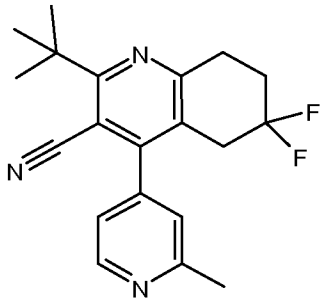
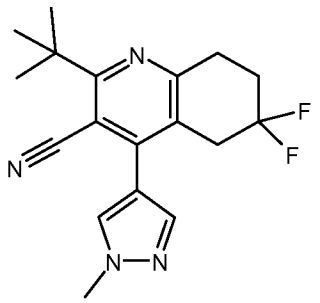
Intermediate	Name and Structure	MS	Method	Reagents
N264	2-[1-(Methoxymethyl)cyclopentyl]-4-(3-methylsulfonylphenyl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 425.6	V	Intermediate B94, 3-(methylsulfonyl)benzaldehyde, cyclohexanone
N265	2-[1-(Methoxymethyl)cyclopentyl]-4-(3-methoxyphenyl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 377.6	V	Intermediate B94, 3-methoxybenzaldehyde, cyclohexanone

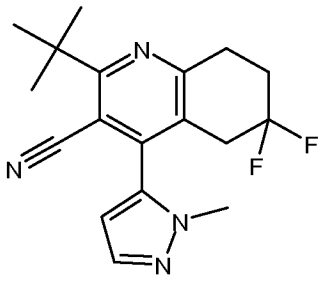
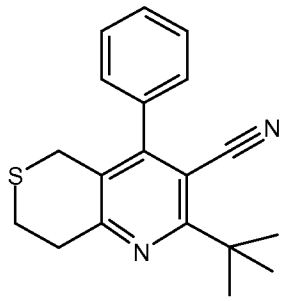
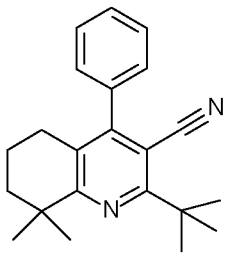
Intermediate	Name and Structure	MS	Method	Reagents
N266	4-(2-Fluoro-5-methoxyphenyl)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 397.6	V	Intermediate B242, 2-fluoro-5-methoxybenzaldehyde, cyclohexanone
N268	2-(1-(Ethoxymethyl)cyclopentyl)-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 361.5	V	Intermediate B268, benzaldehyde, cyclohexanone

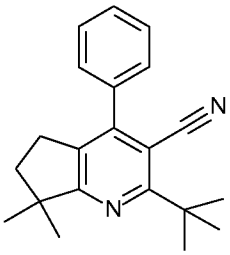
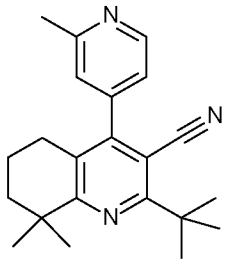
Intermediate	Name and Structure	MS	Method	Reagents
N269R	4-(3-Chlorophenyl)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-6,6-dimethyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 411.5	V	Intermediate B242, 3-chlorobenzaldehyde, 4,4-dimethylcyclohexanone
N271	2-(3,3-Difluorocyclobutyl)-4-(1-methyl-1H-pyrazol-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 343.5	V	3-(3,3-Difluorocyclobutyl)-3-oxopropanenitrile (CAS# 1234616-26-2), 1-methyl-1H-pyrazole-4-carbaldehyde, cycloheptanone

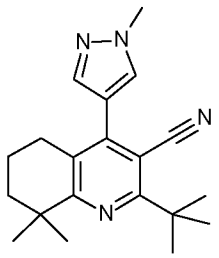
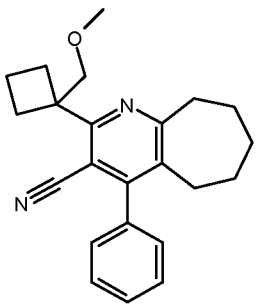
Intermediate	Name and Structure	MS	Method	Reagents
N272	2-(1,5-Dimethyl-1H-pyrazol-4-yl)-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 343.6	V	3-(1,5-Dimethyl-1H-pyrazol-4-yl)-3-oxopropanenitrile(CAS# 1006485-37-5), benzaldehyde, cycloheptanone
N273	2-tert-Butyl-4-(1-methyl-1H-pyrazol-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 309.5	V	4,4-Dimethyl-3-oxopentanenitrile(CAS# 59997-51-2) , 1-methyl-1H-pyrazole-4-carbaldehyde, cycloheptanone

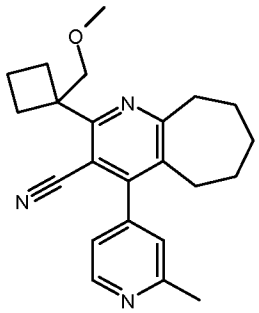
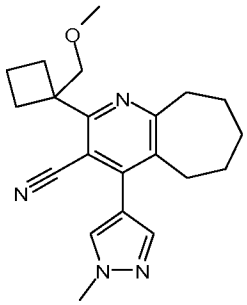
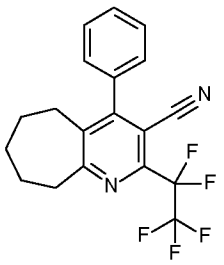
Intermediate	Name and Structure	MS	Method	Reagents
N274	 2-(3,3-Difluorocyclobutyl)-4-(2-methylpyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile	ESP $[M+H]^+$: 354.5	V	3-(3,3-Difluorocyclobutyl)-3-oxopropanenitrile (CAS#1234616-26-2), 2-methylisonicotinaldehyde, cycloheptanone
N275	2-sec-Butyl-4-(1-methyl-1H-pyrazol-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 309.5	V	4-Methyl-3-oxohexanenitrile (CAS# 42124-66-3), 1-methyl-1H-pyrazole-4-carbaldehyde, cycloheptanone

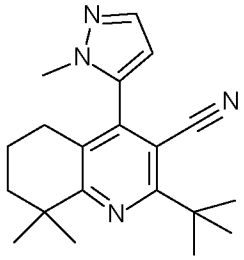
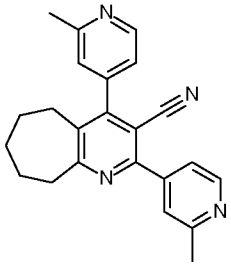
Interme diate	Name and Structure	MS	Method	Reagents
N276	2-tert-Butyl-6,6-difluoro-4-(2-methyl-pyridin-4-yl)-5,6,7,8-tetrahydro-quinoline-3-carbonitrile 	ESP $[M+H]^+$: 342.5	V	4,4-Dimethyl-3-oxopentanenitrile (CAS# 59997-51-2), 2-methylisonicotinaldehyde (CAS#63875-01-4), 4,4-difluorocyclohexanone (CAS# 22515-18-0)
N277	2-tert-Butyl-6,6-difluoro-4-(1-methyl-1H-pyrazol-4-yl)-5,6,7,8-tetrahydro-quinoline-3-carbonitrile 	ESP $[M+H]^+$: 331.0	V	4,4-Dimethyl-3-oxopentanenitrile (CAS# 59997-51-2), 1-methyl-1H-pyrazole-4-carbaldehyde, 4,4-difluorocyclohexanone (CAS# 22515-18-0)

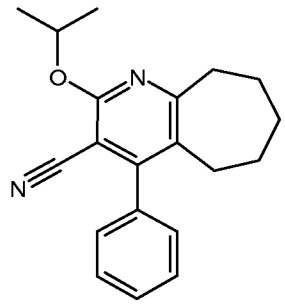
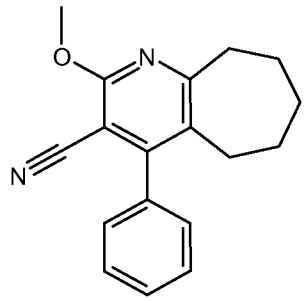
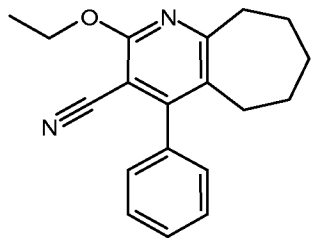
Intermediate	Name and Structure	MS	Method	Reagents
N278	2-tert-Butyl-6,6-difluoro-4-(2-methyl-2H-pyrazol-3-yl)-5,6,7,8-tetrahydro-quinoline-3-carbonitrile 	ESP $[M+H]^+$: 331.5	V	4,4-Dimethyl-3-oxopentanenitrile (CAS# 59997-51-2), 1-methyl-1H-pyrazole-5-carbaldehyde, 4,4-difluorocyclohexanone (CAS# 27258-33-9)
N279	2-tert-Butyl-4-phenyl-7,8-dihydro-5H-thiopyrano[4,3-b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 309.5	V	4,4-Dimethyl-3-oxopentanenitrile (CAS# 59997-51-2), benzaldehyde, dihydro-2H-thiopyran-4(3H)-one (CAS# 1072-72-6)
N280	2-tert-Butyl-8,8-dimethyl-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 319.6	V	4,4-Dimethyl-3-oxopentanenitrile (CAS# 59997-51-2), benzaldehyde, 2,2-dimethylcyclohexanone (CAS# 1193-47-1)

