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(54) **Title**: POSITIVE ALLOSTERIC MODULATORS OF MGLUR2

(57) **Abstract**: The present invention is directed to benzimidazolone derivatives which are positive allosteric modulators of the mGluR2 receptor, useful in the treatment or prevention of neurological and psychiatric disorders associated with glutamate dysfunction and diseases in which the mGluR2 receptor is involved. The invention is also directed to pharmaceutical compositions comprising these compounds and the use of these compounds and compositions in the prevention or treatment of such diseases in which metabotropic glutamate receptors are involved, such as schizophrenia.

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TITLE OF THE INVENTION

POSITIVE ALLOSTERIC MODULATORS OF MGLUR2

BACKGROUND OF THE INVENTION

The excitatory amino acid L-glutamate (sometimes referred to herein simply as glutamate) through its many receptors mediates most of the excitatory neurotransmission within the mammalian central nervous system (CNS). The excitatory amino acids, including glutamate, are of great physiological importance, playing a role in a variety of physiological processes, such as long-term potentiation (learning and memory), the development of synaptic plasticity, motor control, respiration, cardiovascular regulation, and sensory perception.

Glutamate acts via at least two distinct classes of receptors. One class is composed of the ionotropic glutamate (iGlu) receptors that act as ligand-gated ionic channels. Via activation of the iGlu receptors, glutamate is thought to regulate fast neuronal transmission within the synapse of two connecting neurons in the CNS. The second general type of receptor is the G-protein or second messenger-linked "metabotropic" glutamate (mGluR) receptor. Both types of receptors appear not only to mediate normal synaptic transmission along excitatory pathways, but also participate in the modification of synaptic connections during development and throughout life. Schoepp, Bockaert, and Sladeczek, Trends in Pharmacol. Sci., 11, 508 (1990); McDonald and Johnson, Brain Research Reviews, 15, 41 (1990).

The present invention relates to potentiators of mGlu receptors, in particular mGluR2 receptors. The mGluR receptors belong to the Type III G- protein coupled receptor (GPCR) superfamily. This superfamily of GPCR's including the calcium-sensing receptors, GABAB receptors and pheromone receptors, which are unique in that they are activated by binding of effectors to the amino-terminus portion of the receptor protein. The mGlu receptors are thought to mediate glutamate's demonstrated ability to modulate intracellular signal transduction pathways. Ozawa, Kamiya and Tsuzuski, Prog. Neurobio., 54, 581 (1998). They have been demonstrated to be localized both pre- and post-synaptically where they can regulate neurotransmitter release, either glutamate or other neurotransmitters, or modify the post-synaptic response of neurotransmitters, respectively.

At present, there are eight distinct mGlu receptors that have been positively identified, cloned, and their sequences reported. These are further subdivided based on their amino acid sequence homology, their ability to effect certain signal transduction mechanisms, and their known pharmacological properties. Ozawa, Kamiya and Tsuzuski, Prog. Neurobio., 54,

581 (1998). For instance, the Group I mGluR receptors, which include the mGlulR and mGlu5R, are known to activate phospholipase C (PLC) via Gαq-proteins thereby resulting in the increased hydrolysis of phosphoinositides and intracellular calcium mobilization. There are several compounds that are reported to activate the Group I mGlu receptors including DHPG, (R/S)-3,5-dihydroxyphenylglycine. Schoepp, Goldworthy, Johnson, Salhoff and Baker, J. Neurochem., 63, 769 (1994); Ito, et al., keurorep., 3, 1013 (1992). The Group II mGlu receptors consist of the two distinct receptors, mGluR2 and mGluR3 receptors. Both have been found to be negatively coupled to adenylate cyclase via activation of Gαi-protein. These receptors can be activated by a selective compound such as 1S,2S,SR,6S-2 aminobicyclo[3.1.0]hexane-2,6-dicarboxylate. Monn, et al., J. Med. Chem., 40, 528 (1997); Schoepp, et al., Neuropharmacol., 36, 1 (1997). This activitation leads to inhibition of glutamate release in the synapse (Cartmell et al, J Neurochem 75, 889 (2000)). Similarly, the Group III mGlu receptors, including mGluR4, mGluR6, mGluR7 and mGluR8, are negatively coupled to adenylate cyclase via Gαi and are potently activated by L-AP4 (L- (+) -2-amino-4-phosphonobutyric acid). Schoepp, Neurochem. Int., 24, 439 (1994).

Nonselective mGluR2/mGluR3 receptor agonists (Monn, et al., J. Med. Chem., 43, 4893, (2000)) have shown efficacy in numerous animal models of anxiety and psychosis as well as human clinical trials in schizophrenia patients; Patil et al, Nature Medicine, 13, 1102 (2007). Recent reports indicate that mGluR2 but not the mGluR3 receptor mediates the actions of the dual mGluR2/mGluR3 agonist LY379268 in mouse models predictive of antipsychotic activity. Woolley et al, Psycopharmacology, 196, 431 (2008). Additionally, recent animal studies demonstrate that selective potentiation of the mGluR2 receptor has similar effects to such non-selective agonists (Galici et al, Journal of Pharmacology and Experimental Therapeutics, 315, 1181 (2005)) suggesting an alternative strategy concerning the discovery of selective, positive allosteric modulators (PAMs or allosteric potentiators) of mGluR2 (Johnson et al, J. Med. Chem. 46, 3189, (2003); Pinkerton et al., J. Med. Chem., 47, 4595 (2004). These potentiators act by enabling the receptor to produce an enhanced response to endogenous glutamate. Such allosteric potentiators do not bind at the glutamate binding site also known as the "orthosteric site", and may benefit by binding to a site other than the highly conserved orthosteric site. A potential advantage to this approach includes the opportunity to have a distinct pharmacological profile by enhancing the activity of the endogenous ligand upon its binding to the orthosteric site. The pharmacological distinctions include the potential for pharmacological specificity between related receptor types that share the same endogenous ligand. In addition, positive allosteric

modulators of mGluR2 have been shown to potentiate the response of mGluR2 agonists such as LY379268 (Johnson et. Al. Biochemical Soc. Trans. 32, 881 (2004) and this represents an alternative strategy for treatment using mGluR2 selective PAMs.

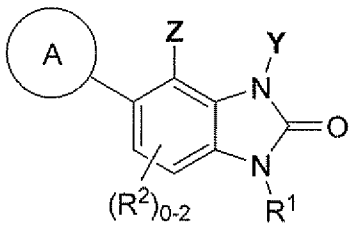
It has become increasingly clear that there is a link between modulation of excitatory amino acid receptors, including the glutamatergic system, through changes in glutamate release or alteration in postsynaptic receptor activation, and a variety of neurological and psychiatric disorders. e.g. Monaghan, Bridges and Cotman, Ann. Rev. Pharmacol. Toxicol., 29, 365-402 (1989); Schoepp and Sacann, Neurobio. Aging, 15, 261-263 (1994); Meldrum and Garthwaite, Tr. Pharmacol. Sci., 11, 379-387 (1990). The medical consequences of such glutamate dysfunction make the abatement of these neurological processes an important therapeutic goal.

SUMMARY OF THE INVENTION

The present invention is directed to benzimidazolone derivatives which are positive allosteric modulators of the mGluR2 receptor, useful in the treatment or prevention of neurological and psychiatric disorders associated with glutamate dysfunction and diseases in which the mGluR2 receptor is involved. The invention is also directed to pharmaceutical compositions comprising these compounds and the use of these compounds and compositions in the prevention or treatment of such diseases in which metabotropic glutamate receptors are involved, such as schizophrenia.

DETAILED DESCRIPTION OF THE INVENTION

The invention encompasses a genus of compounds of Formula I



I

wherein:

Z is selected from H, halo, hydroxy, methyl, methoxy or CN;

Y is cyano, benzyl, C_{1-6}alkyl or C_{2-6}alkenyl, said C_{1-6}alkyl and C_{2-6}alkenyl optionally substituted with cyano;

R^1 is selected from the group consisting of:

(1) C_{2-8}alkyl,

(2) C_{2-8}alkenyl,

(3) C_{2-8}alkynyl,

(4) C_{3-6}cycloalkyl-$(CH_2)_p$-,

(5) aryl-$(CH_2)_p$ -,

(6) heteroaryl-$(CH_2)_p$ -, and

(7) heterocycle-$(CH_2)_p$ -,

wherein wherein p is 0, 1, 2, 3 or 4, and groups (1) to (7) above are optionally substituted with 1 to 4 R^2 groups;

each R^2 is independently selected from the group consisting of: halo, OH, oxo, -CN, C_{1-4}alkyl, C_{1-4}alkoxy, CF_3, $-OCF_3$, -C(O)-O-C_{1-4}alkyl, $-N(R)_2$, pyrimidinyl and –CN;

ring **A** is selected from aryl, heteroaryl and heterocycle, wherein said heterocycle is partially aromatic and wherein said aryl, heteroaryl and heterocycle are optionally substituted with one or more R^3 groups up to the maximum number of substitutable positions;

each R^3 is independently selected from the group consisting of: halo, -CN, $-NO_2$, **X**, $-C(R^4)_2$-N(R)-**X**, $-C(R^4)_2$-N(R)C(O)-**X**, $-C(R^4)_2$-N(R)S(O)$_k$-**X**, $-C(R^4)_2$-N(R)C(O)-O-**X**, -C(O)-**X**, -C(O)-O-**X**, -C(O)-N(R)-**X**, -S(O)$_k$-**X**, -S(O)$_k$N(R)-**X**, -N(R)-**X**, -O-**X**, -N(R)C(O)-**X**, -N(R)S(O)$_k$-**X**, -N(R)C(O)-O-**X**, -N(R)C(O)N(R)-**X** and $-N(R)SO_2N(R)$-**X**,

each **X** is independently selected from the group consisting of: H, C_{1-8}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}cycloalkyl, aryl, heterorayl, heterocycle, C_{3-6}cycloalkyl-$C(R^4)_2$-, aryl-$C(R^4)_2$-, heteroaryl-$C(R^4)_2$- and heterocycle-$C(R^4)_2$-, wherein each member of the group excluding hydrogen is optionally substituted from one up to the maximum number of substitutable positions with one or more substituents independently selected from the group consisting of: CN, halo, R^5, -O-R^5, -N(R)-R^5, -N(R)C(O)-R^5, -N(R)S(O)$_2$-R^5, -N(R)-C(O)-O-R^5, -C(O)-N(R)-R^5, -C(O)-O-R^5, -C(O)-R^5, -C(O)-$C(R^4)_2$-R^5, -C(O)-$C(R^4)_2$-S(O)$_2$-R^5, $-C(R^4)_2$-N(R)-R^5, $-SO_2$-N(R)-R^5, $-Si(CH_3)_2(R^5)$, $-C(R^4)_2$-R^5 and $-SO_2$-R^5;

each k is independently 0, 1 or 2;

each R is independently selected from the group consisting of: H and C_{1-4}alkyl;

each R^4 is independently selected from the group consisting of: H, OH and C_{1-4}alkyl;

each R^5 is independently selected from the group consisting of: H, C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, phenyl, benzyl, heterocycle and heteroaryl, wherein each member of the group excluding hydrogen is optionally substituted with 1 to 3 substituents independently selected from: halogen, cyano, hydroxy and methyl;

aryl at each occurrence is independently selected from the group consisting of: phenyl, naphthyl, anthryl and phenanthryl;

heteroaryl at each occurrence independently means a 5- or 6-membered monocyclic aromatic or 9- or 10-membered bicyclic aromatic, wherein at least one atom in the aromatic is selected from N, O and S, the sulfur optionally oxidized to sulfone or sulfoxide, and the remaining atoms are selected from C, N, O and S, the sulfur optionally oxidized to sulfone or sulfoxide;

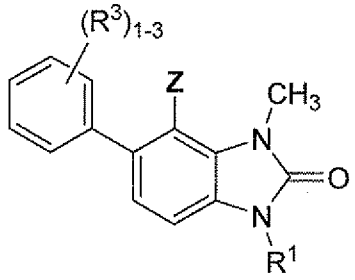
heterocycle at each occurrence independently means a 4- to 7-membered monocyclic non-aromatic ring, an 8- to 11-membered bi-cyclic, including spiro-cyclic, non- or partially-aromatic ring or a 12- to 20-memberd tri-cyclic, including spiro-cyclic portions, non- or partially-aromatic ring, each optionally substituted with 1 to 2 oxo groups, wherein at least one atom is selected from N(R), O and S, the sulfur optionally oxidized to sulfone or sulfoxide, and the remaining atoms are selected from C, N(R), O and S, the sulfur optionally oxidized to sulfone or sulfoxide;

and pharmaceutically acceptable salts thereof.

Within the genus, the invention encompasses a first sub-genus of compounds of Formula I wherein Y is methyl.

Also within the genus, the invention encompasses a second sub-genus of compounds of Formula I wherein R^1 is selected from the group consisting of: cyclopropylmethyl, 2,2-difluorocyclopropylmethyl, 2,2-difluoro-1-methylcyclopropylmethyl, 1-(trifluromethyl)cyclopropylmethyl, 4,4,4-trifluoro-2,2-dimethylbutyl, cyclobutylmethyl, 2,2-dimethylpropyl, prop-2-enyl, biphenyl and benzyl, optionally substituted with methoxy or $-OCF_3$.

Also within the genus, the invention encompasses a third sub-genus of compounds having Formula Ia

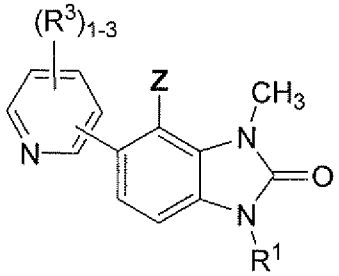


Ia

or a pharmaceutically acceptable salt thereof.

Within the third sub-genus, the invention encompasses a first class of compounds of Formula Ia wherein R^3 is selected from the group consisting of: halo, -CN, -N(O)$_2$, amino, -N(C_{1-4}alkyl)$_2$, -C(O)-O-C_{1-4}alkyl, -C(O)-C_{1-4}alkyl, -S(O)$_2$-C_{1-4}alkyl, C_{3-6}cycloalkyl, -C(C_{1-4}alkyl)$_2$-NHC(O)-O-C_{1-4}alkyl and C_{1-8}alkyl optionally substituted with 1 to 4 substituents independently selected from hydroxy and halo.

Also within the genus, the invention encompasses a fourth sub-genus of compounds having Formula Ib

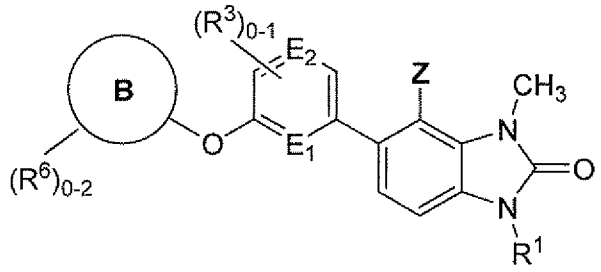


Ib

or a pharmaceutically acceptable salt thereof.

Within the fourth sub-genus, the invention encompasses a second class of compounds of Formula Ib wherein R^3 is selected from the group consisting of: halo, -CN, -N(O)$_2$, amino, -N(C_{1-4}alkyl)$_2$, -C(O)-O-C_{1-4}alkyl, -C(O)-C_{1-4}alkyl, -S(O)$_2$-C_{1-4}alkyl, C_{3-6}cycloalkyl and C_{1-8}alkyl optionally substituted with 1 to 4 substituents independently selected from hydroxy and halo.

Also within the genus, the invention encompasses a fifth sub-genus of compounds having Formula Ic



Ic

or a pharmaceutically acceptable salt thereof, wherein

E_1 and E_2 are independently C or N;

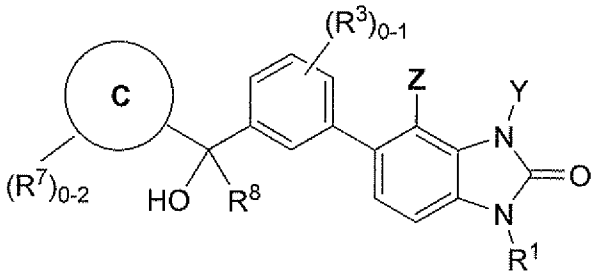
ring **B** is phenyl or heteroaryl,

R^3 is CN, halo or C_{1-4}alkyl, optionally substituted with 1-5 halo atoms, and

each R^6 is independently selected from the group consisting of: CN, halo, R^5, -O-R^5, -N(R)-R^5, -N(R)C(O)-R^5, -N(R)S(O)$_2$-R^5, -N(R)-C(O)-O-R^5, -C(O)-N(R)-R^5, -C(O)-O-R^5, -C(O)-R^5, -C(O)-C(R^4)$_2$-R^5, -C(O)-C(R^4)$_2$-S(O)$_2$-R^5, -C(R^4)$_2$-N(R)-R^5, -SO$_2$-N(R)-R^5, -Si(CH_3)$_2$(R^5), –C(R^4)$_2$-R^5 and -SO$_2$-R^5.

Within the fifth sub-genus, the invention encompasses a third class of compounds of Formula Ic wherein ring **B** is phenyl. Also within the fifth sub-genus, the invention encompasses a fourth class of compounds of Formula Ic wherein ring **B** is pyridyl. Also within the fifth sub-genus, the invention encompasses a fifth class of compounds of Formula Ic wherein E_1 is C and E_2 is C. Also within the fifth sub-genus, the invention encompasses a sixth class of compounds of Formula Ic wherein E_1 is N and E_2 is C. Also within the fifth sub-genus, the invention encompasses a seventh class of compounds of Formula Ic wherein E_1 is C and E_2 is N.

Also within the genus, the invention encompasses an eighth sub-genus of compounds having Formula Id



Id

or a pharmaceutically acceptable salt thereof, wherein

ring **C** is phenyl or heteroaryl,

R^3 is CN, halo or C_{1-4}alkyl, optionally substituted with 1-5 halo atoms, and

each R^7 is independently selected from the group consisting of: CN, halo, R^5, -O-R^5, -N(R)-R^5, -N(R)C(O)-R^5, -N(R)S(O)$_2$-R^5, -N(R)-C(O)-O-R^5, -C(O)-N(R)-R^5, -C(O)-O-R^5, -C(O)-R^5, -C(O)-C(R^4)$_2$-R^5, -C(O)-C(R^4)$_2$-S(O)$_2$-R^5, -C(R^4)$_2$-N(R)-R^5, -SO$_2$-N(R)-R^5, -Si(CH_3)$_2$(R^5), –C(R^4)$_2$-R^5 and -SO$_2$-R^5;

R^8 is H or methyl.

The invention also encompasses the examples that follow.

The invention also encompasses a pharmaceutical composition comprising a compound of Formula I in combination with a pharmaceutically acceptable carrier.

The invention also encompasses a method for treating a neurological or psychiatric disorder associated with glutamate dysfunction in a patient in need thereof comprising administering to the patient a therapeutically effective amount of a compound of Formula I. The invention also encompasses this method wherein the neurological or psychiatric disorder associated with glutamate dysfunction is schizophrenia.

The invention also encompasses the use of a compound of Formula I for the preparation of a medicament for the treatment of a neurological or psychiatric disorder associated with glutamate dysfunction. The invention also encompasses a compound of Formula I for use in the treatment of a neurological or psychiatric disorder associated with glutamate dysfunction

"Alkyl", as well as other groups having the prefix "alk", such as alkoxy, alkanoyl, means carbon chains which may be linear or branched or combinations thereof. Examples of alkyl groups include methyl, ethyl, propyl, isopropyl, butyl, sec- and tert-butyl, pentyl, hexyl, heptyl, octyl, nonyl, and the like.

"Alkenyl" means carbon chains which contain at least one carbon-carbon double bond, and which may be linear or branched or combinations thereof. Examples of alkenyl include vinyl, allyl, isopropenyl, pentenyl, hexenyl, heptenyl, 1-propenyl, 2-butenyl, 2-methyl-2-butenyl, and the like.

"Alkynyl" means carbon chains which contain at least one carbon-carbon triple bond, and which may be linear or branched or combinations thereof. Examples of alkynyl include ethynyl, propargyl, 3-methyl-1-pentynyl, 2-heptynyl and the like.

"Cycloalkyl" means mono-, bi- or tri-cyclic structures, optionally combined with linear or branched structures, having the indicated number of carbon atoms. Examples of

cycloalkyl groups include cyclopropyl, cyclopentyl, cycloheptyl, adamantyl, cyclododecylmethyl, 2-ethyl-1- bicyclo[4.4.0]decyl, and the like.

"Alkoxy" means alkoxy groups of a straight or branched having the indicated number of carbon atoms. C_{1-6}alkoxy, for example, includes methoxy, ethoxy, propoxy, isopropoxy, and the like.

"Cycloalkoxy" means cycloalkyl as defined above bonded to an oxygen atom, such as cyclopropyloxy.

Examples of heteroaryl include pyrrolyl, isoxazolyl, isothiazolyl, pyrazolyl, pyridyl, oxazolyl, oxadiazolyl, thiadiazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, furanyl, triazinyl, thienyl, pyrimidyl, pyridazinyl, pyrazinyl, benzoxazolyl, benzothiazolyl, benzimidazolyl, benzofuranyl, benzothiophenyl, furo(2,3-b)pyridyl, quinolyl, indolyl, isoquinolyl, and the like.

"Halogen" and "halo" includes fluorine, chlorine, bromine and iodine.

The point of attachment for Heterocycle may be through a carbon or nitrogen atom.

A heteroaryl group may be attached to the remainder of the molecule via a ring carbon or a ring nitrogen, provided that this is consistent with preservation of aromaticity.

The compounds of the present invention are potentiators of metabotropic glutamate (mGluR) receptor function, in particular they are potentiators of mGluR2 receptors. That is, the compounds of the present invention do not appear to bind at the glutamate recognition site on the mGluR receptor, but in the presence of glutamate or a glutamate agonist, the compounds of the present invention increase mGluR receptor response. The present potentiators are expected to have their effect at mGluR receptors by virtue of their ability to increase the response of such receptors to glutamate or glutamate agonists, enhancing the function of the receptors. It is recognized that the compounds of the present invention would be expected to increase the effectiveness of glutamate and glutamate agonists of the mGluR2 receptor. Thus, the potentiators of the present invention are expected to be useful in the treatment of various neurological and psychiatric disorders associated with glutamate dysfunction described to be treated herein and others that can be treated by such potentiators as are appreciated by those skilled in the art.

The compounds of the present invention may contain one or more asymmetric centers and can thus occur as racemates and racemic mixtures, single enantiomers, diastereomeric mixtures and individual diastereomers. Additional asymmetric centers may be

present depending upon the nature of the various substituents on the molecule. Each such asymmetric center will independently produce two optical isomers and it is intended that all of the possible optical isomers and diastereomers in mixtures and as pure or partially purified compounds are included within the ambit of this invention. Any formulas, structures or names of compounds described in this specification that do not specify a particular stereochemistry are meant to encompass any and all existing isomers as described above and mixtures thereof in any proportion. When stereochemistry is specified, the invention is meant to encompass that particular isomer in pure form or as part of a mixture with other isomers in any proportion.

The independent syntheses of these diastereomers or their chromatographic separations may be achieved as known in the art by appropriate modification of the methodology disclosed herein. Their absolute stereochemistry may be determined by the x-ray crystallography of crystalline products or crystalline intermediates which are derivatized, if necessary, with a reagent containing an asymmetric center of known absolute configuration.

If desired, racemic mixtures of the compounds may be separated so that the individual enantiomers are isolated. The separation can be carried out by methods well known in the art, such as the coupling of a racemic mixture of compounds to an enantiomerically pure compound to form a diastereomeric mixture, followed by separation of the individual diastereomers by standard methods, such as fractional crystallization or chromatography. The coupling reaction is often the formation of salts using an enantiomerically pure acid or base. The diastereomeric derivatives may then be converted to the pure enantiomers by cleavage of the added chiral residue. The racemic mixture of the compounds can also be separated directly by chromatographic methods utilizing chiral stationary phases, which methods are well known in the art.

Alternatively, any enantiomer of a compound may be obtained by stereoselective synthesis using optically pure starting materials or reagents of known configuration by methods well known in the art.

In the compounds of generic formula I, the atoms may exhibit their natural isotopic abundances, or one or more of the atoms may be artificially enriched in a particular isotope having the same atomic number, but an atomic mass or mass number different from the atomic mass or mass number predominantly found in nature. The present invention is meant to include all suitable isotopic variations of the compounds of generic Formula I. For example, different isotopic forms of hydrogen (H) include protium (^{1}H) and deuterium (^{2}H). Protium is the predominant hydrogen isotope found in nature. Enriching for deuterium may afford certain

therapeutic advantages, such as increasing *in vivo* half-life or reducing dosage requirements, or may provide a compound useful as a standard for characterization of biological samples. Isotopically-enriched compounds within generic Formula I can be prepared without undue experimentation by conventional techniques well known to those skilled in the art or by processes analogous to those described in the Schemes and Examples herein using appropriate isotopically-enriched reagents and/or intermediates.

The term "pharmaceutically acceptable salts" refers to salts prepared from pharmaceutically acceptable non-toxic bases or acids including inorganic or organic bases and inorganic or organic acids. Salts derived from inorganic bases include aluminum, ammonium, calcium, copper, ferric, ferrous, lithium, magnesium, manganic salts, manganous, potassium, sodium, zinc, and the like. Salts in the solid form may exist in more than one crystal structure, and may also be in the form of hydrates. Salts derived from pharmaceutically acceptable organic non-toxic bases include salts of primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines, and basic ion exchange resins, such as arginine, betaine, caffeine, choline, N,N'-dibenzylethylene-diamine, diethylamine, 2-diethylaminoethanol, 2-dimethylaminoethanol, ethanolamine, ethylenediamine, N-ethyl-morpholine, N-ethylpiperidine, glucamine, glucosamine, histidine, hydrabamine, isopropylamine, lysine, methylglucamine, morpholine, piperazine, piperidine, polyamine resins, procaine, purines, theobromine, triethylamine, trimethylamine, tripropylamine, tromethamine, and the like.

When the compound of the present invention is basic, salts may be prepared from pharmaceutically acceptable non-toxic acids, including inorganic and organic acids. Such acids include acetic, benzenesulfonic, benzoic, camphorsulfonic, citric, ethanesulfonic, fumaric, gluconic, glutamic, hydrobromic, hydrochloric, isethionic, lactic, maleic, malic, mandelic, methanesulfonic, mucic, nitric, pamoic, pantothenic, phosphoric, succinic, sulfuric, tartaric, p-toluenesulfonic acid, and the like. It will be understood that, as used herein, references to the compounds of Formula I are meant to also include a pharmaceutically acceptable salts.

Exemplifying the invention are the examples described below. The subject compounds are useful in a method of potentiating metabotropic glutamate receptor activity in a patient such as a mammal in need of such inhibition comprising the administration of an effective amount of the compound. The present invention is directed to the use of the subject compounds disclosed herein as potentiators of metabotropic glutamate receptor activity. In addition to primates, especially humans, a variety of other mammals can be treated according to the method of the present invention.

The present invention is further directed to a method for the manufacture of a medicament for potentiating metabotropic glutamate receptor activity in humans and animals comprising combining a compound of the present invention with a pharmaceutical carrier or diluent.

The subject treated in the present methods is generally a mammal, preferably a human being, male or female, in whom potentiation of metabotropic glutamate receptor activity is desired. The term "therapeutically effective amount" means the amount of the subject compound that will elicit the biological or medical response of a tissue, system, animal or human that is being sought by the researcher, veterinarian, medical doctor or other clinician. It is recognized that one skilled in the art may affect the neurological and psychiatric disorders by treating a patient presently afflicted with the disorders or by prophylactically treating a patient afflicted with the disorders with an effective amount of the compound of the present invention. As used herein, the terms "treatment" and "treating" refer to all processes wherein there may be a slowing, interrupting, arresting, controlling, or stopping of the progression of the neurological and psychiatric disorders described herein, but does not necessarily indicate a total elimination of all disorder symptoms, as well as the prophylactic therapy of the mentioned conditions, particularly in a patient who is predisposed to such disease or disorder.

The term "composition" as used herein is intended to encompass a product comprising the specified ingredients in the specified amounts, as well as any product which results, directly or indirectly, from combination of the specified ingredients in the specified amounts. Such term in relation to pharmaceutical composition, is intended to encompass a product comprising the active ingredient(s), and the inert ingredient(s) that make up the carrier, as well as any product which results, directly or indirectly, from combination, complexation or aggregation of any two or more of the ingredients, or from dissociation of one or more of the ingredients, or from other types of reactions or interactions of one or more of the ingredients. Accordingly, the pharmaceutical compositions of the present invention encompass any composition made by admixing a compound of the present invention and a pharmaceutically acceptable carrier. By "pharmaceutically acceptable" it is meant the carrier, diluent or excipient must be compatible with the other ingredients of the formulation and not deleterious to the recipient thereof.

The terms "administration of" and or "administering a" compound should be understood to mean providing a compound of the invention or a prodrug of a compound of the invention to the individual in need of treatment.

The utility of the compounds in accordance with the present invention as potentiators of metabotropic glutamate receptor activity, in particular mGluR2 activity, may be demonstrated by methodology known in the art. Activity in potentiating the mGluR2 receptor may be determined as follows. The compounds of the present invention are tested in a fluorescence laser imaging plate reader (FLIPR) based assay. This assay is a common functional assay to monitor Ca^{2+} mobilization in whole cells expressing recombinant receptor coupled with a promiscuous G-protein. CHO dhfr- cells stably expressing recombinant human mGluR2 and Gα16 loaded with Fluo-4 AM (Invitrogen, Carlsbad CA) are treated with dose responses of compounds and the Ca^{2+} response is monitored on a FLIPR384 (Molecular Devices, Sunnydale CA) for agonist activity. The potentiation response is monitored after a subsequent addition of an EC20 concentration of glutamate (900 nM). The maximum calcium response at each concentration of compound for agonist or potentiation are plotted as dose responses and the curves are fitted with a four parameters logistic equation giving EC50 and Hill coefficient using the iterative non linear curve fitting software program.

The compounds of the present invention may also be tested in a [^{35}S]-GTPγS assay. The stimulation of [^{35}S]-GTPγS binding is a common functional assay to monitor Gαi-coupled receptor in native and recombinant receptor membrane preparation. Membrane from cells stably expressing hmGlu2 CHO-K1 (50μg) are incubated in a 96 well plate for 1 hour in the presence of GTPγS^{35} (0.05nM), GDP (5μM) and compounds. The reaction is stopped by rapid filtration over Unifilter GF/B plate (Packard, Bioscience, Meriden CT) using a 96-well cell harvester (Brandel Gaithersburg, MD). The filter plates are counted using Topcount counter (Packard, Bioscience, Meriden CT, USA). When compounds are evaluated as potentiators they are tested in the presence of glutamate (1μM). The activation (agonist) or the potentiation of glutamate (potentiator) curves are fitted with a four parameters logistic equation giving EC_{50} and Hill coefficient using the iterative non linear curve fitting software GraphPad (San Diego CA, USA).

Certain compounds of the invention were tested and demonstrated activity in potentiating the mGluR2 receptor in the FLIPR assay with an EC_{50} of less than about 10 μM. Exs. 1-201 (12 μM), 1-202 (>30 μM), 1-203 (>30 μM), 1-205 (> 30 μM) and 1-206 (20 μM) exhibited potency outside this range. Compounds within the present invention had activity in potentiating the mGluR2 receptor in the FLIPR and GTPγS assays with an EC_{50} of less than about 1 μM. Certain compounds of the invention resulted in a minimum 1.8-fold potentiation of

glutamate response in the presence of an EC20 concentration of glutamate (900nM). Such results are indicative of the intrinsic activity of the compounds in use as potentiators of mGluR2 receptor activity.

Representative FLIPR EC_{50} Values

Ex.	EC50	N
1-9	264 nM	2
1-61	2658 nM	1
1-94	41 nM	2
1-148	126 nM	2
1-187	182 nM	2
2-4	496 nM	3
2-38	41 nM	2
3-3	3655 nM	1
4-8	1251 nM	1
5-12	3346 nM	1
5-22	364 nM	1
6-9	45 nM	2
7-19	781 nM	1
7-47	77 nM	2
8-5	40 nM	2
10-3	129 nM	2
10-5	225 nM	2

Metabotropic glutamate receptors including the mGluR2 receptor have been implicated in a wide range of biological functions. This has suggested a potential role for these receptors in a variety of disease processes in humans or other species.

The compounds of the present invention have utility in treating, preventing, ameliorating, controlling or reducing the risk of a variety of neurological and psychiatric disorders associated with glutamate dysfunction, including one or more of the following conditions or diseases: acute neurological and psychiatric disorders such as cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma,

head trauma, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, dementia (including AIDS-induced dementia), Alzheimer's disease, Huntington's Chorea, amyotrophic lateral sclerosis, ocular damage, retinopathy, cognitive disorders, idiopathic and drug-induced Parkinson's disease, muscular spasms and disorders associated with muscular spasticity including tremors, epilepsy, convulsions, migraine (including migraine headache), urinary incontinence, substance tolerance, substance withdrawal (including, substances such as opiates, nicotine, tobacco products, alcohol, benzodiazepines, cocaine, sedatives, hypnotics, etc.), psychosis, schizophrenia, anxiety (including generalized anxiety disorder, panic disorder, and obsessive compulsive disorder), mood disorders (including depression, mania, bipolar disorders), trigeminal neuralgia, hearing loss, tinnitus, macular degeneration of the eye, emesis, brain edema, pain (including acute and chronic pain states, severe pain, intractable pain, neuropathic pain, and post-traumatic pain), tardive dyskinesia, sleep disorders (including narcolepsy), autism, autism spectrum disorders, attention deficit/hyperactivity disorder, and conduct disorder.

In an embodiment the present invention provides a method for treating migraine, comprising: administering to a patient in need thereof an effective amount of a compound of formula I. In another embodiment the present invention provides a method for preventing or treating anxiety, comprising: administering to a patient in need thereof an effective amount of a compound of formula I. Particular anxiety disorders of the invention are generalized anxiety disorder, panic disorder, and obsessive compulsive disorder. In another embodiment the present invention provides a method for treating schizophrenia, comprising: administering to a patient in need thereof an effective amount of a compound of formula I. In yet another embodiment the present invention provides a method for treating epilepsy, comprising: administering to a patient in need thereof an effective amount of a compound of formula I.

In an embodiment, the present invention provides a method for the treatment of schizophrenia comprising: administering to a patient in need thereof an effective amount of a compound of formula I or a pharmaceutical composition thereof. In one of the available sources of diagnostic tools, The Merck Manual (2006-2007), schizophrenia is characterized by psychosis (loss of contact with reality), hallucinations (false perceptions), delusions (false beliefs), disorganized speech and behavior, flattened affect (restricted range of emotions), cognitive deficits (impaired reasoning and problem solving), and occupational and social dysfunction. The skilled artisan will recognize that there are alternative nomenclatures, nosologies, and classification systems for neurological and psychiatric disorders, including migraine, and that these systems evolve with medical scientific progress

Thus, in an embodiment the present invention provides a method for treating migraine, comprising: administering to a patient in need thereof an effective amount of a compound of formula I or a pharmaceutical composition thereof. In one of the available sources of diagnostic tools, Dorland's Medical Dictionary (23'd Ed., 1982, W. B. Saunders Company, Philidelphia, PA), migraine is defined as a symptom complex of periodic headaches, usually temporal and unilateral, often with irritability, nausea, vomiting, constipation or diarrhea, and photophobia. As used herein the term "migraine" includes these periodic headaches, both temporal and unilateral, the associated irritability, nausea, vomiting, constipation or diarrhea, photophobia, and other associated symptoms. The skilled artisan will recognize that there are alternative nomenclatures, nosologies, and classification systems for neurological and psychiatric disorders, including migraine, and that these systems evolve with medical scientific progress.

In another embodiment the present invention provides a method for treating anxiety, comprising: administering to a patient in need thereof an effective amount of a compound of Formula I or a pharmaceutical composition thereof. At present, the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (1994, American Psychiatric Association, Washington, D.C.), provides a diagnostic tool including anxiety and related disorders. These include: panic disorder with or without agoraphobia, agoraphobia without history of panic disorder, specific phobia, social phobia, obsessive- compulsive disorder, post-traumatic stress disorder, acute stress disorder, generalized anxiety disorder, anxiety disorder due to a general medical condition, substance-induced anxiety disorder and anxiety disorder not otherwise specified. As used herein the term "anxiety" includes treatment of those anxiety disorders and related disorder as described in the DSM-IV. The skilled artisan will recognize that there are alternative nomenclatures, nosologies, and classification systems for neurological and psychiatric disorders, and particular anxiety, and that these systems evolve with medical scientific progress. Thus, the term "anxiety" is intended to include like disorders that are described in other diagnostic sources.

In another embodiment the present invention provides a method for treating depression, comprising: administering to a patient in need thereof an effective amount of a compound of Formula I or a pharmaceutical composition thereof. At present, DSM-IV provides a diagnostic tool including depression and related disorders. Depressive disorders include, for example, single episodic or recurrent major depressive disorders, and dysthymic disorders, depressive neurosis, and neurotic depression; melancholic depression including anorexia, weight loss, insomnia and early morning waking, and psychomotor retardation; atypical depression (or

reactive depression) including increased appetite, hypersomnia, psychomotor agitation or irritability, anxiety and phobias; seasonal affective disorder; or bipolar disorders or manic depression, for example, bipolar I disorder, bipolar II disorder and cyclothymic disorder. As used herein the term "depression" includes treatment of those depression disorders and related disorder as described in the DSM-IV.

In another embodiment the present invention provides a method for treating epilepsy, comprising: administering to a patient in need thereof an effective amount of a compound of Formula I or a pharmaceutical composition thereof. At present, there are several types and subtypes of seizures associated with epilepsy, including idiopathic, symptomatic, and cryptogenic. These epileptic seizures can be focal (partial) or generalized. They can also be simple or complex. Epilepsy is described in the art, such as Epilepsy: A comprehensive textbook. Ed. by Jerome Engel, Jr. and Timothy A. Pedley. (Lippincott-Raven, Philadelphia, 1997). At present, the International Classification of Diseases, Ninth Revision, (ICD-9) provides a diagnostic tool including epilepsy and related disorders. These include: generalized nonconvulsive epilepsy, generalized convulsive epilepsy, petit mal status epilepticus, grand mal status epilepticus, partial epilepsy with impairment of consciousness, partial epilepsy without impairment of consciousness, infantile spasms, epilepsy partialis continua, other forms of epilepsy, epilepsy, unspecified, NOS. As used herein the term "epilepsy" includes these all types and subtypes. The skilled artisan will recognize that there are alternative nomenclatures, nosologies, and classification systems for neurological and psychiatric disorders, including epilepsy, and that these systems evolve with medical scientific progress.

The subject compounds are further useful in a method for the prevention, treatment, control, amelioration, or reduction of risk of the diseases, disorders and conditions noted herein.

The subject compounds are further useful in a method for the prevention, treatment, control, amelioration, or reduction of risk of the aforementioned diseases, disorders and conditions in combination with other agents, including an mGluR agonist.

The term "potentiated amount" refers to an amount of an mGluR agonist, that is, the dosage of agonist which is effective in treating the neurological and psychiatric disorders described herein when administered in combination with an effective amount of a compound of the present invention. A potentiated amount is expected to be less than the amount that is required to provided the same effect when the mGluR agonist is administered without an effective amount of a compound of the present invention.

A potentiated amount can be readily determined by the attending diagnostician, as one skilled in the art, by the use of conventional techniques and by observing results obtained under analogous circumstances. In determining a potentiated amount, the dose of an mGluR agonist to be administered in combination with a compound of formula I, a number of factors are considered by the attending diagnostician, including, but not limited to: the mGluR agonist selected to be administered, including its potency and selectivity; the compound of formula I to be coadministered; the species of mammal; its size, age, and general health; the specific disorder involved; the degree of involvement or the severity of the disorder; the response of the individual patient; the modes of administration; the bioavailability characteristics of the preparations administered; the dose regimens selected; the use of other concomitant medication; and other relevant circumstances.

A potentiated amount of an mGluR agonist to be administered in combination with an effective amount of a compound of formula I is expected to vary from about 0.1 milligram per kilogram of body weight per day (mg/kg/day) to about 100 mg/kg/day and is expected to be less than the amount that is required to provided the same effect when administered without an effective amount of a compound of formula I. Preferred amounts of a co-administered mGlu agonist are able to be determined by one skilled in the art.

The compounds of the present invention may be used in combination with one or more other drugs in the treatment, prevention, control, amelioration, or reduction of risk of diseases or conditions for which compounds of Formula I or the other drugs may have utility, where the combination of the drugs together are safer or more effective than either drug alone. Such other drug(s) may be administered, by a route and in an amount commonly used therefor, contemporaneously or sequentially with a compound of Formula I. When a compound of Formula I is used contemporaneously with one or more other drugs, a pharmaceutical composition in unit dosage form may be utilized containing such other drugs and the compound of Formula I. However, the combination therapy may also includes therapies in which the compound of Formula I and one or more other drugs are administered on different overlapping schedules. It is also contemplated that when used in combination with one or more other active ingredients, the compounds of the present invention and the other active ingredients may be used in lower doses than when each is used singly. Accordingly, the pharmaceutical compositions of the present invention include those that contain one or more other active ingredients, in addition to a compound of Formula I.

The above combinations include combinations of a compound of the present invention not only with one other active compound, but also with two or more other active compounds.

Likewise, compounds of the present invention may be used in combination with other drugs that are used in the prevention, treatment, control, amelioration, or reduction of risk of the diseases or conditions for which compounds of the present invention are useful. Such other drugs may be administered, by a route and in an amount commonly used therefor, contemporaneously or sequentially with a compound of the present invention. When a compound of the present invention is used contemporaneously with one or more other drugs, a pharmaceutical composition containing such other drugs in addition to the compound of the present invention may be utilized. Accordingly, the pharmaceutical compositions of the present invention include those that also contain one or more other active ingredients, in addition to a compound of the present invention.

The weight ratio of the compound of the compound of the present invention to the second active ingredient may be varied and will depend upon the effective dose of each ingredient. Generally, an effective dose of each will be used. Thus, for example, when a compound of the present invention is combined with another agent, the weight ratio of the compound of the present invention to the other agent will generally range from about 1000:1 to about 1:1000, preferably about 200:1 to about 1:200. Combinations of a compound of the present invention and other active ingredients will generally also be within the aforementioned range, but in each case, an effective dose of each active ingredient should be used.

In such combinations the compound of the present invention and other active agents may be administered separately or in conjunction. In addition, the administration of one element may be prior to, concurrent to, or subsequent to the administration of other agent(s).

The compounds of the present invention may be administered by oral, parenteral (e.g., intramuscular, intraperitoneal, intravenous, ICV, intracisternal injection or infusion, subcutaneous injection, or implant), by inhalation spray, nasal, vaginal, rectal, sublingual, or topical routes of administration and may be formulated, alone or together, in suitable dosage unit formulations containing conventional non-toxic pharmaceutically acceptable carriers, adjuvants and vehicles appropriate for each route of administration. In addition to the treatment of warm-blooded animals such as mice, rats, horses, cattle, sheep, dogs, cats, monkeys, etc., the compounds of the invention are effective for use in humans.

The pharmaceutical compositions for the administration of the compounds of this invention may conveniently be presented in dosage unit form and may be prepared by any of the methods well known in the art of pharmacy. All methods include the step of bringing the active ingredient into association with the carrier which constitutes one or more accessory ingredients. In general, the pharmaceutical compositions are prepared by uniformly and intimately bringing the active ingredient into association with a liquid carrier or a finely divided solid carrier or both, and then, if necessary, shaping the product into the desired formulation. In the pharmaceutical composition the active object compound is included in an amount sufficient to produce the desired effect upon the process or condition of diseases. As used herein, the term "composition" is intended to encompass a product comprising the specified ingredients in the specified amounts, as well as any product which results, directly or indirectly, from combination of the specified ingredients in the specified amounts.

Pharmaceutical compositions intended for oral use may be prepared according to any method known to the art for the manufacture of pharmaceutical compositions and such compositions may contain one or more agents selected from the group consisting of sweetening agents, flavoring agents, coloring agents and preserving agents in order to provide pharmaceutically elegant and palatable preparations. Tablets contain the active ingredient in admixture with non-toxic pharmaceutically acceptable excipients which are suitable for the manufacture of tablets. These excipients may be for example, inert diluents, such as calcium carbonate, sodium carbonate, lactose, calcium phosphate or sodium phosphate; granulating and disintegrating agents, for example, corn starch, or alginic acid; binding agents, for example starch, gelatin or acacia, and lubricating agents, for example magnesium stearate, stearic acid or talc. The tablets may be uncoated or they may be coated by known techniques to delay disintegration and absorption in the gastrointestinal tract and thereby provide a sustained action over a longer period. Compositions for oral use may also be presented as hard gelatin capsules wherein the active ingredient is mixed with an inert solid diluent, for example, calcium carbonate, calcium phosphate or kaolin, or as soft gelatin capsules wherein the active ingredient is mixed with water or an oil medium, for example peanut oil, liquid paraffin, or olive oil.

Aqueous suspensions contain the active materials in admixture with excipients suitable for the manufacture of aqueous suspensions. Oily suspensions may be formulated by suspending the active ingredient in a suitable oil. Oil-in-water emulsions may also be employed. Dispersible powders and granules suitable for preparation of an aqueous suspension by the

addition of water provide the active ingredient in admixture with a dispersing or wetting agent, suspending agent and one or more preservatives.

Pharmaceutical compositions of the present compounds may be in the form of a sterile injectable aqueous or oleagenous suspension. The compounds of the present invention may also be administered in the form of suppositories for rectal administration. For topical use, creams, ointments, jellies, solutions or suspensions, etc., containing the compounds of the present invention may be employed. The compounds of the present invention may also be formulated for administered by inhalation. The compounds of the present invention may also be administered by a transdermal patch by methods known in the art.

The pharmaceutical composition and method of the present invention may further comprise other therapeutically active compounds as noted herein which are usually applied in the treatment of the above mentioned pathological conditions.

In the treatment, prevention, control, amelioration, or reduction of risk of conditions which require potentiation of metabotorpic glutamate receptor activity an appropriate dosage level will generally be about 0.01 to 500 mg per kg patient body weight per day which can be administered in single or multiple doses. Preferably, the dosage level will be about 0.1 to about 250 mg/kg per day; more preferably about 0.5 to about 100 mg/kg per day. A suitable dosage level may be about 0.01 to 250 mg/kg per day, about 0.05 to 100 mg/kg per day, or about 0.1 to 50 mg/kg per day. Within this range the dosage may be 0.05 to 0.5, 0.5 to 5 or 5 to 50 mg/kg per day. For oral administration, the compositions are preferably provided in the form of tablets containing 1.0 to 1000 milligrams of the active ingredient, particularly 1.0, 5.0, 10.0, 15.0. 20.0, 25.0, 50.0, 75.0, 100.0, 150.0, 200.0, 250.0, 300.0, 400.0, 500.0, 600.0, 750.0, 800.0, 900.0, and 1000.0 milligrams of the active ingredient for the symptomatic adjustment of the dosage to the patient to be treated. The compounds may be administered on a regimen of 1 to 4 times per day, preferably once or twice per day.

When treating, preventing, controlling, ameliorating, or reducing the risk of neurological and psychiatric disorders associated with glutamate dysfunction or other diseases for which compounds of the present invention are indicated, generally satisfactory results are obtained when the compounds of the present invention are administered at a daily dosage of from about 0.1 milligram to about 100 milligram per kilogram of animal body weight, preferably given as a single daily dose or in divided doses two to six times a day, or in sustained release form. For most large mammals, the total daily dosage is from about 1.0 milligrams to about 1000 milligrams, preferably from about 1 milligrams to about 50 milligrams. In the case of a 70 kg

adult human, the total daily dose will generally be from about 7 milligrams to about 350 milligrams. This dosage regimen may be adjusted to provide the optimal therapeutic response.

It will be understood, however, that the specific dose level and frequency of dosage for any particular patient may be varied and will depend upon a variety of factors including the activity of the specific compound employed, the metabolic stability and length of action of that compound, the age, body weight, general health, sex, diet, mode and time of administration, rate of excretion, drug combination, the severity of the particular condition, and the host undergoing therapy.

Several methods for preparing the compounds of this invention are illustrated in the following Schemes and Examples. Starting materials are made according to procedures known in the art or as illustrated herein. The compounds of the present invention can be prepared in a variety of fashions.

Abbreviations used in the description of the chemistry and in the Examples that follow are: Ac2O (acetic anhydride); AcOH (acetic acid); AEBSF (p-aminoethylbenzenesulfonyl fluoride); Boc (di-tert-butyl carbamate); $(Boc)_2O$ (di-tert-butyl dicarbonate); BSA (bovine serum albumin); BuLi (n-Butyl lithium); CDCl3 (chloroform-d); CuI (copper iodide); CuSO4 (copper sulfate); DBU (1,8-DIAZABICYCLO[5.4.0]UNDEC-7-ENE); DCE (dichloroethane); DCM (dichloromethane); DEAD (diethyl azodicarboxylate); DIPEA (diisopropylethylamine); DMBA (1,3-dimethylbarbituric acid); DMF (N,N-dimethylformamide); DMP (Dess-Martin periodinane); DMSO (dimethyl sulfoxide); DPPA (diphenylphosphoryl azide); DTT (dithiothreitol); EDTA (ethylene-diamine-tetra-acetic acid); EGTA (ethylene-glycol-tetra-acetic acid); Et2O (diethylether); EtOAc (ethyl acetate); EtOH (ethanol); HOAc (acetic acid); HPLC (high-performance liquid chromatography); HRMS (high resolution mass spectrum); LAH (lithium aluminum hydride); LCMS (liquid chromatograph-mass spectrometer); LHMDS (lithium bis(trimethylsilyl)amide); LRMS (low resolution mass spectrum); mCPBA (3-chloroperoxybenzoic acid); MeOH (methanol); MOM-Cl (methoxymethyl chloride); MP-B(CN)H3 (Macroporous cyanoborohydride); NaHCO3 (sodium bicarbonate); Na2SO4 (sodium sulfate); Na(OAc)3BH (sodium triacetoxyborohydride); NH4OAc (ammonium acetate); NBS (N-bromosuccinamide); NFSi (N-fluorobenzenesulfonimide); NMP (1-methyl-2-pyrrolidinone); NMR (nuclear magnetic resonance); PBS (phosphate buffered saline); PCR (polymerase chain reaction); Pd(dppf) ([1,1'-bis(diphenylphosphino)ferrocene] palladium); Pd(Ph3)4 (palladium(0) tetrakis-triphenylphosphine); POCl3 (phosphorous oxychloride); PS-DIEA (polystyrene diisopropylethylamine); PS-PPh3 (polystyrene-triphenyl phosphine); PTSA (para-toluene

sulfonic acid); Pyr (pyridine); Selectfluor (1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate); TBAF (tetrabutylammonium fluoride); T-BuOH (tert-butanol); THF (tetrahydrofuran); Tf (trifluoromethanesulfonyl); TFA (trifluoroacteic acid); and TMSCH2N2 (trimethylsilyldiazomethane).

The compounds of this invention may be prepared by employing reactions as shown in the following Reaction Schemes, in addition to other standard manipulations that are known in the literature or exemplified in the experimental procedures. The illustrative Reaction Schemes below, therefore, are not limited by the compounds listed or by any particular substituents employed for illustrative purposes. Substituent numbering as shown in the Reaction Schemes do not necessarily correlate to that used in the claims and often, for clarity, a single substituent is shown attached to the compound where multiple substituents are optionally allowed under the definitions of Formula A hereinabove.

Reactions used to generate the compounds of this invention are prepared by employing reactions as shown in Reaction Schemes **A-J**.

Synopsis of Reaction Schemes

Reaction Scheme A: S_NAr (nucleophilic aromatic substitution) displacement of the fluorine in **A-1** with the an amine produces the nitro compound **A-2**, which can be reduced to the dianiline **A-3** with Zinc and Acetic acid. **A-3** can be cyclized with carbonyldiimidazole (CDI) to establish the benzimidazolinone core. Direct alkylation with an alkyl halide provides **A-5**, and Pd-catalyzed coupling of **A-5** with a boronic acid yields the final compound, **A-6**.

Reaction Scheme B: The functionalized benzimidazolinone, **A-5**, can be cross-coupled with the phenol boronic acid to provide **B-1**, which can then participate in an S_NAr displacement with various heterocyclic chlorides or fluorides.

Reaction Scheme C: The phenol **C-1** can be treated with various benzyl alcohols via a Mitsunobu reaction to yield the series of benzyl alcohols **C-2**.

Reaction Scheme D: Alternatively, the phenol **C-1** can undergo Cu-mediated coupling with substituted aryl halides to afford biaryl benzimidazolinones **D-1**.

Reaction Scheme E: Halogenated benzimidazolinone **A-5** can be converted to its cooresponding pinacol borane ester, **E-1**, which is then cross-coupled with 6-chloro-2-bromopyridine to produce **E-2**. **E-2** can then undergo SNAR displacement to afford the series of pyridyl biaryl benzimidazolinones, **E-3**.

Reaction Scheme F: Isocyanate **F-1** is converted to the urea, **F-2**, with the appropriate amine, then cyclized via intramolecular SNAR displacement to produce benzimidazolinone **F-3**. **F-3** can undergo Pd-catalzyed cross-coupling to produce biaryl **F-4**, which can substituted with various alkyl halides to provide the series **F-5**.

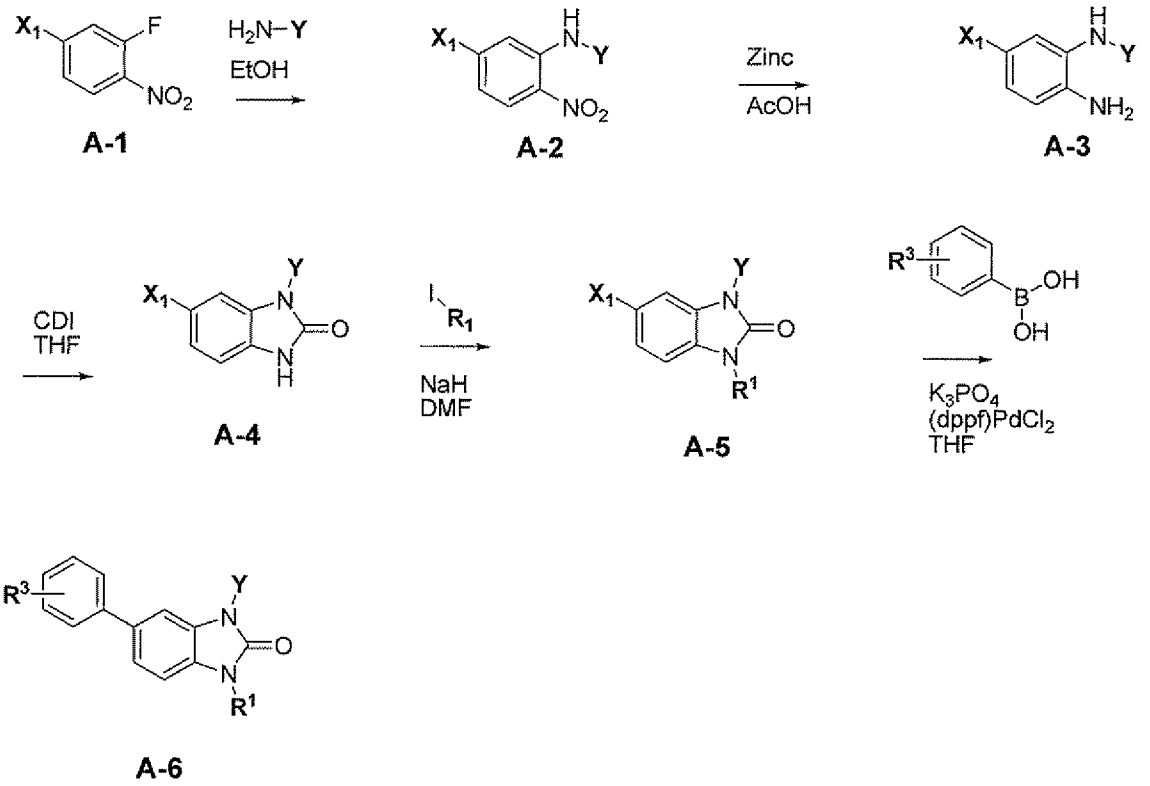
Reaction Scheme G: Difluoro nitro anisole **G-1** is selectively substituted to afford **G-2**, which is then reduced with Fe and Acetic acid to the dianiline **G-3**. CDI cyclization yields benzimidazolinone **G-4**, followed by alkylation yields **G-5**. Demethylation to the phenol **G-6**, with subsequent conversion to the triflate **G-7** allows for Pd-catalyzed cross-coupling with the appropriate boronic acid to provide biaryl **G-8**.

Reaction Scheme H: The phenol **H-1** can participate in an S_NAr displacement to produce biaryl ether **H-2**.

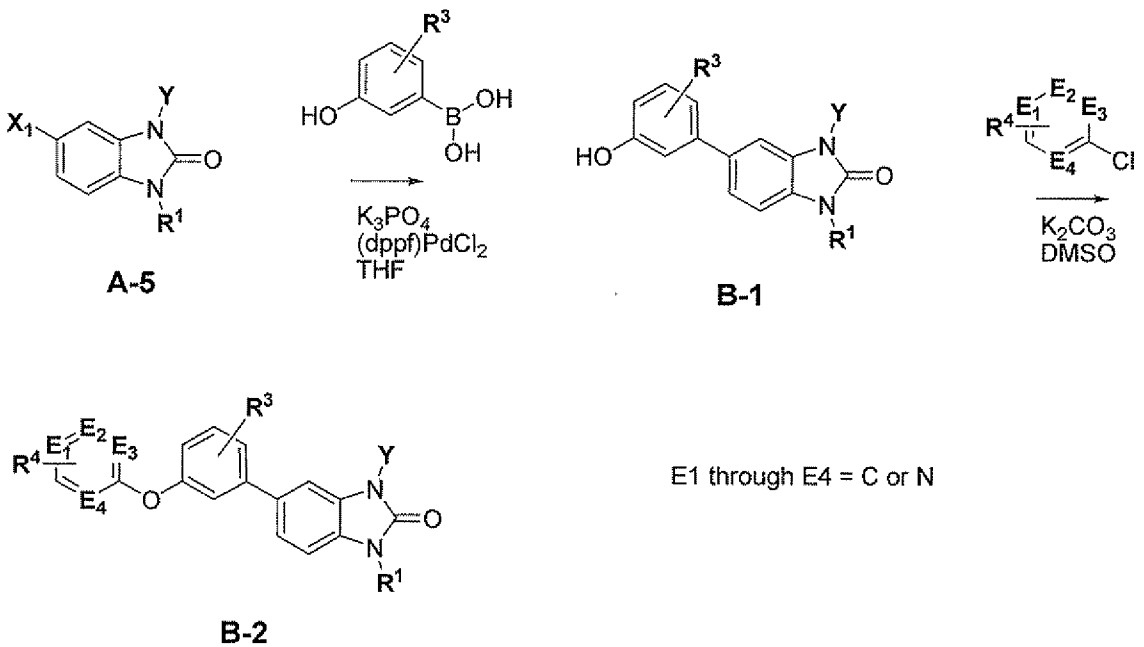
Reaction Scheme I: Alternatively, phenol **H-1** can undergo a Cu-mediated coupling reaction with aryl halides to afford biaryl ethers such as **I-1**.

Reaction Scheme J: The addition of a Grignard reagent across the aryl acetyl **J-1** can afford the tertiary alcohol **J-2**.

Reaction Scheme A

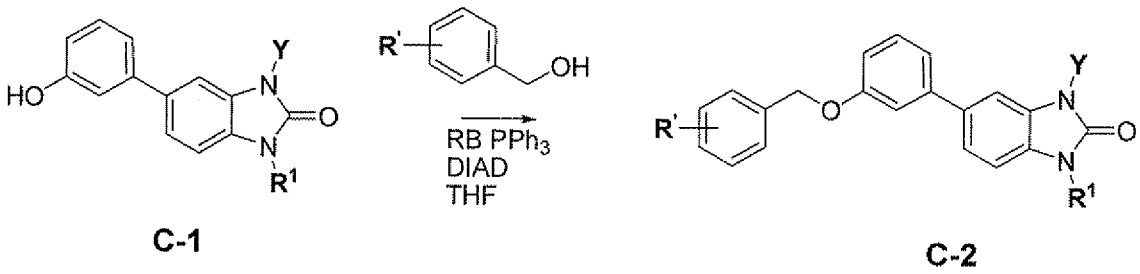


Reaction Scheme B

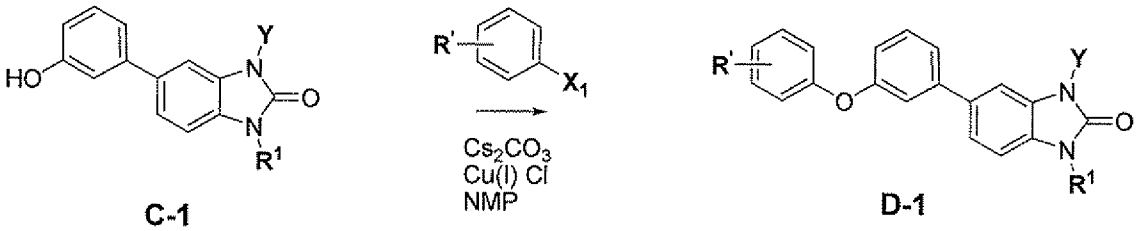


5

Reaction Scheme C



Reaction Scheme D



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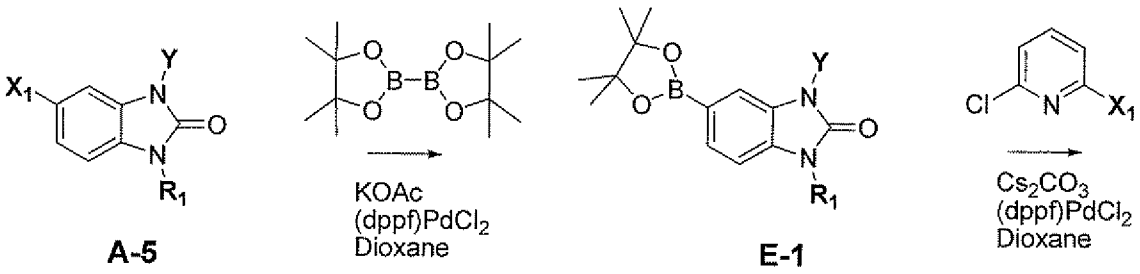
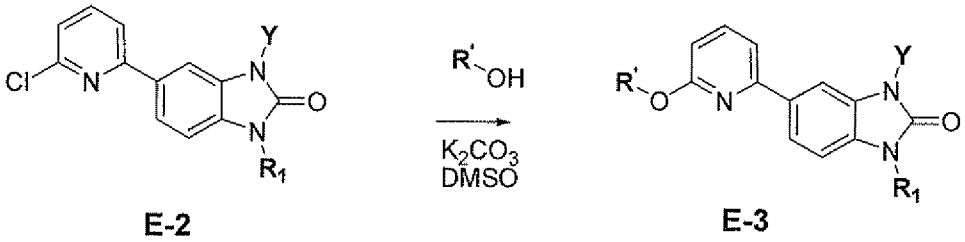
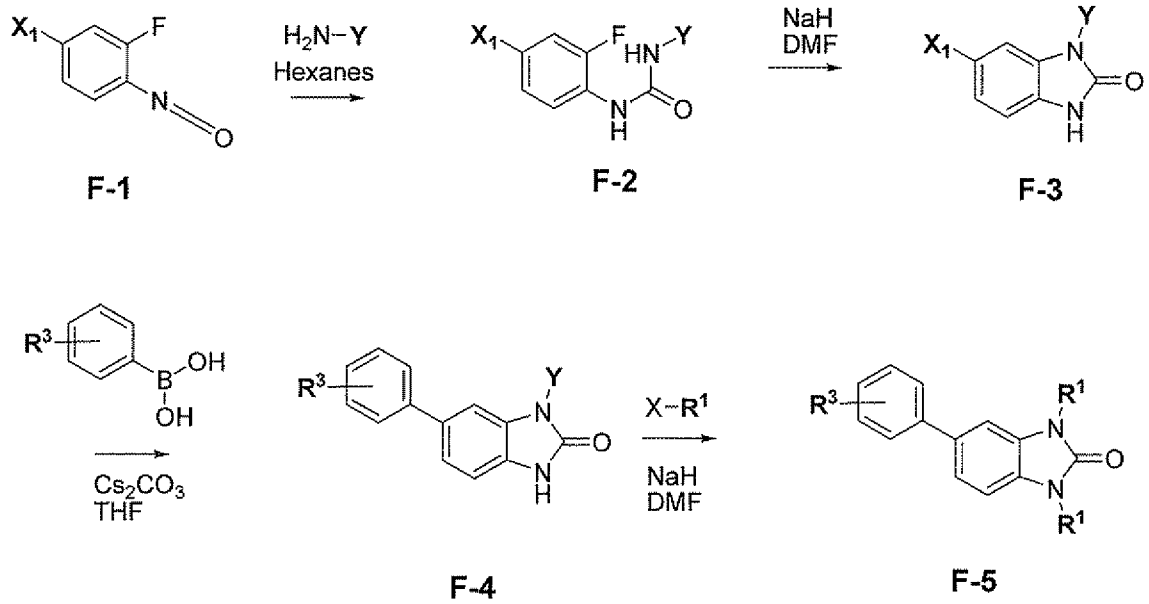
Reaction Scheme E



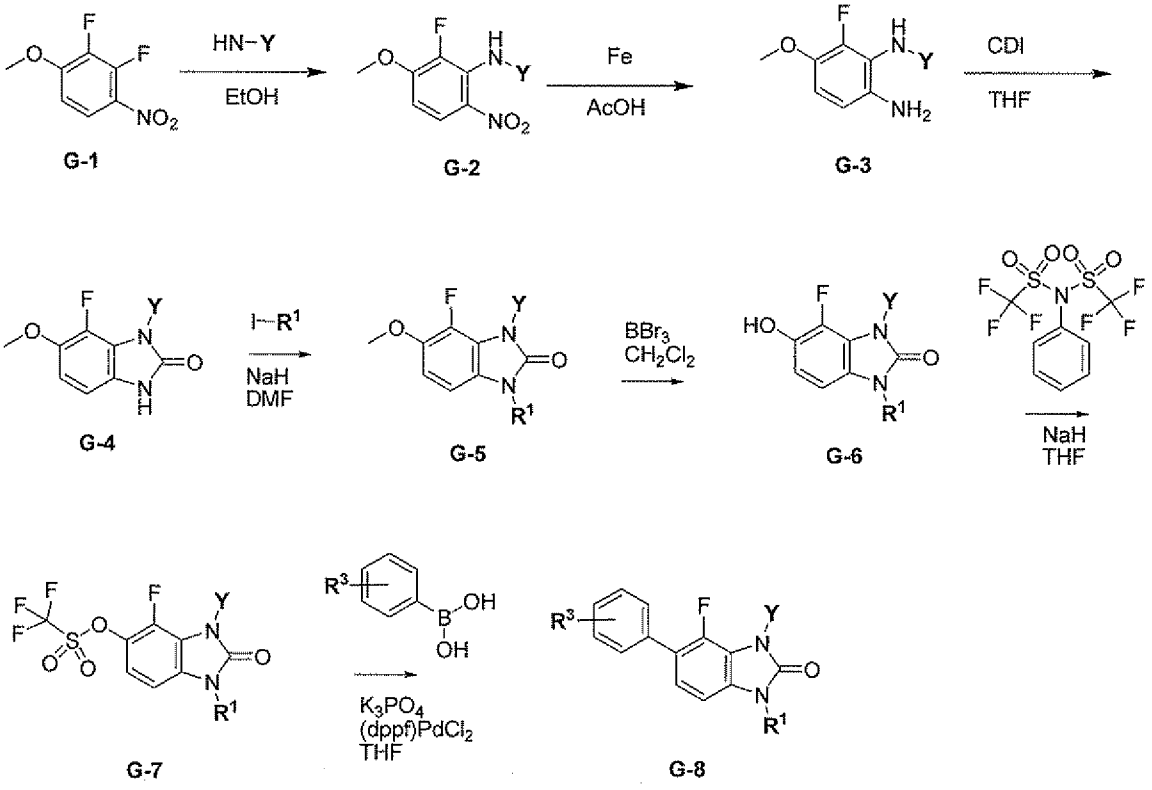


Reaction Scheme F

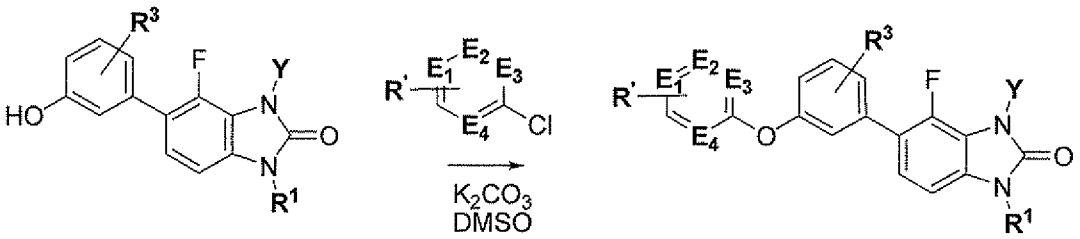


5

Reaction Scheme G

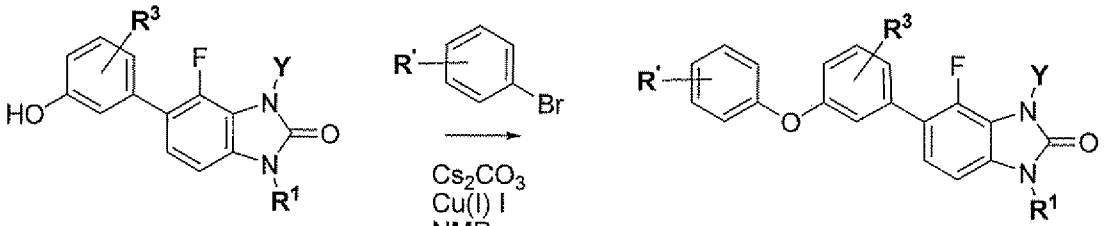


Reaction Scheme H



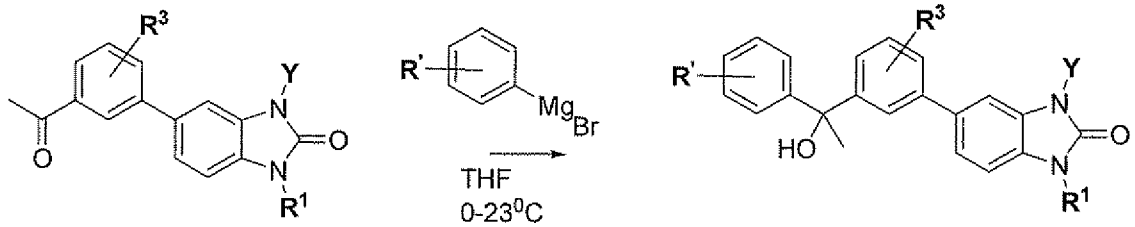
H-1 H-2

Reaction Scheme I



H-1 I-1

Reaction Scheme J



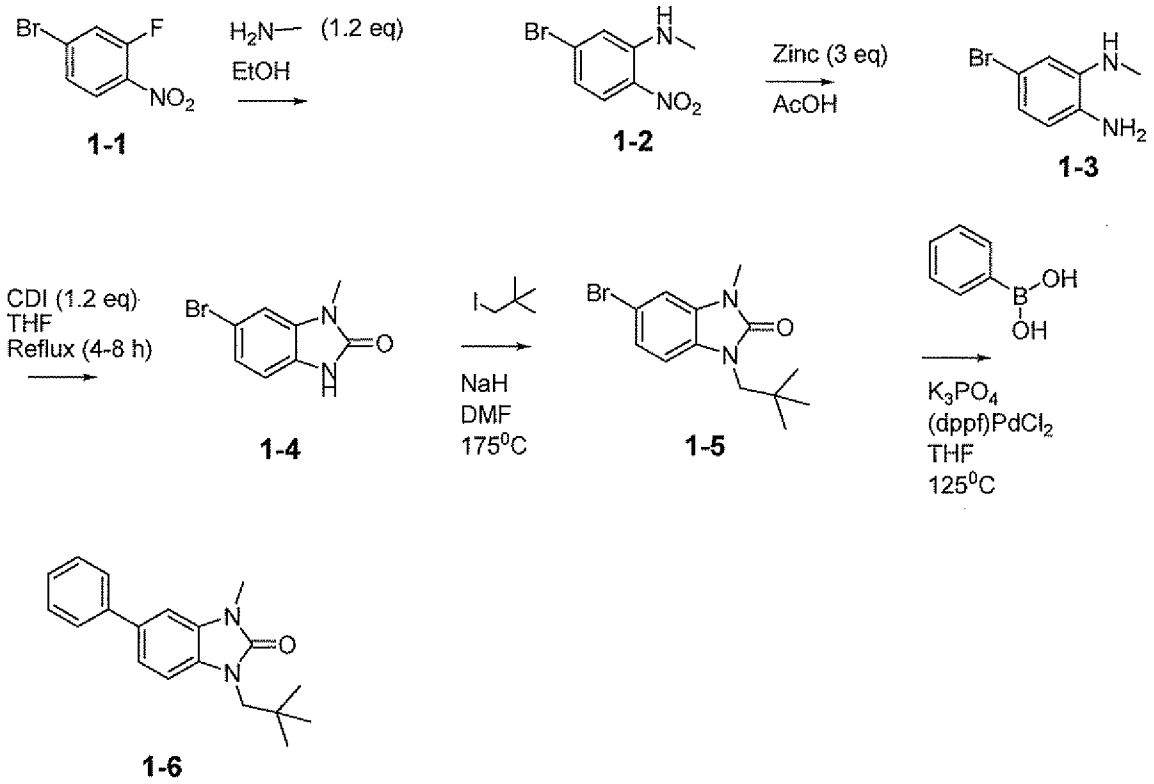
J-1 J-2

EXAMPLES

Examples provided are intended to assist in a further understanding of the invention. Particular materials employed, species and conditions are intended to be further

illustrative of the invention and not limitative of the reasonable scope thereof. The reagents utilized in synthesizing the compounds depicted in the following Tables are either commercially available or are readily prepared by one of ordinary skill in the art.

Scheme 1



5-bromo-N-methyl-2-nitroaniline (1-2)

A solution of 4-Bromo-2-fluoronitrobenzene (**1-1**, 10.5 g, 47.7 mmol) in EtOH (100 ml) was treated with Methylamine (2M in MeOH, 28.6 ml, 57.3 mmol, 1.2 eq) and the resulting dark maroon solution was stirred at 23 deg C for 13 h. The reaction was then concentrated *in vacuo*, and the residual yellow-orange solid was partitioned between EtOAc (2x250 ml) and water (300 ml). The combined organic layers were dried over Na2SO4 and concentrated, leaving the title compound, 5-bromo-N-methyl-2-nitroaniline (**1-2**), as a bright orange solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (d, 1H, *J*=9.15 Hz), 7.01 (sd, 1H, *J*=1.83 Hz), 6.77 (dd, 1H, *J*=7.02 Hz), 3.02 (d, 3H, *J*=4.88 Hz). LRMS *m/z*: Calc'd for $C_7H_7BrN_2O_2$ (M+H) 232.1, found 232.8.

4-bromo-N^2-methylbenzene-1,2-diamine (1-3)

An orange solution consisting of 5-bromo-N-methyl-2-nitroaniline (**1-2**, 10.5 g, 45.4 mmol) in Acetic acid (200 ml) was treated with Zinc dust (8.92 g, 136 mmol, 3.0 eq), generating a mild exotherm. The cloudy maroon reaction mixture was capped and stirred for 20 min. The reaction was >80% complete, so an additional amount of Zinc dust (1.0 g, 16 mmol, 0.35 eq) was added and the reaction was stirred for 15 min. LC/MS showed complete reduction, so the reaction mixture was filtered through Celite and washed with MeOH. The residual filtrate was concentrated *in vacuo*, then partitioned between EtOAc (2x300 ml) and saturated aqueous $NaHCO_3$ (350 ml). The combined organic layers were dried over Na_2SO_4 and concentrated, affording the title compound, 4-bromo-N^2-methylbenzene-1,2-diamine (1-3), as a brown solid with >90% purity. LRMS *m/z*: Calc'd for $C_7H_9BrN_2$ (M+H) 202.1, found 202.8.

6-bromo-1-methyl-1,3-dihydro-2H-benzimidazol-2-one (1-4)

4-bromo-N^2-methylbenzene-1,2-diamine (**1-3**, 9.31 g, 46.3 mmol) was dissolved in anhydrous THF (45 ml) and treated with CDI (9.01 g, 55.6 mmol, 1.2 eq). The resulting orange solution was stirred at reflux for 4 h, then cooled to 23 deg C and stirred for 13 h. The cyclized product was partitioned between EtOAc (2x160 ml) and water (185 ml), and the combined organic layers were dried over Na_2SO_4 and concentrated.

The crude mixture contained a tan solid which was not readily soluble in EtOAc or Methylene Chloride. The material was collected via filtration and was found to only contain alittle bit of the desired product, mostly impurity. The filtrate was dried over Na2SO4, and concentrated. Obtained 6.79 g of the desired product as a brown-orange solid with >90% purity. LRMS *m/z*: Calc'd for $C_8H_7BrN_2O$ (M+H) 228.1, found 228.8.

5-bromo-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one (1-5)

A solution of 6-bromo-1-methyl-1,3-dihydro-2H-benzimidazol-2-one (**1-4**, 500 mg, 2.20 mmol) in DMF (10 ml) was treated with Sodium hydride (176 mg, 4.40 mmol, 2.0 eq) followed by the 1-Iodo-2,2-Dimethylpropane (585 µL, 4.40 mmol, 2.0 eq). The reaction was irradiated at 175 deg C for 20 min in a microwave. The reaction was complete by LC/MS, so it was partitioned between EtOAc (2x125 ml) and water (150 ml). The combined organic layers

were dried over Na_2SO_4 and concentrated. The crude maroon-orange oil was purified via flash column chromatography (SiO_2: 100% Hex to 60:40 Hex:EtOAc), affording the title compound, 5-bromo-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one (**1-5**), as a yellow solid with >95% purity. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.18 (dd, 1H, *J*= Hz), 7.10 (s, 1H), 6.88 (d, 1H, *J*= Hz), 3.63 (s, 2H), 3.40 (s, 3H), 1.02 (s, 9H). LRMS *m/z*: Calc'd for $C_7H_7BrN_2O_2$ (M+H) 232.1, found 232.8.

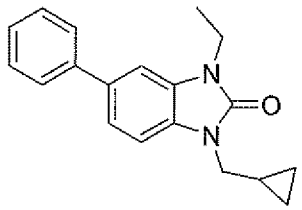
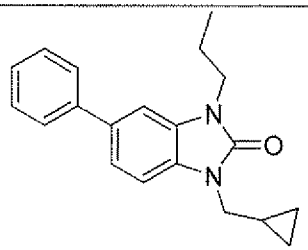
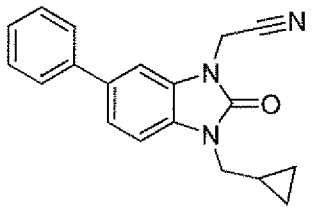
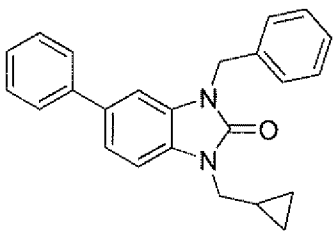
1-(2,2-dimethylpropyl)-3-methyl-5-phenyl-1,3-dihydro-2H-benzimidazol-2-one (1-6)

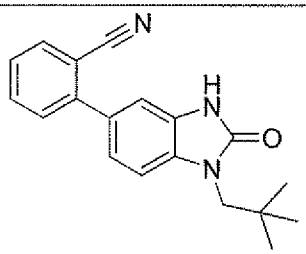
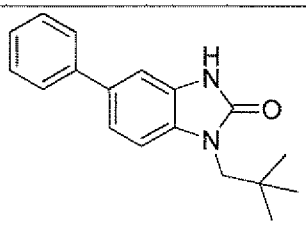
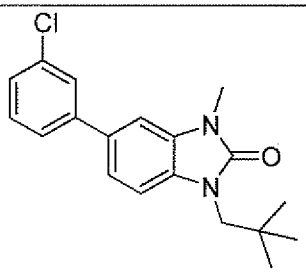
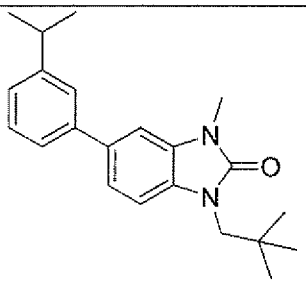
An aqueous solution of Cesium carbonate (54.8 mg, 0.17 mmol, 5.0 eq) in water (2 mL) was charged with a solution of 5-bromo-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one (**1-5**, 10 mg, 0.034 mmol) and phenylboronic acid (8.21 mg, 0.067 mmol, 2.0 eq), then deoxygenated. The 1,1'-Bis(diphenylphosphino)ferrocene-palladium(II)dichloride dichloromethane complex (1.37 mg, 1.68 μmol, 0.05 eq) was introduced and the mixture was irradiated in a microwave at 125 deg C for 15 min. LC/MS showed complete conversion, so the reaction was partitioned between EtOAc (2x85 ml) and saturated aqueous $NaHCO_3$ (95 ml). The combined organic layers were dried over Na_2SO_4 and concentrated. The crude oil was purified via reverse-phase HPLC (Acetonitrile/ Water gradient with 0.1% TFA present), affording the desired compound, 1-(2,2-dimethylpropyl)-3-methyl-5-phenyl-1,3-dihydro-2H-benzimidazol-2-one (**1-6**), with >95% purity. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (d, 2H, *J*=7.3 Hz), 7.45 (t, 2H, *J*=7.3 Hz), 7.30-7.36 (m, 2H), 7.19 (s, 1H), 7.10 (d, 1H, *J*=8.2 Hz), 3.70 (s, 2H), 3.49 (s, 3H), 1.07 (s, 9H). LRMS *m/z*: Calc'd for $C_{19}H_{22}N_2O$ (M+H) 295.4, found 295.1.

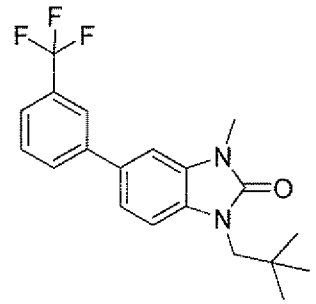
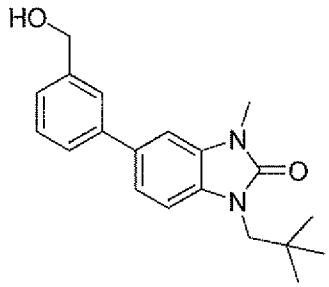
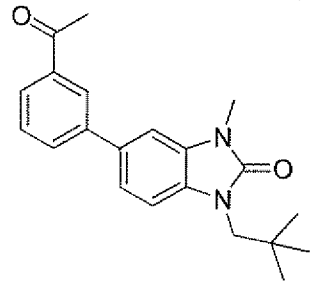
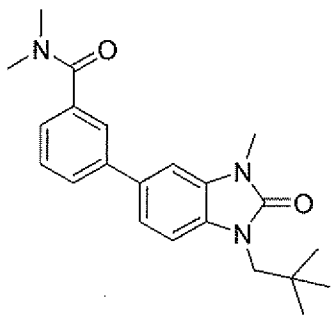
Table 1 for Scheme 1

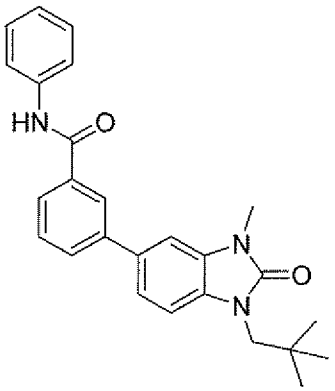
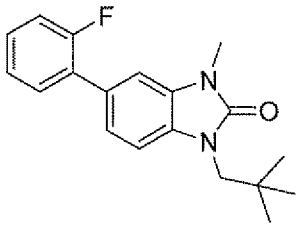
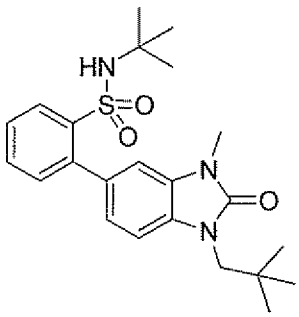
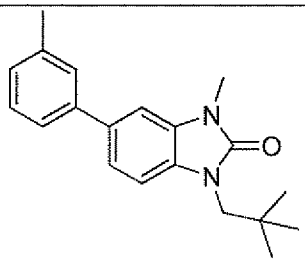
Table 1 for Scheme 1.