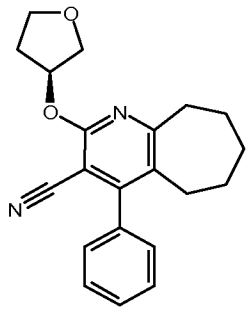
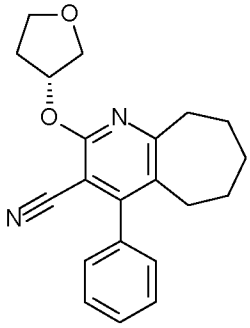
Intermediate	Name and Structure	MS	Method	Reagents
N281	2-tert-Butyl-7,7-dimethyl-4-phenyl-6,7-dihydro-5H-cyclopenta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 305.6	V	4,4-Dimethyl-3-oxopentanenitrile (CAS# 59997-51-2), benzaldehyde, 2,2-dimethylcyclopentanone (CAS# 4541-20-1)
N282	2-tert-Butyl-8,8-dimethyl-4-(2-methylpyridin-4-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 334.6	V	4,4-Dimethyl-3-oxopentanenitrile, 2-methylisonicotinaldehyde, 2,2-dimethylcyclohexanone

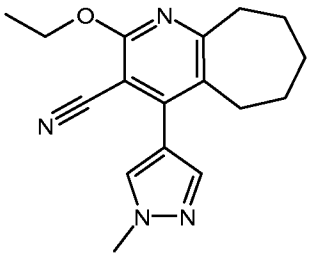
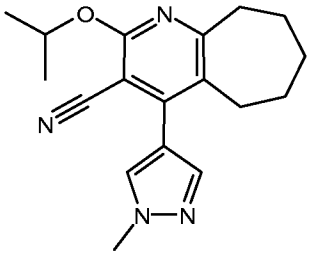
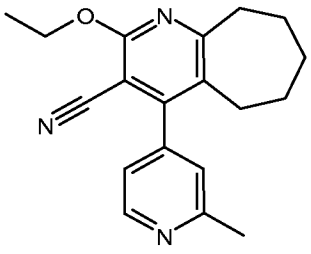
Intermediate	Name and Structure	MS	Method	Reagents
N283	2-tert-Butyl-8,8-dimethyl-4-(1-methyl-1H-pyrazol-4-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 323.5	V	4,4-Dimethyl-3-oxopentanenitrile, 2,2-dimethylcyclohexanone, 1-methyl-1H-pyrazole-4-carbaldehyde (CAS# 25016-11-9)
N284	2-(1-(Methoxymethyl)cyclobutyl)-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 347.2	V	Intermediate B284 (3-(1-(methoxymethyl)cyclobutyl)-3-oxopropanenitrile), benzaldehyde, cycloheptanone

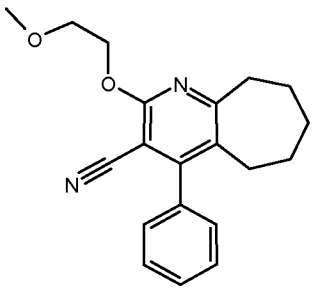
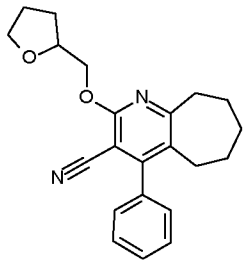
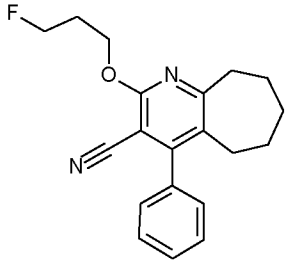
Intermediate	Name and Structure	MS	Method	Reagents
N285	2-(1-(Methoxymethyl)cyclobutyl)-4-(2-methylpyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 362.6	V	Intermediate B284 (3-(1-(methoxymethyl)cyclobutyl)-3-oxopropanenitrile), 2-methylisonicotinaldehyde, cycloheptanone
N286	2-(1-(Methoxymethyl)cyclobutyl)-4-(1-methyl-1H-pyrazol-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 351.6	V	Intermediate B284 (3-(1-(methoxymethyl)cyclobutyl)-3-oxopropanenitrile), 1-methyl-1H-pyrazole-4-carbaldehyde , cycloheptanone
N287	2-(Perfluoroethyl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine 	ESP $[M]^+$: 366	V	4,4,5,5,5-Pentafluoro-3-oxo-pentanenitrile (CAS# 110234-69-0), benzaldehyde, cycloheptanone

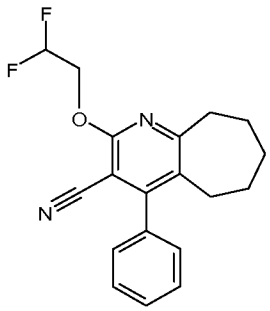
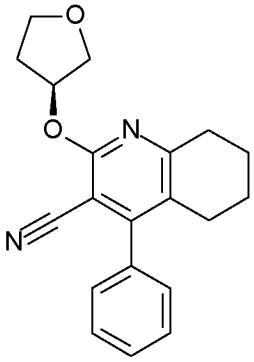
Intermediate	Name and Structure	MS	Method	Reagents
N288	2-tert-Butyl-8,8-dimethyl-4-(1-methyl-1H-pyrazol-5-yl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 323.6	V	4,4-Dimethyl-3-oxopentanenitrile(CAS# 59997-51-2), 1-methyl-1H-pyrazole-5-carbaldehyde (CAS# 27258-33-9), 2,2-dimethylcyclohexanone
N289	2,4-Bis(2-methylpyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 355.6	V	3-(2-Methylpyridin-4-yl)-3-oxopropanenitrile(CAS# 1240521-95-2), 2-methylisonicotinaldehyde, cycloheptanone

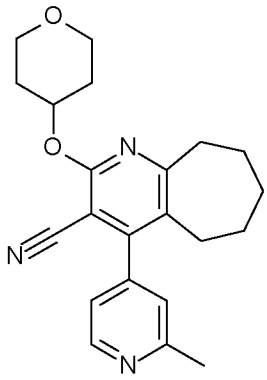
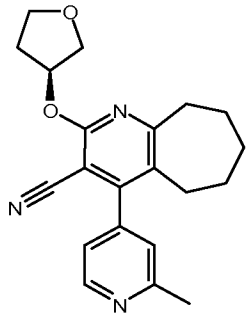
Intermediate	Name and Structure	MS	Method	Reagents
N290	2-Isopropoxy-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 307.5	Y	2-Oxo-4-phenyl-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile (Intermediate P30), isopropanol
N291	2-Methoxy-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 279.5	Y	2-Oxo-4-phenyl-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile (Intermediate P30), methanol
N292	2-Ethoxy-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 293.5	Y	2-Oxo-4-phenyl-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile (Intermediate P30), ethanol

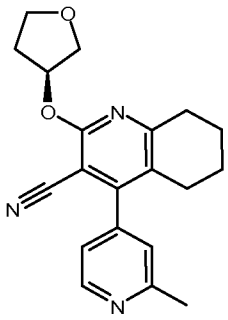
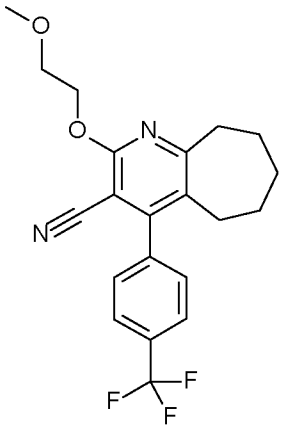
Intermediate	Name and Structure	MS	Method	Reagents
N293	(S)-4-Phenyl-2-(tetrahydrofuran-3-yloxy)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 335.5	Y	2-Oxo-4-phenyl-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile (Intermediate P30), (S)-tetrahydrofuran-3-ol
N294	(R)-4-Phenyl-2-(tetrahydrofuran-3-yloxy)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 335.6	Y	2-Oxo-4-phenyl-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile (Intermediate P30), (R)-tetrahydrofuran-3-ol

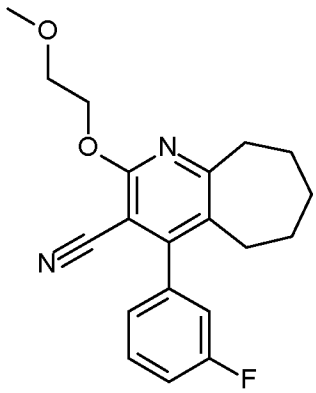
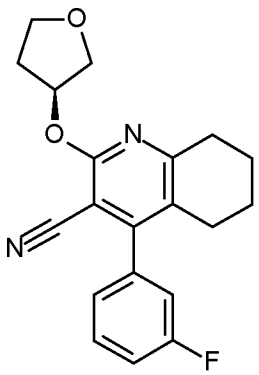
Intermediate	Name and Structure	MS	Method	Reagents
N295	2-Ethoxy-4-(1-methyl-1H-pyrazol-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 297.5	Y	Intermediate P295, ethanol
N296	2-Isopropoxy-4-(1-methyl-1H-pyrazol-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 311.5	Y	Intermediate P295, isopropanol
N297	2-Ethoxy-4-(2-methylpyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 308.5	Y	Intermediate P297, ethanol

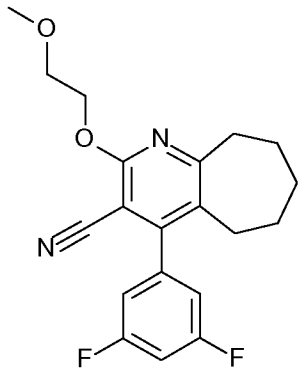
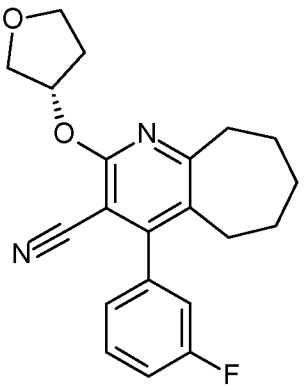
Intermediate	Name and Structure	MS	Method	Reagents
N298	2-(2-Methoxyethoxy)-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 323.5	Y	2-Oxo-4-phenyl-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile (Intermediate P30), methoxyethanol
N299	4-Phenyl-2-((tetrahydrofuran-2-yl)methoxy)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 249.6	Y	2-Oxo-4-phenyl-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile (Intermediate P30), tetrahydrofuran-2-ylmethanol
N300	2-(3-Fluoropropoxy)-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 325.5	Y	2-Oxo-4-phenyl-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile (Intermediate P30), 3-fluoro-1-propanol