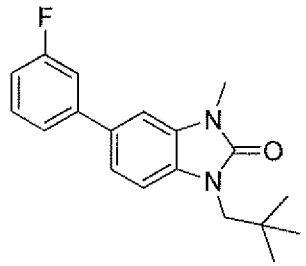
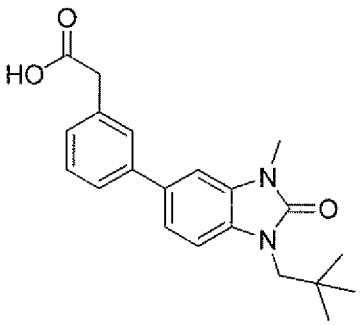
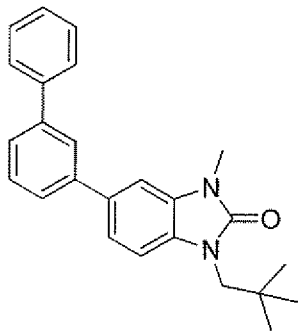
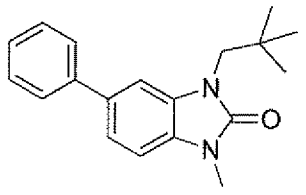
Cmp	Structure	Name	LRMS *m/z* (M+H)

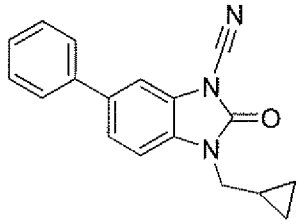
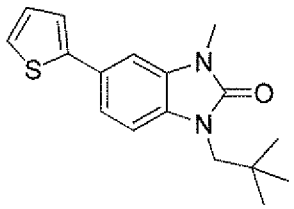
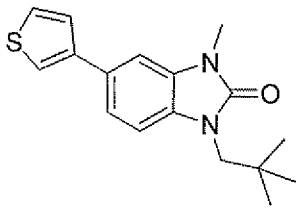
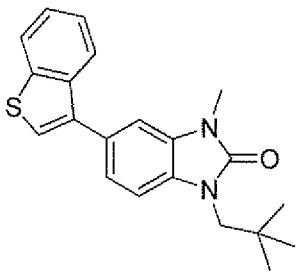
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-7		1-(cyclopropylmethyl)-3-ethyl-5-phenyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS *m/z* (M+H) 293.1 found, 293.4 required.
1-8		1-(cyclopropylmethyl)-5-phenyl-3-propyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS *m/z* (M+H) 307.1 found, 307.4 required.
1-9		[3-(cyclopropylmethyl)-2-oxo-6-phenyl-2,3-dihydro-1H-benzimidazol-1-yl]acetonitrile	LRMS *m/z* (M+H) 304.1 found, 304.4 required.
1-10		3-benzyl-1-(cyclopropylmethyl)-5-phenyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS *m/z* (M+H) 355.1 found, 355.5 required.

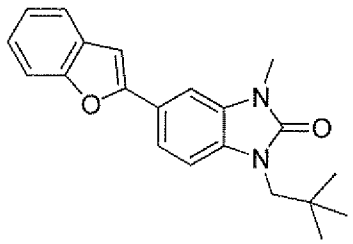
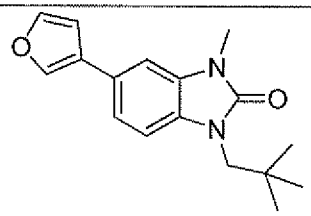
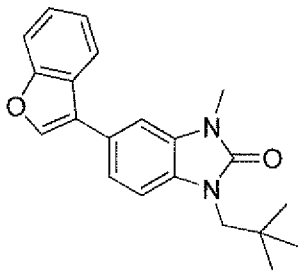
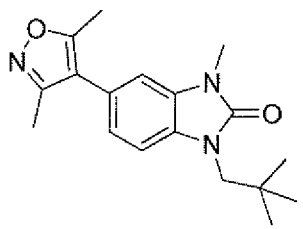
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-11		2-[1-(2,2-dimethylpropyl)-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile	LRMS *m/z* (M+H) 306.1 found, 306.4 required.
1-12		1-(2,2-dimethylpropyl)-5-phenyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 281.0 found, 281.4 required.
1-13		5-(3-chlorophenyl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 329.1 found, 329.4 required.
1-14		1-(2,2-dimethylpropyl)-5-(3-isopropylphenyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 337.2 found, 337.5 required.

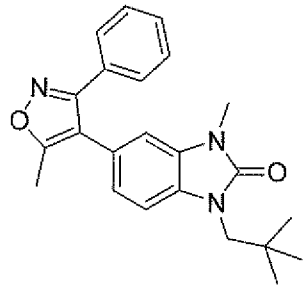
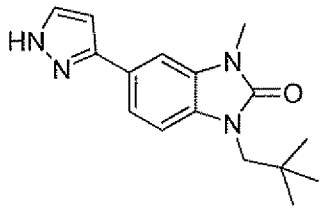
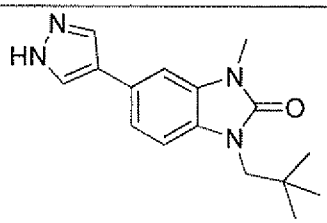
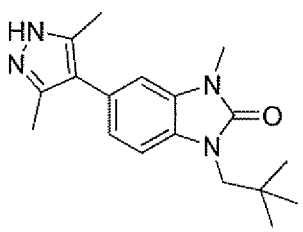
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-15		1-(2,2-dimethylpropyl)-3-methyl-5-[3-(trifluoromethyl)phenyl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 363.2 found, 363.4 required.
1-16		1-(2,2-dimethylpropyl)-5-[3-(hydroxymethyl)phenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 325.2 found, 325.4 required.
1-17		5-(3-acetylphenyl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 337.2 found, 337.4 required.
1-18		3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-N,N-dimethylbenzamide	LRMS m/z (M+H) 366.2 found, 366.5 required.

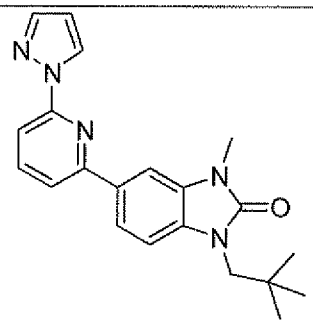
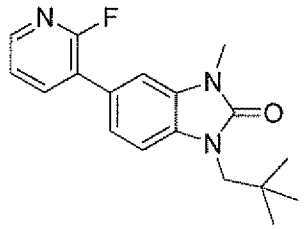
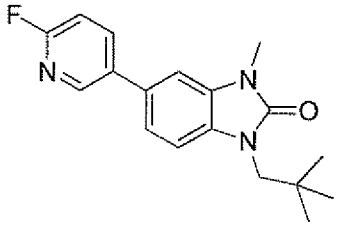
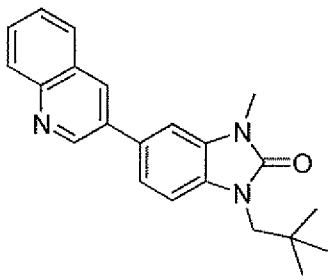
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-19		3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-N-phenylbenzamide	LRMS m/z (M+H) 414.2 found, 414.5 required.
1-20		1-(2,2-dimethylpropyl)-5-(2-fluorophenyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 313.2 found, 313.4 required.
1-21		N-(tert-butyl)-2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzenesulfonamide	LRMS m/z (M+H) 430.2 found, 430.6 required.
1-22		1-(2,2-dimethylpropyl)-3-methyl-5-(3-methylphenyl)-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 309.2 found, 309.4 required.

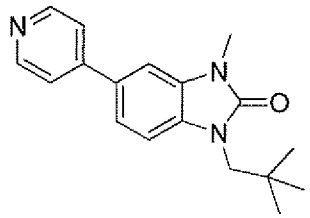
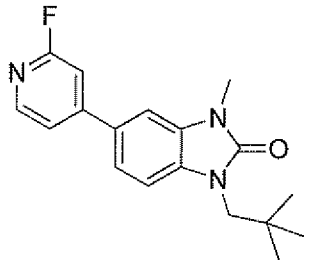
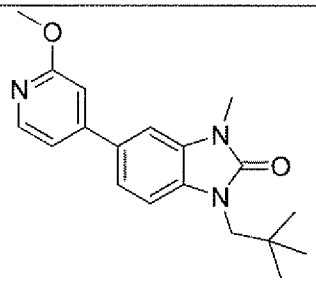
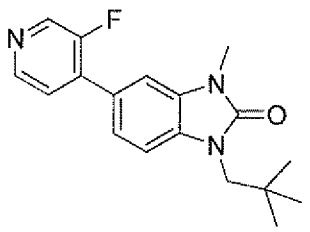
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-23		1-(2,2-dimethylpropyl)-5-(3-fluorophenyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 313.2 found, 313.4 required.
1-24		{3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenyl}acetic acid	LRMS m/z (M+H) 353.2 found, 353.4 required.
1-25		5-biphenyl-3-yl-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 371.2 found, 371.5 required.
1-26		3-(2,2-dimethylpropyl)-1-methyl-5-phenyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 295.1 found, 295.4 required.

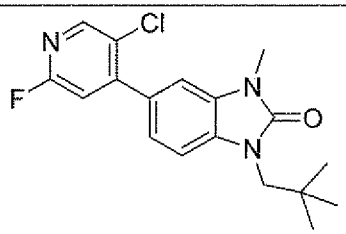
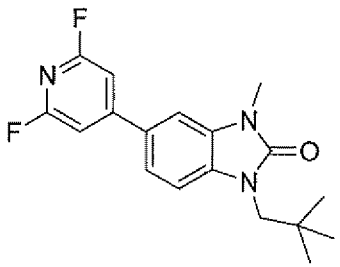
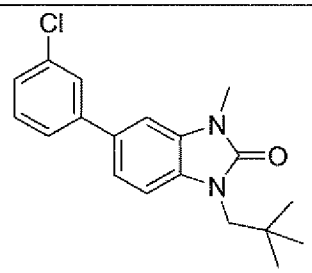
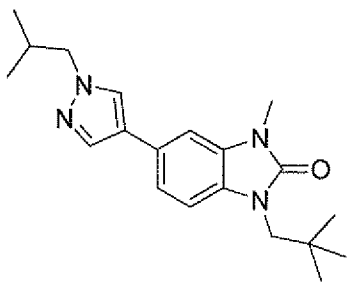
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-27		3-(cyclopropylmethyl)-2-oxo-6-phenyl-2,3-dihydro-1H-benzimidazole-1-carbonitrile	LRMS m/z (M+H) 290.1 found, 290.3 required.
1-28		1-(2,2-dimethylpropyl)-3-methyl-5-(2-thienyl)-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 301.1 found, 301.4 required.
1-29		1-(2,2-dimethylpropyl)-3-methyl-5-(3-thienyl)-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 301.1 found, 301.4 required.
1-30		5-(1-benzothien-3-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 351.1 found, 351.5 required.

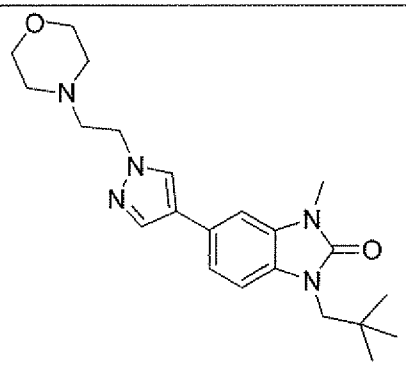
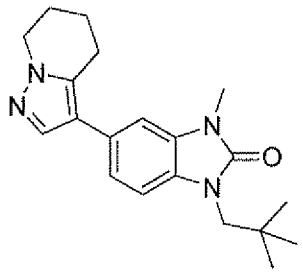
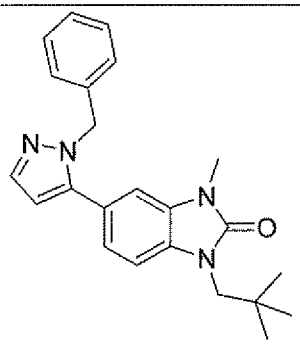
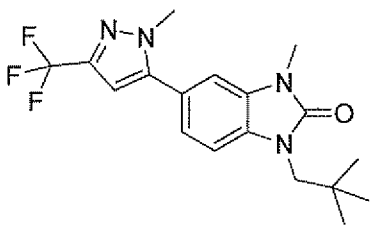
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-31		5-(1-benzofuran-2-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 335.2 found, 335.4 required.
1-32		1-(2,2-dimethylpropyl)-5-(3-furyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 285.1 found, 285.4 required.
1-33		5-(1-benzofuran-3-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 335.2 found, 335.4 required.
1-34		5-(3,5-dimethylisoxazol-4-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 314.2 found, 314.4 required.

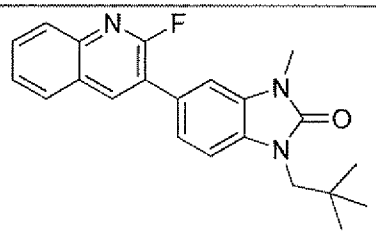
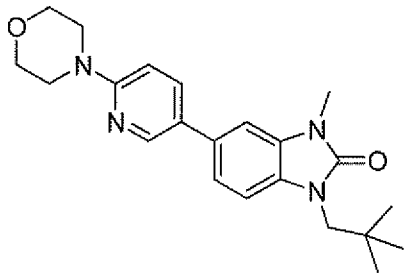
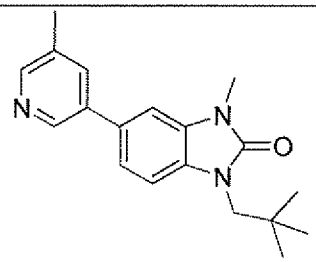
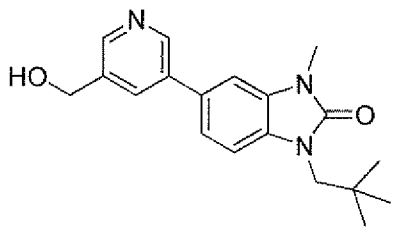
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-34		1-(2,2-dimethylpropyl)-3-methyl-5-(5-methyl-3-phenylisoxazol-4-yl)-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 376.2 found, 376.5 required.
1-35		1-(2,2-dimethylpropyl)-3-methyl-5-(1H-pyrazol-3-yl)-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 285.2 found, 285.4 required.
1-36		1-(2,2-dimethylpropyl)-3-methyl-5-(1H-pyrazol-4-yl)-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 285.2 found, 285.4 required.
1-37		1-(2,2-dimethylpropyl)-5-(3,5-dimethyl-1H-pyrazol-4-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 313.2 found, 313.4 required.

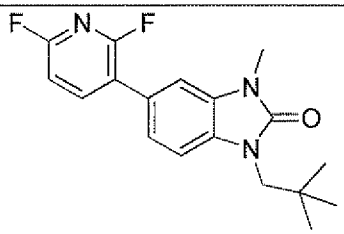
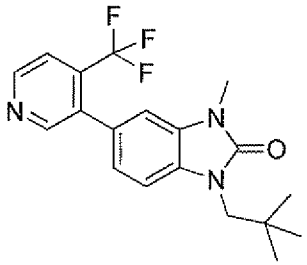
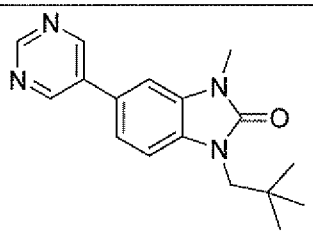
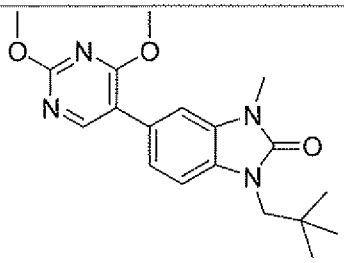
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-38		1-(2,2-dimethylpropyl)-3-methyl-5-[6-(1H-pyrazol-1-yl)pyridin-2-yl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 362.2 found, 362.5 required.
1-39		1-(2,2-dimethylpropyl)-5-(2-fluoropyridin-3-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 314.2 found, 314.4 required.
1-40		1-(2,2-dimethylpropyl)-5-(6-fluoropyridin-3-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 314.1 found, 314.4 required.
1-41		1-(2,2-dimethylpropyl)-3-methyl-5-quinolin-3-yl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 346.2 found, 346.5 required.

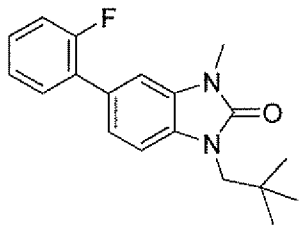
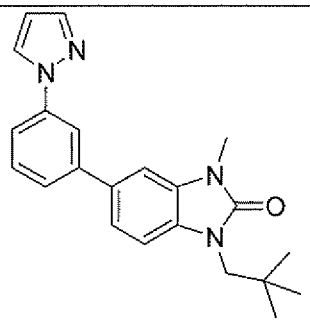
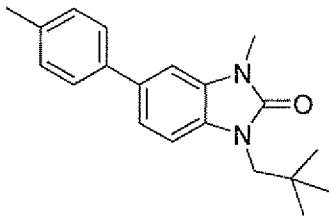
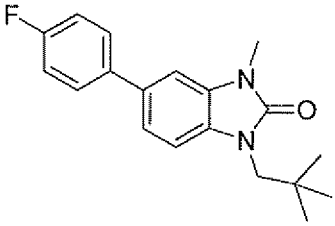
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-42		1-(2,2-dimethylpropyl)-3-methyl-5-pyridin-4-yl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 296.2 found, 296.4 required.
1-43		1-(2,2-dimethylpropyl)-5-(2-fluoropyridin-4-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 314.2 found, 314.4 required.
1-44		1-(2,2-dimethylpropyl)-5-(2-methoxypyridin-4-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 326.2 found, 326.4 required.
1-45		1-(2,2-dimethylpropyl)-5-(3-fluoropyridin-4-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 314.2 found, 314.4 required.

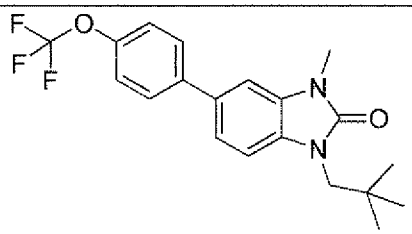
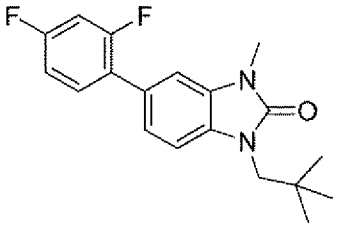
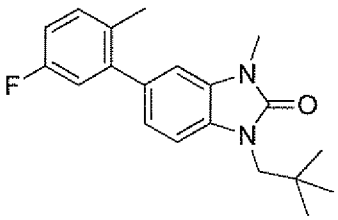
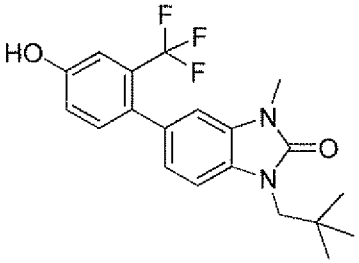
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-46		5-(5-chloro-2-fluoropyridin-4-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 348.1 found, 348.8 required.
1-47		5-(2,6-difluoropyridin-4-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 332.1 found, 332.4 required.
1-48		5-(3-chlorophenyl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 329.1 found, 329.9 required.
1-49		1-(2,2-dimethylpropyl)-5-(1-isobutyl-1H-pyrazol-4-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 341.2 found, 341.5 required.

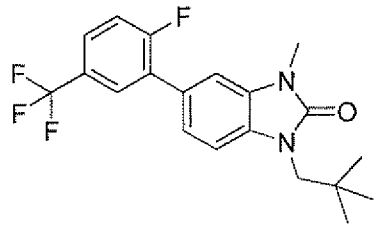
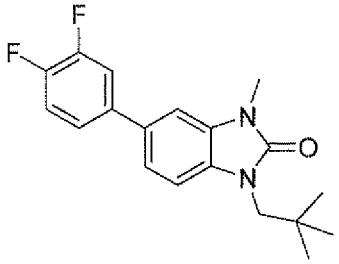
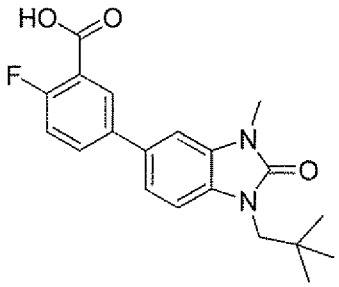
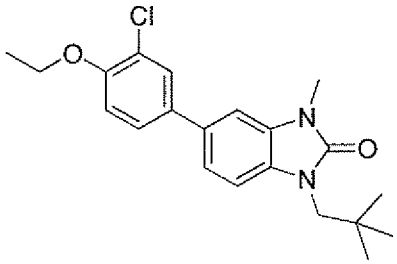
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-50		1-(2,2-dimethylpropyl)-3-methyl-5-[1-(2-morpholin-4-ylethyl)-1H-pyrazol-4-yl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 398.2 found, 398.5 required.
1-51		1-(2,2-dimethylpropyl)-3-methyl-5-(4,5,6,7-tetrahydropyrazolo[1,5-a]pyridin-3-yl)-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 339.2 found, 339.5 required.
1-52		5-(1-benzyl-1H-pyrazol-5-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 375.2 found, 375.5 required.
1-53		1-(2,2-dimethylpropyl)-3-methyl-5-[1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 367.1 found, 367.4 required.

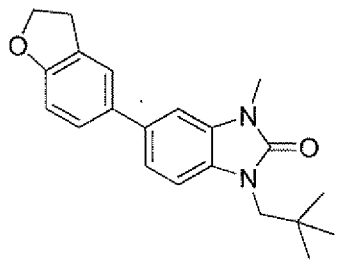
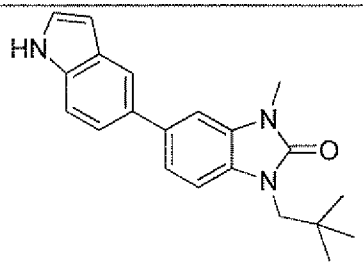
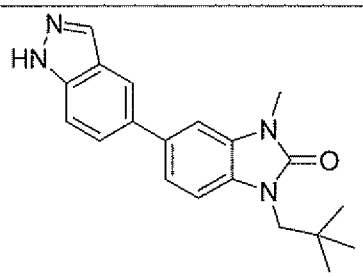
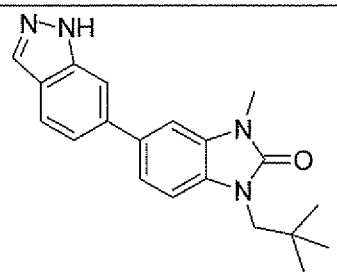
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-54		1-(2,2-dimethylpropyl)-5-(2-fluoroquinolin-3-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 364.2 found, 364.4 required.
1-55		1-(2,2-dimethylpropyl)-3-methyl-5-(6-morpholin-4-ylpyridin-3-yl)-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 381.2 found, 381.5 required.
1-56		1-(2,2-dimethylpropyl)-3-methyl-5-(5-methylpyridin-3-yl)-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 310.2 found, 310.4 required.
1-57		1-(2,2-dimethylpropyl)-5-[5-(hydroxymethyl)pyridin-3-yl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 326.2 found, 326.4 required.

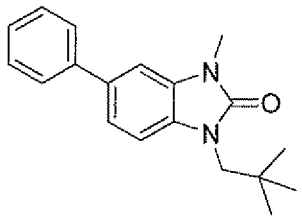
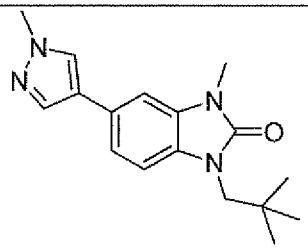
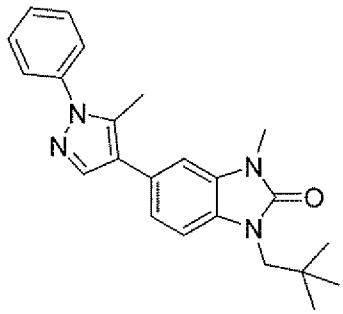
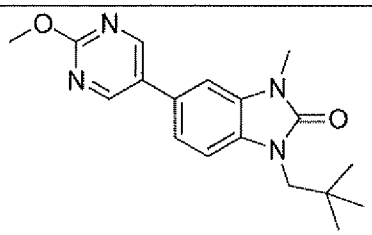
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-58		5-(2,6-difluoropyridin-3-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 332.1 found, 332.4 required.
1-59		1-(2,2-dimethylpropyl)-3-methyl-5-[4-(trifluoromethyl)pyridin-3-yl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 364.1 found, 364.4 required.
1-60		1-(2,2-dimethylpropyl)-3-methyl-5-pyrimidin-5-yl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 297.2 found, 297.4 required.
1-61		5-(2,4-dimethoxypyrimidin-5-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H--benzimidazol-2-one	LRMS m/z (M+H) 357.2 found, 357.4 required.

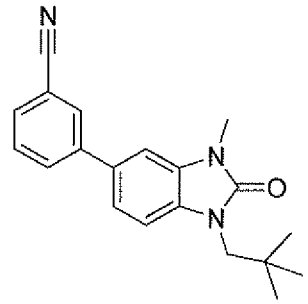
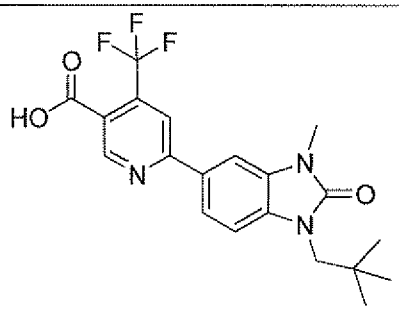
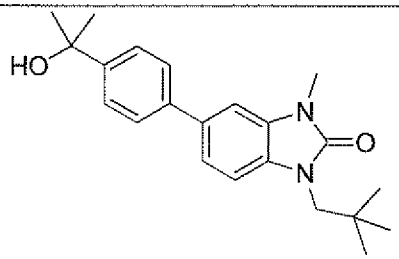
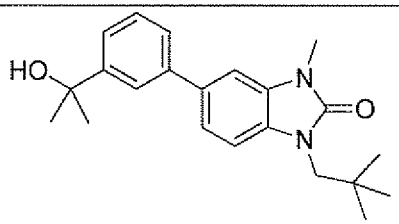
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-62		1-(2,2-dimethylpropyl)-5-(2-fluorophenyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 313.2 found, 313.4 required.
1-63		1-(2,2-dimethylpropyl)-3-methyl-5-[3-(1H-pyrazol-1-yl)phenyl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 361.2 found, 361.5 required.
1-64		1-(2,2-dimethylpropyl)-3-methyl-5-(4-methylphenyl)-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 309.2 found, 309.4 required.
1-65		1-(2,2-dimethylpropyl)-5-(4-fluorophenyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 313.2 found, 313.4 required.

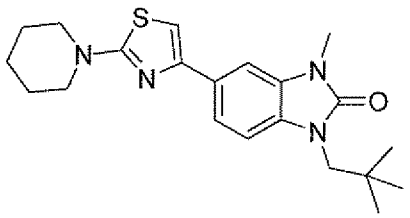
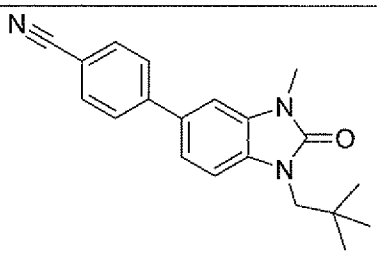
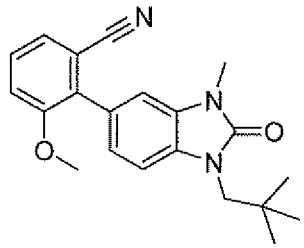
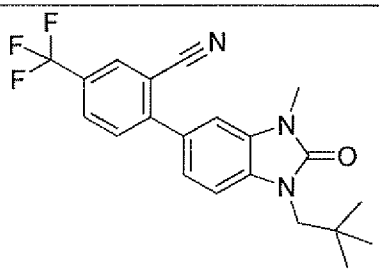
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-66		1-(2,2-dimethylpropyl)-3-methyl-5-[4-(trifluoromethoxy)phenyl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 379.1 found, 379.4 required.
1-67		5-(2,4-difluorophenyl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 331.1 found, 331.4 required.
1-68		1-(2,2-dimethylpropyl)-5-(5-fluoro-2-methylphenyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 327.2 found, 327.4 required.
1-69		1-(2,2-dimethylpropyl)-5-[4-hydroxy-2-(trifluoromethyl)phenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 379.1 found, 379.4 required.

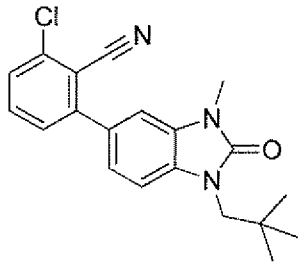
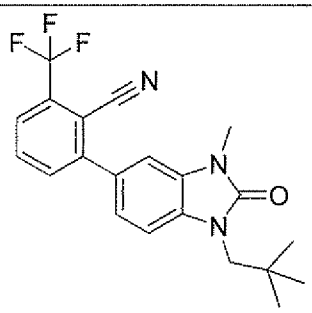
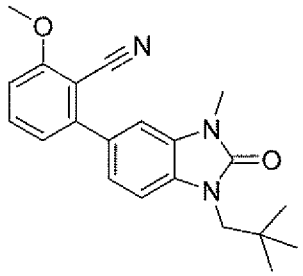
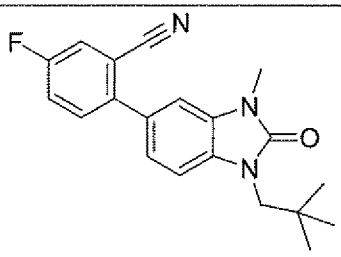
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-70		1-(2,2-dimethylpropyl)-5-[2-fluoro-5-(trifluoromethyl)phenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 381.1 found, 381.4 required.
1-71		5-(3,4-difluorophenyl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 331.1 found, 331.4 required.
1-72		5-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-2-fluorobenzoic acid	LRMS m/z (M+H) 357.1 found, 357.4 required.
1-73		5-(3-chloro-4-ethoxyphenyl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 373.1 found, 373.9 required.

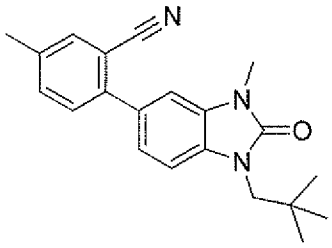
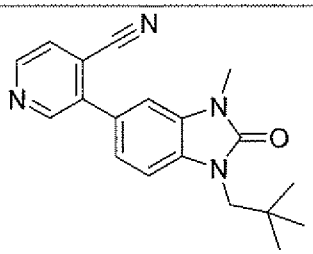
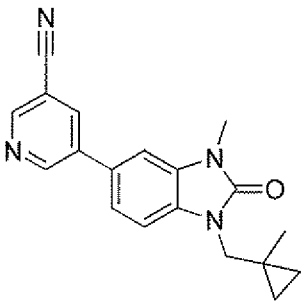
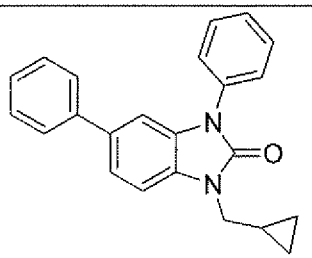
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-74		5-(2,3-dihydro-1-benzofuran-5-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 337.2 found, 337.4 required.
1-75		1-(2,2-dimethylpropyl)-5-(1H-indol-5-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 334.2 found, 334.4 required.
1-76		1-(2,2-dimethylpropyl)-5-(1H-indazol-5-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 335.2 found, 335.4 required.
1-77		1-(2,2-dimethylpropyl)-5-(1H-indazol-6-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 335.2 found, 335.4 required.

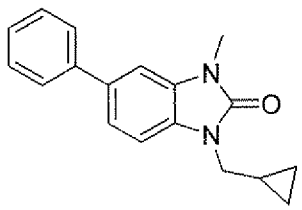
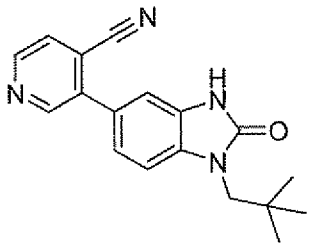
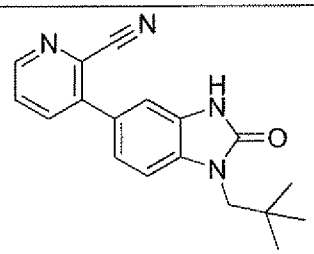
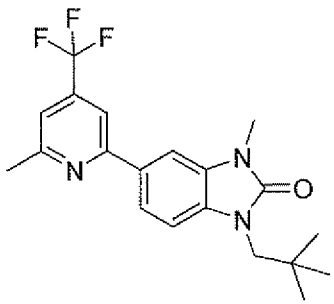
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-78		1-(2,2-dimethylpropyl)-3-methyl-5-phenyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 295.1 found, 295.4 required.
1-79		1-(2,2-dimethylpropyl)-3-methyl-5-(1-methyl-1H-pyrazol-4-yl)-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 299.1 found, 299.4 required.
1-80		1-(2,2-dimethylpropyl)-3-methyl-5-(5-methyl-1-phenyl-1H-pyrazol-4-yl)-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 375.2 found, 375.5 required.
1-81		1-(2,2-dimethylpropyl)-5-(2-methoxypyrimidin-5-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 327.2 found, 327.4 required.

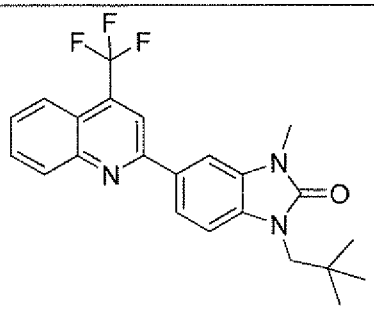
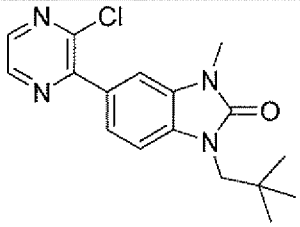
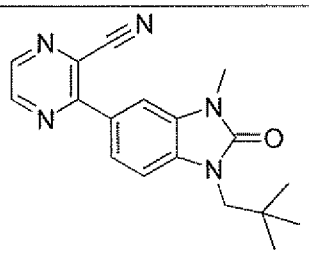
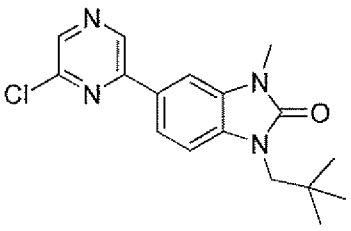
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-82		3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile	LRMS m/z (M+H) 320.2 found, 320.4 required.
1-83		6-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-4-(trifluoromethyl)nicotinic acid	LRMS m/z (M+H) 408.2 found, 408.4 required.
1-84		1-(2,2-dimethylpropyl)-5-[4-(1-hydroxy-1-methylethyl)phenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 353.2 found, 353.5 required.
1-85		1-(2,2-dimethylpropyl)-5-[3-(1-hydroxy-1-methylethyl)phenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 353.2 found, 353.5 required.

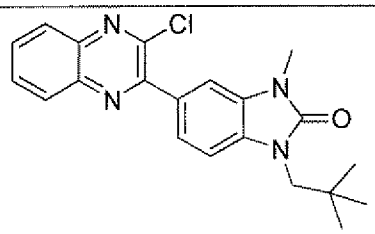
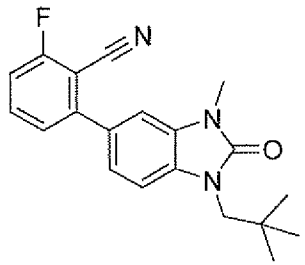
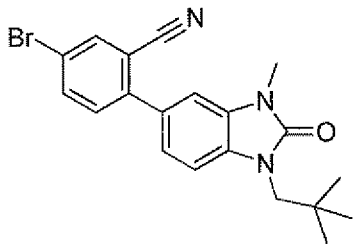
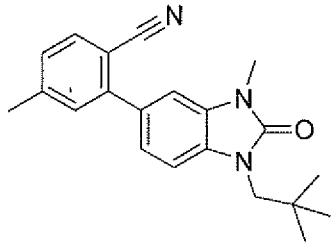
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-86		1-(2,2-dimethylpropyl)-3-methyl-5-(2-piperidin-1-yl-1,3-thiazol-4-yl)-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 385.2 found, 385.5 required.
1-87		4-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile	LRMS m/z (M+H) 320.2 found, 320.4 required.
1-88		2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-3-methoxybenzonitrile	LRMS m/z (M+H) 350.1 found, 350.4 required.
1-89		2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-5-(trifluoromethyl)benzonitrile	LRMS m/z (M+H) 388.1 found, 388.4 required.

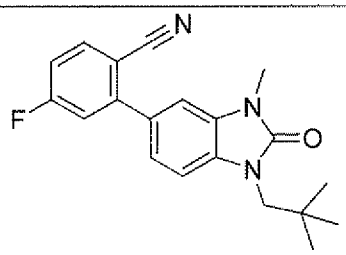
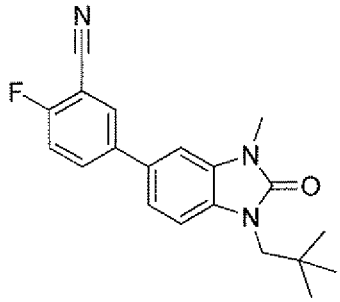
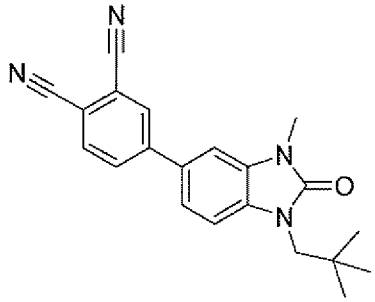
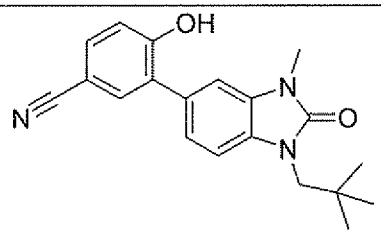
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-90		2-chloro-6-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile	LRMS m/z (M+H) 354.1 found, 354.9 required.
1-91		2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-6-(trifluoromethyl)benzonitrile	LRMS m/z (M+H) 388.1 found, 388.4 required.
1-92		2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-6-methoxybenzonitrile	LRMS m/z (M+H) 350.1 found, 350.4 required.
1-93		2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-5-fluorobenzonitrile	LRMS m/z (M+H) 338.0 found, 338.4 required.

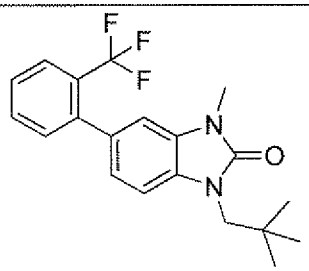
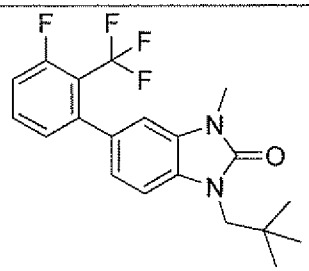
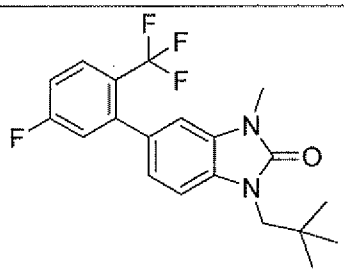
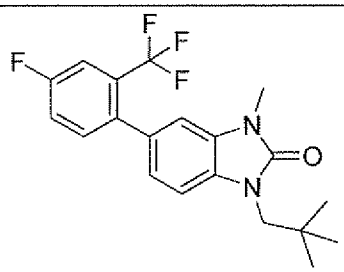
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-94		2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-5-methylbenzonitrile	LRMS m/z (M+H) 334.1 found, 334.4 required.
1-95		3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]isonicotinonitrile	LRMS m/z (M+H) 321.0 found, 321.4 required.
1-96		5-{3-methyl-1-[(1-methylcyclopropyl)methyl]-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl}nicotinonitrile	LRMS m/z (M+H) 319.2 found, 319.4 required.
1-97		1-(cyclopropylmethyl)-3,5-diphenyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 341.1 found, 341.4 required.

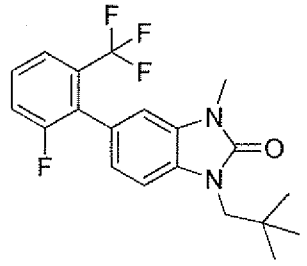
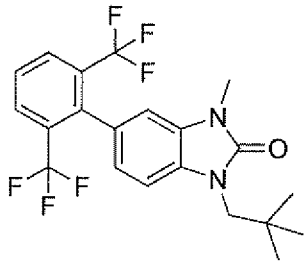
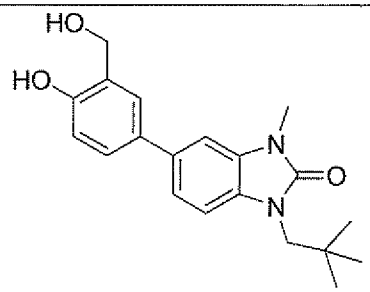
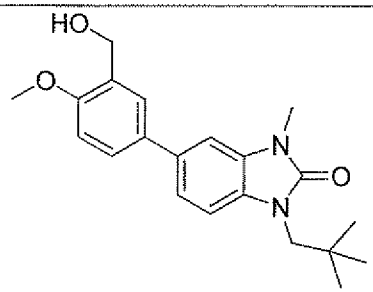
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-98		1-(cyclopropylmethyl)-3-methyl-5-phenyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 279.1 found, 279.4 required.
1-99		3-[1-(2,2-dimethylpropyl)-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]isonicotinonitrile	HRMS m/z (M+H) 307.1549 found, 307.1553 required.
1-100		3-[1-(2,2-dimethylpropyl)-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]pyridine-2-carbonitrile	LRMS m/z (M+H) 307.1 found, 307.4 required.
1-101		1-(2,2-dimethylpropyl)-3-methyl-5-[6-methyl-4-(trifluoromethyl)pyridin-2-yl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 378.2 found, 378.4 required.

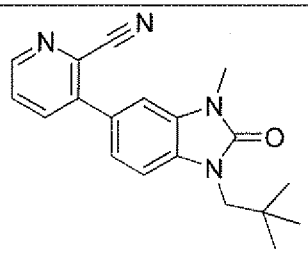
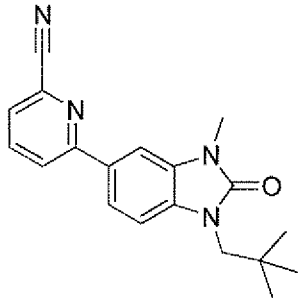
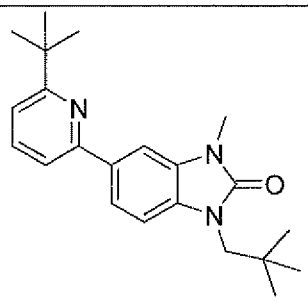
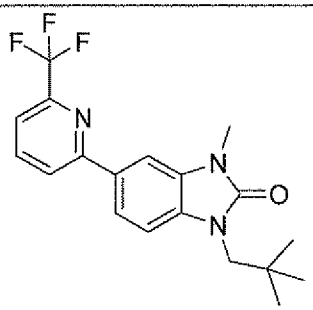
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-102		1-(2,2-dimethylpropyl)-3-methyl-5-[4-(trifluoromethyl)quinolin-2-yl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 414.2 found, 414.4 required.
1-103		5-(3-chloropyrazin-2-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 331.1 found, 331.8 required.
1-104		3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]pyrazine-2-carbonitrile	LRMS m/z (M+H) 322.2 found, 322.4 required.
1-105		5-(6-chloropyrazin-2-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 331.1 found, 331.8 required.

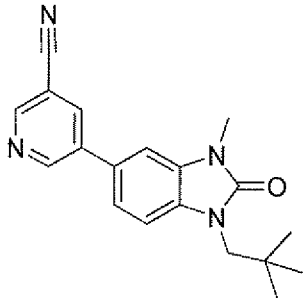
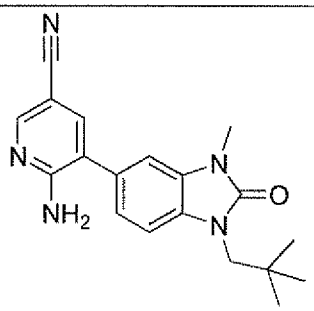
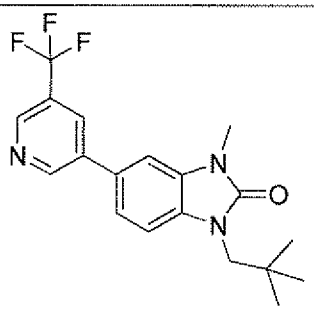
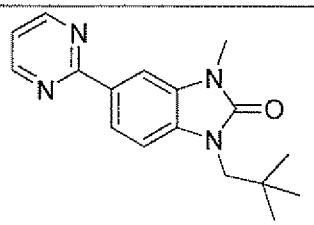
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-106		5-(3-chloroquinoxalin-2-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 381.2 found, 381.9 required.
1-107		2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-6-fluorobenzonitrile	LRMS m/z (M+H) 338.2 found, 338.4 required.
1-108		5-bromo-2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile	LRMS m/z (M+H) 398.1 found, 399.3 required.
1-109		2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-4-methylbenzonitrile	LRMS m/z (M+H) 334.2 found, 334.4 required.

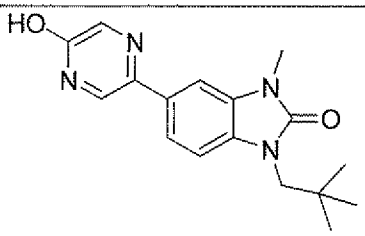
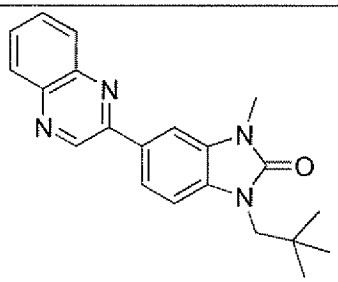
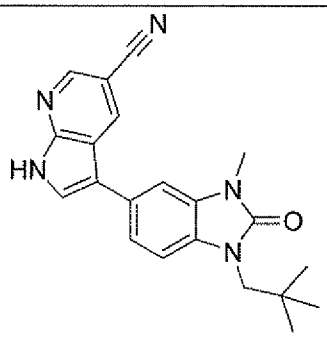
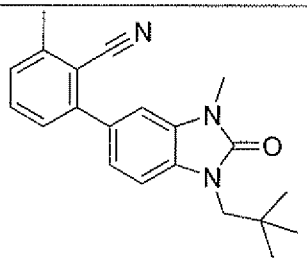
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-110		2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-4-fluorobenzonitrile	LRMS m/z (M+H) 338.2 found, 338.4 required.
1-111		5-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-2-fluorobenzonitrile	LRMS m/z (M+H) 338.2 found, 338.4 required.
1-112		4-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phthalonitrile	LRMS m/z (M+H) 345.2 found, 345.4 required.
1-113		3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-4-hydroxybenzonitrile	LRMS m/z (M+H) 336.2 found, 336.4 required.

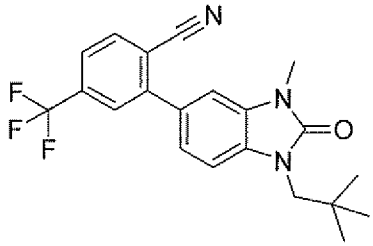
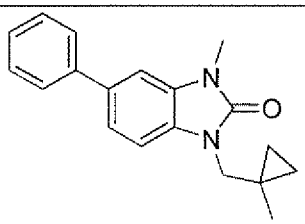
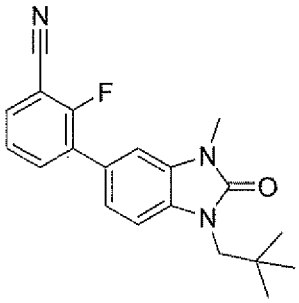
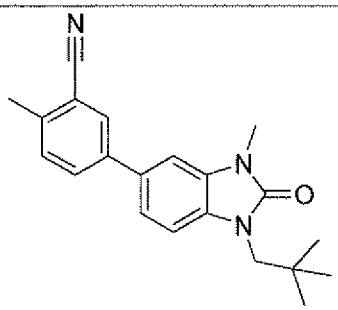
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-114		1-(2,2-dimethylpropyl)-3-methyl-5-[2-(trifluoromethyl)phenyl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 363.2 found, 363.4 required.
1-115		1-(2,2-dimethylpropyl)-5-[3-fluoro-2-(trifluoromethyl)phenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 381.2 found, 381.4 required.
1-116		1-(2,2-dimethylpropyl)-5-[5-fluoro-2-(trifluoromethyl)phenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 381.2 found, 381.4 required.
1-117		1-(2,2-dimethylpropyl)-5-[4-fluoro-2-(trifluoromethyl)phenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 381.2 found, 381.4 required.

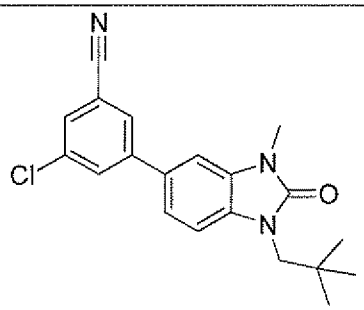
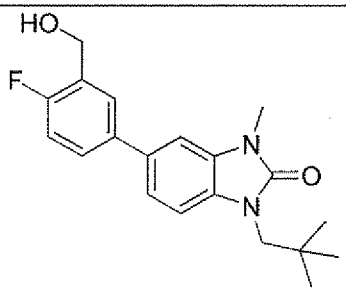
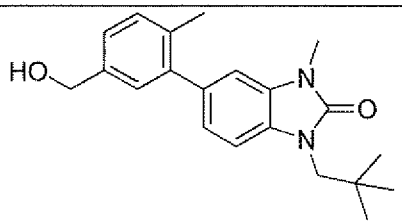
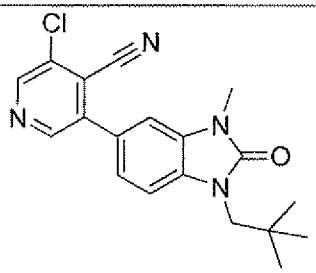
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-118		1-(2,2-dimethylpropyl)-5-[2-fluoro-6-(trifluoromethyl)phenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 381.2 found, 381.4 required.
1-119		5-[2,6-bis(trifluoromethyl)phenyl]-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 431.2 found, 431.4 required.
1-120		1-(2,2-dimethylpropyl)-5-[4-hydroxy-3-(hydroxymethyl)phenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 341.2 found, 341.4 required.
1-121		1-(2,2-dimethylpropyl)-5-[3-(hydroxymethyl)-4-methoxyphenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 355.2 found, 355.4 required.

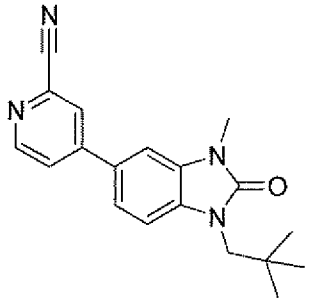
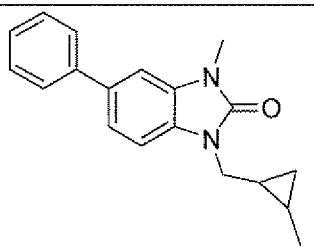
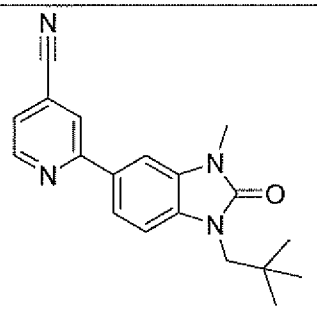
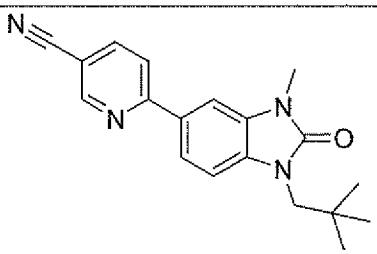
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-122		3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]pyridine-2-carbonitrile	LRMS m/z (M+H) 321.2 found, 321.4 required.
1-123		6-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]pyridine-2-carbonitrile	LRMS m/z (M+H) 321.2 found, 321.4 required.
1-124		5-(6-tert-butylpyridin-2-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 352.2 found, 352.5 required.
1-125		1-(2,2-dimethylpropyl)-3-methyl-5-[6-(trifluoromethyl)pyridin-2-yl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 364.2 found, 364.4 required.

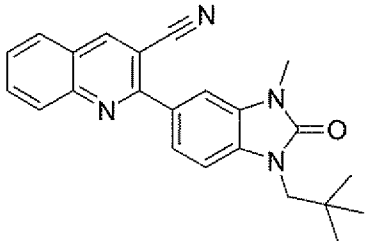
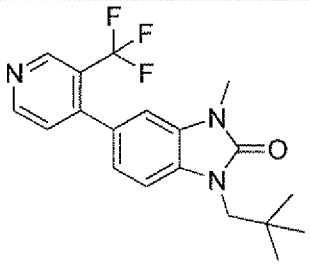
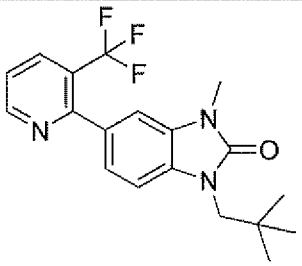
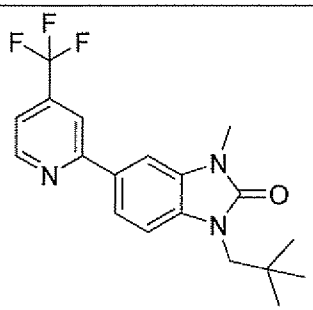
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-126		5-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]nicotinonitrile	LRMS m/z (M+H) 321.2 found, 321.4 required.
1-127		6-amino-5-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]nicotinonitrile	LRMS m/z (M+H) 336.2 found, 336.4 required.
1-128		1-(2,2-dimethylpropyl)-3-methyl-5-[5-(trifluoromethyl)pyridin-3-yl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 364.2 found, 364.4 required.
1-129		1-(2,2-dimethylpropyl)-3-methyl-5-pyrimidin-2-yl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 297.2 found, 297.4 required.

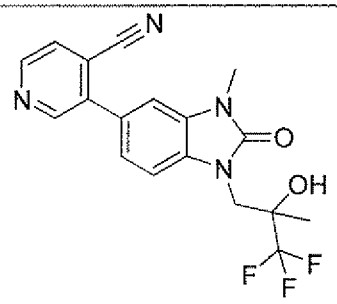
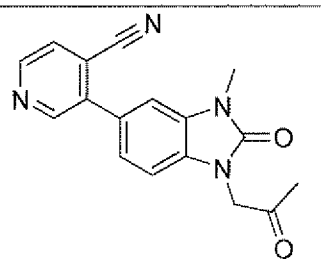
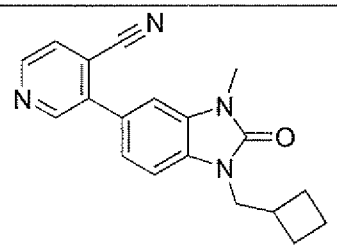
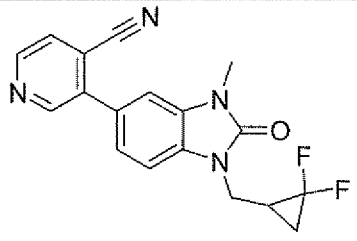
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-130		1-(2,2-dimethylpropyl)-5-(5-hydroxypyrazin-2-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 313.2 found, 313.4 required.
1-131		1-(2,2-dimethylpropyl)-3-methyl-5-quinoxalin-2-yl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 347.2 found, 347.4 required.
1-132		3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-1H-pyrrolo[2,3-b]pyridine-5-carbonitrile	LRMS m/z (M+H) 360.2 found, 360.4 required.
1-133		2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-6-methylbenzonitrile	LRMS m/z (M+H) 334.2 found, 334.4 required.

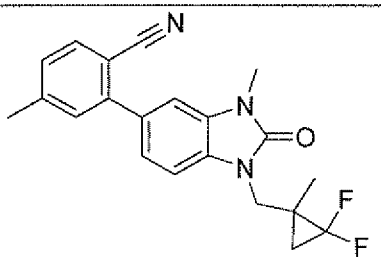
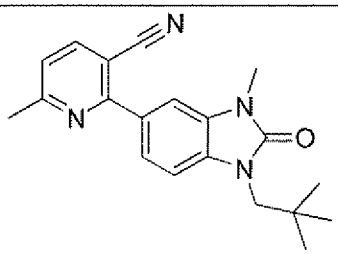
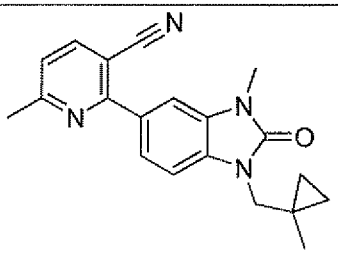
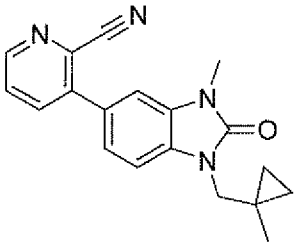
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-134		2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-4-(trifluoromethyl)benzonitrile	LRMS m/z (M+H) 388.2 found, 388.4 required.
1-135		3-methyl-1-[(1-methylcyclopropyl)methyl]-5-phenyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 293.1 found, 293.4 required.
1-136		3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-2-fluorobenzonitrile	LRMS m/z (M+H) 338.1 found, 338.4 required.
1-137		5-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-2-methylbenzonitrile	LRMS m/z (M+H) 334.2 found, 334.4 required.

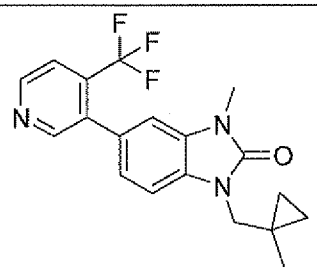
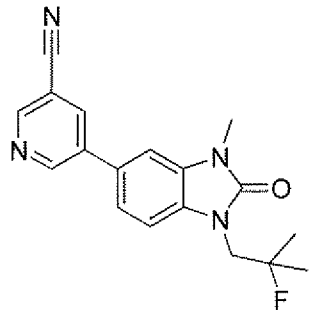
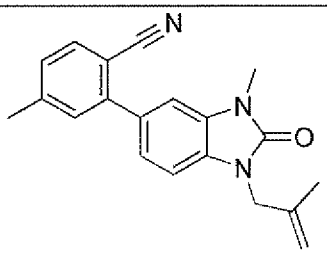
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-138		3-chloro-5-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile	LRMS m/z (M+H) 354.1 found, 354.9 required.
1-139		1-(2,2-dimethylpropyl)-5-[4-fluoro-3-(hydroxymethyl)phenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 343.2 found, 343.4 required.
1-140		1-(2,2-dimethylpropyl)-5-[5-(hydroxymethyl)-2-methylphenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 339.2 found, 339.5 required.
1-141		3-chloro-5-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]isonicotinonitrile	LRMS m/z (M+H) 355.1 found, 355.9 required.

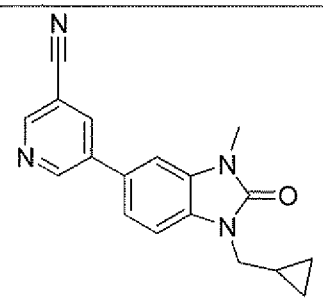
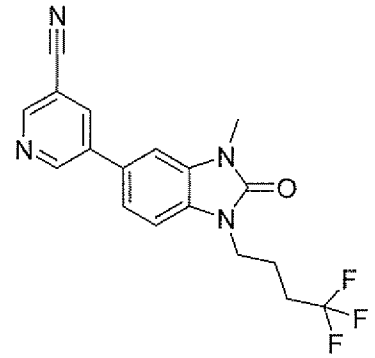
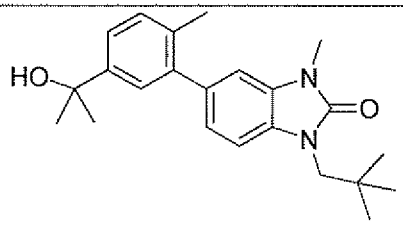
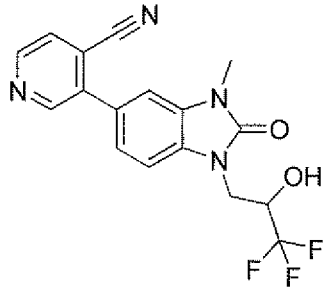
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-142		4-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]pyridine-2-carbonitrile	LRMS m/z (M+H) 321.2 found, 321.4 required.
1-143		3-methyl-1-[(2-methylcyclopropyl)methyl]-5-phenyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 293.2 found, 293.4 required.
1-144		2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]isonicotinonitrile	LRMS m/z (M+H) 321.2 found, 321.4 required.
1-145		6-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]nicotinonitrile	LRMS m/z (M+H) 321.2 found, 321.4 required.

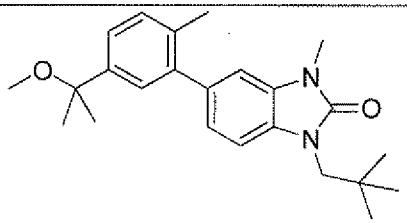
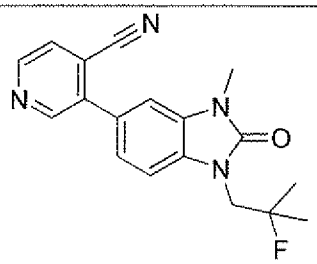
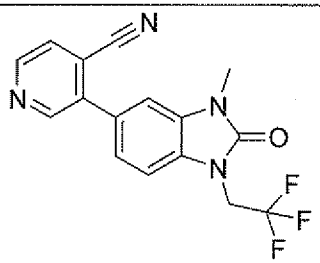
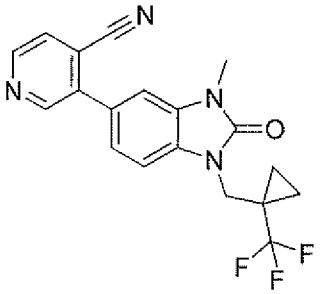
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-146		2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]quinoline-3-carbonitrile	LRMS m/z (M+H) 371.2 found, 371.5 required.
1-147		1-(2,2-dimethylpropyl)-3-methyl-5-[3-(trifluoromethyl)pyridin-4-yl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 364.2 found, 364.4 required.
1-148		1-(2,2-dimethylpropyl)-3-methyl-5-[3-(trifluoromethyl)pyridin-2-yl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 364.2 found, 364.4 required.
1-149		1-(2,2-dimethylpropyl)-3-methyl-5-[4-(trifluoromethyl)pyridin-2-yl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 364.1 found, 364.4 required.

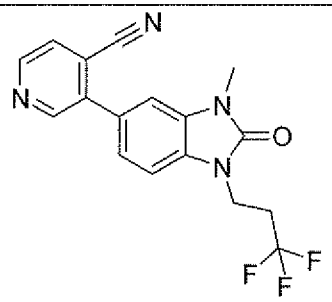
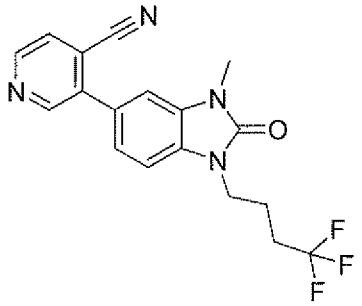
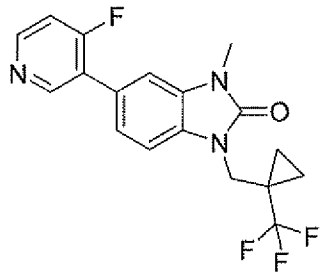
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-150		3-[3-methyl-2-oxo-1-(3,3,3-trifluoro-2-hydroxy-2-methylpropyl)-2,3-dihydro-1H-benzimidazol-5-yl]isonicotinonitrile	LRMS m/z (M+H) 377.2 found, 377.3 required.
1-151		3-[3-methyl-2-oxo-1-(2-oxopropyl)-2,3-dihydro-1H-benzimidazol-5-yl]isonicotinonitrile	LRMS m/z (M+H) 307.2 found, 307.3 required.
1-152		3-[1-(cyclobutylmethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]isonicotinonitrile	LRMS m/z (M+H) 319.1 found, 319.4 required.
1-153		3-{1-[(2,2-difluorocyclopropyl)methyl]-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl}isonicotinonitrile	LRMS m/z (M+H) 341.1 found, 341.3 required.

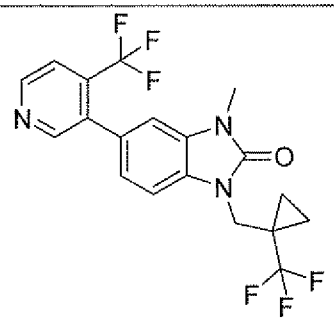
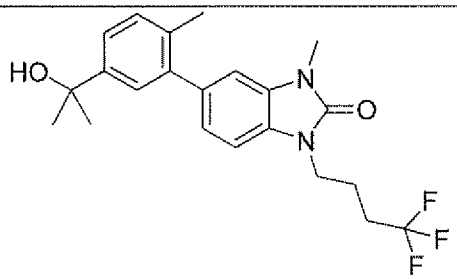
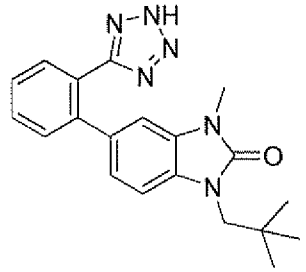
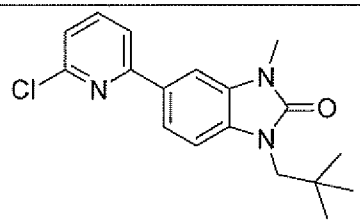
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-154		2-{1-[(2,2-difluoro-1-methylcyclopropyl)methyl]-3-methyl-2-oxo-2,3-dihyro-1H-benzimidazol-5-yl}-4-methylbenzonitrile	LRMS m/z (M+H) 368.3 found, 368.4 required.
1-155		2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-6-methylnicotinonitrile	LRMS m/z (M+H) 335.1 found, 335.4 required.
1-156		6-methyl-2-{3-methyl-1-[(1-methylcyclopropyl)methyl]-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl}nicotinonitrile	LRMS m/z (M+H) 333.1 found, 333.4 required.
1-157		3-{3-methyl-1-[(1-methylcyclopropyl)methyl]-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl}pyridine-2-carbonitrile	LRMS m/z (M+H) 319.1 found, 319.4

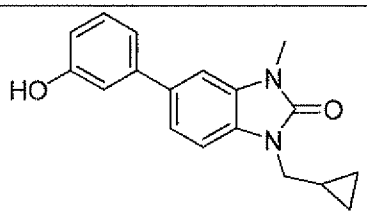
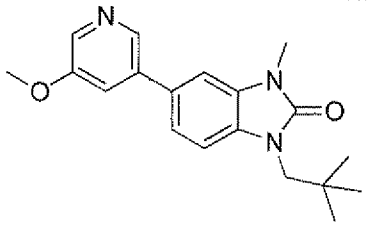
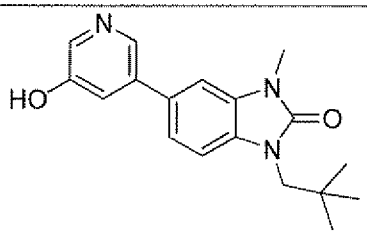
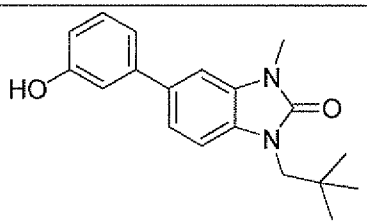
Cmp	Structure	Name	LRMS *m/z* (M+H)
			required.
1-158		3-methyl-1-[(1-methylcyclopropyl)methyl]-5-[4-(trifluoromethyl)pyridin-3-yl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 362.1 found, 362.4 required.
1-159		5-[1-(2-fluoro-2-methylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]nicotinonitrile	LRMS m/z (M+H) 325.1 found, 325.4 required.
1-160		4-methyl-2-[3-methyl-1-(2-methylprop-2-en-1-yl)-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile	LRMS m/z (M+H) 318.2 found, 318.4 required.

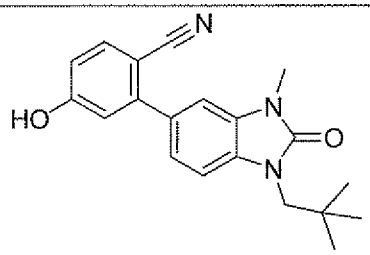
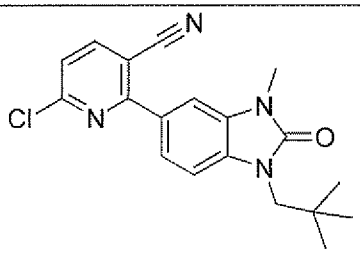
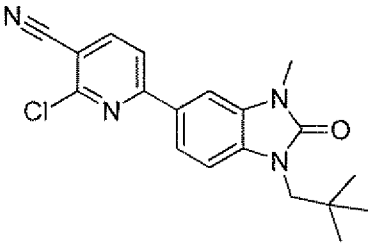
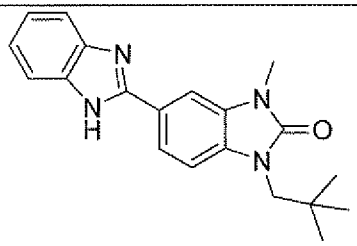
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-161		5-[1-(cyclopropylmethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]nicotinonitrile	LRMS m/z (M+H) 305.1 found, 305.4 required.
1-162		5-[3-methyl-2-oxo-1-(4,4,4-trifluorobutyl)-2,3-dihydro-1H-benzimidazol-5-yl]nicotinonitrile	LRMS m/z (M+H) 361.1 found, 361.3 required.
1-163		1-(2,2-dimethylpropyl)-5-[5-(1-hydroxy-1-methylethyl)-2-methylphenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	HRMS m/z (M+H) 367.2385 found, 367.2380 required.
1-164		3-[3-methyl-2-oxo-1-(3,3,3-trifluoro-2-hydroxypropyl)-2,3-dihydro-1H-benzimidazol-5-yl]isonicotinonitrile	LRMS m/z (M+H) 363.1 found, 363.3 required.

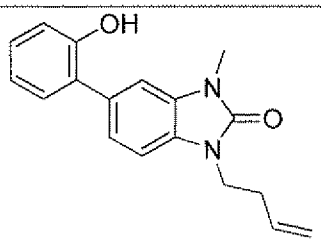
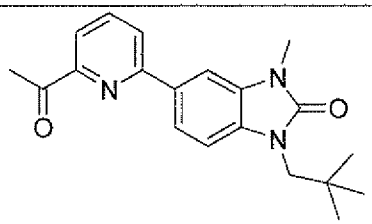
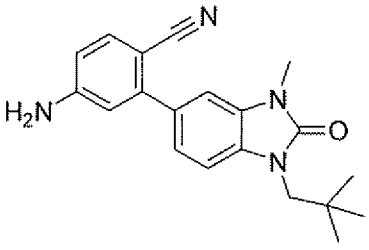
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-165		1-(2,2-dimethylpropyl)-5-[5-(1-methoxy-1-methylethyl)-2-methylphenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	HRMS m/z (M+H) 381.2538 found, 381.2537 required.
1-166		3-[1-(2-fluoro-2-methylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]isonicotinonitrile	LRMS m/z (M+H) 325.1 found, 325.4 required.
1-167		3-[3-methyl-2-oxo-1-(2,2,2-trifluoroethyl)-2,3-dihydro-1H-benzimidazol-5-yl]isonicotinonitrile	LRMS m/z (M+H) 333.1 found, 333.3 required.
1-168		3-(3-methyl-2-oxo-1-{[1-(trifluoromethyl)cyclopropyl]methyl}-2,3-dihydro-1H-benzimidazol-5-yl)isonicotinonitrile	LRMS m/z (M+H) 373.1 found, 373.4

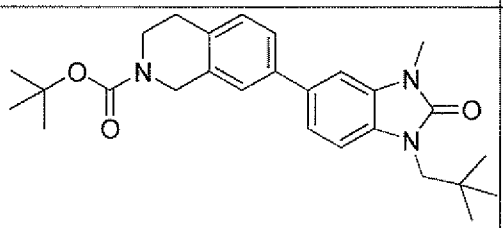
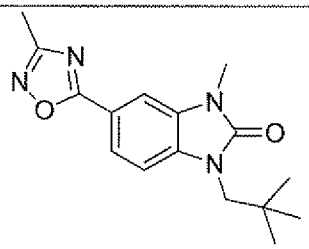
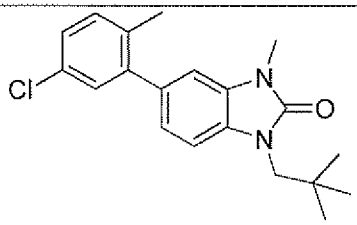
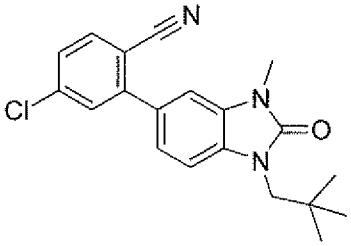
Cmp	Structure	Name	LRMS *m/z* (M+H)
			required.
1-169		3-[3-methyl-2-oxo-1-(3,3,3-trifluoropropyl)-2,3-dihydro-1H-benzimidazol-5-yl]isonicotinonitrile	LRMS m/z (M+H) 347.1 found, 347.3 required.
1-170		3-[3-methyl-2-oxo-1-(4,4,4-trifluorobutyl)-2,3-dihydro-1H-benzimidazol-5-yl]isonicotinonitrile	LRMS m/z (M+H) 361.1 found, 361.3 required.
1-171		5-(4-fluoropyridin-3-yl)-3-methyl-1-{[1-(trifluoromethyl)cyclopropyl]methyl}-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 366.1 found, 366.3 required.

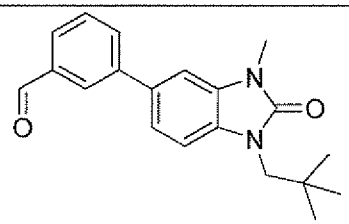
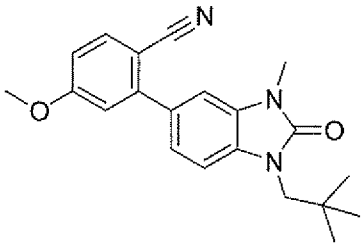
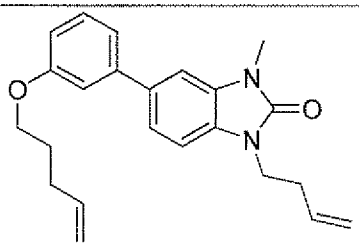
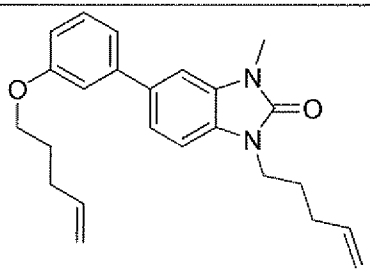
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-172		3-methyl-1-{[1-(trifluoromethyl)cyclopropyl]methyl}-5-[4-(trifluoromethyl)pyridin-3-yl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 416.1 found, 416.3 required.
1-173		5-[5-(1-hydroxy-1-methylethyl)-2-methylphenyl]-3-methyl-1-(4,4,4-trifluorobutyl)-1,3-dihydro-2H-benzimidazol-2-one	HRMS m/z (M+H) 407.1951 found, 407.1941 required.
1-174		1-(2,2-dimethylpropyl)-3-methyl-5-[2-(2H-tetrazol-5-yl)phenyl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 363.2 found, 362.4 required.
1-175		5-(6-chloropyridin-2-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 330.1 found, 330.8 required.

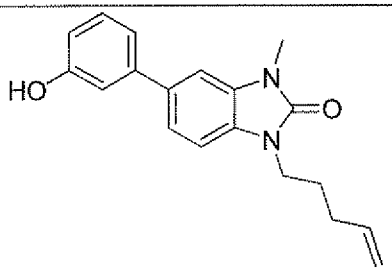
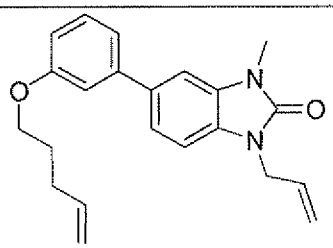
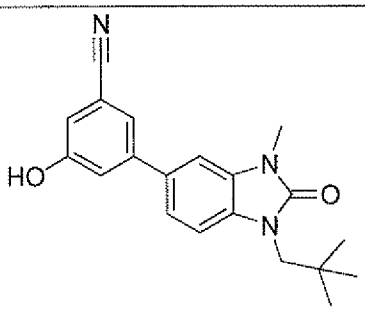
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-176		1-(cyclopropylmethyl)-5-(3-hydroxyphenyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 295.0 found, 295.4 required.
1-177		1-(2,2-dimethylpropyl)-5-(5-methoxypyridin-3-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 326.1 found, 326.4 required.
1-178		1-(2,2-dimethylpropyl)-5-(5-hydroxypyridin-3-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 312.1 found, 312.4 required.
1-179		1-(2,2-dimethylpropyl)-5-(3-hydroxyphenyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 311.0 found, 311.4 required.

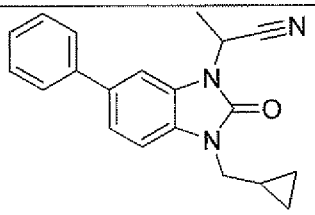
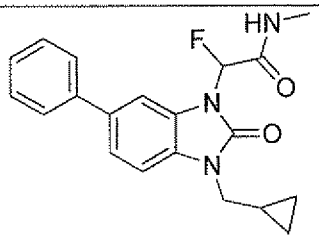
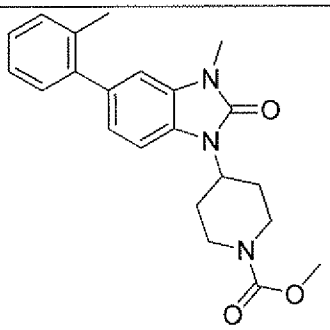
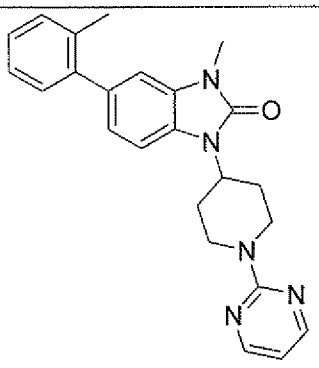
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-180		2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-4-hydroxybenzonitrile	LRMS m/z (M+H) 336.0 found, 336.4 required.
1-181		6-chloro-2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]nicotinonitrile	LRMS m/z (M+H) 355.0 found, 355.8 required.
1-182		2-chloro-6-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]nicotinonitrile	LRMS m/z (M+H) 355.0 found, 355.8 required.
1-183		1'-(2,2-dimethylpropyl)-3'-methyl-1',3'-dihydro-1H-2'H-2,5'-bibenzimidazol-2'-one	LRMS m/z (M+H) 335.1 found, 335.4 required.

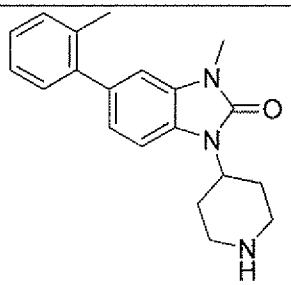
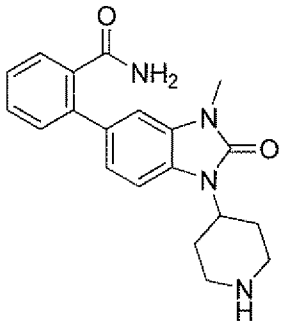
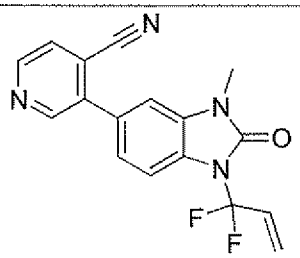
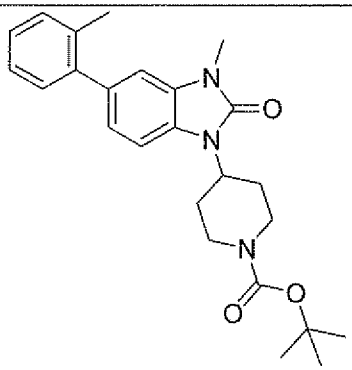
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-184		1-but-3-en-1-yl-5-(2-hydroxyphenyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 295.0 found, 295.4 required.
1-185		5-(6-acetylpyridin-2-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 338.0 found, 338.4 required.
1-186		4-amino-2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile	LRMS m/z (M+H) 335.0 found, 335.4 required.

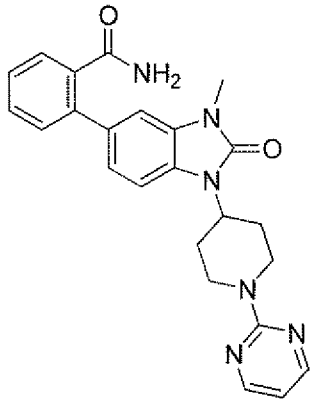
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-187		tert-butyl 7-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-3,4-dihydroisoquinoline-2(1H)-carboxylate	HRMS m/z (M+H) 450.2756 found, 450.2751 required.
1-188		1-(2,2-dimethylpropyl)-3-methyl-5-(3-methyl-1,2,4-oxadiazol-5-yl)-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 301.1661 found, 301.1659 required.
1-189		5-(5-chloro-2-methylphenyl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 343.0 found, 343.9 required.
1-190		4-chloro-2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile	LRMS m/z (M+H) 354.0 found, 354.9 required.

Cmp	Structure	Name	LRMS *m/z* (M+H)
1-191		3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzaldehyde	LRMS m/z (M+H) 323.0 found, 323.4 required.
1-192		2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-4-methoxybenzonitrile	LRMS m/z (M+H) 350.0 found, 350.4 required.
1-193		1-but-3-en-1-yl-3-methyl-5-[3-(pent-4-en-1-yloxy)phenyl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 363.1 found, 363.5 required.
1-194		3-methyl-1-pent-4-en-1-yl-5-[3-(pent-4-en-1-yloxy)phenyl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 377.2 found, 377.5 required.