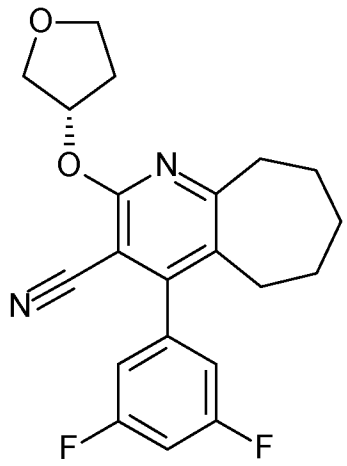
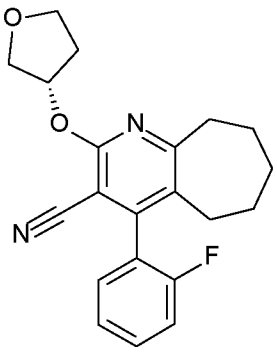
Intermediate	Name and Structure	MS	Method	Reagents
N301	2-(2,2-Difluoroethoxy)-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 329.5	Y	2-Oxo-4-phenyl-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile (Intermediate P30), 2,2-difluoroethanol
N302	(S)-4-Phenyl-2-(tetrahydrofuran-3-yloxy)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 321.5	Y	2-Oxo-4-phenyl-1,2,5,6,7,8-hexahydroquinoline-3-carbonitrile (intermediate P302), (S)-tetrahydrofuran-3-ol

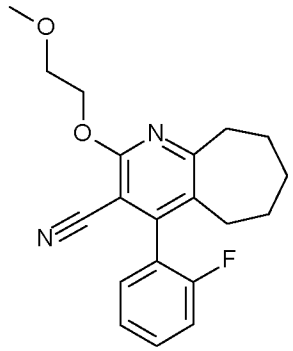
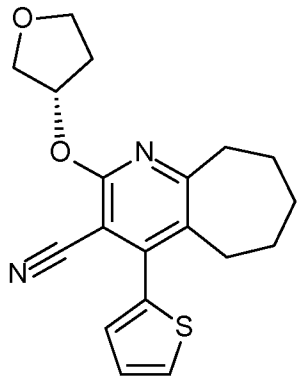
Intermediate	Name and Structure	MS	Method	Reagents
N303	4-(2-Methylpyridin-4-yl)-2-(tetrahydro-2H-pyran-4-yloxy)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 364.5	Y	4-(2-Methylpyridin-4-yl)-2-oxo-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile (Intermediate P297), tetrahydro-2H-pyran-4-ol
N304	(S)-4-(2-Methylpyridin-4-yl)-2-(tetrahydrofuran-3-yloxy)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 350.5	Y	4-(2-Methylpyridin-4-yl)-2-oxo-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile (Intermediate P297), (S)-tetrahydrofuran-3-ol

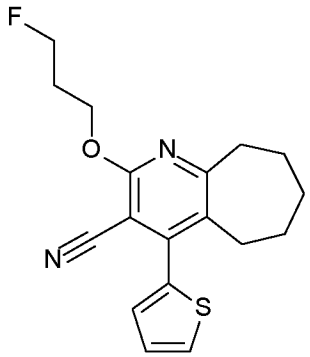
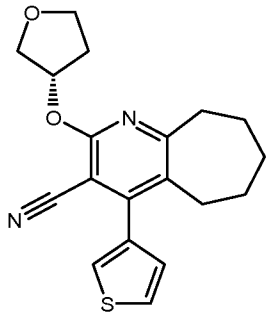
Intermediate	Name and Structure	MS	Method	Reagents
N305	(S)-4-(2-Methylpyridin-4-yl)-2-(tetrahydrofuran-3-yloxy)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 379.5	Y	4-(2-Methylpyridin-4-yl)-2-oxo-1,2,5,6,7,8-hexahydroquinoline-3-carbonitrile (Intermediate P305), (S)-tetrahydrofuran-3-ol
N306	2-(2-Methoxyethoxy)-4-(4-(trifluoromethyl)phenyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 391.4	Y	2-Oxo-4-(4-(trifluoromethyl)phenyl)-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile (Intermediate P306), 2-methoxyethanol

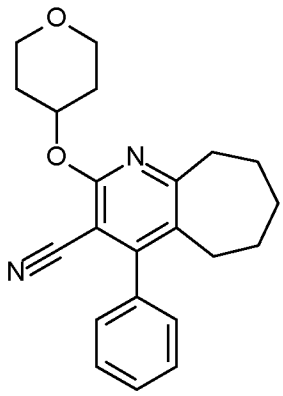
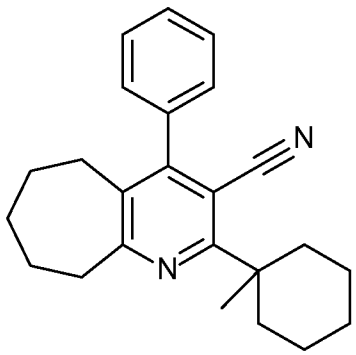
Intermediate	Name and Structure	MS	Method	Reagents
N307	4-(3-Fluorophenyl)-2-(2-methoxyethoxy)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 341.4	Y	4-(3-Fluorophenyl)-2-oxo-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile (Intermediate P307), 2-methoxyethanol
N308	(S)-4-(3-Fluorophenyl)-2-(tetrahydrofuran-3-yloxy)-5,6,7,8-tetrahydroquinoline-3-carbonitrile 	ESP $[M+H]^+$: 339.4	Y	(S)-4-(3-Fluorophenyl)-2-(tetrahydrofuran-3-yloxy)-5,6,7,8-tetrahydroquinoline-3-carbonitrile (Intermediate P308), 2-(S)-tetrahydrofuran-3-ol

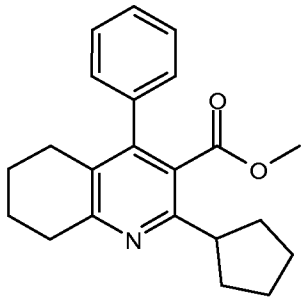
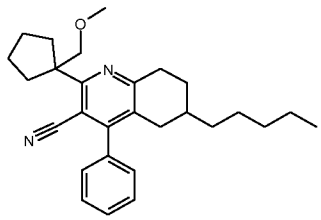
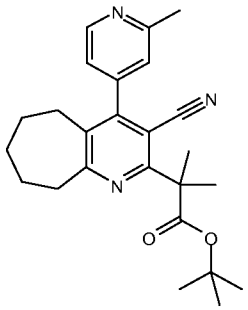
Intermediate	Name and Structure	MS	Method	Reagents
N309	4-(3,5-Difluorophenyl)-2-(2-methoxyethoxy)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 359.4	Y	4-(3,5-Difluorophenyl)-2-oxo-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile (Intermediate P309), 2-methoxyethanol,
N310	(S)-4-(3-Fluorophenyl)-2-(tetrahydrofuran-3-yloxy)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 353.5	Y	4-(3-Fluorophenyl)-2-oxo-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile (Intermediate P307), (S)-tetrahydrofuran-3-ol

Intermediate	Name and Structure	MS	Method	Reagents
N311	(S)-4-(3,5-Difluorophenyl)-2-(tetrahydrofuran-3-yloxy)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 371.4	Y	4-(3,5-Difluorophenyl)-2-oxo-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile (Intermediate 309), (S)-tetrahydrofuran-3-ol
N312	4-(2-Fluorophenyl)-2-((S)-tetrahydrofuran-3-yloxy)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 353.5	Y	4-(2-Fluorophenyl)-2-oxo-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile (Intermediate P312), (S)-tetrahydrofuran-3-ol

Intermediate	Name and Structure	MS	Method	Reagents
N313	4-(2-Fluorophenyl)-2-(2-methoxyethoxy)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 341.4	Y	4-(2-Fluorophenyl)-2-oxo-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile (Intermediate P312), 2-methoxyethanol
N314	(S)-2-(Tetrahydrofuran-3-yloxy)-4-(thiophen-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 341.4	Y	2-Oxo-4-(thiophen-2-yl)-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile, (Intermediate P314), (S)-tetrahydrofuran-3-ol

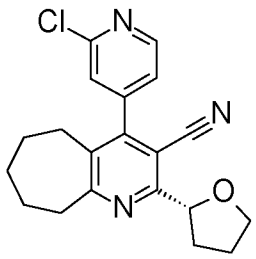
Intermediate	Name and Structure	MS	Method	Reagents
N315	2-(3-Fluoropropoxy)-4-(thiophen-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 331.5	Y	2-Oxo-4-(thiophen-2-yl)-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile, (Intermediate P314), 3-fluoropropan-1-ol
N316	(S)-2-(Tetrahydrofuran-3-yloxy)-4-(thiophen-3-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 341.3	Y	2-Oxo-4-(3-thienyl)-1,5,6,7,8,9-hexahydrocyclohepta[b]pyridine-3-carbonitrile (Intermediate P316), (S)-tetrahydrofuran-3-ol