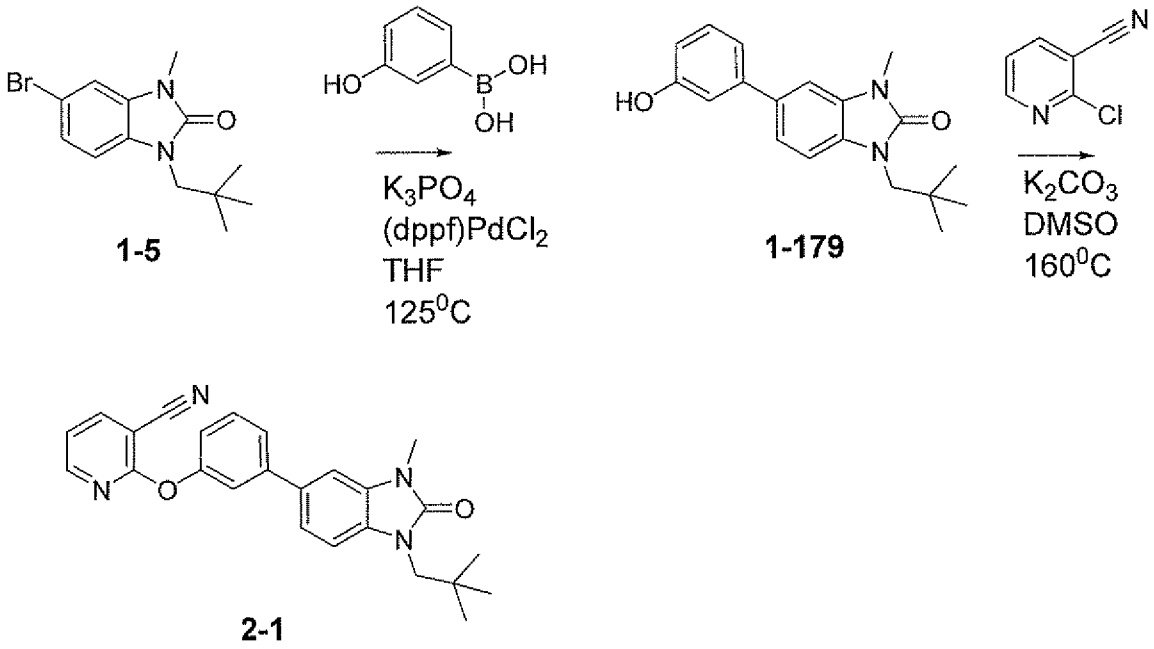
Cmp	Structure	Name	LRMS *m/z* (M+H)
1-195		5-(3-hydroxyphenyl)-3-methyl-1-pent-4-en-1-yl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 309.1 found, 309.4 required.
1-196		1-allyl-3-methyl-5-[3-(pent-4-en-1-yloxy)phenyl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 349.1 found, 349.5 required.
1-197		3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-5-hydroxybenzonitrile	LRMS m/z (M+H) 336.1 found, 336.4 required.

Cmp	Structure	Name	LRMS *m/z* (M+H)
1-198		2-[3-(cyclopropylmethyl)-2-oxo-6-phenyl-2,3-dihydro-1H-benzimidazol-1-yl]propanenitrile	LRMS m/z (M+H) 318.1 found, 318.4 required.
1-199		2-[3-(cyclopropylmethyl)-2-oxo-6-phenyl-2,3-dihydro-1H-benzimidazol-1-yl]-2-fluoro-N-methylacetamide	LRMS m/z (M+H) 354.1 found, 354.4 required.
1-200		methyl-4-[3-methyl-5-(2-methylphenyl)-2-oxo-2,3-dihydro-1H-benzimidazol-1-yl]piperidine-1-carboxylate	HRMS m/z (M+H) 380.1967 found, 380.1969 required.
1-201		3-methyl-5-(2-methylphenyl)-1-(1-pyrimidin-2-ylpiperidin-4-yl)-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 400.3 found, 400.5 required.

Cmp	Structure	Name	LRMS *m/z* (M+H)
1-202		3-methyl-5-(2-methylphenyl)-1-piperidin-4-yl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 322.3 found, 322.4 required.
1-203		2-(3-methyl-2-oxo-1-piperidin-4-yl-2,3-dihydro-1H-benzimidazol-5-yl)benzamide	LRMS m/z (M+H) 351.2 found, 351.4 required.
1-204		3-[1-(1,1-difluoroprop-2-en-1-yl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]isonicotinonitrile	HRMS m/z (M+H) 327.1046 found, 327.1052 required.
1-205		tert-butyl 4-[3-methyl-5-(2-methylphenyl)-2-oxo-2,3-dihydro-1H-benzimidazol-1-yl]piperidine-1-carboxylate	LRMS m/z (M-56) 366.3 found, 366.5 required.

Cmp	Structure	Name	LRMS *m/z* (M+H)
1-206		2-[3-methyl-2-oxo-1-(1-pyrimidin-2-ylpiperidin-4-yl)-2,3-dihydro-1H-benzimidazol-5-yl]benzamide	LRMS m/z (M+H) 429.3 found, 429.5 required.

Scheme 2



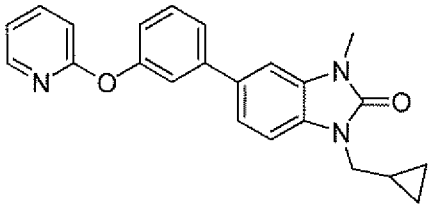
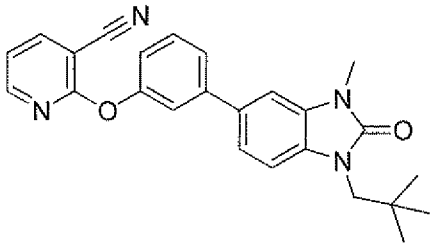
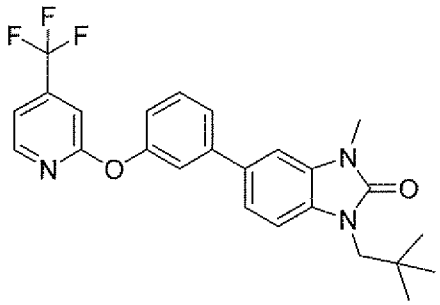
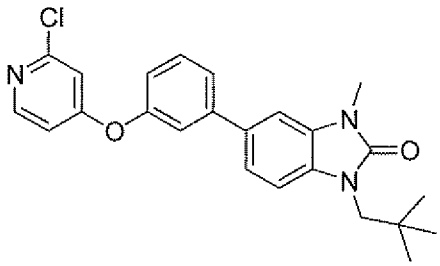
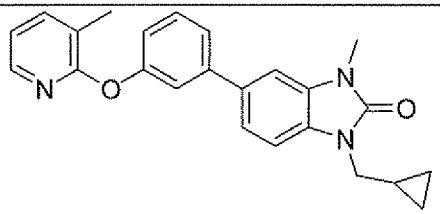
1-(2,2-dimethylpropyl)-5-(3-hydroxyphenyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one (1-179)

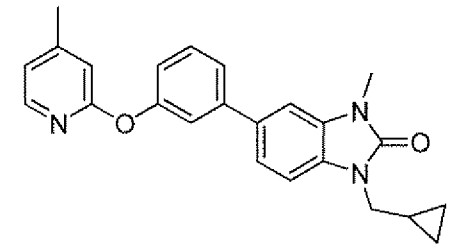
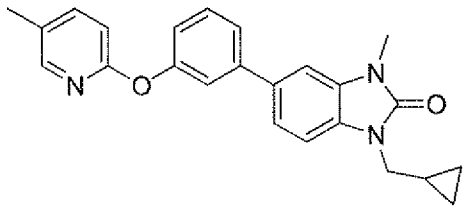
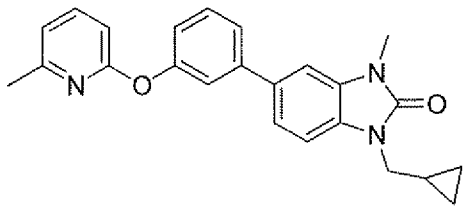
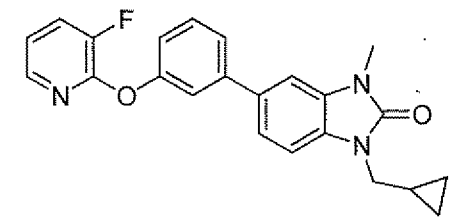
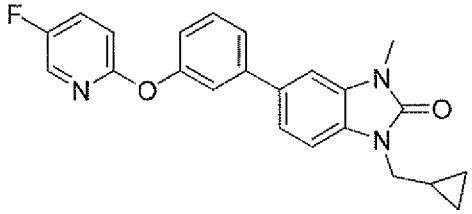
A solution of Cesium carbonate (3.66 g, 11.2 mmol, 3.0 eq) in Water (1 ml) was charged with a solution of 5-bromo-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one (**1-5**, 1.37 g, 3.74 mmol) dissolved in anhydrous THF (19 ml). 3-Hydroxyphenyl boronic acid was introduced and the solution was deoxygenated. The 1,1'-Bis(diphenylphosphino) ferrocene-palladium(II)dichloride dichloromethane complex (153 mg, 0.19 mmol, 0.05 eq) was introduced and the mixture was irradiated in a microwave at 125 deg C for 15 min. LC/MS analysis showed ~50% conversion, so more of each reagent was added and the reaction was irradiated again at 120 deg C for 30 min. The completed reaction was partitioned between EtOAc (2x25 ml) and saturated aqueous $NaHCO_3$ (25 ml), and the combined organic layers were dried over Na_2SO_4 and concentrated. The crude product was purified via flash column chromatography (SiO_2: 100% Hex to 60:40 EtOAc/ Hex), affording 1-(2,2-dimethylpropyl)-5-(3-hydroxyphenyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one **(1-179)** as a pink-orange solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34-7.29 (m, 2H), 7.21-7.15 (m, 2H), 7.11-7.06 (m, 2H), 6.81 (d, 1H, *J*=5.4 Hz), 3.68 (s, 2H), 3.47 (s, 3H), 1.07 (s, 9H). LRMS *m/z*: Calc'd for $C_{19}H_{22}N_2O_2$ (M+H) 311.4, found 311.1.

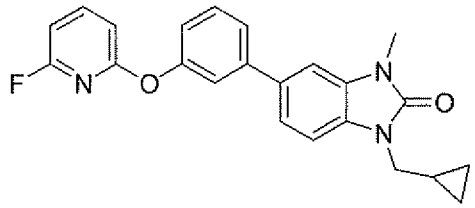
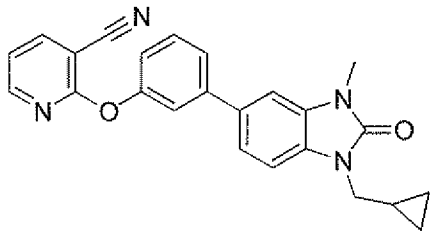
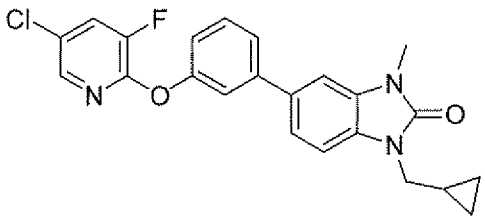
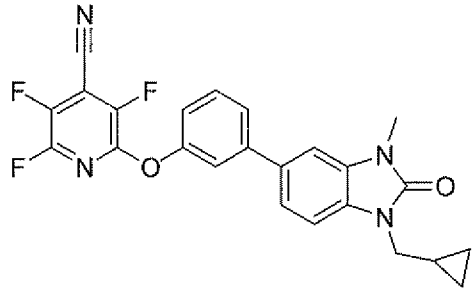
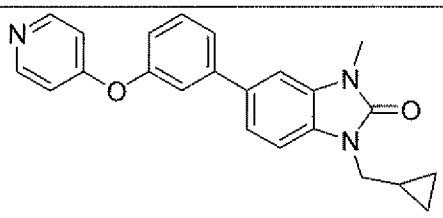
2-{3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}nicotinonitrile (2-1)

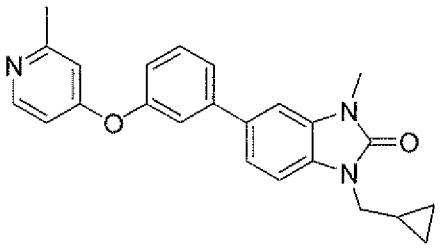
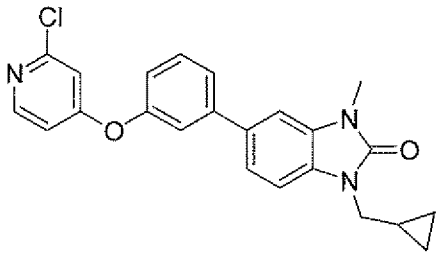
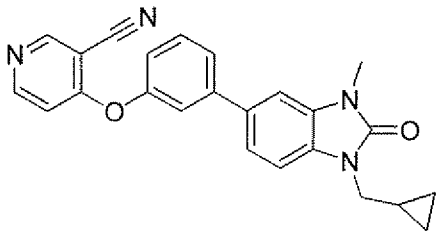
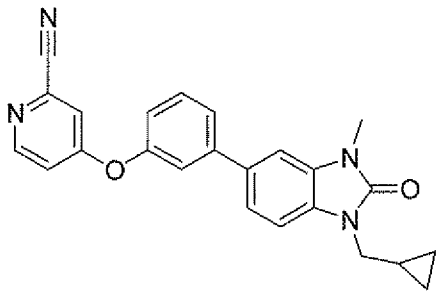
A solution of 1-(2,2-dimethylpropyl)-5-(3-hydroxyphenyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one (**1-179**, 23 mg, 0.07 mmol) in DMSO (2 ml) was charged with Potassium carbonate (20.5 mg, 0.15 mmol, 2.0 eq) and 2-Chloro-3-cyanopyridine (15.4 mg, 0.11 mmol, 1.5 eq). The mixture was irradiated in a microwave at 160 deg C for 20 min. The resulting dark mixture was purified via reverse-phase HPLC (Acetonitrile/ Water gradient with 0.1% TFA present), providing the title compound, 2-{3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy} nicotinonitrile **(2-1)**, as a tan solid-oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, 1H, *J*=3.3 Hz), 8.03 (d, 1H, *J*=5.9 Hz), 7.51-7.50 (m, 2H), 7.42 (s, 1H), 7.32 (d, 1H, *J*=8.2 Hz), 7.20-7.17 (m, 2H), 7.13-7.09 (m, 2H), 3.70 (s, 2H), 3.49 (s, 3H), 1.06 (s, 9H). LRMS *m/z*: Calc'd for $C_{25}H_{24}N_4O_2$ (M+H) 413.4, found 413.2.

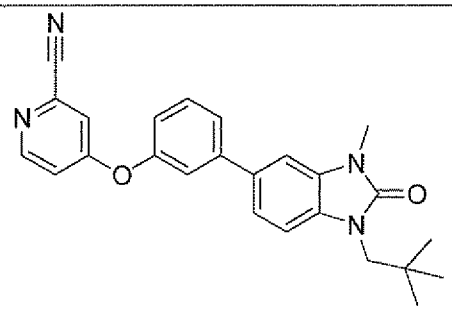
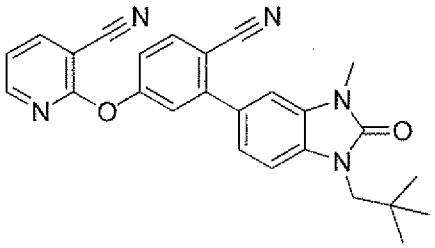
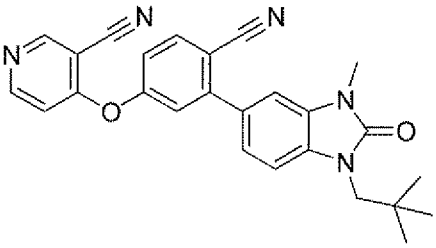
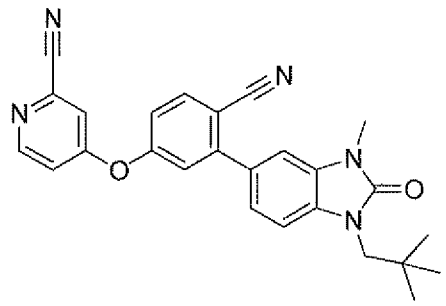
Table 1 for Scheme 2

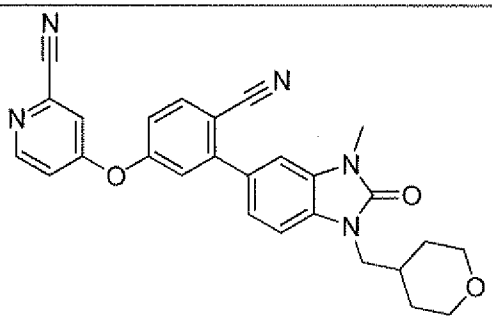
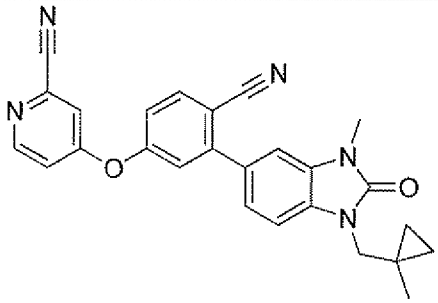
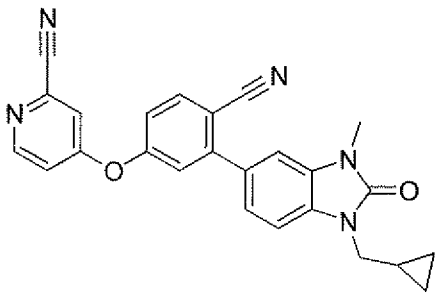
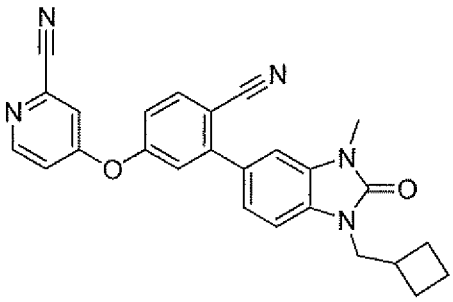
Cmp	Structure	Name	LRMS *m/z* (M+H)
2-2		1-(cyclopropylmethyl)-3-methyl-5-[3-(pyridin-2-yloxy)phenyl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS *m/z* (M+H) 372.2 found, 372.4 required.
2-3		2-{3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}nicotinonitrile	LRMS *m/z* (M+H) 413.2 found, 413.5 required.
2-4		1-(2,2-dimethylpropyl)-3-methyl-5-(3-{[4-(trifluoromethyl)pyridin-2-yl]oxy}phenyl)-1,3-dihydro-2H-benzimidazol-2-one	LRMS *m/z* (M+H) 456.3 found, 456.5 required.
2-5		5-{3-[(2-chloropyridin-4-yl)oxy]phenyl}-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS *m/z* (M+H) 422.2 found, 422.9 required.
2-6		1-(cyclopropylmethyl)-3-methyl-5-{3-[(3-methylpyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-benzimidazol-2-one	LRMS *m/z* (M+H) 386.2 found, 386.5 required.

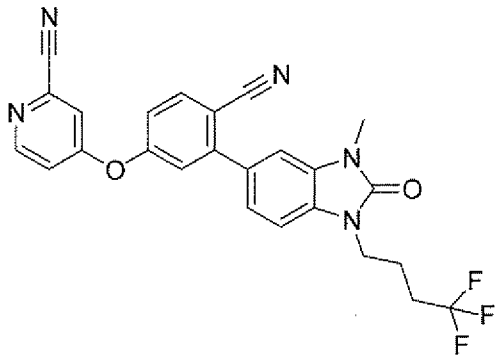
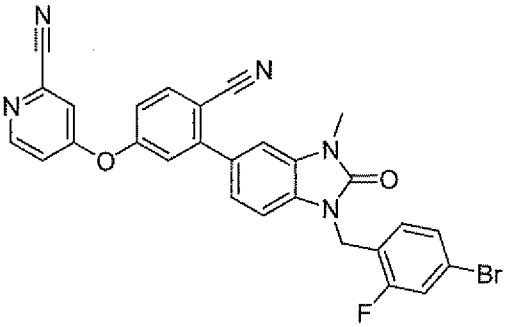
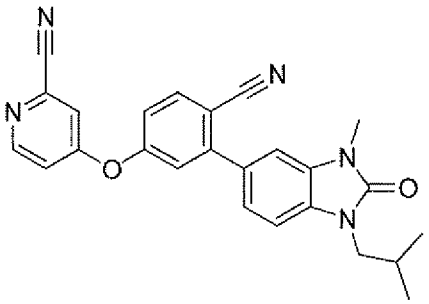
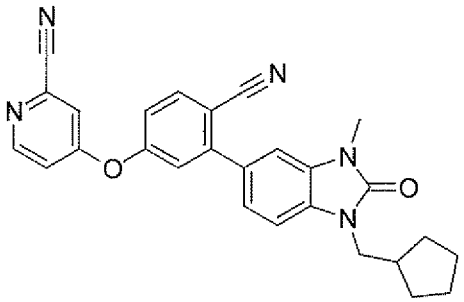
Cmp	Structure	Name	LRMS *m/z* (M+H)
2-7		1-(cyclopropylmethyl)-3-methyl-5-{3-[(4-methylpyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 386.2 found, 386.5 required.
2-8		1-(cyclopropylmethyl)-3-methyl-5-{3-[(5-methylpyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 386.2 found, 386.5 required.
2-9		1-(cyclopropylmethyl)-3-methyl-5-{3-[(6-methylpyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 386.2 found, 386.5 required.
2-10		1-(cyclopropylmethyl)-5-{3-[(3-fluoropyridin-2-yl)oxy]phenyl}-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 390.2 found, 390.4 required.
2-11		1-(cyclopropylmethyl)-5-{3-[(5-fluoropyridin-2-yl)oxy]phenyl}-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 390.1 found, 390.4 required.

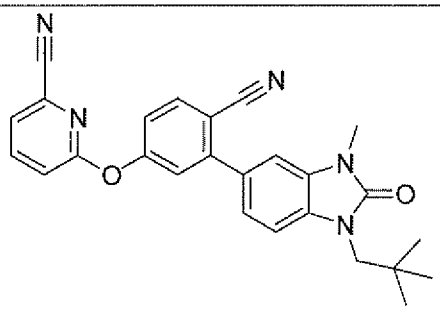
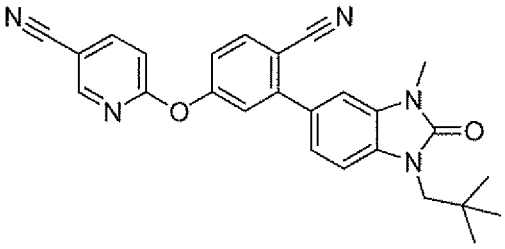
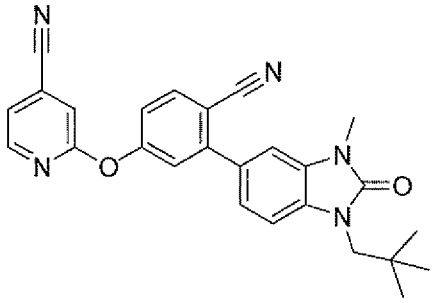
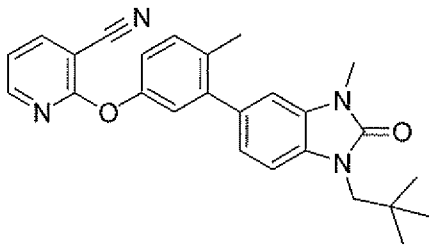
Cmp	Structure	Name	LRMS *m/z* (M+H)
2-12		1-(cyclopropylmethyl)-5-{3-[(6-fluoropyridin-2-yl)oxy]phenyl}-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 390.1 found, 390.4 required.
2-13		2-{3-[1-(cyclopropylmethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}nicotinonitrile	LRMS m/z (M+H) 397.2 found, 397.5 required.
2-14		5-{3-[(5-chloro-3-fluoropyridin-2-yl)oxy]phenyl}-1-(cyclopropylmethyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 424.1 found, 424.9 required.
2-15		2-{3-[1-(cyclopropylmethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}-3,5,6-trifluoroisonicotinonitrile	LRMS m/z (M+H) 451.1 found, 451.4 required.
2-16		1-(cyclopropylmethyl)-3-methyl-5-[3-(pyridin-4-yloxy)phenyl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 371.2 found, 372.4 required.

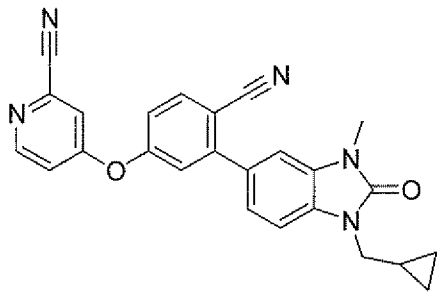
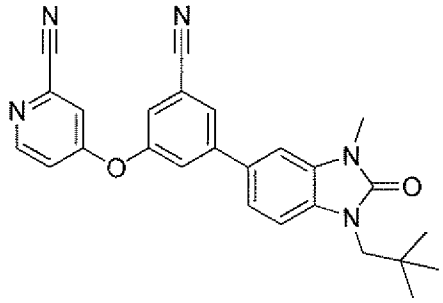
Cmp	Structure	Name	LRMS *m/z* (M+H)
2-17		1-(cyclopropylmethyl)-3-methyl-5-{3-[(2-methylpyridin-4-yl)oxy]phenyl}-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 386.2 found, 386.5 required.
2-18		5-{3-[(2-chloropyridin-4-yl)oxy]phenyl}-1-(cyclopropylmethyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 406.1 found, 406.5 required.
2-19		4-{3-[1-(cyclopropylmethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}nicotinonitrile	LRMS m/z (M+H) 397.2 found, 397.5 required.
2-20		4-{3-[1-(cyclopropylmethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}pyridine-2-carbonitrile	LRMS m/z (M+H) 397.1 found, 397.5 required.

Cmp	Structure	Name	LRMS *m/z* (M+H)
2-21		4-{3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}pyridine-2-carbonitrile	LRMS m/z (M+H) 413.2 found, 413.5 required.
2-22		2-{4-cyano-3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}nicotinonitrile	LRMS m/z (M+H) 438.1 found, 438.5 required.
2-23		4-{4-cyano-3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}nicotinonitrile	LRMS m/z (M+H) 438.1 found, 438.5 required.
2-24		4-{4-cyano-3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}pyridine-2-carbonitrile	LRMS m/z (M+H) 438.1 found, 438.5 required.

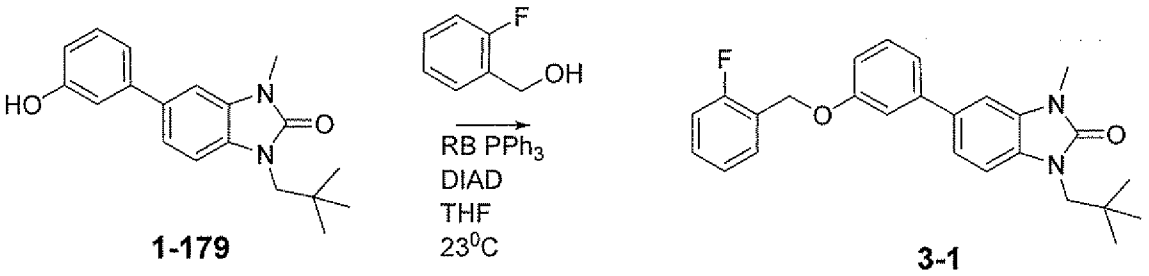
Cmp	Structure	Name	LRMS *m/z* (M+H)
2-25		4-{4-cyano-3-[3-methyl-2-oxo-1-(tetrahydro-2H-pyran-4-ylmethyl)-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}pyridine-2-carbonitrile	LRMS m/z (M+H) 466.2 found, 466.5 required.
2-26		4-(4-cyano-3-{3-methyl-1-[(1-methylcyclopropyl)methyl]-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl}phenoxy)pyridine-2-carbonitrile	LRMS m/z (M+H) 436.2 found, 436.5 required.
2-27		4-{4-cyano-3-[1-(cyclopropylmethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}pyridine-2-carbonitrile	LRMS m/z (M+H) 422.1 found, 422.5 required.
2-28		4-{4-cyano-3-[1-(cyclobutylmethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}pyridine-2-carbonitrile	LRMS m/z (M+H) 436.2 found, 436.5 required.

Cmp	Structure	Name	LRMS *m/z* (M+H)
2-29		4-{4-cyano-3-[3-methyl-2-oxo-1-(4,4,4-trifluorobutyl)-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}pyridine-2-carbonitrile	LRMS m/z (M+H) 478.1 found, 478.5 required.
2-30		4-{3-[1-(4-bromo-2-fluorobenzyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-4-cyanophenoxy}pyridine-2-carbonitrile	LRMS m/z (M+H) 555.1 found, 555.4 required.
2-31		4-[4-cyano-3-(1-isobutyl-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl)phenoxy]pyridine-2-carbonitrile	LRMS m/z (M+H) 424.2 found, 424.5 required.
2-32		4-{4-cyano-3-[1-(cyclopentylmethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}pyridine-2-carbonitrile	LRMS m/z (M+H) 450.2 found, 450.5 required.

Cmp	Structure	Name	LRMS *m/z* (M+H)
2-33		6-{4-cyano-3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}pyridine-2-carbonitrile	LRMS m/z (M+H) 438.1 found, 438.5 required.
2-34		6-{4-cyano-3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}nicotinonitrile	LRMS m/z (M+H) 438.1 found, 438.5 required.
2-35		2-{4-cyano-3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}isonicotinonitrile	LRMS m/z (M+H) 438.1 found, 438.5 required.
2-36		2-{3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-4-methylphenoxy}nicotinonitrile	LRMS m/z (M+H) 427.1 found, 427.5 required.

Cmp	Structure	Name	LRMS *m/z* (M+H)
2-37		4-{4-cyano-3-[1-(cyclopropylmethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}pyridine-2-carbonitrile	LRMS m/z (M+H) 422.0 found, 422.5 required.
2-38		4-{3-cyano-5-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}pyridine-2-carbonitrile	LRMS m/z (M+H) 438.2 found, 438.5 required.

Scheme 3

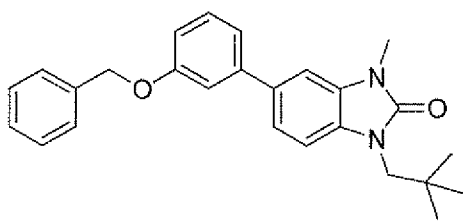


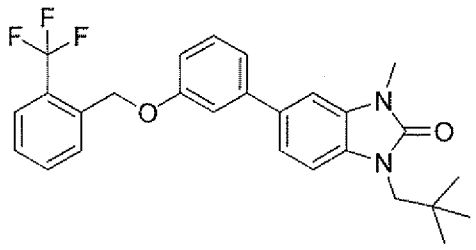
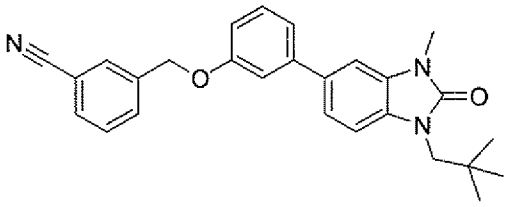
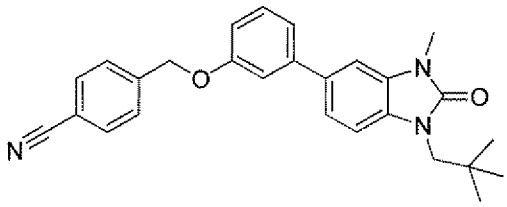
1-179 **3-1**

1-(2,2-dimethylpropyl)-5-{3-[(2-fluorobenzyl)oxy]phenyl}-3-methyl-1,3-dihydro-2H-benzimidazol-2-one (3-1)

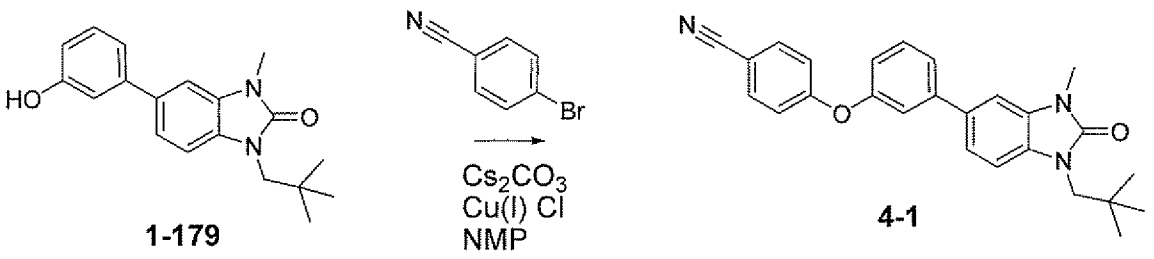
An orange solution of 1-(2,2-dimethylpropyl)-5-(3-hydroxyphenyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one (**1-179**, 70 mg, 0.23 mmol) in Dichloromethane (10 ml) was treated with polymer bound-Triphenylphosphine (177 mg, 0.68 mmol, 3.0 eq) and the 2-Fluorobenzyl alcohol (56.9 mg, 0.45 mmol, 2.0 eq). The mixture was charged, in portions, with Di-*tert*-butyl azodicarboxylate (104 mg, 0.45 mmol, 2.0 eq) and the resulting maroon-orange solution was stirred at 23 deg C for 1 h. The reaction mixture was filtered through a frit and the filtrate was purified via flash column chromatography (SiO_2: 100% Hex to 75:25% Hex:EtOAc) to afford the title compound, 1-(2,2-dimethylpropyl)-5-{3-[(2-fluorobenzyl)oxy]phenyl}-3-methyl-1,3-dihydro-2H-benzimidazol-2-one **(3-1)**, as an orange oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (t, 1H, *J*=7.0 Hz), 7.38-7.26 (m, 3H), 7.22-7.15 (m, 3H), 7.13-7.06 (m, 3H), 6.97 (d, 1H, *J*=7.1 Hz), 5.21 (s, 2H), 3.68 (s, 2H), 3.47 (s, 3H), 1.06 (s, 9H). LRMS *m/z*: Calc'd for $C_{26}H_{27}FN_2O_2$ (M+H) 419.2, found 419.3.

Table for Scheme 3

Cmp	Structure	Name	LRMS *m/z* (M+H)
3-2		5-[3-(benzyloxy)phenyl]-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS *m/z* (M+H) 401.3 found, 401.5 required.

Cmp	Structure	Name	LRMS *m/z* (M+H)
3-3		1-(2,2-dimethylpropyl)-3-methyl-5-(3-{[2-(trifluoromethyl)benzyl]oxy}phenyl)-1,3-dihydro-2H-benzimidazol-2-one	LRMS *m/z* (M+H) 469.3 found, 469.5 required.
3-4		3-({3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}methyl)benzonitrile	LRMS *m/z* (M+H) 426.3 found, 426.5 required.
3-5		4-({3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}methyl)benzonitrile	LRMS *m/z* (M+H) 426.3 found, 426.5 required.

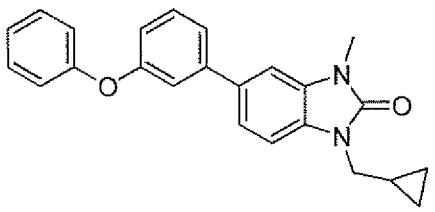
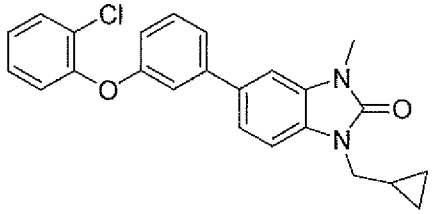
Scheme 4

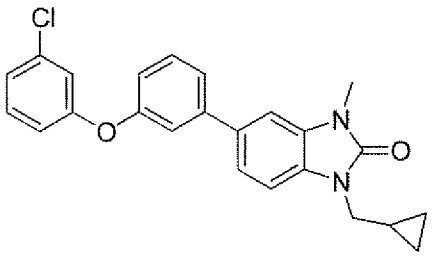
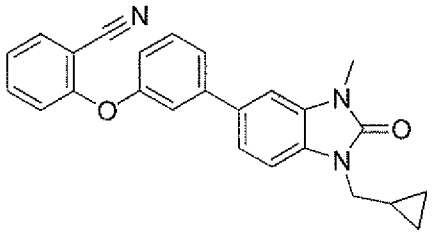
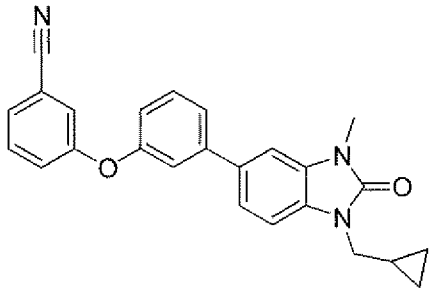
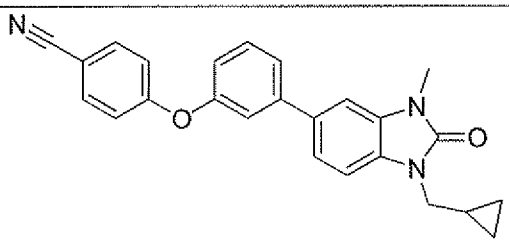
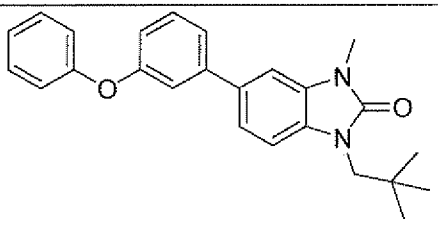


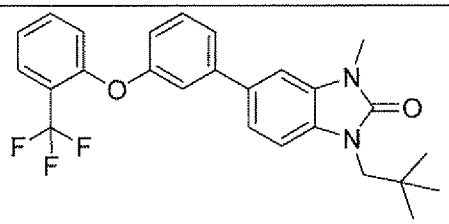
4-{3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}benzonitrile (4-1)

A solution of 1-(2,2-dimethylpropyl)-5-(3-hydroxyphenyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one (**1-179**, 70 mg, 0.23 mmol) and Cesium carbonate (73.5 mg, 0.23 mmol, 1.0 eq) in N-Methylpyrrolidine (1 ml) was stirred at 23 deg C for 45 min. 4-Bromobenzonitrile and Copper (I) Chloride were added and the resulting mixture was irradiated in a microwave at 150 deg C for 5 min. LC/MS analysis showed very little conversion, so the reaction was capped and heated in an oil bath at 175 deg C for 16 h. The resulting crude, dark mixture was run through a filter disk, then purified via reverse-phase HPLC (Acetonitrile/ Water gradient with 0.1% TFA present), providing 4-{3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}benzonitrile **(4-1)** as a tan solid-oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, 2H, *J*=8.7 Hz), 7.48-7.47 (m, 2H), 7.30-7.28 (m, 2H), 7.08 (s, 1H), 7.08-7.02 (m, 4H), 3.69 (s, 2H), 3.47 (s, 3H), 1.06 (s, 9H). LRMS *m/z*: Calc'd for $C_{26}H_{25}N_3O_2$ (M+H) 412.5, found 412.3.

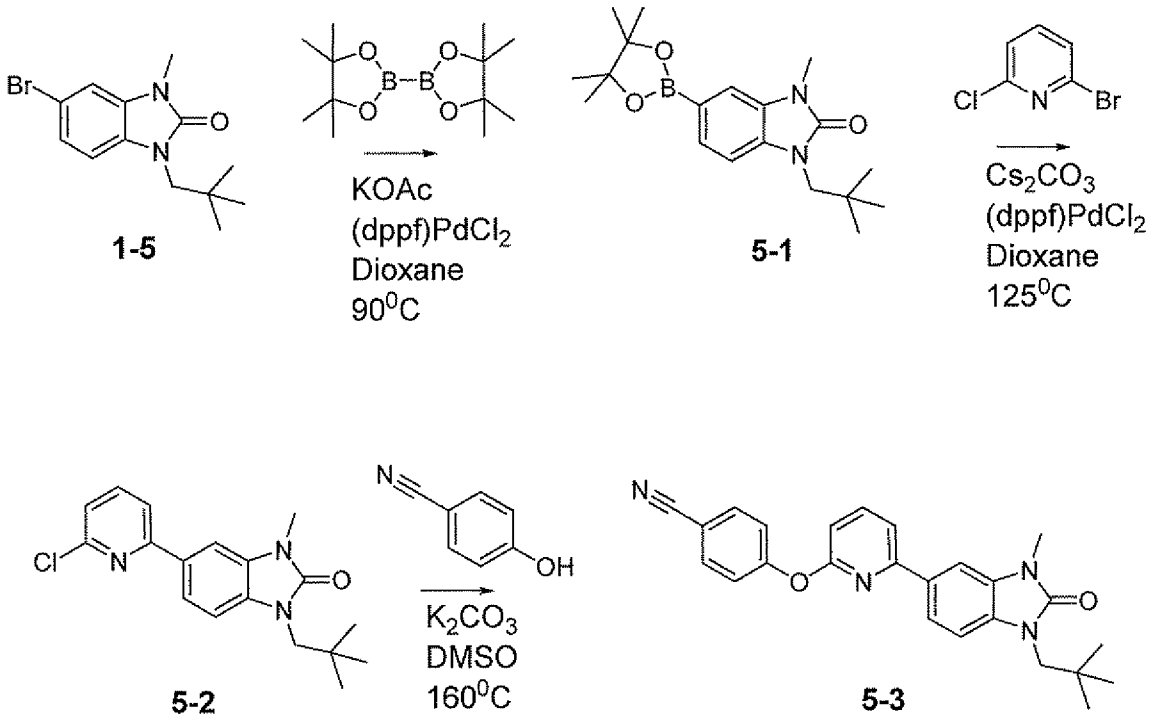
Table 1 for Scheme 4

Cmp	Structure	Name	LRMS *m/z* (M+H)
4-2		1-(cyclopropylmethyl)-3-methyl-5-(3-phenoxyphenyl)-1,3-dihydro-2H-benzimidazol-2-one	LRMS *m/z* (M+H) 371.2 found, 371.5 required.
4-3		5-[3-(2-chlorophenoxy)phenyl]-1-(cyclopropylmethyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS *m/z* (M+H) 405.1 found, 405.9 required.

Cmp	Structure	Name	LRMS *m/z* (M+H)
4-4		5-[3-(3-chlorophenoxy)phenyl]-1-(cyclopropylmethyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS *m/z* (M+H) 405.1 found, 405.9 required.
4-5		2-{3-[1-(cyclopropylmethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}benzonitrile	LRMS *m/z* (M+H) 396.2 found, 396.5 required.
4-6		3-{3-[1-(cyclopropylmethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}benzonitrile	LRMS *m/z* (M+H) 396.2 found, 396.5 required.
4-7		4-{3-[1-(cyclopropylmethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}benzonitrile	LRMS m/z (M+H) 396.1 found, 396.5 required.
4-8		1-(2,2-dimethylpropyl)-3-methyl-5-(3-phenoxyphenyl)-1,3-dihydro-2H-	LRMS m/z (M+H) 387.2 found, 387.5 required.

Cmp	Structure	Name	LRMS *m/z* (M+H)
		benzimidazol-2-one	
4-9		1-(2,2-dimethylpropyl)-3-methyl-5-{3-[2-(trifluoromethyl)phenoxy]phenyl}-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 455.3 found, 455.5 required.

Scheme 5



1-(2,2-dimethylpropyl)-3-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3-dihydro-2H-benzimidazol-2-one (5-1)

A solution of 5-bromo-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one (**1-5**, 300 mg, 1.01 mmol), Bis(pinacolato)diboron (308 mg, 1.21 mmol, 1.2 eq), and Potassium acetate (297 mg, 3.03 mmol, 3.0 eq) in Dioxane (10 ml) was deoxygenated, then treated with 1,1'-Bis(diphenylphosphino) ferrocene-palladium(II)dichloride dichloromethane complex (41.2 mg, 0.05 mmol, 0.05 eq). The resulting mixture was heated to 90 deg C and stirred for 15 h. The reaction was partially complete, so an additional amount of bis(pinacoloto)diboron (308 mg, 1.21 mmol, 1.2 eq) and Pd catalyst (41.2 mg, 0.05 mmol, 0.05 eq) was added and the reaction was stirred at 90 deg C for 16 h. The reaction was diluted with water (70 ml) and the resulting gray solid was filtered and washed with water (25 ml). The solid was then dissolved in EtOAc (70 ml) and the insoluble material was removed by filtration. The resulting orange filtrate was concentrated *in vacuo*, affording the title compound, 1-(2,2-dimethylpropyl)-3-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3-dihydro-2H-benzimidazol-2-one **(5-1)**, as a maroon-orange oil. LRMS *m/z*: Calc'd for $C_{19}H_{29}BN_2O_3$ (M+H) 345.3, found 345.2.

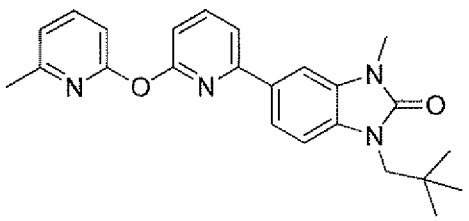
5-(6-chloropyridin-2-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one (5-2)

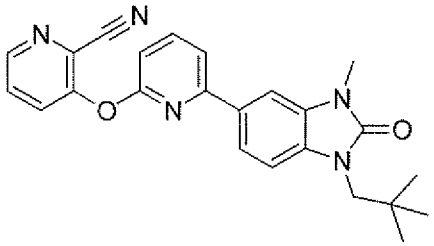
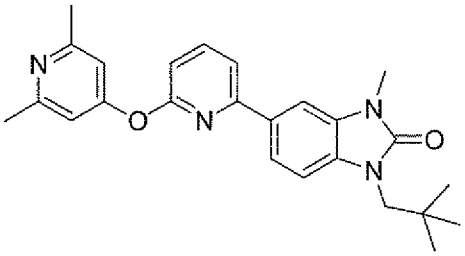
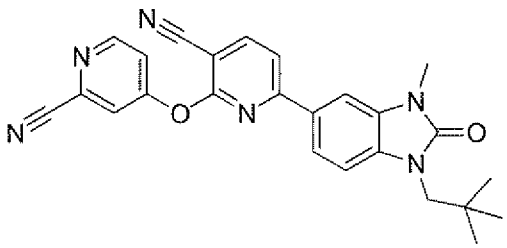
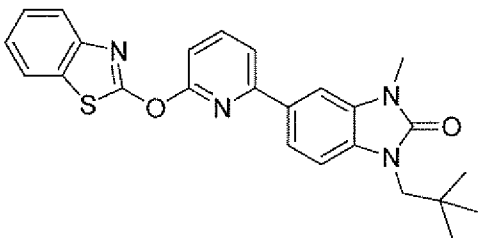
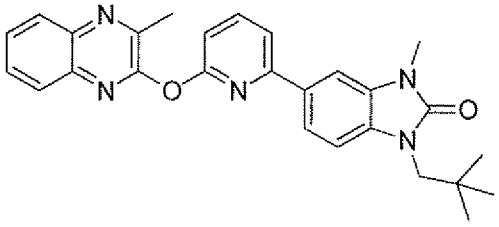
Cesium carbonate (852 mg, 2.61 mmol, 3.0 eq) was added to a solution of 1-(2,2-dimethylpropyl)-3-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3-dihydro-2H-benzimidazol-2-one (**5-1**, 300 mg, 0.87 mmol) dissolved in anhydrous Dioxane (5 ml). 2-Chloro-4-hydroxybenzonitrile (335 mg, 1.74 mmol, 2.0 eq) was introduced followed by 1,1'-Bis(diphenylphosphino) ferrocene-palladium(II)dichloride dichloromethane complex (35.6 mg, 0.04 mmol, 0.05 eq). The reaction mixture was irradiated at 125 deg C for 15 min. The reaction not complete, so more 2-Chloro-4-hydroxybenzonitrile (335 mg, 1.74 mmol, 2.0 eq) and Pd catalyst (35.6 mg, 0.04 mmol, 0.05 eq) was added and the reaction was irradiated again at 150 deg C for 30 min. The reaction was partitioned between EtOAc (2x100 ml) and saturated aqueous $NaHCO_3$ (90 ml). The combined organic layers were dried over Na_2SO_4 and concentrated, and the crude product was purified via flash column chromatography (SiO_2: 100% Hex to 60:40 Hex/ EtOAc), providing 5-(6-chloropyridin-2-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one **(5-2)** as a yellow. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70-7.63 (m, 4H), 7.22 (d, 2H, *J*=6.8 Hz), 7.07 (d, 1H, *J*=8.3 Hz), 3.69 (s, 2H), 3.50 (s, 3H), 1.05 (s, 9H). LRMS *m/z*: Calc'd for $C_{18}H_{20}ClN_3O$ (M+H) 330.8, found 330.1.

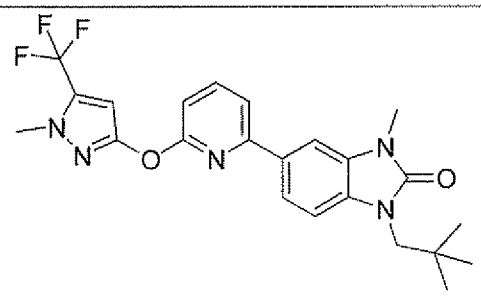
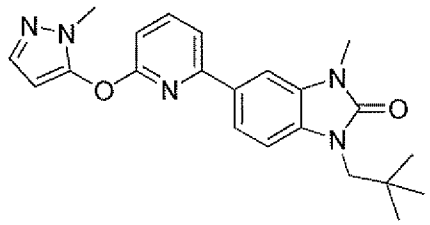
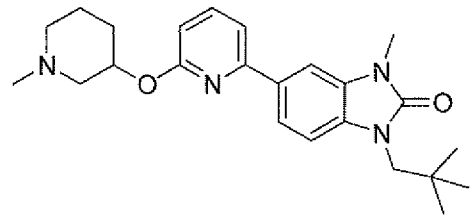
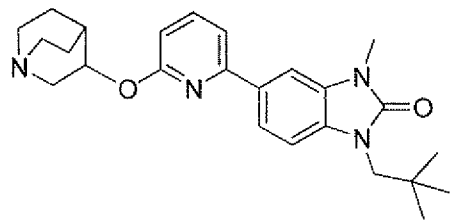
4-({6-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]pyridin-2-yl}oxy)benzonitrile (5-3)

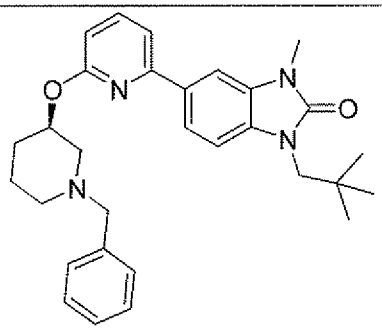
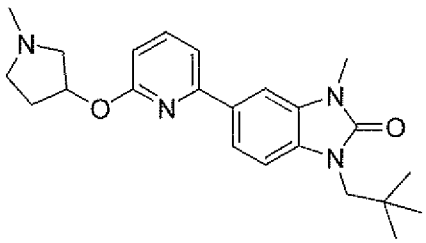
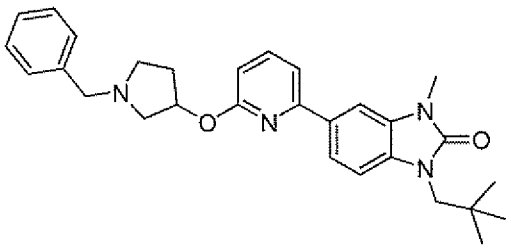
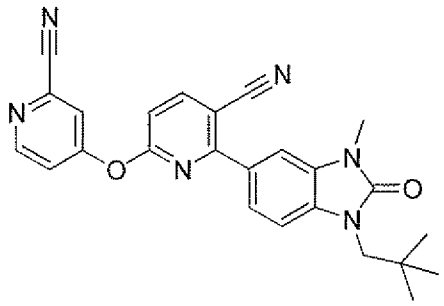
A solution of 5-(6-chloropyridin-2-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one (**5-2**, 55 mg, 0.17 mmol) in DMSO (1 ml), was charged with Potassium carbonate (34.6 mg, 0.25 mmol, 1.5 eq) and 4-Cyanophenol (39.7 mg, 0.33 mmol, 2.0 eq), then irradiated in a microwave at 160 deg C for 20 min. A second addition of Potassium carbonate (34.6 mg, 0.25 mmol, 1.5 eq) and 4-Cyanophenol (39.7 mg, 0.33 mmol, 2.0 eq) was necessary, then the reaction was irradiated again at 160 deg C for 20 min. The crude, dark mixture was filtered through a fritted disk, then purified via reverse-phase HPLC (Acetonitrile/ Water gradient with 0.1% TFA present) to afford the title compound, 4-({6-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]pyridin-2-yl}oxy)benzonitrile **(5-3)**, as an orange oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (t, 1H, *J*= Hz), 7.71 (d, 2H, *J*=9.0 Hz), 7.62 (d, 1H, *J*=7.1 Hz), 7.55 (d, 1H, *J*=7.3 Hz), 7.51 (s, 1H), 7.34-7.31 (m, 2H), 7.06-7.04 (d, 2H, 8.3 Hz), 6.87 (d, 1H, *J*=8.1 Hz), 3.68 (s, 2H), 3.44 (s, 3H), 1.04 (s, 9H). LRMS *m/z*: Calc'd for $C_{25}H_{25}N_4O_2$ (M+H) 414.2, found 414.3.

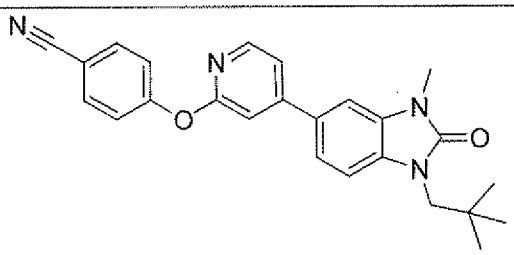
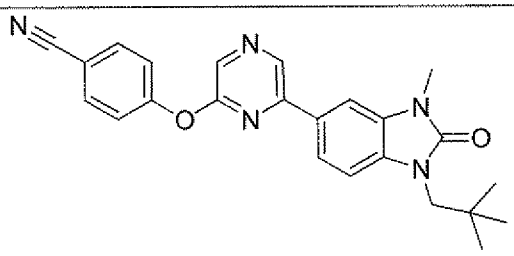
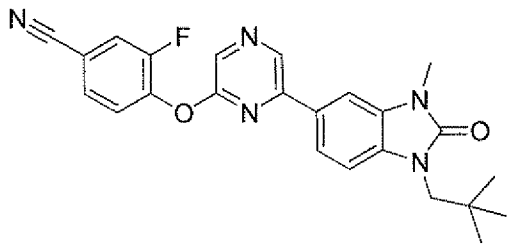
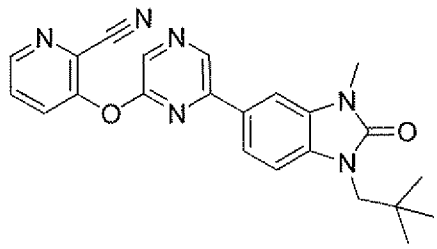
Table 1 for Scheme 5

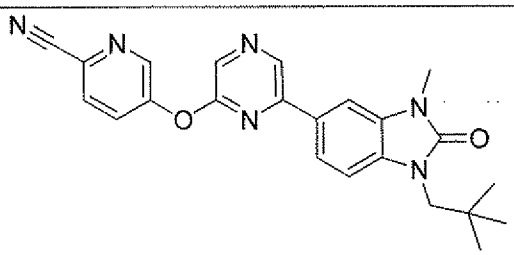
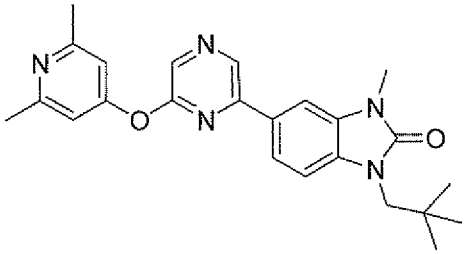
Cmp	Structure	Name	LRMS *m/z* (M+H)
5-4		1-(2,2-dimethylpropyl)-3-methyl-5-{6-[(6-methylpyridin-2-yl)oxy]pyridin-2-yl}-1,3-dihydro-2H-benzimidazol-2-one	LRMS *m/z* (M+H) 403.2 found, 403.5 required.
5-5		3-({6-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-	LRMS *m/z* (M+H) 414.2 found, 414.5 required.

Cmp	Structure	Name	LRMS *m/z* (M+H)
		yl]pyridin-2-yl}oxy)pyridine-2-carbonitrile	
5-6		1-(2,2-dimethylpropyl)-5-{6-[(2,6-dimethylpyridin-4-yl)oxy]pyridin-2-yl}-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS *m/z* (M+H) 417.2 found, 417.5 required.
5-7		4-({3-cyano-6-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]pyridin-2-yl}oxy)pyridine-2-carbonitrile	LRMS *m/z* (M+H) 439.1 found, 439.5 required.
5-8		5-[6-(1,3-benzothiazol-2-yloxy)pyridin-2-yl]-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 445.1 found, 445.6 required.
5-9		1-(2,2-dimethylpropyl)-3-methyl-5-{6-[(3-methylquinoxalin-2-yl)oxy]pyridin-2-yl}-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 454.2 found, 454.5 required.

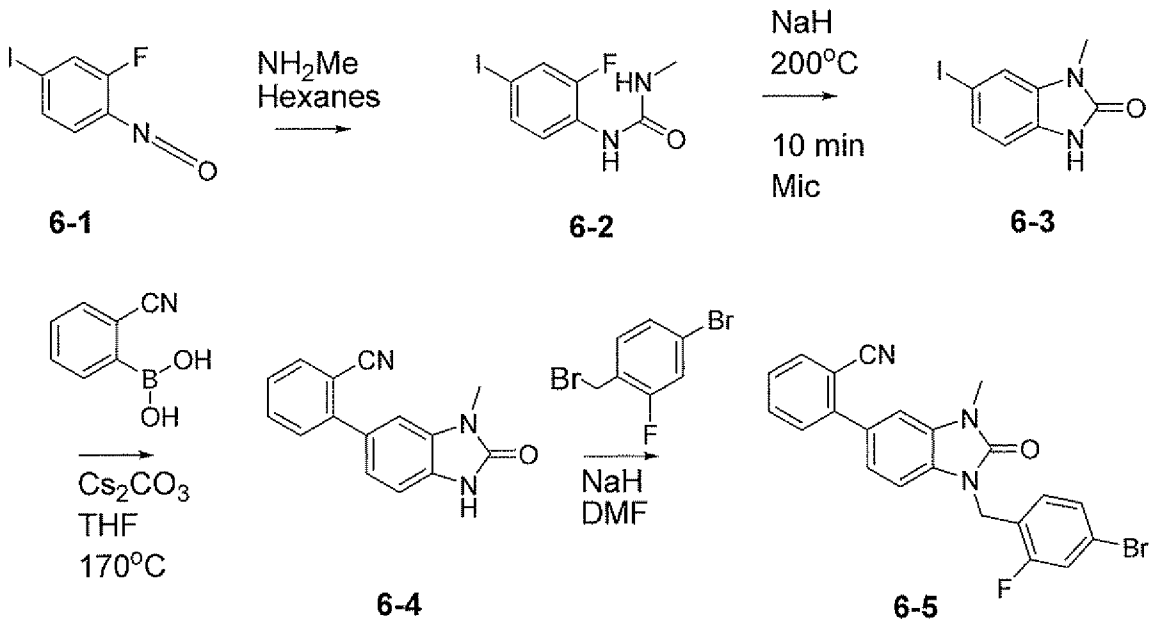
Cmp	Structure	Name	LRMS *m/z* (M+H)
5-10		1-(2,2-dimethylpropyl)-3-methyl-5-(6-{[1-methyl-5-(trifluoromethyl)-1H-pyrazol-3-yl]oxy}pyridin-2-yl)-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 460.1 found, 460.5 required.
5-11		1-(2,2-dimethylpropyl)-3-methyl-5-{6-[(1-methyl-1H-pyrazol-5-yl)oxy]pyridin-2-yl}-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 392.1 found, 392.5 required.
5-12		1-(2,2-dimethylpropyl)-3-methyl-5-{6-[(1-methylpiperidin-3-yl)oxy]pyridin-2-yl}-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 409.1 found, 409.5 required.
5-13		5-[6-(1-azabicyclo[2.2.2]oct-3-yloxy)pyridin-2-yl]-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 421.2 found, 421.6 required.
5-14		5-(6-{[(3R)-1-benzylpiperidin-3-yl]oxy}pyridin-2-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-	LRMS m/z (M+H) 485.2 found, 485.6 required.

Cmp	Structure	Name	LRMS *m/z* (M+H)
		2H-benzimidazol-2-one	
5-15		1-(2,2-dimethylpropyl)-3-methyl-5-{6-[(1-methylpyrrolidin-3-yl)oxy]pyridin-2-yl}-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 395.1 found, 395.5 required.
5-16		5-{6-[(1-benzylpyrrolidin-3-yl)oxy]pyridin-2-yl}-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 471.2 found, 471.6 required.
5-17		4-({5-cyano-6-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]pyridin-2-yl}oxy)pyridine-2-carbonitrile	LRMS m/z (M+H) 439.1 found, 439.5 required.
5-18		4-({4-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-	LRMS m/z (M+H) 413.2 found, 413.5 required.

Cmp	Structure	Name	LRMS *m/z* (M+H)
		yl]pyridin-2-yl}oxy)benzonitrile	
5-19		4-({6-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]pyrazin-2-yl}oxy)benzonitrile	LRMS m/z (M+H) 414.2 found, 414.5 required.
5-20		4-({6-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]pyrazin-2-yl}oxy)-3-fluorobenzonitrile	LRMS m/z (M+H) 432.2 found, 432.5 required.
5-21		3-({6-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]pyrazin-2-yl}oxy)pyridine-2-carbonitrile	LRMS m/z (M+H) 415.2 found, 415.5 required.
5-22		5-({6-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-	LRMS m/z (M+H) 415.2 found, 415.5 required.

Cmp	Structure	Name	LRMS *m/z* (M+H)
		benzimidazol-5-yl]pyrazin-2-yl}oxy)pyridine-2-carbonitrile	
5-23		1-(2,2-dimethylpropyl)-5-{6-[(2,6-dimethylpyridin-4-yl)oxy]pyrazin-2-yl}-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 418.2 found, 418.5 required.

Scheme 6



N-(2-fluoro-4-iodophenyl)-N'-methylurea (6-2)

A solution of 4-Iodo-2-fluorophenyl isocyanate (**6-1**, 5.15 g, 19.6 mmol) in Hexanes (80 ml) was treated with a solution of Methylamine (2M in THF, 9.8 mL, 19.6 mmol,

1.0 eq). A white precipitate formed as the mixture stirred at 23 deg C for 30 min. The precipitate was collected via filtration and air dried, affording the title compound, N-(2-fluoro-4-iodophenyl)-N'-methylurea **(6-2)**, as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (t, 2H, *J*=8.6 Hz), 7.47-7.38 (m, 2H), 6.31 (bs, 1H), 4.58 (bs, 1H), 2.88 (d, 3H, *J*=4.9 Hz). LRMS *m/z*: Calc'd for $C_8H_8FIN_2O$ (M+H) 295.1, found 294.9.

6-iodo-1-methyl-1,3-dihydro-2H-benzimidazol-2-one (6-3)

A solution of N-(2-fluoro-4-iodophenyl)-N'-methylurea (**6-2**, 2.9 g, 9.86 mmol) in DMF (12 ml) were treated with Sodium Hydride (308 mg, 12.8 mmol, 1.3 eq). The reaction mixture was irradiated in a microwave at 200 deg C for 10 min. The starting material was consumed, so it was partitioned between EtOAc (2x75 ml) and water (85 ml), and the combined organic layers were dried over Na_2SO_4 and concentrated. The residual crude maroon oil was purified via flash column chromatography (SiO_2: 100% Hex to 50:50 Hex/EtOAc), which afforded the title compound, 6-iodo-1-methyl-1,3-dihydro-2H-benzimidazol-2-one **(6-3)**, as a tan solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.64 (bs, 1H), 7.39 (d, 1H, *J*=6.6 Hz), 7.30 (s, 1H), 6.87 (d, 1H, *J*=8.1 Hz), 3.39 (s, 3H). LRMS *m/z*: Calc'd for $C_8H_7IN_2O$ (M+H) 275.1, found 274.9.

2-(3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl)benzonitrile (6-4)

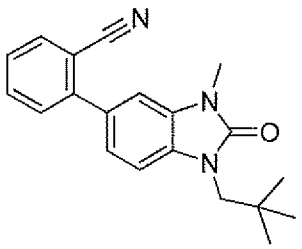
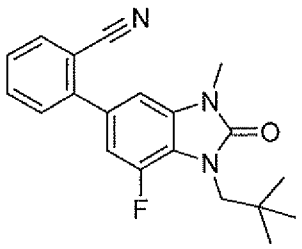
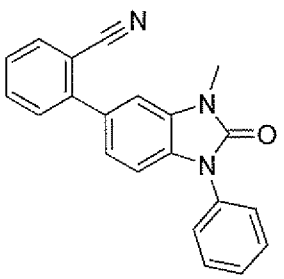
A solution of Cesium carbonate (1100 mg, 3.38 mmol, 5.0 eq) was treated with a solution of 6-iodo-1-methyl-1,3-dihydro-2H-benzimidazol-2-one (**6-3**, 185 mg, 0.68 mmol) and 2-Cyanophenylboronic acid (198 mg, 1.35 mmol, 2.0 eq). The 1,1'-Bis(diphenylphosphino)ferrocene-palladium(II)dichloride dichloromethane complex (27.6 mg, 0.03 mmol, 0.05 eq) was introduced and the mixture was irradiated in a microwave at 140 deg C for 15 min. The product was worked up by partitioning between EtOAc (2x85 ml) and saturated aqueous $NaHCO_3$ (95 ml), and the combined organic layers were dried over Na_2SO_4 and concentrated. Afforded 2-(3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl)benzonitrile **(6-4)**, as a maroon-orange solid.

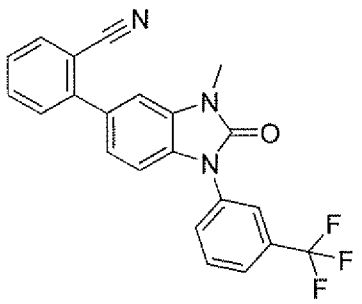
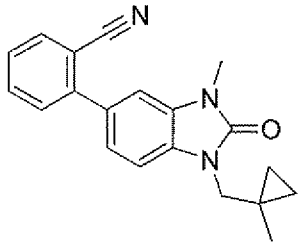
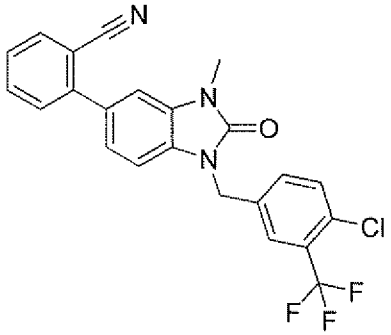
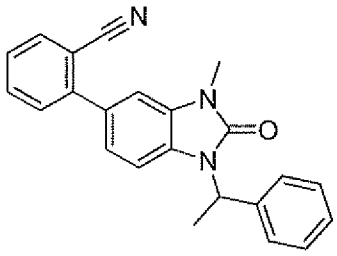
LRMS *m/z*: Calc'd for $C_{15}H_{11}N_3O$ (M+H) 250.3, found 250.0.

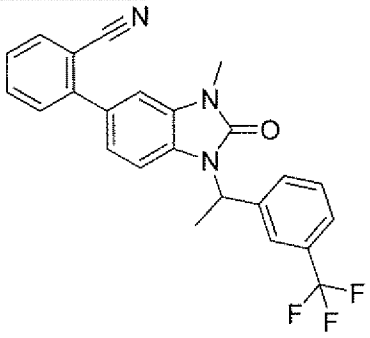
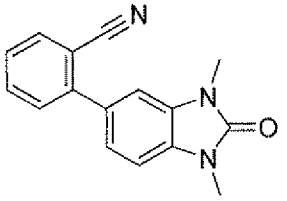
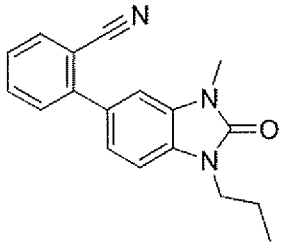
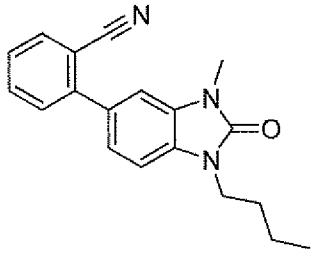
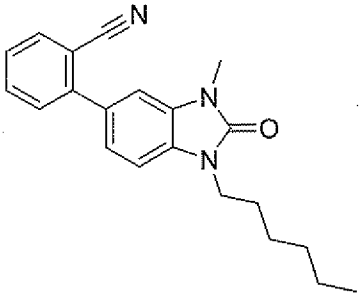
2-[1-(4-bromo-2-fluorobenzyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile (6-5)

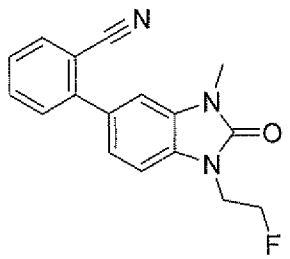
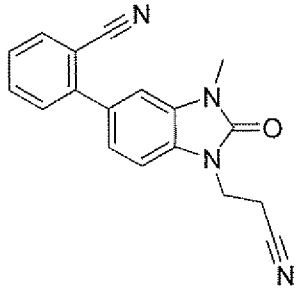
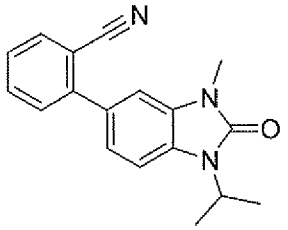
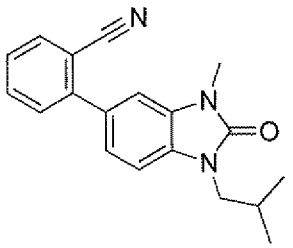
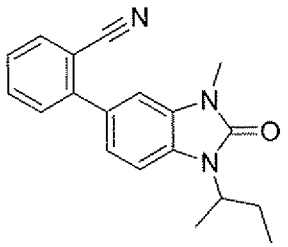
A solution of 2-(3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl)benzonitrile (**6-4**, 20 mg, 0.08 mmol) in anhydrous DMF (1 ml) was charged with Sodium Hydride (6.42 mg, 0.16 mmol, 2.0 eq) and 4-Bromo-2-fluorobenzyl bromide (42.5 mg, 0.16 mmol, 2.0 eq). The resulting dark mixture was irradiated in a microwave at 200 deg C for 15 min, then quenched with water, filtered and purified via reverse-phase HPLC (Acetonitrile/ Water gradient with 0.1% TFA present) to afford the title compound, 2-[1-(4-bromo-2-fluorobenzyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile **(6-5)**, as an orange-tan solid-oil. LRMS *m/z*: Calc'd for $C_{22}H_{15}BrFN_3O$ (M+H) 436.0, found 435.9.

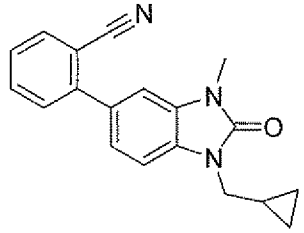
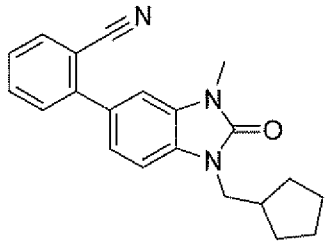
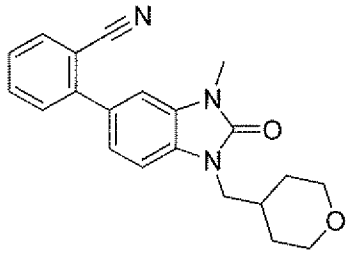
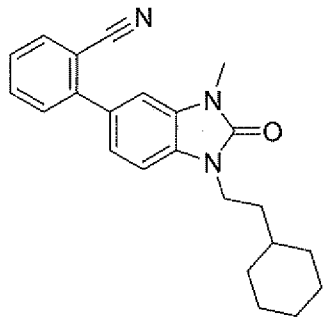
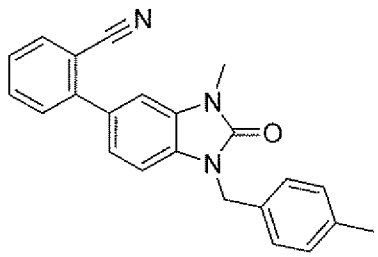
Table 1 for Scheme 6

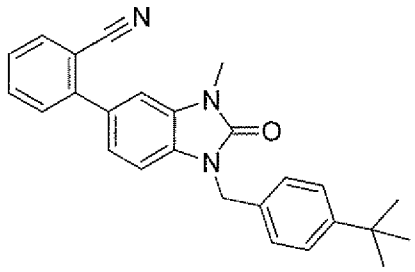
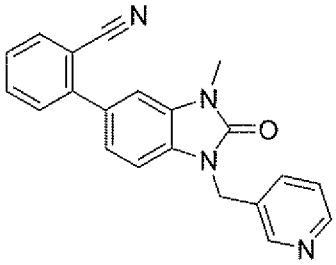
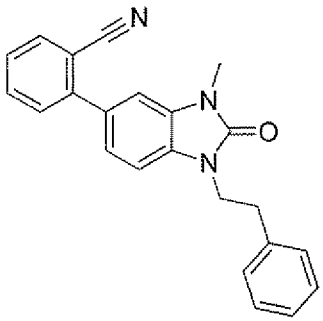
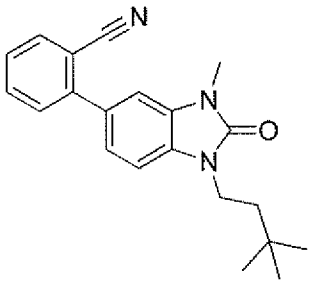
Cmp	Structure	Name	LRMS *m/z* (M+H)
6-6		2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile	LRMS *m/z* (M+H) 320.1 found, 320.4 required.
6-7		2-[1-(2,2-dimethylpropyl)-7-fluoro-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile	LRMS *m/z* (M+H) 338.0 found, 338.4 required.
6-8		2-(3-methyl-2-oxo-1-phenyl-2,3-dihydro-1H-benzimidazol-5-yl)benzonitrile	LRMS *m/z* (M+H) 326.0 found, 326.1 required.

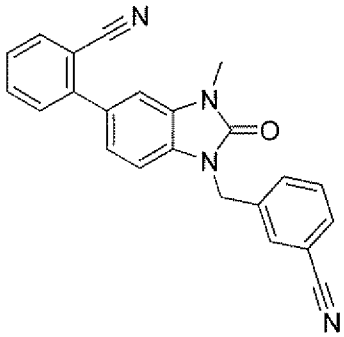
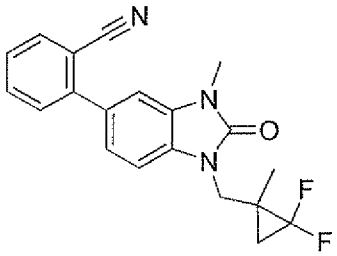
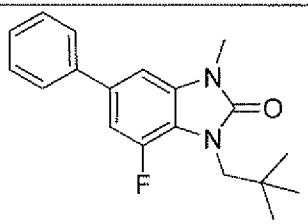
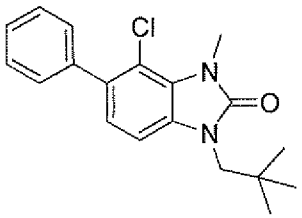
Cmp	Structure	Name	LRMS *m/z* (M+H)
6-9		2-{3-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-2,3-dihydro-1H-benzimidazol-5-yl}benzonitrile	LRMS *m/z* (M+H) 394.1 found, 394.1 required.
6-10		2-{3-methyl-1-[(1-methylcyclopropyl)methyl]-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl}benzonitrile	LRMS m/z (M+H) 318.0 found, 318.4 required.
6-11		2-{1-[4-chloro-3-(trifluoromethyl)benzyl]-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl}benzonitrile	LRMS m/z (M+H) 442.0 found, 442.8 required.
6-12		2-[3-methyl-2-oxo-1-(1-phenylethyl)-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile	LRMS m/z (M+H) 354.1 found, 354.4 required.
6-13		2-(3-methyl-2-oxo-1-{1-[3-(trifluoromethyl)phenyl]ethyl}-2,3-dihydro-1H-benzimidazol-5-	LRMS m/z (M+H) 422.1 found, 422.4 required.

Cmp	Structure	Name	LRMS *m/z* (M+H)
		yl)benzonitrile	
6-14		2-(1,3-dimethyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl)benzonitrile	LRMS m/z (M+H) 264.1 found, 264.3 required.
6-15		2-(3-methyl-2-oxo-1-propyl-2,3-dihydro-1H-benzimidazol-5-yl)benzonitrile	LRMS m/z (M+H) 292.1 found, 292.4 required.
6-16		2-(1-butyl-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl)benzonitrile	LRMS m/z (M+H) 306.1 found, 306.4 required.
6-17		2-(1-hexyl-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl)benzonitrile	LRMS m/z (M+H) 334.2 found, 334.4 required.

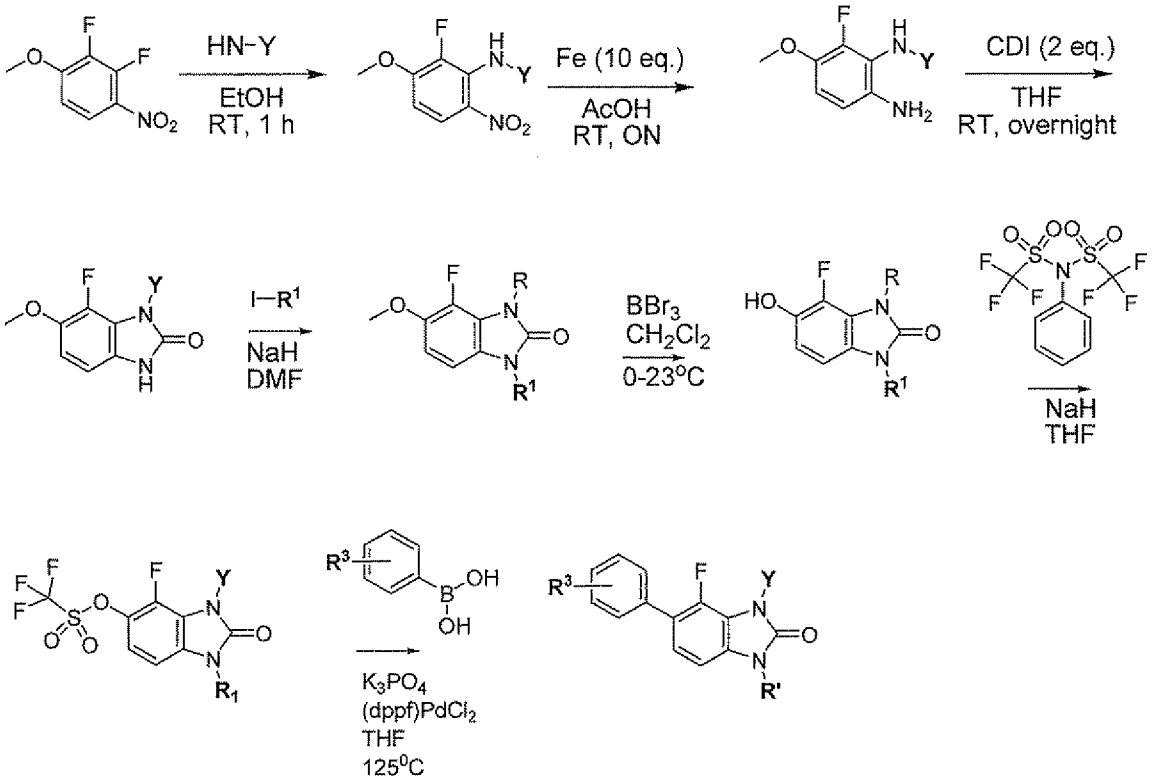
Cmp	Structure	Name	LRMS *m/z* (M+H)
6-18		2-[1-(2-fluoroethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile	LRMS m/z (M+H) 296.1 found, 296.4 required.
6-19		2-[1-(2-cyanoethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile	LRMS m/z (M+H) 303.2 found, 303.3 required.
6-20		2-(1-isopropyl-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl)benzonitrile	LRMS m/z (M+H) 292.1 found, 292.4 required.
6-21		2-(1-isobutyl-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl)benzonitrile	LRMS m/z (M+H) 306.2 found, 306.4 required.
6-22		2-(1-sec-butyl-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl)benzonitrile	LRMS m/z (M+H) 306.2 found, 306.4 required.

Cmp	Structure	Name	LRMS *m/z* (M+H)
6-23		2-[1-(cyclopropylmethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile	LRMS m/z (M+H) 304.1 found, 304.4 required.
6-24		2-[1-(cyclopentylmethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile	LRMS m/z (M+H) 332.2 found, 332.4 required.
6-25		2-[3-methyl-2-oxo-1-(tetrahydro-2H-pyran-4-ylmethyl)-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile	LRMS m/z (M+H) 348.1 found, 348.4 required.
6-26		2-[1-(2-cyclohexylethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile	LRMS m/z (M+H) 360.1 found, 360.5 required.
6-27		2-[3-methyl-1-(4-methylbenzyl)-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile	LRMS m/z (M+H) 354.1 found, 354.4 required.

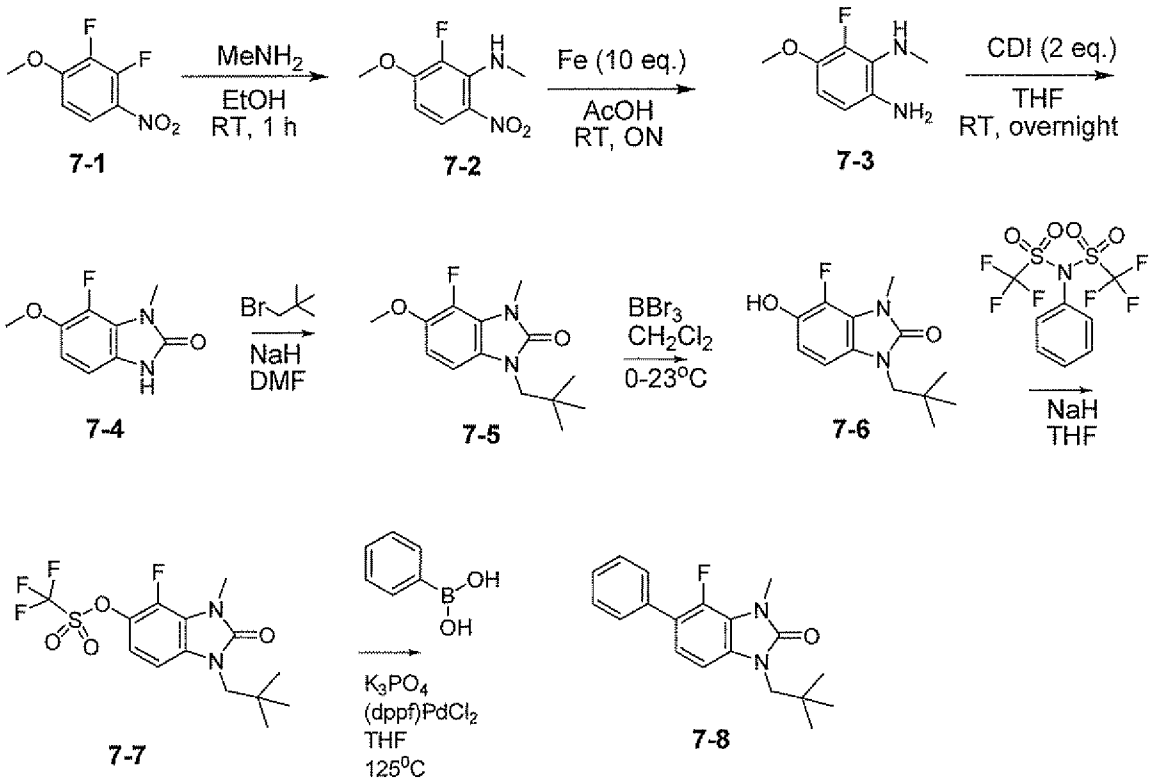
Cmp	Structure	Name	LRMS *m/z* (M+H)
6-28		2-[1-(4-tert-butylbenzyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile	LRMS m/z (M+H) 396.1 found, 396.5 required.
6-29		2-[3-methyl-2-oxo-1-(pyridin-3-ylmethyl)-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile	LRMS m/z (M+H) 341.0 found, 341.4 required.
6-30		2-[3-methyl-2-oxo-1-(2-phenylethyl)-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile	LRMS m/z (M+H) 354.1 found, 354.4 required.
6-31		2-[1-(3,3-dimethylbutyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile	LRMS m/z (M+H) 334.2 found, 334.4 required.
6-32		2-[1-(3-cyanobenzyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile	LRMS m/z (M+H) 365.1 found, 365.4 required.