Interme diate	Name and Structure	MS	Method	Reagents
N317	4-phenyl-2-(tetrahydro-2H-pyran-4-yloxy)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 	ESP $[M+H]^+$: 349.5	Y	2-Oxo-4-phenyl-2,5,6,7,8,9-hexahydro-1H-cyclohepta[b]pyridine-3-carbonitrile (Intermediate P30), tetrahydro-2H-pyran-4-ol
N321	2-(1-Methylcyclohexyl)-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile, contains traces of 2-cyclohexyl-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile 		V	Intermediate B171, benzaldehyde, cycloheptanone

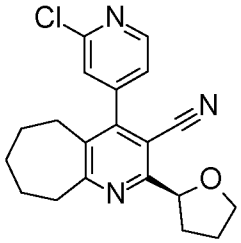
Intermediate	Name and Structure	MS	Method	Reagents
E325	Methyl 2-cyclopentyl-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carboxylate 	ESP $[M+H]^+$: 336.6	P	Intermediate K6, cyclohexanone
N326	2-(1-(Methoxymethyl)cyclopentyl)-6-pentyl-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile 		V	Intermediate B94, benzaldehyde, 4-pentylcyclohexanone
N327	tert-Butyl 2-(3-cyano-4-(2-methylpyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-yl)-2-methylpropanoate 	ESP $[M+H]^+$: 406.6	V	tert-Butyl 4-cyano-2,2-dimethyl-3-oxobutanoate (Intermediate B327), 2-methylisonicotinaldehyde, cycloheptanone

Intermediates N149 and N150

(R)-4-(2-chloropyridin-4-yl)-2-(tetrahydrofuran-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile and (S)-4-(2-chloropyridin-4-yl)-2-(tetrahydrofuran-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile



and



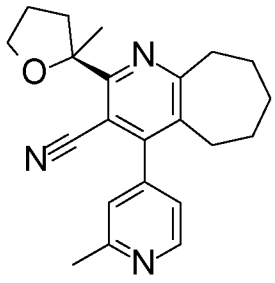
Intermediate N149R was separated into the enantiomers using chiral chromatography (Chiralpak AD, isopropanol/heptane 1:9) to give the title compounds as off-white solids.

N149 First-eluting enantiomer (+), ESP $[M+H]^+$: 354.5

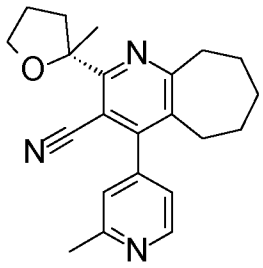
N150 Second-eluting enantiomer (-), ESP $[M+H]^+$: 354.5

Intermediates N161 and N162

2-[(2S)-2-methyloxolan-2-yl]-4-(2-methylpyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile and 2-[(2R)-2-methyloxolan-2-yl]-4-(2-methylpyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile



and



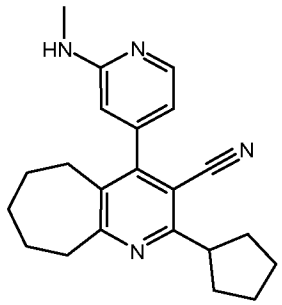
Intermediate N160 was separated into the enantiomers using chiral chromatography (Reprosil Chiral NR, 15% EtOH in heptane) to give the title compounds as light yellow solids.

N161 First-eluting enantiomer (-), ESP $[M+H]^+$: 348.5

N162 Second-eluting enantiomer (+), ESP $[M+H]^+$: 348.5

Intermediate N194

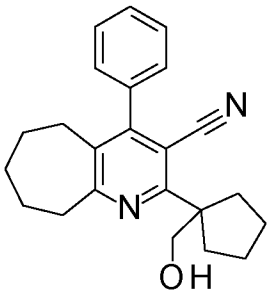
2-Cyclopentyl-4-(2-(methylamino)pyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile



4-(2-Chloropyridin-4-yl)-2-cyclopentyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile (Intermediate N103, 209 mg) and methylamine (8M in ethanol, 5 ml) were stirred 18h in a stainless steel autoclave at 150 °C. The reaction mixture was evaporated and purified by chromatography (SiO_2, 0-50% EtOAc in heptane) to give the title compound (66 mg) as a light yellow solid. ESP $[M+H]^+$: 347.6

Intermediate N205

2-[1-(Hydroxymethyl)cyclopentyl]-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile



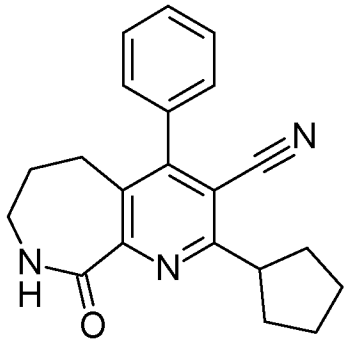
2-(1-(Methoxymethyl)cyclopentyl)-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile (Intermediate N184, 200 mg) was combined with acetonitrile (2.5 ml) to give a colorless solution. Then a suspension of sodium iodide (166 mg) in acetonitrile (2.5 ml) and

trimethylchlorosilane (121 mg) were added at r.t. After stirring at r.t. for 1.5 h, the mixture was stirred for 33 h at 60 °C and for 17 days at r.t. Additional portions of trimethylchlorosilane (121 mg) and sodium iodide (166 mg) were added twice during this time. 5 g Silica gel was added and the reaction mixture was evaporated. The crude material was purified by flash chromatography (silical gel, 0% to 50% EtOAc in n-heptane)

followed by preparative TLC (silica gel, 2.0 mm, 1:1 n-heptane/AcOEt) to give the title compound (not totally pure) as a light brown foam (114 mg) which was used for the next step without further purification. ESP $[M+H]^+$: 347.6

Intermediate N212

2-Cyclopentyl-9-oxo-4-phenyl-6,7,8,9-tetrahydro-5H-pyrido[2,3-c]azepine-3-carbonitrile

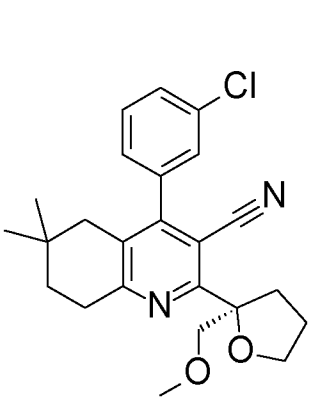


3-(Piperidin-1-yl)-6,7-dihydro-1H-azepin-2(5H)-one (3 g), benzaldehyde (1.64 g), 3-cyclopentyl-3-oxopropanenitrile (2.12 g) and ammonium acetate (5.95 g) were mixed with toluene (45.0 ml) and refluxed for 90 min while water was removed using a Dean-Stark-trap. The reaction mixture was evaporated. The residual brown semisolid was suspended in acetone (75.0 ml). After slow addition of a solution of ceric ammonium nitrate (16.9 g) in water (30.0 ml) the reaction mixture was stirred 30 min at rt. The reaction mixture was diluted with water and ethyl acetate and separated, extracted once more with ethyl acetate. The organic layers were washed once with water, dried over sodium sulphate and evaporated. The residual red-brown gum was purified by chromatography (SiO_2, 0-100% EtOAc in heptane) followed by trituration with isopropyl ether to give the title compound (1.25 g) as an off-white solid. ESP $[M+H]^+$: 332.6

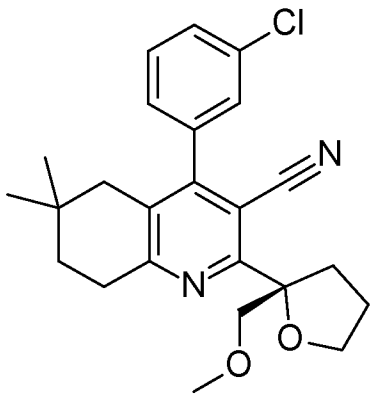
As a side product there was obtained 2-cyclopentyl-5-oxo-4-phenyl-6,7,8,9-tetrahydro-5H-pyrido[3,2-c]azepine-3-carbonitrile (1.04 g).

Intermediates N269 and N270

(R)-4-(3-chlorophenyl)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-6,6-dimethyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile and (S)-4-(3-chlorophenyl)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-6,6-dimethyl-5,6,7,8-tetrahydroquinoline-3-carbonitrile



and



Intermediate N269R was separated into the enantiomers using chiral chromatography (Reprosil Chiral NR, 10% EtOH in heptane) to give the title compounds as colorless solids.
N269 First-eluting enantiomer (-), ESP $[M+H]^+$: 411.5
N270 Second-eluting enantiomer (+), ESP $[M+H]^+$: 411.5

Example A

A compound of formula (I) can be used in a manner known per se as the active ingredient for the production of tablets of the following composition:

	Per tablet
Active ingredient	200 mg
Microcrystalline cellulose	155 mg
Corn starch	25 mg
Talc	25 mg

Hydroxypropylmethylcellulose	20 mg
	425 mg

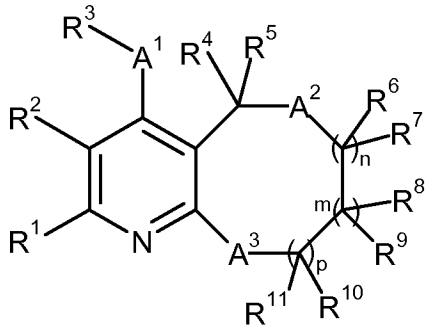
Example B

A compound of formula (I) can be used in a manner known per se as the active ingredient for the production of capsules of the following composition:

	Per capsule
Active ingredient	100.0 mg
Corn starch	20.0 mg
Lactose	95.0 mg
Talc	4.5 mg
Magnesium stearate	0.5 mg
	220.0 mg