Cmp	Structure	Name	LRMS *m/z* (M+H)
			
6-33		2-{1-[(2,2-difluoro-1-methylcyclopropyl)methyl]-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl}benzonitrile	LRMS m/z (M+H) 354.3 found, 354.4 required.
6-34		3-(2,2-dimethylpropyl)-4-fluoro-1-methyl-6-phenyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 313.0 found, 313.4 required.
6-35		4-chloro-1-(2,2-dimethylpropyl)-3-methyl-5-phenyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 329.0 found, 329.9 required.

REACTION SCHEME 7


HN-Y
EtOH
RT, 1 h
Fe (10 eq.)
AcOH
RT, ON
CDI (2 eq.)
THF
RT, overnight
I—R1
NaH
DMF
BBr3
CH2Cl2
0-23°C
NaH
THF
K3PO4
(dppf)PdCl2
THF
125°C

Scheme 7



2-fluoro-3-methoxy-N-methyl-6-nitroaniline (7-2)

A solution of 2,3-Difluoro-4-nitroanisole (**7-1**, 1.0 g, 5.29 mmol) in EtOH (20 ml) was treated with Methylamine (2M in THF, 3.17 ml, 6.35 mmol, 1.2 eq) and the resulting yellow solution was stirred at 23 deg C for 1 h. The reaction was complete by LC/MS, but allowed to stir at 23 deg C for an additional 17 h. The residual bright orange-yellow solution was concentrated *in vacuo*, then partitioned between EtOAc (2x80 ml) and water (90 ml). The combined organic layers were dried over Na_2SO_4 and concentrated, leaving the title compound, 2-fluoro-3-methoxy-N-methyl-6-nitroaniline **(7-2)**, as an orange solid with >90% purity. ^1H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, 1H, *J*=1.9 Hz), 7.84 (bs, 1H), 6.81-6.83 (m, 1H), 3.95 (s, 3H), 3.24 (m, 3H). LRMS *m/z*: Calc'd for $C_8H_9FN_2O_3$ (M+H) 201.2, found 200.9.

3-fluoro-4-methoxy-N^2-methylbenzene-1,2-diamine (7-3)

A solution of 2-fluoro-3-methoxy-N-methyl-6-nitroaniline (**7-2**, 1.04 g, 5.20 mmol) in Acetic acid (25 ml) was charged with Iron (powder). The resulting mixture was stirred

at 23 deg C for 22 h. The reduced material concentrated *in vacuo*, and the residual oil was taken up in Methylene Chloride and filtered through Celite. The filtrate was again concentrated *in vacuo*, leaving the title compound, 3-fluoro-4-methoxy-N^2-methylbenzene-1,2-diamine **(7-3)**, as a maroon oil with >80% purity. LRMS *m/z*: Calc'd for $C_8H_{11}FN_2O$ (M+H) 171.2, found 170.9.

7-fluoro-6-methoxy-1-methyl-1,3-dihydro-2H-benzimidazol-2-one (7-4)

3-fluoro-4-methoxy-N^2-methylbenzene-1,2-diamine (**7-3**, 1.09 g, 6.40 mmol) was dissolved in anhydrous THF (15 ml) and treated with CDI (1.25 g, 7.69 mmol, 1.2 eq). The resulting orange solution was stirred at reflux for 6 h, then cooled to 23 deg C. The remaining dark reaction mixture was partitioned between EtOAc (2x40 ml) and water (45 ml). The combined organic layers were dried over Na_2SO_4 and concentrated. The crude mixture was purified via flash column chromatography (SiO_2: 100% Hex to 50:50 Hex:EtOAc), affording the title compound, 7-fluoro-6-methoxy-1-methyl-1,3-dihydro-2H-benzimidazol-2-one **(7-4)**, as a maroon oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 (s, 1H), 6.68-6.74 (m, 2H), 3.89 (s, 3H), 3.60 (s, 3H). LRMS *m/z*: Calc'd for $C_9H_9FN_2O_2$ (M+H) 197.2, found 196.9.

1-(2,2-dimethylpropyl)-4-fluoro-5-methoxy-3-methyl-1,3-dihydro-2H-benzimidazol-2-one (7-5)

A solution of 7-fluoro-6-methoxy-1-methyl-1,3-dihydro-2H-benzimidazol-2-one (**7-4**, 250 mg, 1.27 mmol) in anhydrous DMF (1.5 ml) was treated with NaH and 1-Bromo-2,2-dimethylpropane. The reaction was then irradiated in a microwave at 175 deg C for 25 min. The reaction was partitioned between EtOAc (2x60 ml) and water (75 ml). The combined organic layers were dried over Na_2SO_4 and concentrated, affording the title compound, 1-(2,2-dimethylpropyl)-4-fluoro-5-methoxy-3-methyl-1,3-dihydro-2H-benzimidazol-2-one **(7-5)**, as an orange oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.65-6.70 (m, 2H), 3.88 (s, 3H), 3.60 (m, 5H), 1.03 (s, 9H). LRMS *m/z*: Calc'd for $C_{14}H_{19}FN_2O_2$ (M+H) 267.3, found 267.0.

1-(2,2-dimethylpropyl)-4-fluoro-5-hydroxy-3-methyl-1,3-dihydro-2H-benzimidazol-2-one (7-6)

A solution of 1-(2,2-dimethylpropyl)-4-fluoro-5-methoxy-3-methyl-1,3-dihydro-2H-benzimidazol-2-one (**7-5**, 193 mg, 0.73 mmol) in anhydrous Dichloromethane (10 ml) was cooled to -78 deg C (Acetone/ dry ice) and treated with Boron tribromide (1M in DCM, 1.45 ml, 1.45 mmol, 2 eq). The resulting mixture was allowed to slowly warm to 23 deg C over 15 h. The reaction was only ~75% complete by LC/MS, so it was treated with more BBr_3 (360 ml, 0.36 mmol, 0.5 eq). The reaction was stirred at 23 deg C for 1 h, then was carefully quenched by pouring directly into a solution of saturated aqueous $NaHCO_3$ cooled to 0 deg C. The aqueous mixture was extracted with Methylene Chloride (2x200 ml), and the combined organic layers were dried over Na_2SO_4 and concentrated, thereby providing the title compound, 1-(2,2-dimethylpropyl)-4-fluoro-5-hydroxy-3-methyl-1,3-dihydro-2H-benzimidazol-2-one **(7-6)**, as a green-tan solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.65-6.73 (m, 2H), 3.61 (m, 5H), 1.02 (s, 9H). LRMS *m/z*: Calc'd for $C_{13}H_{17}FN_2O_2$ (M+H) 253.3, found 253.0.

1-(2,2-dimethylpropyl)-4-fluoro-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl trifluoromethanesulfonate (7-7)

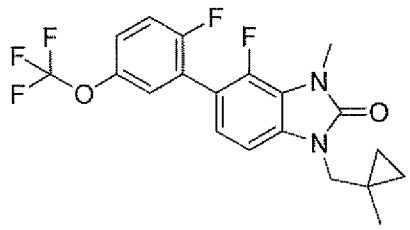
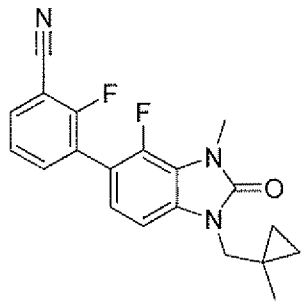
1-(2,2-dimethylpropyl)-4-fluoro-5-hydroxy-3-methyl-1,3-dihydro-2H-benzimidazol-2-one (**7-6**, 125 mg, 0.50 mmol) was dissolved in anhydrous THF (8 ml) and cooled to 0 deg C (water/ wet ice). The resulting maroon solution was treated with NaH (27.7 mg, 0.69 mmol, 1.4 eq) causing it to become dark green-black. The mixture then became maroon-orange again upon addition of N-Phenylbis (trifluoromethanesulfonimide) (266 mg, 0.74 mmol, 1.5 eq). The reaction mixture was allowed to slowly warm to 23 deg C over 16 h. The reaction mixture was then partitioned between EtOAc (2x55 ml) and water (65 ml). The residual maroon-orange oil containing the title compound, 1-(2,2-dimethylpropyl)-4-fluoro-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl trifluoromethanesulfonate **(7-7)**, was used crude. LRMS *m/z*: Calc'd for $C_{14}H_{16}F_4N_2O_4S$ (M+H) 385.3, found 385.1.

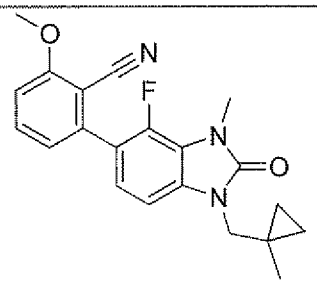
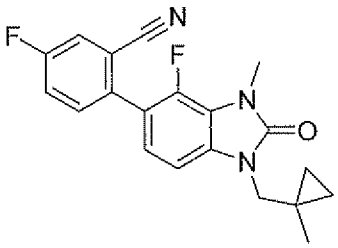
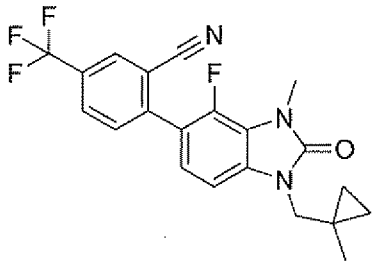
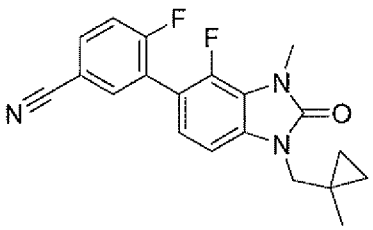
1-(2,2-dimethylpropyl)-4-fluoro-3-methyl-5-phenyl-1,3-dihydro-2H-benzimidazol-2-one (7-8)

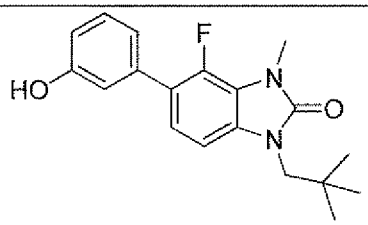
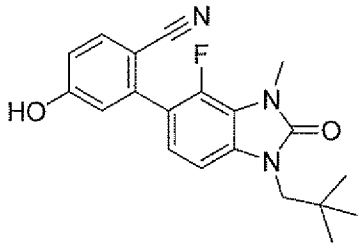
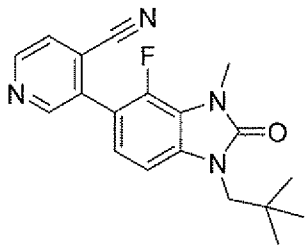
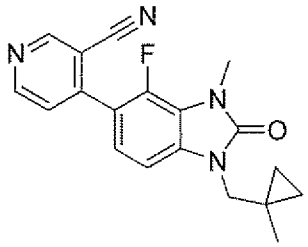
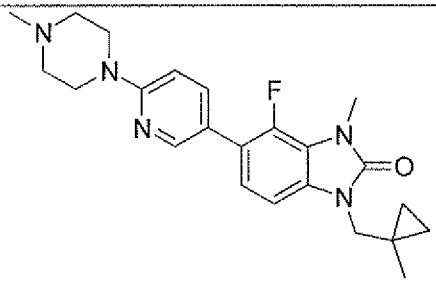
A solution of Cesium carbonate was treated with a solution of 1-(2,2-dimethylpropyl)-4-fluoro-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl trifluoromethanesulfonate (**7-7**, 80 mg, 0.21 mmol) and Phenylboronic acid (50.8 mg, 0.42 mmol, 2.0 eq) in anhydrous THF (5 ml). The mixture was deoxygenated, and 1,1'-

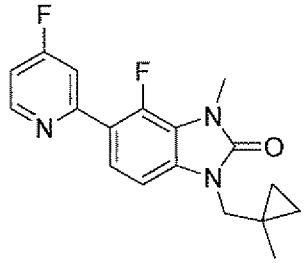
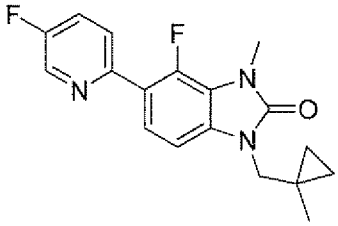
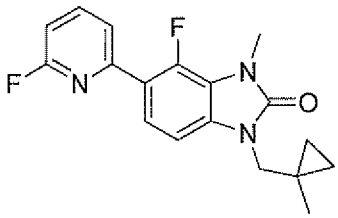
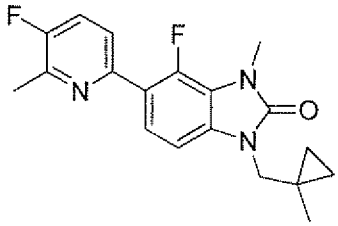
Bis(diphenylphosphino)ferrocene-palladium(II)dichloride dichloromethane complex was introduced (8.5 mg, 10.4 μmol, 0.05 eq) and the mixture was irradiated in a microwave at 140 deg C for 15 min. The reaction was not complete, so more Phenylboronic acid (26 mg, 0.24 mmol, 1.0 eq) and catalyst (8.5 mg, 10.4 μmol, 0.05 eq) was added and the reaction was irradiated again at 170 deg C for 25 min. LC/MS showed complete conversion, so the crude maroon oil was partitioned between EtOAc (2x45 ml) and aqueous saturated $NaHCO_3$ (55 ml), the combined organic layers were dried over Na_2SO_4 and concentrated, then purified via reverse-phase HPLC (Acetonitrile/ Water gradient with 0.1% TFA present). The title compound, 1-(2,2-dimethylpropyl)-4-fluoro-3-methyl-5-phenyl-1,3-dihydro-2H-benzimidazol-2-one **(7-8)**, was obtained as a brown oil with >95% purity. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54-7.52 (m, 2H), 7.45 (t, 2H, *J*=5.86 Hz), 7.38-7.35 (m, 1H), 7.09 (t, 1H, *J*=5.38 Hz), 6.89 (d, 1H, *J*=6.35 Hz), 3.69 (s, 2H), 3.66 (s, 3H), 1.06 (s, 9H). LRMS *m/z*: Calc'd for $C_{19}H_{21}FN_2O$ (M+H) 313.4, found 313.1.

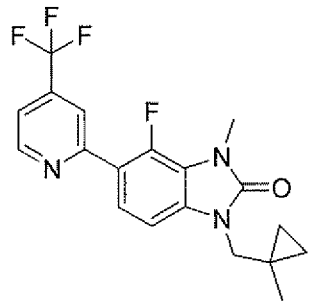
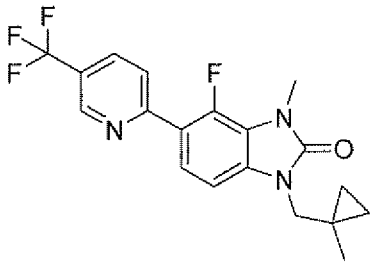
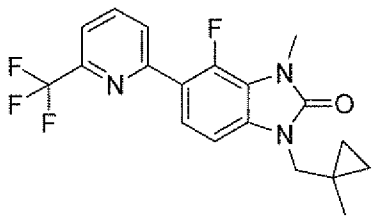
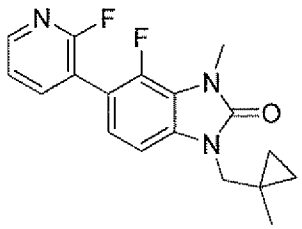
Table 1 for Scheme 7

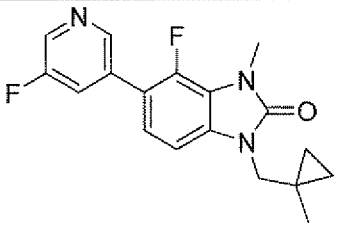
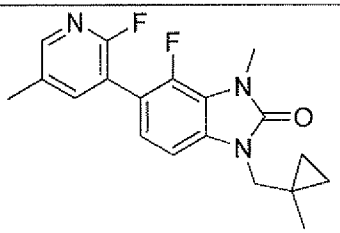
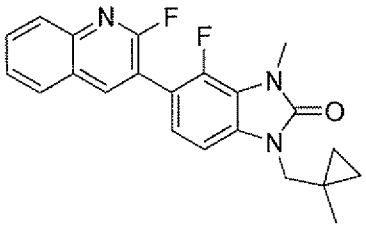
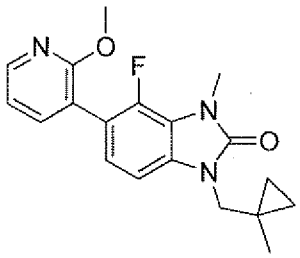
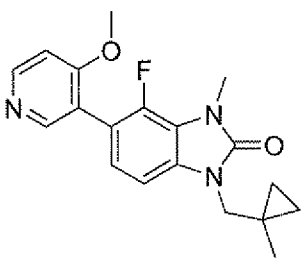
Cmp	Structure	Name	LRMS *m/z* (M+H)
7-9		4-fluoro-5-[2-fluoro-5-(trifluoromethoxy)phenyl]-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS *m/z* (M+H) 413.1 found, 413.4 required.
7-10		2-fluoro-3-{4-fluoro-3-methyl-1-[(1-methylcyclopropyl)methyl]-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl}benzonitrile	LRMS *m/z* (M+H) 354.1 found, 354.4 required.

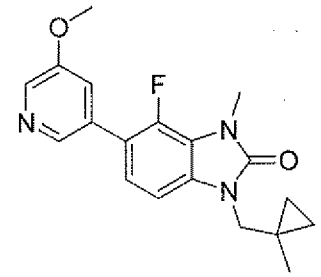
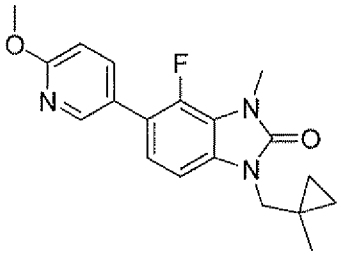
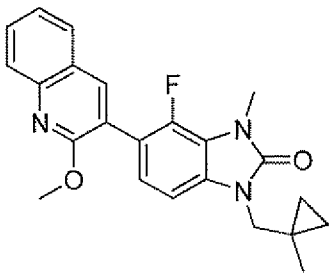
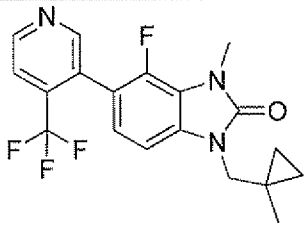
Cmp	Structure	Name	LRMS *m/z* (M+H)
7-11		2-{4-fluoro-3-methyl-1-[(1-methylcyclopropyl)methyl]-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl}-6-methoxybenzonitrile	LRMS *m/z* (M+H) 366.1 found, 366.4 required.
7-12		5-fluoro-2-{4-fluoro-3-methyl-1-[(1-methylcyclopropyl)methyl]-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl}benzonitrile	LRMS *m/z* (M+H) 354.1 found, 354.4 required.
7-13		2-{4-fluoro-3-methyl-1-[(1-methylcyclopropyl)methyl]-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl}-5-(trifluoromethyl)benzonitrile	LRMS m/z (M+H) 404.1 found, 404.4 required.
7-14		4-fluoro-3-{4-fluoro-3-methyl-1-[(1-methylcyclopropyl)methyl]-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl}benzonitrile	LRMS m/z (M+H) 354.2 found, 354.5 required.
7-15		1-(2,2-dimethylpropyl)-4-fluoro-5-(3-hydroxyphenyl)-3-methyl-1,3-dihydro-	LRMS m/z (M+H) 329.1 found, 329.4 required.

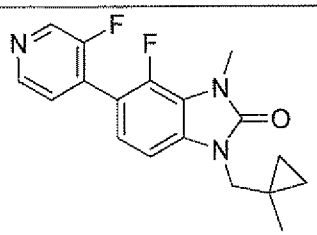
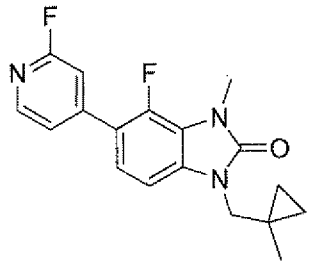
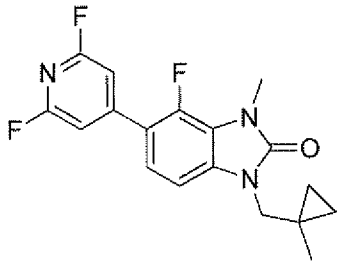
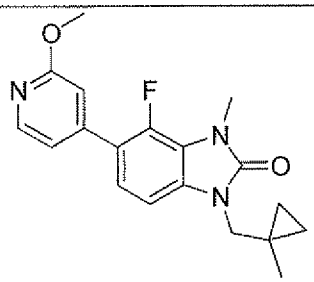
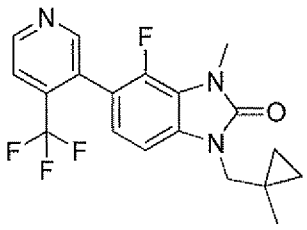
Cmp	Structure	Name	LRMS *m/z* (M+H)
		2H-benzimidazol-2-one	
7-16		2-[1-(2,2-dimethylpropyl)-4-fluoro-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-4-hydroxybenzonitrile	LRMS m/z (M+H) 353.8 found, 354.4 required.
7-17		3-[1-(2,2-dimethylpropyl)-4-fluoro-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]isonicotinonitrile	LRMS m/z (M+H) 339.1 found, 339.4 required.
7-18		4-{4-fluoro-3-methyl-1-[(1-methylcyclopropyl)methyl]-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl}nicotinonitrile	LRMS m/z (M+H) 337.1 found, 337.4 required.
7-19		4-fluoro-3-methyl-1-[(1-methylcyclopropyl)methyl]-5-[6-(4-methylpiperazin-1-yl)pyridin-3-yl]-1,3-dihydro-2H-	LRMS m/z (M+H) 410.2 found, 410.5 required.

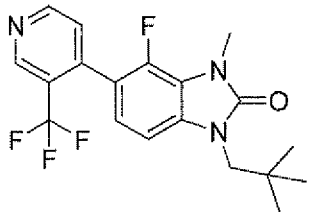
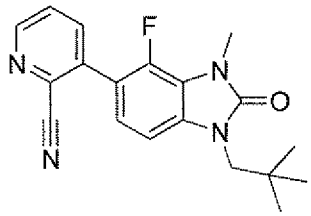
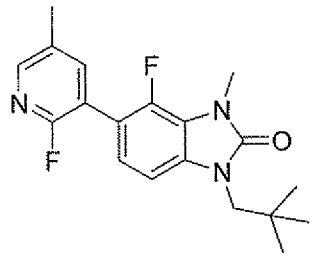
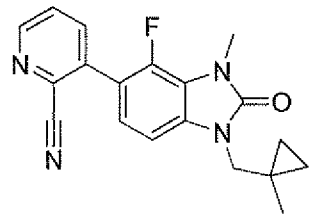
Cmp	Structure	Name	LRMS *m/z* (M+H)
		benzimidazol-2-one	
7-20		4-fluoro-5-(4-fluoropyridin-2-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 330.1 found, 330.4 required.
7-21		4-fluoro-5-(5-fluoropyridin-2-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 330.1 found, 330.4 required.
7-22		4-fluoro-5-(6-fluoropyridin-2-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 330.1 found, 330.4 required.
7-23		4-fluoro-5-(5-fluoro-6-methylpyridin-2-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 344.1 found, 344.4 required.

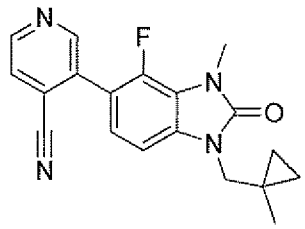
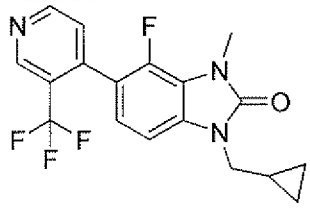
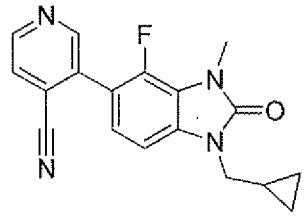
Cmp	Structure	Name	LRMS *m/z* (M+H)
7-24		4-fluoro-3-methyl-1-[(1-methylcyclopropyl)methyl]-5-[4-(trifluoromethyl)pyridin-2-yl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 380.1 found, 380.4 required.
7-25		4-fluoro-3-methyl-1-[(1-methylcyclopropyl)methyl]-5-[5-(trifluoromethyl)pyridin-2-yl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 380.1 found, 380.4 required.
7-26		4-fluoro-3-methyl-1-[(1-methylcyclopropyl)methyl]-5-[6-(trifluoromethyl)pyridin-2-yl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 380.1 found, 380.4 required.
7-27		4-fluoro-5-(2-fluoropyridin-3-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 330.1 found, 330.4 required.

Cmp	Structure	Name	LRMS *m/z* (M+H)
7-28		4-fluoro-5-(5-fluoropyridin-3-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 330.2 found, 330.5 required.
7-29		4-fluoro-5-(2-fluoro-5-methylpyridin-3-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 344.1 found, 344.4 required.
7-30		4-fluoro-5-(2-fluoroquinolin-3-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 380.1 found, 380.4 required.
7-31		4-fluoro-5-(2-methoxypyridin-3-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 342.1 found, 342.4 required.
7-32		4-fluoro-5-(4-methoxypyridin-3-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 342.1 found, 342.4 required.

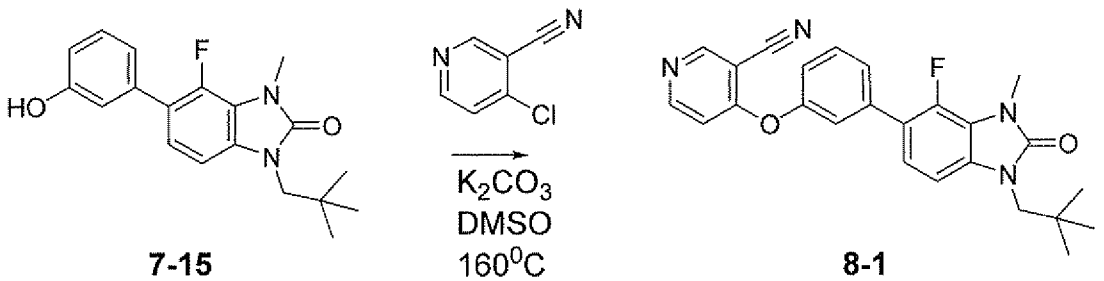
Cmp	Structure	Name	LRMS *m/z* (M+H)
7-33		4-fluoro-5-(5-methoxypyridin-3-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 342.1 found, 342.4 required.
7-34		4-fluoro-5-(6-methoxypyridin-3-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 342.2 found, 342.2 required.
7-35		4-fluoro-5-(2-methoxyquinolin-3-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 392.2 found, 392.4 required.
7-36		4-fluoro-3-methyl-1-[(1-methylcyclopropyl)methyl]-5-[4-(trifluoromethyl)pyridin-3-yl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 380.1 found, 380.4 required.

Cmp	Structure	Name	LRMS *m/z* (M+H)
7-37		4-fluoro-5-(3-fluoropyridin-4-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 330.1 found, 330.4 required.
7-38		4-fluoro-5-(2-fluoropyridin-4-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 330.1 found, 330.4 required.
7-39		5-(2,6-difluoropyridin-4-yl)-4-fluoro-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 348.1 found, 348.4 required.
7-40		4-fluoro-5-(2-methoxypyridin-4-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 342.1 found, 342.4 required.
7-41		4-fluoro-3-methyl-1-[(1-methylcyclopropyl)methyl]-5-[4-(trifluoromethyl)pyridin-3-yl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 380.1 found, 380.4 required.

Cmp	Structure	Name	LRMS *m/z* (M+H)
7-42		1-(2,2-dimethylpropyl)-4-fluoro-3-methyl-5-[3-(trifluoromethyl)pyridin-4-yl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 382.1 found, 382.4 required.
7-43		3-[1-(2,2-dimethylpropyl)-4-fluoro-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]pyridine-2-carbonitrile	LRMS m/z (M+H) 339.1 found, 339.4 required.
7-44		1-(2,2-dimethylpropyl)-4-fluoro-5-(2-fluoro-5-methylpyridin-3-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 346.1 found, 346.4 required.
7-45		3-{4-fluoro-3-methyl-1-[(1-methylcyclopropyl)methyl]-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl}pyridine-2-carbonitrile	LRMS m/z (M+H) 337.1 found, 337.4 required.

Cmp	Structure	Name	LRMS *m/z* (M+H)
7-46		4-fluoro-5-(2-methoxyquinolin-3-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 337.1 found, 337.4 required.
7-47		1-(cyclopropylmethyl)-4-fluoro-3-methyl-5-[3-(trifluoromethyl)pyridin-4-yl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS m/z (M+H) 366.1 found, 366.3 required.
7-48		3-[1-(cyclopropylmethyl)-4-fluoro-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]isonicotinonitrile	LRMS m/z (M+H) 323.1 found, 323.3 required.

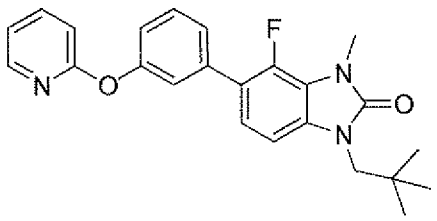
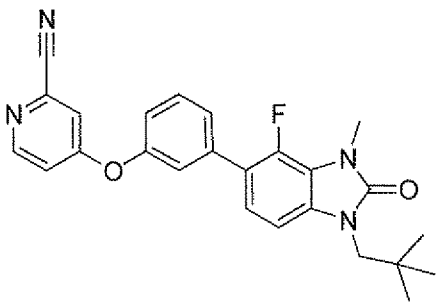
REACTION SCHEME 8

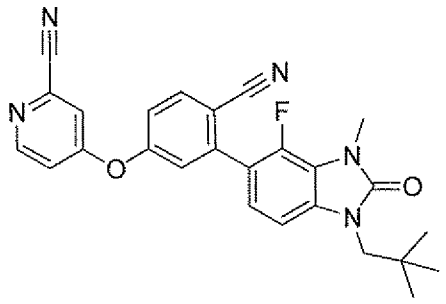
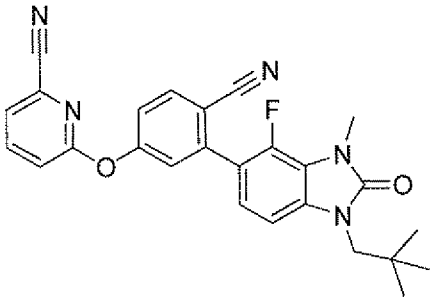


4-{3-[1-(2,2-dimethylpropyl)-4-fluoro-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}nicotinonitrile (8-1)

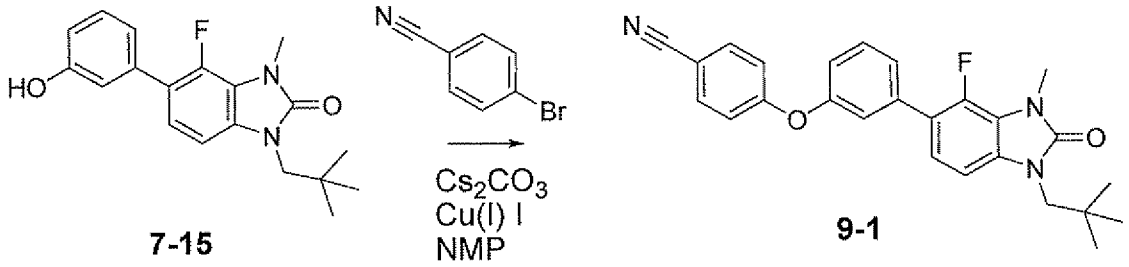
A solution of 1-(2,2-dimethylpropyl)-4-fluoro-5-(3-hydroxyphenyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one (**7-15**, 55 mg, 0.17 mmol) in DMSO (1 ml) was charged with Potassium carbonate (46.3 mg, 0.34 mmol, 2.0 eq) and 4-Chloro-3-cyanopyridine (34.8 mg, 0.25 mmol, 1.5 eq). The mixture was irradiated in a microwave at 160 deg C for 20 min, then purified via reverse-phase HPLC (Acetonitrile/ Water gradient with 0.1% TFA present) providing 4-{3-[1-(2,2-dimethylpropyl)-4-fluoro-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}nicotinonitrile **(8-1)** as a tan solid-oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (bs, 1H), 7.60-7.53 (m, 2H), 7.35 (s, 1H), 7.27 (s, 1H), 7.17-7.14 (m, 1H), 7.11-7.07 (m, 1H), 6.91 (d, 2H, *J*=8.24 Hz), 3.69 (s, 2H), 3.66 (s, 3H), 1.10 (s, 9H). LRMS *m/z*: Calc'd for $C_{25}H_{23}FN_4O_2$ (M+H) 431.4, found 431.5.

Table 1 for Scheme 8

Cmp	Structure	Name	LRMS *m/z* (M+H)
8-2		1-(2,2-dimethylpropyl)-4-fluoro-3-methyl-5-[3-(pyridin-2-yloxy)phenyl]-1,3-dihydro-2H-benzimidazol-2-one	LRMS *m/z* (M+H) 406.2 found, 406.5 required.
8-3		4-{3-[1-(2,2-dimethylpropyl)-4-fluoro-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}pyridine-2-carbonitrile	LRMS *m/z* (M+H) 431.2 found, 431.5 required.

Cmp	Structure	Name	LRMS *m/z* (M+H)
8-4		4-{4-cyano-3-[1-(2,2-dimethylpropyl)-4-fluoro-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}pyridine-2-carbonitrile	LRMS *m/z* (M+H) 456.0 found, 456.5 required.
8-5		6-{4-cyano-3-[1-(2,2-dimethylpropyl)-4-fluoro-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}pyridine-2-carbonitrile	LRMS *m/z* (M+H) 456.0 found, 456.5 required.

Scheme 9

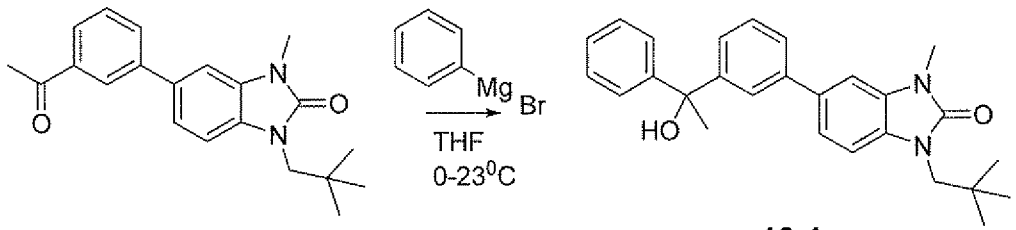


4-{3-[1-(2,2-dimethylpropyl)-4-fluoro-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}benzonitrile (9-1)

A solution of 1-(2,2-dimethylpropyl)-4-fluoro-5-(3-hydroxyphenyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one (**7-15**, 55 mg, 0.17 mmol) in NMP (1 ml) was sequentially charged with 4-Bromobenzonitrile (61.0 mg, 0.34 mmol, 2.0 eq), Cesium carbonate (109 mg, 0.34 mmol, 2.0 eq) and Copper(I) iodide (31.9 mg, 0.17 mmol, 1.0 eq). The resulting mixture

was irradiated in a microwave at 195 deg C for 2 h. LC/MS analysis showed only partial conversion, therefore additional amounts of 4-Bromobenzonitrile (61.0 mg, 0.34 mmol, 2.0 eq) and Cu(I)I (31.9 mg, 0.17 mmol, 1.0 eq) were added and the reaction was irradiated again at 195 deg C for 1 h. The completed reaction was filtered and the filtrate purified via reverse-phase HPLC (Acetonitrile/ Water gradient with 0.1% TFA present) to afford the title compound, 4-{3-[1-(2,2-dimethylpropyl)-4-fluoro-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}benzonitrile **(9-1)**, as a tan solid-oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, 2H, *J*=8.9 Hz), 7.50-7.46 (m, 1H), 7.39 (m, 1H), 7.25 (s, 1H), 7.09-7.04 (m, 4H), 6.87 (d, 1H, *J*=8.2 Hz), 3.67 (s, 2H), 3.64 (s, 3H), 1.05 (s, 9H). LRMS *m/z*: Calc'd for $C_{26}H_{24}FN_3O_2$ (M+H) 430.2, found 430.5.

Scheme 10



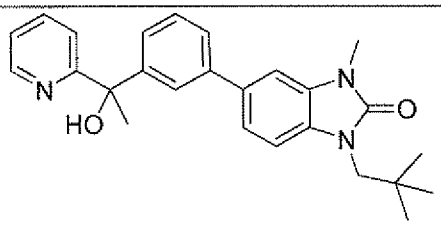
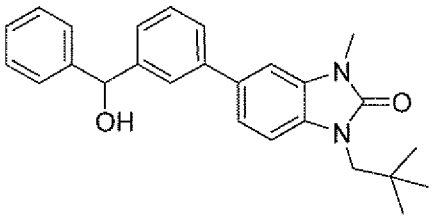
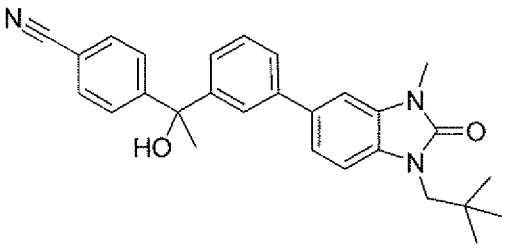
1-17 **10-1**

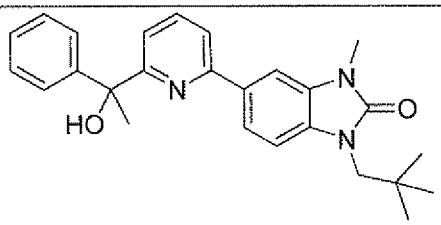
1-(2,2-dimethylpropyl)-5-[3-(1-hydroxy-1-phenylethyl)phenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one (10-1)

A solution of 5-(3-acetylphenyl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one (**1-17**, 170 mg, 0.51 mmol) in anhydrous THF (5 ml) was cooled to -78 deg C and treated with Phenyl magnesium chloride (1.8 M in THF, 365 µL, 0.66 mmol, 1.3 eq). The reaction mixture was warmed to 0 deg C and stirred for 1 h. The reaction was only ~30% complete, so more of the Grignard reagent (1.8 M in THF, 365 µL, 0.66 mmol, 1.3 eq) was added at 0 deg C and the reaction was maintained there for 30 min. The completed reaction was partitioned between EtOAc (50 ml) and water (55 ml) and the cloudy, white precipitate present which was removed via filtration. The filtrate was separated in a separatory funnel and the aqueous layer was re-extracted with EtOAc (50 ml). The combined organic layers were dried over Na_2SO_4, concentrated, then purified via flash column chromatography (SiO_2: 100% Hex to 50:50 Hex/ EtOAc), affording the title compound, 1-(2,2-dimethylpropyl)-5-[3-(1-hydroxy-1-

phenylethyl)phenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one **(10-1)** as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.48-7.45 (m, 3H), 7.40-7.31 (m, 4H), 7.27-7.24 (m, 2H), 7.12 (s, 1H), 7.05 (d, 1H, *J*=8.15 Hz), 3.67 (s, 2H), 3.45 (s, 3H), 2.02 (s, 3H), 1.05 (s, 9H). LRMS *m/z*: Calc'd for $C_{27}H_{30}N_2O_2$ (M+H) 415.2, found 415.5.

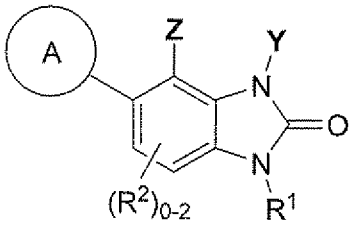
Table 1 for Scheme 10

Cmp	Structure	Name	LRMS *m/z* (M+H)
10-2		1-(2,2-dimethylpropyl)-5-[3-(1-hydroxy-1-pyridin-2-ylethyl)phenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS *m/z* (M+H) 416.1 found, 416.5 required.
10-3		1-(2,2-dimethylpropyl)-5-{3-[hydroxy(phenyl)methyl]phenyl}-3-methyl-1,3-dihydro-2H-benzimidazol-2-one	LRMS *m/z* (M+H) 401.1 found, 401.5 required.
10-4		4-(1-{3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenyl}-1-hydroxyethyl)benzonitrile	LRMS *m/z* (M+H) 440.1 found, 440.6 required.
10-5		1-(2,2-dimethylpropyl)-5-[6-(1-hydroxy-1-phenylethyl)pyridin-2-yl]-3-methyl-1,3-	LRMS *m/z* (M+H) 416.1 found, 416.5 required.