Claims

1. Compounds of formula (I)



(I)

wherein

R^1 is alkyl, haloalkyl, cycloalkyl, substituted cycloalkyl, alkoxy, alkoxyalkyl, alkoxyalkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, carboxy, carboxyalkyl, haloalkyl, haloalkoxy, haloalkoxyalkyl, cycloalkoxy, substituted cycloalkoxy, cycloalkoxylalkyl, substituted cycloalkoxyalkyl, hydroxyalkyl, aryl, substituted aryl, heterocycloalkyl, substituted heterocycloalkyl, heterocycloalkoxy, substituted heterocycloalkoxy, heterocycloalkylalkoxy, substituted heterocycloalkylalkoxy, heteroaryl, substituted heteroaryl, amino, substituted amino, aminocarbonyl or substituted aminocarbonyl, wherein substituted cycloalkyl, substituted cycloalkoxy, substituted cycloalkoxyalkyl, substituted aryl, substituted heterocycloalkyl, substituted heterocycloalkoxy, substituted heterocycloalkylalkoxy and substituted heteroaryl are substituted with one to three substituents independently selected from hydroxy, oxo, halogen, alkyl, cycloalkyl, haloalkyl, alkylcycloalkyl, cycloalkylalkyl, alkylcycloalkylalkyl, hydroxyalkyl, alkylsulfonyl, alkylsulfonylalkyl, alkoxycarbonyl, alkoxy and alkoxyalkyl and wherein substituted amino and substituted aminocarbonyl are substituted on the nitrogen atom with one to two substituents independently selected from alkyl, cycloalkyl, haloalkyl, alkylcycloalkyl, cycloalkylalkyl, alkylcycloalkylalkyl, hydroxyalkyl and alkoxyalkyl;

R^2 is -COOH, tetrazol-5-yl, [1,3,4]oxadiazol-2-on-5-yl, [1,3,4]oxadiazole-2-thion-5-yl, [1,2,4]oxadiazol-5-on-3-yl, [1,2,4]oxadiazole-5-thion-3-yl, [1,2,3,5]oxathiadiazole-2-oxide-4-yl, [1,2,4]thiadiazol-5-on-3-yl, isoxazol-3-ol-5-yl, 5-alkylisoxazol-3-ol-4-yl, 5-cycloalkylisoxazol-3-ol-4-yl, furazan-3-ol-4-yl, 5-alkylsulfonylamino-[1,3,4]oxadiazol-2-yl, 5-cycloalkylsulfonylamino-[1,3,4]oxadiazol-2-yl, 5-

alkylsulfonylamino-[1,2,4]triazol-3-yl, 5-cycloalkylsulfonylamino-[1,2,4]triazol-3-yl, 5-alkylisothiazol-3-ol-4-yl, 5-cycloalkylisothiazol-3-ol-4-yl, [1,2,5]thiadiazol-3-ol-4-yl, 1,4-dihydro-tetrazol-5-on-1-yl, tetrazol-5-ylcarbamoyl, tetrazole-5-carbonyl, [1,2,4]oxadiazolidine-3,5-dion-2-y, [1,2,4]oxadiazol-5-on-3-yl, 2,4-dihydro-[1,2,4]triazol-3-on-5-sulfanyl, [1,2,4]triazole-3-sulfanyl, [1,2,4]triazole-3-sulfinyl, [1,2,4]triazole-3-sulfonyl, 4-alkyl-pyrazol-1-ol-5-yl, 4-cycloalkyl-pyrazol-1-ol-5-yl, 4-alkyl-[1,2,3]triazol-1-ol-5-yl, 4-cycloalkyl-[1,2,3]triazol-1-ol-5-yl, 5-alkyl-imidazol-1-ol-2-yl, 5-cycloalkyl-imidazol-1-ol-2-yl, 4-alkyl-imidazol-1-ol-5-yl, 4-cycloalkyl-imidazol-1-ol-5-yl, 4-alkyl-1,1-dioxo-1λ^6-[1,2,5]thiadiazolidin-3-on-5-yl, 4,4-dialkyl-1,1-dioxo-1λ^6-[1,2,5]thiadiazolidin-3-on-5-yl, 4-cycloalkyl-1,1-dioxo-1λ^6-[1,2,5]thiadiazolidin-3-on-5-yl, 4,4-dicycloalkyl-1,1-dioxo-1λ^6-[1,2,5]thiadiazolidin-3-on-5-yl, thiazolidine-2,4-dion-5-yl, oxazolidine-2,4-dion-5-yl, 3-[1-hydroxy-meth-(E)-ylidene]-pyrrolidine-2,4-dion-1-yl, 3-[1-hydroxy-meth-(Z)-ylidene]-pyrrolidine-2,4-dion-1-yl, 5-methyl-4-hydroxyfuran-2-on-3-yl, 5,5-dialkyl-4-hydroxyfuran-2-on-3-yl, 5-cycloalkyl-4-hydroxyfuran-2-on-3-yl, 5,5-dicycloalkyl-4-hydroxyfuran-2-on-3-yl, 3-hydroxycyclobut-3-ene-1,2-dion-4-yl or 3-hydroxycyclobut-3-ene-1,2-dion-4-amino;

R^3 is phenyl, substituted phenyl, substituted dihydropyridinyl, heteroaryl or substituted heteroaryl, wherein substituted phenyl, substituted dihydropyridinyl and substituted heteroaryl are substituted with one to three substituents independently selected from hydroxy, oxo, halogen, alkyl, cycloalkyl, haloalkyl, haloalkoxy, alkylcycloalkyl, cycloalkylalkyl, alkylcycloalkylalkyl, hydroxyalkyl, hydroxyalkoxy, alkoxy, alkoxyalkyl, alkylsulfonyl, amino and amino substituted on the nitrogen atom with one to two substituents independently selected from alkyl, cycloalkyl, haloalkyl, alkylcycloalkyl, cycloalkylalkyl, alkylcycloalkylalkyl, hydroxyalkyl and alkoxyalkyl;

A^1 is a bond or $CR^{12}R^{13}$;

A^2 is $-CR^{14}R^{15}-$, $-NR^{16}-$, -O-, -S-, -S(O)- or $-S(O)_2-$;

A^3 is $-CR^{17}R^{18}-$, $-C(O)NR^{19}-$, $-NR^{19}-$, -O-, -S-, -S(O)- or $-S(O)_2-$;

R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11}, R^{14}, R^{15}, R^{17} and R^{18} are independently selected from H, halogen, alkyl, alkoxy, cycloalkyl, cycloalkylalkoxy, haloalkoxy and haloalkyl.

R^{12} and R^{13} are independently selected from hydrogen, alkyl, cycloalkyl and haloalkyl.

R^{16} and R^{19} are independently selected from hydrogen, alkyl, cycloalkyl, haloalkyl and alkylcarbonyl.

n, m and p are independently selected from zero and 1;

or pharmaceutically acceptable salts.

2. A compound according to claim 1, wherein R^1 is alkyl, cycloalkyl, substituted cycloalkyl, alkoxy, alkoxyalkyl, alkoxyalkoxy, alkoxycarbonylalkyl, carboxyalkyl, haloalkyl, haloalkoxy, substituted aryl, heterocycloalkyl, substituted heterocycloalkyl, heterocycloalkoxy, substituted heterocycloalkylalkoxy, heteroaryl, substituted heteroaryl, amino or substituted amino, wherein substituted cycloalkyl, substituted aryl, substituted heterocycloalkyl, substituted heterocycloalkylalkoxy and substituted heteroaryl are substituted with one to three substituents independently selected from halogen, alkyl, haloalkyl, hydoxyalkyl, alkylsulfonylalkyl, alkoxycarbonyl and alkoxyalkyl and wherein substituted amino is substituted on the nitrogen atom with two alkyl.

3. A compound according to claim 1 or 2, wherein R^1 is cycloalkyl, substituted cycloalkyl, heterocycloalkyl, substituted heterocycloalkyl, heterocycloalkylalkoxy or substituted amino, wherein substituted cycloalkyl and substituted heterocycloalkyl are substituted with one alkyl or alkoxyalkyl and wherein substituted amino is substituted on the nitrogen atom with two alkyl.

4. A compound according to any one of claims 1 to 3, wherein R^1 is cyclopentyl, substituted cyclopentyl, tetrahydrofuranyl, substituted tetrahydrofuranyl, tetrahydrofuranyloxy, piperidinyl or substituted amino, wherein substituted cyclopentyl and substituted tetrahydrofuranyl are substituted with one alkyl or alkoxyalkyl and wherein substituted amino is substituted on the nitrogen atom with two alkyl.

5. A compound according to any one of claims 1 to 4, wherein R^2 is -COOH, tetrazol-5-yl or [1,3,4]oxadiazol-2-thion-5-yl.

6. A compound according to any one of claims 1 to 5, wherein R^2 is tetrazol-5-yl.

7. A compound according to any one of claims 1 to 6, wherein R^3 is phenyl, substituted phenyl, substituted dihydropyridinyl, heteroaryl or substituted heteroaryl, wherein substituted phenyl, substituted dihydropyridinyl and substituted heteroaryl are substituted

with one to three substituents independently selected from hydroxy, oxo, halogen, alkyl, cycloalkyl, haloalkyl, haloalkoxy, hydroxyalkoxy, alkoxy, alkylsulfonyl and amino substituted on the nitrogen atom with one to two substituents independently selected from alkyl, cycloalkyl, haloalkyl, alkylcycloalkyl, cycloalkylalkyl, alkylcycloalkylalkyl, hydroxyalkyl and alkoxyalkyl.

8. A compound according to any one of claims 1 to 7, wherein R^3 is phenyl, substituted phenyl or substituted heteroaryl, wherein substituted phenyl and substituted heteroaryl are substituted with one to three substituents independently selected from halogen and alkyl.

9. A compound according to any one of claims 1 to 8, wherein R^3 is phenyl, substituted phenyl, substituted pyrazolyl or substituted pyridinyl, wherein substituted phenyl, substituted pyrazolyl and substituted pyridinyl are substituted with one to three substituents independently selected from halogen and alkyl.

10. A compound according to any one of claims 1 to 9, wherein R^3 is substituted pyrazolyl or substituted pyridinyl, wherein substituted pyrazolyl and substituted pyridinyl are substituted with one alkyl.

11. A compound according to any one of claims 1 to 10, wherein R^3 is pyridinyl substituted with one alkyl or halogen.

12. A compound according to any one of claims 1 to 11, wherein A^1 is a bond.

13. A compound according to any one of claims 1 to 12, wherein A^2 is $-CR^{14}R^{15}-$, $-NR^{16}-$, -O- and -S-.

14. A compound according to any one of claims 1 to 13, wherein A^2 is $-CR^{14}R^{15}$.

15. A compound according to any one of claims 1 to 14, wherein A^3 is $-CR^{17}R^{18}-$, $-C(O)NR^{19}$ or $-NR^{19}$.

16. A compound according to any one of claims 1 to 15, wherein A^3 is $-CR^{17}R^{18}-$.

17. A compound according to any one of claims 1 to 16, wherein n is 1.

18. A compound according to any one of claims 1 to 17, wherein p is zero.

19. A compound according to any one of claims 1 to 18, wherein R^4, R^5, R^6, R^7, R^8, R^9, R^{10} and R^{11} are H.

20. A compound according to any one of claims 1 to 19, wherein R^{14} and R^{15} are independently selected from H, halogen and alkyl.

21. A compound according to any one of claims 1 to 20, wherein R^{17} and R^{18} are independently selected from H and alkyl.

22. A compound according to any one of claims 1 to 21, wherein R^{16} is haloalkyl or alkylcarbonyl.

23. A compound according to any one of claims 1 to 22, wherein R^{19} is alkyl or alkylcarbonyl.

24. A compound according to any one of claims 1 to 23, selected from

2-isopropyl-6,8-dimethyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylic acid;

8-acetyl-2-isopropyl-6-methyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylic acid;

8-ethyl-2-isopropyl-6-methyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylic acid;

4-(3-chlorophenyl)-2-cyclohexyl-8-ethyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylic acid;

2-cyclohexyl-8-ethyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylic acid;

2-cyclopentyl-8-ethyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylic acid;

2-cyclopentyl-8-ethyl-6-methyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylic acid;

2-cyclopentyl-6,8-dimethyl-4-phenyl-5,6,7,8-tetrahydro-1,8-naphthyridine-3-carboxylic acid;

2-isopropyl-6-methyl-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carboxylic acid;

6-ethyl-2-isopropyl-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carboxylic acid;

2-isopropyl-6,6-dimethyl-4-phenyl-5,6,7,8-tetrahydro-quinoline-3-carboxylic acid;

2-cyclopentyl-4-(6-methoxypyridin-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid;

2-cyclopentyl-4-(6-oxo-1,6-dihydropyridin-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid;

4-phenyl-2-(piperidin-1-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid;

2-(2-methylpyrrolidin-1-yl)-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid;

6-methyl-4-phenyl-2-(piperidin-1-yl)-5,6,7,8-tetrahydroquinoline-3-carboxylic acid;

2-(diethylamino)-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid;

6-methyl-2-(2-methylpyrrolidin-1-yl)-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carboxylic acid;

2-(diethylamino)-6-methyl-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carboxylic acid;

4-(3-chlorophenyl)-6-methyl-2-(pyrrolidin-1-yl)-5,6,7,8-tetrahydroquinoline-3-carboxylic acid;

4-phenyl-2-(piperidin-1-yl)-6,7-dihydro-5H-cyclopenta[b]pyridine-3-carboxylic acid;

2-(diethylamino)-4-phenyl-6,7-dihydro-5H-cyclopenta[b]pyridine-3-carboxylic acid;

4-(3-chlorophenyl)-6-methyl-2-(piperidin-1-yl)-5,6,7,8-tetrahydroquinoline-3-carboxylic acid;

5-(6-methyl-4-phenyl-2-(piperidin-1-yl)-5,6,7,8-tetrahydroquinolin-3-yl)-1,3,4-oxadiazole-2(3H)-thione;

6-methyl-4-phenyl-2-(piperidin-1-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

N,N-diethyl-6-methyl-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinolin-2-amine;

4-phenyl-2-(piperidin-1-yl)-3-(2H-tetrazol-5-yl)-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinoline;

N,N-diethyl-4-phenyl-3-(2H-tetrazol-5-yl)-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinolin-2-amine;

6-methyl-4-(1-methyl-1H-pyrazol-5-yl)-2-(piperidin-1-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

4-phenyl-2-(piperidin-1-yl)-3-(2H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

N,N-diethyl-4-phenyl-3-(2H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine;

4-(3-chlorophenyl)-2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(3-chlorophenyl)-N,N-diethyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine;

4-(1-methyl-1H-pyrazol-5-yl)-2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(4-fluorophenyl)-6-methyl-2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

4-(4-fluorophenyl)-2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-7,8-dihydro-5H-pyrano[4,3-b]pyridine;

4-(1-methyl-1H-pyrazol-5-yl)-2-(2-methylpyrrolidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(5-chlorothiophen-2-yl)-N,N-diethyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine;

4-(5-chlorothiophen-2-yl)-2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

N,N-diethyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine;

5-methyl-3-(2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)isoxazole;

N,N-diethyl-4-(5-methylisoxazol-3-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine;

4-(1-methyl-1H-pyrazol-5-yl)-2-(2-methylpyrrolidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(piperidin-1-yl)-4-(pyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

N,N-diethyl-4-(pyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine;

4-(5-methylfuran-2-yl)-2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

N,N-diethyl-4-(5-methylfuran-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine;

4-(1,5-dimethyl-1H-pyrazol-4-yl)-2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(1,5-dimethyl-1H-pyrazol-4-yl)-N,N-diethyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine;

4-(5-chlorothiophen-2-yl)-2-(3-fluoropiperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(5-chlorothiophen-2-yl)-2-(3,3-difluoropiperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(5-chlorothiophen-2-yl)-2-(4,4-difluoropiperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(5-chlorothiophen-2-yl)-2-(4-fluoropiperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(5-chlorothiophen-2-yl)-3-(1H-tetrazol-5-yl)-2-(4-(trifluoromethyl)piperidin-1-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(5-chlorothiophen-2-yl)-2-(3,3-difluoroazetidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

N,N-diethyl-4-(4-methylthiazol-5-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine;

4-methyl-5-(2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)thiazole;

N,N-diethyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8,9,10-hexahydrocycloocta[b]pyridin-2-amine;

4-(5-chlorothiophen-2-yl)-2-(3,3-difluoropyrrolidin-1-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(1-methyl-1H-pyrazol-5-yl)-2-(piperidin-1-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8,9,10-hexahydrocycloocta[b]pyridine;

diethyl-[4-pyrimidin-5-yl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-yl]-amine;

N,N-diethyl-4-(3-fluoropyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine;

N,N-diethyl-4-(2-methoxypyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine;

4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine;

2-propyl-4-(pyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(1-methyl-1H-pyrazol-5-yl)-2-(pentan-3-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(3-chlorophenyl)-2-cyclobutyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclohexyl-4-pyridin-4-yl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-H-cyclohepta[b]pyridine;

4-(3-chloro-phenyl)-2-cyclopentyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-H-cyclohepta[b]pyridine;

2-cyclohexyl-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

5-(2-cyclohexyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)pyridin-2(1H)-one;

5-(2-cyclohexyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)-1-ethylpyridin-2(1H)-one;

5-(2-cyclohexyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)-1-methylpyridin-2(1H)-one;

2-cyclohexyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclopentyl-4-(pyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclopentyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

1-(4-(3-chlorophenyl)-2-cyclobutyl-3-(1H-tetrazol-5-yl)-7,8-dihydro-1,6-naphthyridin-6(5H)-yl)ethanone;

2-cyclopentyl-4-(6-methoxypyridin-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-phenyl-2-(tetrahydro-2H-pyran-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclopentyl-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-phenyl-2-(tetrahydrofuran-3-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclopentyl-4-(2-methoxypyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclohexyl-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclopentyl-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-phenyl-2-(tetrahydrofuran-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclohexyl-4-(3-fluoropyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclopentyl-4-(3-fluoropyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-phenyl-2-(tetrahydro-2H-pyran-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclohexyl-4-(2-methylpyrimidin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

5-(2-cyclobutyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)-1-methylpyridin-2(1H)-one;

2-cyclohexyl-4-(pyrimidin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclopentyl-4-(pyrimidin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclopentyl-4-(2-methylpyrimidin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-(methoxymethyl)cyclopentyl)-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclopentyl-4-(pyridazin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclopentyl-4-(6-methylpyridin-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclopentyl-4-(pyridin-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-isopropyl-4-(2-isopropylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclopentyl-4-(pyrimidin-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(2-(2-cyclopentyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)phenoxy)ethanol;

2-cyclopentyl-4-(2-isopropylpyrimidin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-isopropyl-4-(2-isopropylpyrimidin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-chloropyridin-4-yl)-2-cyclopentyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-(methoxymethyl)cyclopentyl)-4-(2-methoxypyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-isopropylpyridin-4-yl)-2-(pentan-3-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(1-methyl-1H-pyrazol-5-yl)-2-(pentan-3-yl)-3-(2H-tetrazol-5-yl)-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinoline;

2-cyclohexyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinoline;

2-cyclohexyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinoline;

2-cyclohexyl-6-methyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-cyclohexyl-6-methyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-cyclopentyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinoline;

2-cyclopentyl-6,6-difluoro-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-cyclopentyl-6-methyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