Cmp	Structure	Name	LRMS *m/z* (M+H)
		dihydro-2H-benzimidazol-2-one	

WHAT IS CLAIMED IS:

1. A compound according to Formula I



I

wherein:

Z is selected from H, halo, hydroxy, methyl, methoxy or CN;

Y is cyano, benzyl, C_{1-6}alkyl or C_{2-6}alkenyl, said C_{1-6}alkyl and C_{2-6}alkenyl optionally substituted with cyano;

R^1 is selected from the group consisting of:

(1) C_{2-8}alkyl,
(2) C_{2-8}alkenyl,
(3) C_{2-8}alkynyl,
(4) C_{3-6}cycloalkyl-$(CH_2)_p$-,
(5) aryl-$(CH_2)_p$ -,
(6) heteroaryl-$(CH_2)_p$ -, and
(7) heterocycle-$(CH_2)_p$ -,

wherein wherein p is 0, 1, 2, 3 or 4, and groups (1) to (7) above are optionally substituted with 1 to 4 R^2 groups;

each R^2 is independently selected from the group consisting of: halo, OH, oxo, -CN, C_{1-4}alkyl, C_{1-4}alkoxy, CF_3, -OCF_3, -C(O)-O-C_{1-4}alkyl, -$N(R)_2$, pyrimidinyl and –CN;

ring **A** is selected from aryl, heteroaryl and heterocycle, wherein said heterocycle is partially aromatic and wherein said aryl, heteroaryl and heterocycle are optionally substituted with one or more R^3 groups up to the maximum number of substitutable positions;

each R^3 is independently selected from the group consisting of: halo, -CN, $-NO_2$, **X**, $-C(R^4)_2-N(R)-$**X**, $-C(R^4)_2-N(R)C(O)-$**X**, $-C(R^4)_2-N(R)S(O)_k-$**X**, $-C(R^4)_2-N(R)C(O)-O-$**X**, -C(O)-**X**, -C(O)-O-**X**, -C(O)-N(R)-**X**, $-S(O)_k-$**X**, $-S(O)_kN(R)-$**X**, -N(R)-**X**, -O-**X**, -N(R)C(O)-**X**, $-N(R)S(O)_k-$**X**, -N(R)C(O)-O-**X**, -N(R)C(O)N(R)-**X** and $-N(R)SO_2N(R)-$**X**,

each **X** is independently selected from the group consisting of: H, C_{1-8}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}cycloalkyl, aryl, heterorayl, heterocycle, C_{3-6}cycloalkyl-$C(R^4)_2-$, aryl-$C(R^4)_2-$, heteroaryl-$C(R^4)_2-$ and heterocycle-$C(R^4)_2-$, wherein each member of the group excluding hydrogen is optionally substituted from one up to the maximum number of substitutable positions with one or more substituents independently selected from the group consisting of: CN, halo, R^5, $-O-R^5$, $-N(R)-R^5$, $-N(R)C(O)-R^5$, $-N(R)S(O)_2-R^5$, $-N(R)-C(O)-O-R^5$, $-C(O)-N(R)-R^5$, $-C(O)-O-R^5$, $-C(O)-R^5$, $-C(O)-C(R^4)_2-R^5$, $-C(O)-C(R^4)_2-S(O)_2-R^5$, $-C(R^4)_2-N(R)-R^5$, $-SO_2-N(R)-R^5$, $-Si(CH_3)_2(R^5)$, $-C(R^4)_2-R^5$ and $-SO_2-R^5$;

each k is independently 0, 1 or 2;

each R is independently selected from the group consisting of: H and C_{1-4}alkyl;

each R^4 is independently selected from the group consisting of: H, OH and C_{1-4}alkyl;

each R^5 is independently selected from the group consisting of: H, C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{3-6}cycloalkyl, phenyl, benzyl, heterocycle and heteroaryl, wherein each member of the group excluding hydrogen is optionally substituted with 1 to 3 substituents independently selected from: halogen, cyano, hydroxy and methyl;

aryl at each occurrence is independently selected from the group consisting of: phenyl, naphthyl, anthryl and phenanthryl;

heteroaryl at each occurrence independently means a 5- or 6-membered monocyclic aromatic or 9- or 10-membered bicyclic aromatic, wherein at least one atom in the aromatic is selected from N, O and S, the sulfur optionally oxidized to sulfone or sulfoxide, and the remaining atoms are selected from C, N, O and S, the sulfur optionally oxidized to sulfone or sulfoxide;

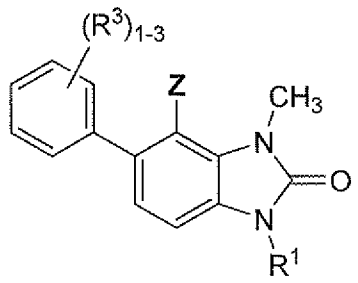
heterocycle at each occurrence independently means a 4- to 7-membered monocyclic non-aromatic ring, an 8- to 11-membered bi-cyclic, including spiro-cyclic, non- or partially-aromatic ring or a 12- to 20-memberd tri-cyclic, including spiro-cyclic portions, non- or partially-aromatic ring, each optionally substituted with 1 to 2 oxo groups, wherein at least one atom is selected from N(R), O and S, the sulfur optionally oxidized to sulfone or sulfoxide, and the remaining atoms are selected from C, N(R), O and S, the sulfur optionally oxidized to sulfone or sulfoxide;

and pharmaceutically acceptable salts thereof.

2. The compound according to Claim 1 wherein Y is methyl.

3. The compound according to Claim 1 wherein R^1 is selected from the group consisting of: cyclopropylmethyl, 2,2-difluorocyclopropylmethyl, 2,2-difluoro-1-methylcyclopropylmethyl, 1-(trifluromethyl)cyclopropylmethyl, 4,4,4-trifluoro-2,2-dimethylbutyl, cyclobutylmethyl, 2,2-dimethylpropyl, prop-2-enyl, biphenyl and benzyl, optionally substituted with methoxy or $-OCF_3$.

4. The compound according to Claim 1 of Formula Ia

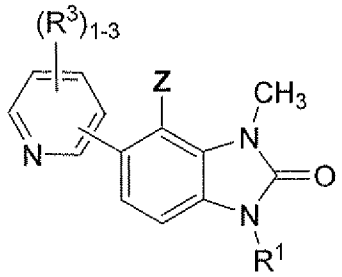


Ia

or a pharmaceutically acceptable salt thereof.

5. The compound according to Claim 4 wherein R^3 is selected from the group consisting of: halo, -CN, -N(O)2, amino, -N(C_{1-4}alkyl)2, -C(O)-O-C_{1-4}alkyl, -C(O)-C_{1-4}alkyl, -S(O)2-C_{1-4}alkyl, C_{3-6}cycloalkyl, -C(C_{1-4}alkyl)2-NHC(O)-O-C_{1-4}alkyl and C_{1-8}alkyl optionally substituted with 1 to 4 substituents independently selected from hydroxy and halo.

6. The compound according to Claim 1 of Formula Ib

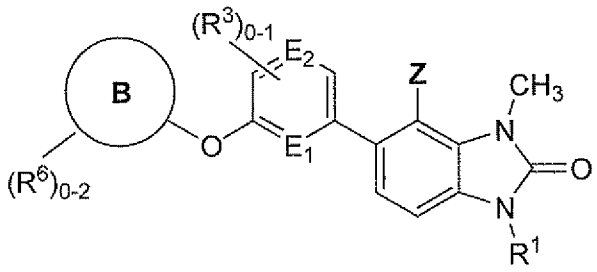


Ib

or a pharmaceutically acceptable salt thereof.

7. The compound according to Claim 6 wherein R^3 is selected from the group consisting of: halo, -CN, -N(O)2, amino, -N(C_{1-4}alkyl)2, -C(O)-O-C_{1-4}alkyl, -C(O)-C_{1-4}alkyl, -S(O)2-C_{1-4}alkyl, C_{3-6}cycloalkyl and C_{1-8}alkyl optionally substituted with 1 to 4 substituents independently selected from hydroxy and halo.

8. The compound according to Claim 1 of Formula Ic



Ic

or a pharmaceutically acceptable salt thereof, wherein

E_1 and E_2 are independently C or N;

ring **B** is phenyl or heteroaryl,

R^3 is CN, halo or C_{1-4}alkyl, optionally substituted with 1-5 halo atoms, and

each R^6 is independently selected from the group consisting of: CN, halo, R^5, -O-R^5, -N(R)-R^5, -N(R)C(O)-R^5, -N(R)S(O)$_2$-R^5, -N(R)-C(O)-O-R^5, -C(O)-N(R)-R^5, -C(O)-O-R^5, -C(O)-R^5, -C(O)-C(R^4)$_2$-R^5, -C(O)-C(R^4)$_2$-S(O)$_2$-R^5, -C(R^4)$_2$-N(R)-R^5, -SO$_2$-N(R)-R^5, -Si(CH_3)$_2$(R^5), –C(R^4)$_2$-R^5 and -SO$_2$-R^5.

9. The compound according to Claim 8 wherein ring **B** is phenyl.

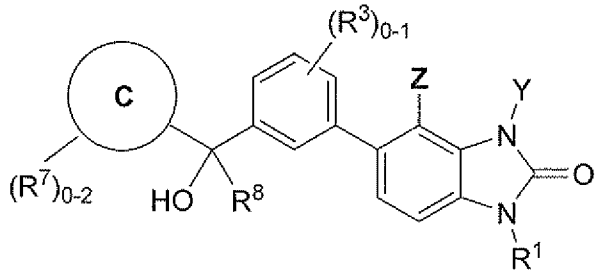
10. The compound according to Claim 8 wherein ring **B** is pyridyl.

11. The compound according to Claim 8 wherein E_1 is C and E_2 is C.

12. The compound according to Claim 8 wherein E_1 is N and E_2 is C.

13. The compound according to Claim 8 wherein E_1 is C and E_2 is N.

14. The compound according to Claim 1 of Formula Id



Id

or a pharmaceutically acceptable salt thereof, wherein

ring **C** is phenyl or heteroaryl,

R^3 is CN, halo or C_{1-4}alkyl, optionally substituted with 1-5 halo atoms, and

each R^7 is independently selected from the group consisting of: CN, halo, R^5, -O-R^5, -N(R)-R^5, -N(R)C(O)-R^5, -N(R)S(O)$_2$-R^5, -N(R)-C(O)-O-R^5, -C(O)-N(R)-R^5, -C(O)-O-R^5, -C(O)-R^5, -C(O)-C(R^4)$_2$-R^5, -C(O)-C(R^4)$_2$-S(O)$_2$-R^5, -C(R^4)$_2$-N(R)-R^5, -SO$_2$-N(R)-R^5, -Si(CH_3)$_2$(R^5), –C(R^4)$_2$-R^5 and -SO$_2$-R^5;

R^8 is H or methyl.

15. A compound according to Claim 1 selected from the following group:

1-(2,2-dimethylpropyl)-3-methyl-5-phenyl-1,3-dihydro-2H-benzimidazol-2-one;
1-(cyclopropylmethyl)-3-ethyl-5-phenyl-1,3-dihydro-2H-benzimidazol-2-one;
1-(cyclopropylmethyl)-5-phenyl-3-propyl-1,3-dihydro-2H-benzimidazol-2-one;
[3-(cyclopropylmethyl)-2-oxo-6-phenyl-2,3-dihydro-1H-benzimidazol-1-yl]acetonitrile;
3-benzyl-1-(cyclopropylmethyl)-5-phenyl-1,3-dihydro-2H-benzimidazol-2-one;
2-[1-(2,2-dimethylpropyl)-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile;
1-(2,2-dimethylpropyl)-5-phenyl-1,3-dihydro-2H-benzimidazol-2-one;
5-(3-chlorophenyl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;
1-(2,2-dimethylpropyl)-5-(3-isopropylphenyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;
1-(2,2-dimethylpropyl)-3-methyl-5-[3-(trifluoromethyl)phenyl]-1,3-dihydro-2H-benzimidazol-2-one;
1-(2,2-dimethylpropyl)-5-[3-(hydroxymethyl)phenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;
5-(3-acetylphenyl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;
3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-N,N-dimethylbenzamide;

3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-N-phenylbenzamide;

1-(2,2-dimethylpropyl)-5-(2-fluorophenyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

N-(tert-butyl)-2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzenesulfonamide;

1-(2,2-dimethylpropyl)-3-methyl-5-(3-methylphenyl)-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-(3-fluorophenyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

{3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenyl}acetic acid;

5-biphenyl-3-yl-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

3-(2,2-dimethylpropyl)-1-methyl-5-phenyl-1,3-dihydro-2H-benzimidazol-2-one;

3-(cyclopropylmethyl)-2-oxo-6-phenyl-2,3-dihydro-1H-benzimidazole-1-carbonitrile;

1-(2,2-dimethylpropyl)-3-methyl-5-(2-thienyl)-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-(3-thienyl)-1,3-dihydro-2H-benzimidazol-2-one;

5-(1-benzothien-3-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

5-(1-benzofuran-2-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-(3-furyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

5-(1-benzofuran-3-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

5-(3,5-dimethylisoxazol-4-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-(5-methyl-3-phenylisoxazol-4-yl)-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-(1H-pyrazol-3-yl)-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-(1H-pyrazol-4-yl)-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-(3,5-dimethyl-1H-pyrazol-4-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-[6-(1H-pyrazol-1-yl)pyridin-2-yl]-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-(2-fluoropyridin-3-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-(6-fluoropyridin-3-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-quinolin-3-yl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-pyridin-4-yl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-(2-fluoropyridin-4-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-(2-methoxypyridin-4-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-(3-fluoropyridin-4-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

5-(5-chloro-2-fluoropyridin-4-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

5-(2,6-difluoropyridin-4-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

5-(3-chlorophenyl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-(1-isobutyl-1H-pyrazol-4-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-[1-(2-morpholin-4-ylethyl)-1H-pyrazol-4-yl]-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-(4,5,6,7-tetrahydropyrazolo[1,5-a]pyridin-3-yl)-1,3-dihydro-2H-benzimidazol-2-one;

5-(1-benzyl-1H-pyrazol-5-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-[1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-(2-fluoroquinolin-3-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-(6-morpholin-4-ylpyridin-3-yl)-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-(5-methylpyridin-3-yl)-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-[5-(hydroxymethyl)pyridin-3-yl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

5-(2,6-difluoropyridin-3-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-[4-(trifluoromethyl)pyridin-3-yl]-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-pyrimidin-5-yl-1,3-dihydro-2H-benzimidazol-2-one;

5-(2,4-dimethoxypyrimidin-5-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-(2-fluorophenyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-[3-(1H-pyrazol-1-yl)phenyl]-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-(4-methylphenyl)-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-(4-fluorophenyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-[4-(trifluoromethoxy)phenyl]-1,3-dihydro-2H-benzimidazol-2-one;

5-(2,4-difluorophenyl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-(5-fluoro-2-methylphenyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-[4-hydroxy-2-(trifluoromethyl)phenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-[2-fluoro-5-(trifluoromethyl)phenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

5-(3,4-difluorophenyl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

5-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-2-fluorobenzoic acid;

5-(3-chloro-4-ethoxyphenyl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

5-(2,3-dihydro-1-benzofuran-5-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-(1H-indol-5-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-(1H-indazol-5-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-(1H-indazol-6-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-phenyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-(1-methyl-1H-pyrazol-4-yl)-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-(5-methyl-1-phenyl-1H-pyrazol-4-yl)-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-(2-methoxypyrimidin-5-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile;

6-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-4-(trifluoromethyl)nicotinic acid;

1-(2,2-dimethylpropyl)-5-[4-(1-hydroxy-1-methylethyl)phenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-[3-(1-hydroxy-1-methylethyl)phenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-(2-piperidin-1-yl-1,3-thiazol-4-yl)-1,3-dihydro-2H-benzimidazol-2-one;

4-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile;

2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-3-methoxybenzonitrile;

2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-5-(trifluoromethyl)benzonitrile;

2-chloro-6-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile;

2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-6-(trifluoromethyl)benzonitrile;

2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-6-methoxybenzonitrile;

2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-5-fluorobenzonitrile;

2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-5-methylbenzonitrile;

3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]isonicotinonitrile;

5-{3-methyl-1-[(1-methylcyclopropyl)methyl]-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl}nicotinonitrile;

1-(cyclopropylmethyl)-3,5-diphenyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(cyclopropylmethyl)-3-methyl-5-phenyl-1,3-dihydro-2H-benzimidazol-2-one;

3-[1-(2,2-dimethylpropyl)-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]isonicotinonitrile;

3-[1-(2,2-dimethylpropyl)-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]pyridine-2-carbonitrile;

1-(2,2-dimethylpropyl)-3-methyl-5-[6-methyl-4-(trifluoromethyl)pyridin-2-yl]-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-[4-(trifluoromethyl)quinolin-2-yl]-1,3-dihydro-2H-benzimidazol-2-one;

5-(3-chloropyrazin-2-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]pyrazine-2-carbonitrile;

5-(6-chloropyrazin-2-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

5-(3-chloroquinoxalin-2-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-6-fluorobenzonitrile;

5-bromo-2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile;

2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-4-methylbenzonitrile;

2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-4-fluorobenzonitrile;

5-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-2-fluorobenzonitrile;

4-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phthalonitrile;

3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-4-hydroxybenzonitrile;

1-(2,2-dimethylpropyl)-3-methyl-5-[2-(trifluoromethyl)phenyl]-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-[3-fluoro-2-(trifluoromethyl)phenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-[5-fluoro-2-(trifluoromethyl)phenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-[4-fluoro-2-(trifluoromethyl)phenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-[2-fluoro-6-(trifluoromethyl)phenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

5-[2,6-bis(trifluoromethyl)phenyl]-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-[4-hydroxy-3-(hydroxymethyl)phenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-[3-(hydroxymethyl)-4-methoxyphenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]pyridine-2-carbonitrile;

6-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]pyridine-2-carbonitrile;

5-(6-tert-butylpyridin-2-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-[6-(trifluoromethyl)pyridin-2-yl]-1,3-dihydro-2H-benzimidazol-2-one;

5-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]nicotinonitrile;

6-amino-5-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]nicotinonitrile;

1-(2,2-dimethylpropyl)-3-methyl-5-[5-(trifluoromethyl)pyridin-3-yl]-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-pyrimidin-2-yl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-(5-hydroxypyrazin-2-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-quinoxalin-2-yl-1,3-dihydro-2H-benzimidazol-2-one;

3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-1H-pyrrolo[2,3-b]pyridine-5-carbonitrile;

2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-6-methylbenzonitrile;

2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-4-(trifluoromethyl)benzonitrile;

3-methyl-1-[(1-methylcyclopropyl)methyl]-5-phenyl-1,3-dihydro-2H-benzimidazol-2-one;

3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-2-fluorobenzonitrile;

5-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-2-methylbenzonitrile;

3-chloro-5-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile;

1-(2,2-dimethylpropyl)-5-[4-fluoro-3-(hydroxymethyl)phenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-[5-(hydroxymethyl)-2-methylphenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

3-chloro-5-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]isonicotinonitrile;

4-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]pyridine-2-carbonitrile;

3-methyl-1-[(2-methylcyclopropyl)methyl]-5-phenyl-1,3-dihydro-2H-benzimidazol-2-one;

2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]isonicotinonitrile;

6-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]nicotinonitrile;

2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]quinoline-3-carbonitrile;

1-(2,2-dimethylpropyl)-3-methyl-5-[3-(trifluoromethyl)pyridin-4-yl]-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-[3-(trifluoromethyl)pyridin-2-yl]-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-[4-(trifluoromethyl)pyridin-2-yl]-1,3-dihydro-2H-benzimidazol-2-one;

3-[3-methyl-2-oxo-1-(3,3,3-trifluoro-2-hydroxy-2-methylpropyl)-2,3-dihydro-1H-benzimidazol-5-yl]isonicotinonitrile;

3-[3-methyl-2-oxo-1-(2-oxopropyl)-2,3-dihydro-1H-benzimidazol-5-yl]isonicotinonitrile;

3-[1-(cyclobutylmethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]isonicotinonitrile;

3-{1-[(2,2-difluorocyclopropyl)methyl]-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl}isonicotinonitrile;

2-{1-[(2,2-difluoro-1-methylcyclopropyl)methyl]-3-methyl-2-oxo-2,3-dihyro-1H-benzimidazol-5-yl}-4-methylbenzonitrile;

2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-6-methylnicotinonitrile;

6-methyl-2-{3-methyl-1-[(1-methylcyclopropyl)methyl]-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl}nicotinonitrile;

3-{3-methyl-1-[(1-methylcyclopropyl)methyl]-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl}pyridine-2-carbonitrile;

3-methyl-1-[(1-methylcyclopropyl)methyl]-5-[4-(trifluoromethyl)pyridin-3-yl]-1,3-dihydro-2H-benzimidazol-2-one;

5-[1-(2-fluoro-2-methylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]nicotinonitrile;

4-methyl-2-[3-methyl-1-(2-methylprop-2-en-1-yl)-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile;

5-[1-(cyclopropylmethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]nicotinonitrile;

5-[3-methyl-2-oxo-1-(4,4,4-trifluorobutyl)-2,3-dihydro-1H-benzimidazol-5-yl]nicotinonitrile;

1-(2,2-dimethylpropyl)-5-[5-(1-hydroxy-1-methylethyl)-2-methylphenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

3-[3-methyl-2-oxo-1-(3,3,3-trifluoro-2-hydroxypropyl)-2,3-dihydro-1H-benzimidazol-5-yl]isonicotinonitrile;

1-(2,2-dimethylpropyl)-5-[5-(1-methoxy-1-methylethyl)-2-methylphenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

3-[1-(2-fluoro-2-methylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]isonicotinonitrile;

3-[3-methyl-2-oxo-1-(2,2,2-trifluoroethyl)-2,3-dihydro-1H-benzimidazol-5-yl]isonicotinonitrile;

3-(3-methyl-2-oxo-1-{[1-(trifluoromethyl)cyclopropyl]methyl}-2,3-dihydro-1H-benzimidazol-5-yl)isonicotinonitrile;

3-[3-methyl-2-oxo-1-(3,3,3-trifluoropropyl)-2,3-dihydro-1H-benzimidazol-5-yl]isonicotinonitrile;

3-[3-methyl-2-oxo-1-(4,4,4-trifluorobutyl)-2,3-dihydro-1H-benzimidazol-5-yl]isonicotinonitrile;

5-(4-fluoropyridin-3-yl)-3-methyl-1-{[1-(trifluoromethyl)cyclopropyl]methyl}-1,3-dihydro-2H-benzimidazol-2-one;

3-methyl-1-{[1-(trifluoromethyl)cyclopropyl]methyl}-5-[4-(trifluoromethyl)pyridin-3-yl]-1,3-dihydro-2H-benzimidazol-2-one;

5-[5-(1-hydroxy-1-methylethyl)-2-methylphenyl]-3-methyl-1-(4,4,4-trifluorobutyl)-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-[2-(2H-tetrazol-5-yl)phenyl]-1,3-dihydro-2H-benzimidazol-2-one;

5-(6-chloropyridin-2-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(cyclopropylmethyl)-5-(3-hydroxyphenyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-(5-methoxypyridin-3-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-(5-hydroxypyridin-3-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-(3-hydroxyphenyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-4-hydroxybenzonitrile;

6-chloro-2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]nicotinonitrile;

2-chloro-6-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]nicotinonitrile;

1'-(2,2-dimethylpropyl)-3'-methyl-1',3'-dihydro-1H-2'H-2,5'-bibenzimidazol-2'-one;

1-but-3-en-1-yl-5-(2-hydroxyphenyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

5-(6-acetylpyridin-2-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

4-amino-2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile;

tert-butyl 7-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-3,4-dihydroisoquinoline-2(1H)-carboxylate;

1-(2,2-dimethylpropyl)-3-methyl-5-(3-methyl-1,2,4-oxadiazol-5-yl)-1,3-dihydro-2H-benzimidazol-2-one;

5-(5-chloro-2-methylphenyl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

4-chloro-2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile;

3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzaldehyde;

2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-4-methoxybenzonitrile;

1-but-3-en-1-yl-3-methyl-5-[3-(pent-4-en-1-yloxy)phenyl]-1,3-dihydro-2H-benzimidazol-2-one;

3-methyl-1-pent-4-en-1-yl-5-[3-(pent-4-en-1-yloxy)phenyl]-1,3-dihydro-2H-benzimidazol-2-one;

5-(3-hydroxyphenyl)-3-methyl-1-pent-4-en-1-yl-1,3-dihydro-2H-benzimidazol-2-one;

1-allyl-3-methyl-5-[3-(pent-4-en-1-yloxy)phenyl]-1,3-dihydro-2H-benzimidazol-2-one;

3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-5-hydroxybenzonitrile;

2-[3-(cyclopropylmethyl)-2-oxo-6-phenyl-2,3-dihydro-1H-benzimidazol-1-yl]propanenitrile;

2-[3-(cyclopropylmethyl)-2-oxo-6-phenyl-2,3-dihydro-1H-benzimidazol-1-yl]-2-fluoro-N-methylacetamide;

methyl-4-[3-methyl-5-(2-methylphenyl)-2-oxo-2,3-dihydro-1H-benzimidazol-1-yl]piperidine-1-carboxylate;

3-[1-(1,1-difluoroprop-2-en-1-yl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]isonicotinonitrile;

2-{3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}nicotinonitrile;

1-(cyclopropylmethyl)-3-methyl-5-[3-(pyridin-2-yloxy)phenyl]-1,3-dihydro-2H-benzimidazol-2-one;

2-{3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}nicotinonitrile;

1-(2,2-dimethylpropyl)-3-methyl-5-(3-{[4-(trifluoromethyl)pyridin-2-yl]oxy}phenyl)-1,3-dihydro-2H-benzimidazol-2-one;

5-{3-[(2-chloropyridin-4-yl)oxy]phenyl}-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(cyclopropylmethyl)-3-methyl-5-{3-[(3-methylpyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-benzimidazol-2-one;

1-(cyclopropylmethyl)-3-methyl-5-{3-[(4-methylpyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-benzimidazol-2-one;

1-(cyclopropylmethyl)-3-methyl-5-{3-[(5-methylpyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-benzimidazol-2-one;

1-(cyclopropylmethyl)-3-methyl-5-{3-[(6-methylpyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-benzimidazol-2-one;

1-(cyclopropylmethyl)-5-{3-[(3-fluoropyridin-2-yl)oxy]phenyl}-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(cyclopropylmethyl)-5-{3-[(5-fluoropyridin-2-yl)oxy]phenyl}-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(cyclopropylmethyl)-5-{3-[(6-fluoropyridin-2-yl)oxy]phenyl}-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

2-{3-[1-(cyclopropylmethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}nicotinonitrile;

5-{3-[(5-chloro-3-fluoropyridin-2-yl)oxy]phenyl}-1-(cyclopropylmethyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

2-{3-[1-(cyclopropylmethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}-3,5,6-trifluoroisonicotinonitrile;

1-(cyclopropylmethyl)-3-methyl-5-[3-(pyridin-4-yloxy)phenyl]-1,3-dihydro-2H-benzimidazol-2-one;

1-(cyclopropylmethyl)-3-methyl-5-{3-[(2-methylpyridin-4-yl)oxy]phenyl}-1,3-dihydro-2H-benzimidazol-2-one;

5-{3-[(2-chloropyridin-4-yl)oxy]phenyl}-1-(cyclopropylmethyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

4-{3-[1-(cyclopropylmethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}nicotinonitrile;

4-{3-[1-(cyclopropylmethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}pyridine-2-carbonitrile;

4-{3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}pyridine-2-carbonitrile;

2-{4-cyano-3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}nicotinonitrile;

4-{4-cyano-3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}nicotinonitrile;

4-{4-cyano-3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}pyridine-2-carbonitrile;

4-{4-cyano-3-[3-methyl-2-oxo-1-(tetrahydro-2H-pyran-4-ylmethyl)-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}pyridine-2-carbonitrile;

4-(4-cyano-3-{3-methyl-1-[(1-methylcyclopropyl)methyl]-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl}phenoxy)pyridine-2-carbonitrile;

4-{4-cyano-3-[1-(cyclopropylmethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}pyridine-2-carbonitrile;

4-{4-cyano-3-[1-(cyclobutylmethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}pyridine-2-carbonitrile;

4-{4-cyano-3-[3-methyl-2-oxo-1-(4,4,4-trifluorobutyl)-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}pyridine-2-carbonitrile;

4-{3-[1-(4-bromo-2-fluorobenzyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-4-cyanophenoxy}pyridine-2-carbonitrile;

4-[4-cyano-3-(1-isobutyl-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl)phenoxy]pyridine-2-carbonitrile;

4-{4-cyano-3-[1-(cyclopentylmethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}pyridine-2-carbonitrile;

6-{4-cyano-3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}pyridine-2-carbonitrile;

6-{4-cyano-3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}nicotinonitrile;

2-{4-cyano-3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}isonicotinonitrile;

2-{3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-4-methylphenoxy}nicotinonitrile;

4-{4-cyano-3-[1-(cyclopropylmethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}pyridine-2-carbonitrile;

4-{3-cyano-5-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}pyridine-2-carbonitrile;

1-(2,2-dimethylpropyl)-5-{3-[(2-fluorobenzyl)oxy]phenyl}-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

5-[3-(benzyloxy)phenyl]-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-(3-{[2-(trifluoromethyl)benzyl]oxy}phenyl)-1,3-dihydro-2H-benzimidazol-2-one;

3-({3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}methyl)benzonitrile;

4-({3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}methyl)benzonitrile;

4-{3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}benzonitrile;

1-(cyclopropylmethyl)-3-methyl-5-(3-phenoxyphenyl)-1,3-dihydro-2H-benzimidazol-2-one;

5-[3-(2-chlorophenoxy)phenyl]-1-(cyclopropylmethyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

5-[3-(3-chlorophenoxy)phenyl]-1-(cyclopropylmethyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

2-{3-[1-(cyclopropylmethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}benzonitrile;

3-{3-[1-(cyclopropylmethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}benzonitrile;

4-{3-[1-(cyclopropylmethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}benzonitrile;

1-(2,2-dimethylpropyl)-3-methyl-5-(3-phenoxyphenyl)-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-{3-[2-(trifluoromethyl)phenoxy]phenyl}-1,3-dihydro-2H-benzimidazol-2-one;

4-({6-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]pyridin-2-yl}oxy)benzonitrile;

1-(2,2-dimethylpropyl)-3-methyl-5-{6-[(6-methylpyridin-2-yl)oxy]pyridin-2-yl}-1,3-dihydro-2H-benzimidazol-2-one;

3-({6-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]pyridin-2-yl}oxy)pyridine-2-carbonitrile;

1-(2,2-dimethylpropyl)-5-{6-[(2,6-dimethylpyridin-4-yl)oxy]pyridin-2-yl}-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

4-({3-cyano-6-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]pyridin-2-yl}oxy)pyridine-2-carbonitrile;

5-[6-(1,3-benzothiazol-2-yloxy)pyridin-2-yl]-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-{6-[(3-methylquinoxalin-2-yl)oxy]pyridin-2-yl}-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-(6-{[1-methyl-5-(trifluoromethyl)-1H-pyrazol-3-yl]oxy}pyridin-2-yl)-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-{6-[(1-methyl-1H-pyrazol-5-yl)oxy]pyridin-2-yl}-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-{6-[(1-methylpiperidin-3-yl)oxy]pyridin-2-yl}-1,3-dihydro-2H-benzimidazol-2-one;

5-[6-(1-azabicyclo[2.2.2]oct-3-yloxy)pyridin-2-yl]-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

5-(6-{[(3R)-1-benzylpiperidin-3-yl]oxy}pyridin-2-yl)-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-3-methyl-5-{6-[(1-methylpyrrolidin-3-yl)oxy]pyridin-2-yl}-1,3-dihydro-2H-benzimidazol-2-one;

5-{6-[(1-benzylpyrrolidin-3-yl)oxy]pyridin-2-yl}-1-(2,2-dimethylpropyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

4-({5-cyano-6-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]pyridin-2-yl}oxy)pyridine-2-carbonitrile;

4-({4-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]pyridin-2-yl}oxy)benzonitrile;

4-({6-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]pyrazin-2-yl}oxy)benzonitrile;

4-({6-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]pyrazin-2-yl}oxy)-3-fluorobenzonitrile;

3-({6-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]pyrazin-2-yl}oxy)pyridine-2-carbonitrile;

5-({6-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]pyrazin-2-yl}oxy)pyridine-2-carbonitrile;

1-(2,2-dimethylpropyl)-5-{6-[(2,6-dimethylpyridin-4-yl)oxy]pyrazin-2-yl}-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

2-[1-(4-bromo-2-fluorobenzyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile;

2-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile;

2-[1-(2,2-dimethylpropyl)-7-fluoro-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile;

2-(3-methyl-2-oxo-1-phenyl-2,3-dihydro-1H-benzimidazol-5-yl)benzonitrile;

2-{3-methyl-2-oxo-1-[3-(trifluoromethyl)phenyl]-2,3-dihydro-1H-benzimidazol-5-yl}benzonitrile;

2-{3-methyl-1-[(1-methylcyclopropyl)methyl]-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl}benzonitrile;

2-{1-[4-chloro-3-(trifluoromethyl)benzyl]-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl}benzonitrile;

2-[3-methyl-2-oxo-1-(1-phenylethyl)-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile;

2-(3-methyl-2-oxo-1-{1-[3-(trifluoromethyl)phenyl]ethyl}-2,3-dihydro-1H-benzimidazol-5-yl)benzonitrile;

2-(1,3-dimethyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl)benzonitrile;

2-(3-methyl-2-oxo-1-propyl-2,3-dihydro-1H-benzimidazol-5-yl)benzonitrile;

2-(1-butyl-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl)benzonitrile;

2-(1-hexyl-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl)benzonitrile;

2-[1-(2-fluoroethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile;

2-[1-(2-cyanoethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile;

2-(1-isopropyl-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl)benzonitrile;

2-(1-isobutyl-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl)benzonitrile;

2-(1-sec-butyl-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl)benzonitrile;

2-[1-(cyclopropylmethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile;

2-[1-(cyclopentylmethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile;

2-[3-methyl-2-oxo-1-(tetrahydro-2H-pyran-4-ylmethyl)-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile;

2-[1-(2-cyclohexylethyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile;

2-[3-methyl-1-(4-methylbenzyl)-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile;

2-[1-(4-tert-butylbenzyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile;

2-[3-methyl-2-oxo-1-(pyridin-3-ylmethyl)-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile;

2-[3-methyl-2-oxo-1-(2-phenylethyl)-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile;

2-[1-(3,3-dimethylbutyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile;

2-[1-(3-cyanobenzyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]benzonitrile;

2-{1-[(2,2-difluoro-1-methylcyclopropyl)methyl]-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl}benzonitrile;

3-(2,2-dimethylpropyl)-4-fluoro-1-methyl-6-phenyl-1,3-dihydro-2H-benzimidazol-2-one;

4-chloro-1-(2,2-dimethylpropyl)-3-methyl-5-phenyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-4-fluoro-3-methyl-5-phenyl-1,3-dihydro-2H-benzimidazol-2-one;

4-fluoro-5-[2-fluoro-5-(trifluoromethoxy)phenyl]-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one;

2-fluoro-3-{4-fluoro-3-methyl-1-[(1-methylcyclopropyl)methyl]-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl}benzonitrile;

2-{4-fluoro-3-methyl-1-[(1-methylcyclopropyl)methyl]-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl}-6-methoxybenzonitrile;

5-fluoro-2-{4-fluoro-3-methyl-1-[(1-methylcyclopropyl)methyl]-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl}benzonitrile;

2-{4-fluoro-3-methyl-1-[(1-methylcyclopropyl)methyl]-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl}-5-(trifluoromethyl)benzonitrile;

4-fluoro-3-{4-fluoro-3-methyl-1-[(1-methylcyclopropyl)methyl]-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl}benzonitrile;

1-(2,2-dimethylpropyl)-4-fluoro-5-(3-hydroxyphenyl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

2-[1-(2,2-dimethylpropyl)-4-fluoro-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]-4-hydroxybenzonitrile;

3-[1-(2,2-dimethylpropyl)-4-fluoro-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]isonicotinonitrile;

4-{4-fluoro-3-methyl-1-[(1-methylcyclopropyl)methyl]-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl}nicotinonitrile;

4-fluoro-3-methyl-1-[(1-methylcyclopropyl)methyl]-5-[6-(4-methylpiperazin-1-yl)pyridin-3-yl]-1,3-dihydro-2H-benzimidazol-2-one;

4-fluoro-5-(4-fluoropyridin-2-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one;

4-fluoro-5-(5-fluoropyridin-2-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one;

4-fluoro-5-(6-fluoropyridin-2-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one;

4-fluoro-5-(5-fluoro-6-methylpyridin-2-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one;

4-fluoro-3-methyl-1-[(1-methylcyclopropyl)methyl]-5-[4-(trifluoromethyl)pyridin-2-yl]-1,3-dihydro-2H-benzimidazol-2-one;

4-fluoro-3-methyl-1-[(1-methylcyclopropyl)methyl]-5-[5-(trifluoromethyl)pyridin-2-yl]-1,3-dihydro-2H-benzimidazol-2-one;

4-fluoro-3-methyl-1-[(1-methylcyclopropyl)methyl]-5-[6-(trifluoromethyl)pyridin-2-yl]-1,3-dihydro-2H-benzimidazol-2-one;

4-fluoro-5-(2-fluoropyridin-3-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one;

4-fluoro-5-(5-fluoropyridin-3-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one;

4-fluoro-5-(2-fluoro-5-methylpyridin-3-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one;

4-fluoro-5-(2-fluoroquinolin-3-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one;

4-fluoro-5-(2-methoxypyridin-3-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one;

4-fluoro-5-(4-methoxypyridin-3-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one;

4-fluoro-5-(5-methoxypyridin-3-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one;

4-fluoro-5-(6-methoxypyridin-3-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one;

4-fluoro-5-(2-methoxyquinolin-3-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one;

4-fluoro-3-methyl-1-[(1-methylcyclopropyl)methyl]-5-[4-(trifluoromethyl)pyridin-3-yl]-1,3-dihydro-2H-benzimidazol-2-one;

4-fluoro-5-(3-fluoropyridin-4-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one;

4-fluoro-5-(2-fluoropyridin-4-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one;

5-(2,6-difluoropyridin-4-yl)-4-fluoro-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one;

4-fluoro-5-(2-methoxypyridin-4-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one;

4-fluoro-3-methyl-1-[(1-methylcyclopropyl)methyl]-5-[4-(trifluoromethyl)pyridin-3-yl]-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-4-fluoro-3-methyl-5-[3-(trifluoromethyl)pyridin-4-yl]-1,3-dihydro-2H-benzimidazol-2-one;

3-[1-(2,2-dimethylpropyl)-4-fluoro-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]pyridine-2-carbonitrile;

1-(2,2-dimethylpropyl)-4-fluoro-5-(2-fluoro-5-methylpyridin-3-yl)-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

3-{4-fluoro-3-methyl-1-[(1-methylcyclopropyl)methyl]-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl}pyridine-2-carbonitrile;

4-fluoro-5-(2-methoxyquinolin-3-yl)-3-methyl-1-[(1-methylcyclopropyl)methyl]-1,3-dihydro-2H-benzimidazol-2-one;

1-(cyclopropylmethyl)-4-fluoro-3-methyl-5-[3-(trifluoromethyl)pyridin-4-yl]-1,3-dihydro-2H-benzimidazol-2-one;

3-[1-(cyclopropylmethyl)-4-fluoro-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]isonicotinonitrile;

4-{3-[1-(2,2-dimethylpropyl)-4-fluoro-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}nicotinonitrile;

1-(2,2-dimethylpropyl)-4-fluoro-3-methyl-5-[3-(pyridin-2-yloxy)phenyl]-1,3-dihydro-2H-benzimidazol-2-one;

4-{3-[1-(2,2-dimethylpropyl)-4-fluoro-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}pyridine-2-carbonitrile;

4-{4-cyano-3-[1-(2,2-dimethylpropyl)-4-fluoro-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}pyridine-2-carbonitrile;

6-{4-cyano-3-[1-(2,2-dimethylpropyl)-4-fluoro-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}pyridine-2-carbonitrile;

4-{3-[1-(2,2-dimethylpropyl)-4-fluoro-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenoxy}benzonitrile;

1-(2,2-dimethylpropyl)-5-[3-(1-hydroxy-1-phenylethyl)phenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-[3-(1-hydroxy-1-pyridin-2-ylethyl)phenyl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

1-(2,2-dimethylpropyl)-5-{3-[hydroxy(phenyl)methyl]phenyl}-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

4-(1-{3-[1-(2,2-dimethylpropyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzimidazol-5-yl]phenyl}-1-hydroxyethyl)benzonitrile; and

1-(2,2-dimethylpropyl)-5-[6-(1-hydroxy-1-phenylethyl)pyridin-2-yl]-3-methyl-1,3-dihydro-2H-benzimidazol-2-one;

and pharmaceutically acceptable salts of any of the foregoing compounds.

16. A pharmaceutical composition comprising a compound according to Claim 1 in combination with a pharmaceutically acceptable carrier.

17. A method for treating a neurological or psychiatric disorder associated with glutamate dysfunction in a patient in need thereof comprising administering to the patient a therapeutically effective amount of a compound according to Claim 1.

18. The method according to Claim 17 wherein the neurological or psychiatric disorder associated with glutamate dysfunction is schizophrenia.

INTERNATIONAL SEARCH REPORT

2011/046677 20.12.2011

International application No.
PCT/US 11/46677

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A01N 43/50; A61K 31/415 (2011.01)
USPC - 514/396; 514/397
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)
USPC - 514/396; 514/397

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC - 514/235.8; 514/400; 514/401; 514/402 (see search terms below)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
USPTO-WEST - PGPB,USPT,USOC,EPAB,JPAB keywords: mGluR2 receptor, potentiators, psychiatric disorders, glutamate dysfunction, treatment, schizophrenia, administration, pharmaceutical composition, benzazole, benzotriazolyl, potentiating glutamate receptor, AMPA receptor potentiator, molecular modeling, binding site, pharmacophore. INTERNET search - G

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2006/091496 A2 (GOVEK et al.) 31 August 2006 (31.08.2006) pg 2, ln 25-28; pg 3, ln 1 - pg 5, ln 32; pg 14, ln 29 - pg 15, ln 6; pg 17, ln 1-6; pg 17, ln 25 - pg 18, ln 2; pg 18, ln 30 - pg 19, ln 13	1-18
Y	WO 02/14275 A2 (FORMAN et al.) 21 February 2002 (21.02.2002) pg 2, ln 3-4; pg 3, ln 5 - pg 4, ln 8; pg 4, ln 18-20, 27-33; pg 5, ln 1-14	1-18
Y	JULLIAN et al. Agonist Selectivity of mGluR1 and mGluR2 Metabotropic Receptors: A Different Environment but Similar Recognition of an Extended Glutamate Conformation. J. Med. Chem., 1999, Vol 42(9), pp 1546-1555; pg 1546 - pg 1553	1-18
Y	US 2008/0293684 A1 (PINKERTON et al.) 27 November 2008 (27.11.2008) para [0006]-[0053]	8-14

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* 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
02 December 2011 (02.12.2011)	20 DEC 2011
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774