4-(2-cyclohexyl-3-(2H-tetrazol-5-yl)-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinolin-4-yl)-3,5-dimethylisoxazole;

4-(2-cyclohexyl-6-methyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinolin-4-yl)-3,5-dimethylisoxazole;

2-cyclopentyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-6-(trifluoromethyl)-5,6,7,8-tetrahydroquinoline;

2-cyclopentyl-4-phenyl-3-(2H-tetrazol-5-yl)-6-(2,2,2-trifluoroethyl)-5,6,7,8-tetrahydro-1,6-naphthyridine;

2-cyclopentyl-6,6-dimethyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-cyclopentyl-6-methoxy-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

6-methyl-4-(2-methylpyridin-4-yl)-2-tert-pentyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-cyclopentyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-cyclohexyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-methoxy-2-methylpropan-2-yl)-6-methyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-cyclopentyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-6,7-dihydro-5H-cyclopenta[b]pyridine;

2-cyclohexyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-6,7-dihydro-5H-cyclopenta[b]pyridine;

2-tert-butyl-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-tert-butyl-4-(3-fluorophenyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-tert-butyl-3-(1H-tetrazol-5-yl)-4-(4-(trifluoromethyl)phenyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-tert-butyl-3-(1H-tetrazol-5-yl)-4-(3-(trifluoromethyl)phenyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-tert-butyl-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(3,3-difluorocyclobutyl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-tert-butyl-4-(4-fluoro-phenyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-tert-butyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)oxazole;

2-tert-butyl-4-(1-methyl-1H-pyrazol-3-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-tert-butyl-4-(4-methyl-1H-pyrazol-5-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-tert-butyl-4-(3-cyclopropyl-1H-pyrazol-5-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-tert-butyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)-2-methyloxazole;

2-tert-butyl-4-(4-chloro-1H-pyrazol-3-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-tert-butyl-3-(1H-tetrazol-5-yl)-4-(4-(trifluoromethyl)-1H-imidazol-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-tert-butyl-3-(1H-tetrazol-5-yl)-4-(1H-1,2,3-triazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-tert-butyl-4-(2-butyl-1H-imidazol-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-furan-2-yl-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-sec-butyl-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(3-fluorophenyl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-sec-butyl-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

and pharmaceutically acceptable salts thereof.

25. A compound according to any one of claims 1 to 23, selected from

4-phenyl-2-(R)-tetrahydro-furan-2-yl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-phenyl-2-(S)-tetrahydro-furan-2-yl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

(R)-4-(2-chloropyridin-4-yl)-2-(tetrahydrofuran-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

(S)-4-(2-chloropyridin-4-yl)-2-(tetrahydrofuran-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-phenyl-2-(tetrahydrofuran-2-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8,9,10-hexahydrocycloocta[b]pyridine;

(S)-4-phenyl-2-(tetrahydrofuran-2-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8,9,10-hexahydrocycloocta[b]pyridine;

(R)-4-phenyl-2-(tetrahydrofuran-2-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8,9,10-hexahydrocycloocta[b]pyridine;

2-(2-methyltetrahydrofuran-2-yl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-((S)-2-methyl-tetrahydro-furan-2-yl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-((R)-2-methyl-tetrahydro-furan-2-yl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(3-methoxyphenyl)-2-(2-methyltetrahydrofuran-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(3-methoxy-phenyl)-2-((S)-2-methyl-tetrahydro-furan-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(3-methoxy-phenyl)-2-((R)-2-methyl-tetrahydro-furan-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-methylpyridin-4-yl)-2-(2-methyltetrahydrofuran-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-[(2S)-2-methyloxolan-2-yl]-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-[(2R)-2-methyloxolan-2-yl]-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(3-chlorophenyl)-2-(2-methyltetrahydrofuran-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(3-chloro-phenyl)-2-((S)-2-methyl-tetrahydro-furan-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(3-chloro-phenyl)-2-((R)-2-methyl-tetrahydro-furan-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-methylcyclopentyl)-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-methylcyclopentyl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-methoxypyridin-4-yl)-2-(1-methylcyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-(1-methylcyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)pyridin-2(1H)-one;

4-(3-chloro-phenyl)-2-(1-methyl-cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(1-methyl-1H-pyrazol-5-yl)-2-(1-methylcyclohexyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-methylcyclohexyl)-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-methoxymethyl-cyclopentyl)-4-(2-methyl-2H-pyrazol-3-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(3-fluoropyridin-4-yl)-2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-(methoxymethyl)cyclopentyl)-4-(4-methyl-1H-pyrazol-3-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(1H-indol-4-yl)-2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-chloropyridin-4-yl)-2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-ethylpyridin-4-yl)-2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

3-(2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)-2-methylphenol;

4-(2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)-2-methyloxazole;

4-(1H-indazol-4-yl)-2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-4-(2-(trifluoromethyl)pyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-4-(2-(2,2,2-trifluoroethoxy)pyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-(methoxymethyl)cyclopentyl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-ethoxypyridin-4-yl)-2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(4-fluoro-3-methoxyphenyl)-2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(4-fluorophenyl)-2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-(methoxymethyl)cyclopentyl)-4-(3-methoxyphenyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-fluoro-5-methoxyphenyl)-2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(3-chloro-phenyl)-2-(1-methoxymethyl-cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(3-(methoxymethyl)pentan-3-yl)-4-(1-methyl-1H-pyrazol-5-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(3-(methoxymethyl)pentan-3-yl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclopentyl-4-(2-ethylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-cyclopentyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-4-yl)-N-methylpyridin-2-amine;

2-cyclopentyl-3-(1H-tetrazol-5-yl)-4-(2-(trifluoromethyl)pyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(1-methyl-1H-pyrazol-5-yl)-2-(3-methylpentan-3-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-ethylpyridin-4-yl)-2-isopropyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-isopropyl-3-(1H-tetrazol-5-yl)-4-(2-(2,2,2-trifluoroethoxy)pyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-ethoxypyridin-4-yl)-2-isopropyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-methoxycyclopentyl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-methoxycyclopentyl)-4-phenyl-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-methoxycyclopentyl)-4-(2-methoxypyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-chloropyridin-4-yl)-2-(1-methoxycyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-methoxycyclopentyl)-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

(1-(4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-yl)cyclopentyl)methanol;

(1-(4-phenyl-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinolin-2-yl)cyclopentyl)methanol;

(1-(4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-yl)cyclopentyl)methanol;

(1-(4-(3-chlorophenyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-yl)cyclopentyl)methanol;

(1-(4-(4-fluorophenyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-yl)cyclopentyl)methanol;

(S)-tert-butyl 2-(4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-yl)pyrrolidine-1-carboxylate;

(S)-4-phenyl-2-(pyrrolidin-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine 2,2,2-trifluoroacetate;

2-cyclopentyl-4-phenyl-3-(1H-tetrazol-5-yl)-7,8-dihydro-5H-pyrido[2,3-c]azepin-9(6H)-one;

2-(1-methoxy-2-methylpropan-2-yl)-6,6-dimethyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

6,6-dimethyl-4-(1-methyl-1H-pyrazol-5-yl)-2-tert-pentyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-methoxy-2-methylpropan-2-yl)-6,6-dimethyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-(methoxymethyl)cyclopentyl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

6,6-difluoro-2-(1-(methoxymethyl)cyclopentyl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

6,6-difluoro-2-(1-methoxymethyl-cyclohexyl)-4-phenyl-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydro-quinoline;

6,6-difluoro-2-(1-(methoxymethyl)cyclopentyl)-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(4-methyltetrahydro-2H-pyran-4-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

6,6-difluoro-2-(4-methyltetrahydro-2H-pyran-4-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-(methoxymethyl)cyclopentyl)-6-methyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-(methoxymethyl)cyclohexyl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

6,6-difluoro-2-(1-(methoxymethyl)cyclopentyl)-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-(methoxymethyl)cyclopentyl)-6,6-dimethyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(2-methyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

6,6-difluoro-2-(2-methyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

6,6-dimethyl-2-(2-methyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

4-(1-methyl-1H-pyrazol-5-yl)-2-(2-methyltetrahydrofuran-2-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

6,6-dimethyl-4-(1-methyl-1H-pyrazol-5-yl)-2-(2-methyltetrahydrofuran-2-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(R)-2-(2-methyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(S)-2-(2-methyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(R)-6,6-difluoro-2-(2-methyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(S)-6,6-difluoro-2-(2-methyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(R)-6,6-dimethyl-2-(2-methyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(S)-6,6-dimethyl-2-(2-methyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-(methoxymethyl)cyclopentyl)-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-(methoxymethyl)cyclohexyl)-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-(methoxymethyl)cyclohexyl)-6,6-dimethyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

6,6-difluoro-2-(1-(methoxymethyl)cyclohexyl)-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

6,6-difluoro-4-(1-methyl-1H-pyrazol-5-yl)-2-(2-methyltetrahydrofuran-2-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-(methoxymethyl)cyclohexyl)-4-(1-methyl-1H-pyrazol-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-6,6-dimethyl-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

6,6-difluoro-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(2-ethyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(2-ethyltetrahydrofuran-2-yl)-6,6-dimethyl-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(2-ethyltetrahydrofuran-2-yl)-6,6-difluoro-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(R)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(S)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(R)-6,6-difluoro-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(S)-6,6-difluoro-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(R)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-6,6-dimethyl-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(S)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-6,6-dimethyl-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(2-ethyltetrahydrofuran-2-yl)-4-(1-methyl-1H-pyrazol-5-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-(methoxymethyl)cyclopentyl)-4-(1-methyl-1H-pyrazol-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

4-(3-chlorophenyl)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

4-(3-chlorophenyl)-2-(2-methyltetrahydrofuran-2-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-4-(3-methoxyphenyl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

4-(4-fluoro-3-methoxyphenyl)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-(methylsulfonylmethyl)cyclopentyl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(R)-4-(4-fluoro-3-methoxyphenyl)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(S)-4-(4-fluoro-3-methoxyphenyl)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-(methoxymethyl)cyclopentyl)-4-(3-(methylsulfonyl)phenyl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-(methoxymethyl)cyclopentyl)-4-(3-methoxyphenyl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

4-(2-fluoro-5-methoxyphenyl)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

4-(2-fluoro-5-methoxyphenyl)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-(ethoxymethyl)cyclopentyl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(R)-4-(3-chlorophenyl)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-6,6-dimethyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(S)-4-(3-chlorophenyl)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-6,6-dimethyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(3,3-difluorocyclobutyl)-4-(1-methyl-1H-pyrazol-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1,5-dimethyl-1H-pyrazol-4-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-tert-butyl-4-(1-methyl-1H-pyrazol-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(3,3-difluorocyclobutyl)-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-sec-butyl-4-(1-methyl-1H-pyrazol-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-tert-butyl-6,6-difluoro-4-(2-methyl-pyridin-4-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydro-quinoline;

2-tert-butyl-6,6-difluoro-4-(1-methyl-1H-pyrazol-4-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydro-quinoline;

2-tert-butyl-6,6-difluoro-4-(2-methyl-2H-pyrazol-3-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydro-quinoline;

2-tert-butyl-4-phenyl-3-(1H-tetrazol-5-yl)-7,8-dihydro-5H-thiopyrano[4,3-b]pyridine;

2-tert-butyl-8,8-dimethyl-4-phenyl-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-tert-butyl-7,7-dimethyl-4-phenyl-3-(1H-tetrazol-5-yl)-6,7-dihydro-5H-cyclopenta[b]pyridine;

2-tert-butyl-8,8-dimethyl-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-tert-butyl-8,8-dimethyl-4-(1-methyl-1H-pyrazol-4-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(1-(methoxymethyl)cyclobutyl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-(methoxymethyl)cyclobutyl)-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-(methoxymethyl)cyclobutyl)-4-(1-methyl-1H-pyrazol-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(perfluoroethyl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-tert-butyl-8,8-dimethyl-4-(1-methyl-1H-pyrazol-5-yl)-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2,4-bis(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-isopropoxy-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-methoxy-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-ethoxy-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

(S)-4-phenyl-2-(tetrahydrofuran-3-yloxy)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile;

(R)-4-phenyl-2-(tetrahydrofuran-3-yloxy)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile;

2-ethoxy-4-(1-methyl-1H-pyrazol-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-isopropoxy-4-(1-methyl-1H-pyrazol-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-ethoxy-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(2-methoxyethoxy)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-phenyl-2-((tetrahydrofuran-2-yl)methoxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(3-fluoropropoxy)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(2,2-difluoroethoxy)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

(S)-4-phenyl-2-(tetrahydrofuran-3-yloxy)-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

4-(2-methylpyridin-4-yl)-2-(tetrahydro-2H-pyran-4-yloxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

(S)-4-(2-methylpyridin-4-yl)-2-(tetrahydrofuran-3-yloxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

(S)-4-(2-methylpyridin-4-yl)-2-(tetrahydrofuran-3-yloxy)-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-(2-methoxyethoxy)-3-(1H-tetrazol-5-yl)-4-(4-(trifluoromethyl)phenyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(3-fluorophenyl)-2-(2-methoxyethoxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

(S)-4-(3-fluorophenyl)-2-(tetrahydrofuran-3-yloxy)-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

4-(3,5-difluorophenyl)-2-(2-methoxyethoxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

(S)-4-(3-fluorophenyl)-2-(tetrahydrofuran-3-yloxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

(S)-4-(3,5-difluorophenyl)-2-(tetrahydrofuran-3-yloxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-fluorophenyl)-2-((S)-tetrahydrofuran-3-yloxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-fluorophenyl)-2-(2-methoxyethoxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

(S)-2-(tetrahydrofuran-3-yloxy)-3-(1H-tetrazol-5-yl)-4-(thiophen-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(3-fluoropropoxy)-3-(1H-tetrazol-5-yl)-4-(thiophen-2-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

(S)-2-(tetrahydrofuran-3-yloxy)-3-(1H-tetrazol-5-yl)-4-(thiophen-3-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-phenyl-2-(tetrahydro-2H-pyran-4-yloxy)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-methylcyclopentyl)-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid;

4-(3-chlorophenyl)-2-(1-methylcyclopentyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid;

4-(1-methyl-1H-pyrazol-5-yl)-2-(1-methylcyclohexyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid;

2-(1-methylcyclohexyl)-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid;

2-cyclohexyl-4-phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid;

2-(1-methylcyclohexyl)-4-(2-methylpyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid;

2-cyclohexyl-4-(2-methylpyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid;

2-cyclopentyl-4-phenyl-5,6,7,8-tetrahydroquinoline-3-carboxylic acid;

2-(1-(methoxymethyl)cyclopentyl)-6-pentyl-4-phenyl-3-(1H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

tert-butyl 2-methyl-2-(4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-yl)propanoate;

2-methyl-2-(4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-yl)propanoic acid;

and pharmaceutically acceptable salts thereof.

26. A compound according to any one of claims 1 to 24, selected from

6-methyl-4-(1-methyl-1H-pyrazol-5-yl)-2-(piperidin-1-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

4-(3-chlorophenyl)-N,N-diethyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-2-amine;

2-cyclopentyl-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-phenyl-2-(tetrahydrofuran-2-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-(methoxymethyl)cyclopentyl)-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-cyclopentyl-6,6-difluoro-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-cyclopentyl-6-methyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

2-cyclopentyl-6,6-dimethyl-4-(2-methylpyridin-4-yl)-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

and pharmaceutically acceptable salts thereof.

27. A compound according to any one of claims 1 to 23 and 25, selected from

2-((R)-2-methyl-tetrahydro-furan-2-yl)-4-phenyl-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

2-(1-methylcyclopentyl)-4-(2-methylpyridin-4-yl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

4-(2-chloropyridin-4-yl)-2-(1-(methoxymethyl)cyclopentyl)-3-(1H-tetrazol-5-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine;

(R)-6,6-dimethyl-2-(2-methyltetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

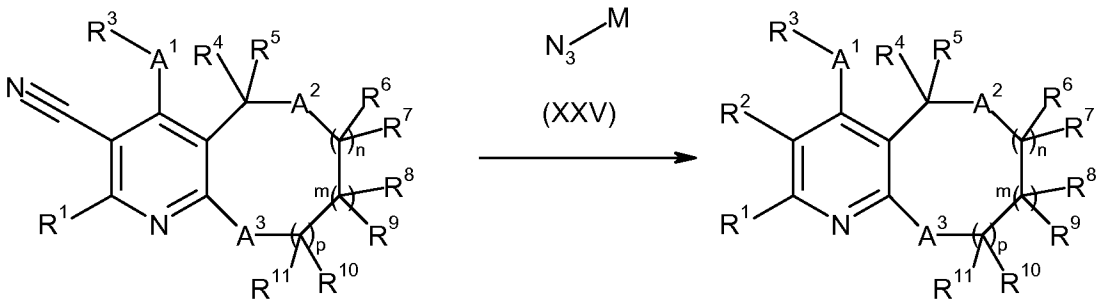
(R)-2-(2-(methoxymethyl)tetrahydrofuran-2-yl)-4-phenyl-3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydroquinoline;

(S)-4-phenyl-2-(tetrahydrofuran-3-yloxy)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carbonitrile;

2-(1-methylcyclohexyl)-4-(2-methylpyridin-4-yl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxylic acid;

and pharmaceutically acceptable salts thereof.

28. A process to prepare a compound according to any one of claims 1 to 27 comprising the reaction of a compound of formula (II) in the presence of a compound of formula (XXV), wherein M is sodium, trialkyltin or trialkylsilyl.



(II) (I)

29. A compound according to any one of claims 1 to 27 for use as therapeutically active substance.

30. A pharmaceutical composition comprising a compound according to any one of claims 1 to 27 and a therapeutically inert carrier.

31. The use of a compound according to any one of claims 1 to 27 for the treatment or prophylaxis of type 2 diabetes, atherosclerosis, cancer, chronic renal disease and non-alcoholic steatohepatitis.

32. A compound according to any one of claims 1 to 27 for the treatment or prophylaxis of type 2 diabetes, atherosclerosis, cancer, chronic renal disease and non-alcoholic steatohepatitis.

33. The use of a compound according to any one of claims 1 to 27 for the preparation of a medicament for the treatment or prophylaxis of type 2 diabetes, atherosclerosis, cancer, chronic renal disease and non-alcoholic steatohepatitis.

34. A method for the treatment or prophylaxis of type 2 diabetes, atherosclerosis, cancer, chronic renal disease and non-alcoholic steatohepatitis, which method comprises administering an effective amount of a compound according to any one of claims 1 to 27.

35. A compound according to any one of claims 1 to 27, when manufactured according to a process of claim 28.

36. The invention as hereinbefore described.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2013/067220

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D401/14 C07D215/48 C07D401/04 C07D401/06 C07D471/04
A61K31/4353 A61K31/47 A61P3/10
ADD.
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07D A61K A61P

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2012/122837 A1 (CHENG CLIFFORD [US] ET AL) 17 May 2012 (2012-05-17) the whole document	1,31

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

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

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

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

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

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

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

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

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

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
14 October 2013	29/10/2013

Name and mailing address of the ISA/	Authorized officer
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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2013/067220

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2012122837 A1	17-05-2012	NONE	