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(54) Titre : 1H-IMIDAZO[4,5-B]PYRIDIN-2(3H)-ONES SUBSTITUEES ET LEUR UTILISATION EN TANT QUE  
MODULATEURS DU RECEPTEUR GLUN2B  
(54) Title: SUBSTITUTED 1H-IMIDAZO[4,5-B]PYRIDIN-2(3H)-ONES AND THEIR USE AS GLUN2B RECEPTOR  
MODULATORS

(57) **Abrégé/Abstract:**

Substituted 1 H-imidazo[4,5-b]pyridin-2(3H)-ones as NR2B receptor ligands. Such compounds may be used in NR2B receptor modulation and in pharmaceutical compositions and methods for the treatment of disease states, disorders, and conditions mediated by NR2B receptor activity.

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(54) Title: SUBSTITUTED 1H-IMIDAZO[4,5-B]PYRIDIN-2(3H)-ONES AND THEIR USE AS GLUN2B RECEPTOR MODULATORS

(57) Abstract: Substituted 1 H-imidazo[4,5-b]pyridin-2(3H)-ones as NR2B receptor ligands. Such compounds may be used in NR2B receptor modulation and in pharmaceutical compositions and methods for the treatment of disease states, disorders, and conditions mediated by NR2B receptor activity.

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## Field of the Invention

## Background of the Invention

N-methyl-D-aspartate (NMDA) receptors are a subtype of ionotropic glutamate receptors that mediate excitatory synaptic transmission in the brain. NMDA receptors are ubiquitously distributed throughout the brain and play a key role in synaptic plasticity, synaptogenesis, excitotoxicity, memory acquisition and learning. NMDA receptors are distinct from other major subtypes of ionotropic glutamate receptors (AMPA and kainate receptors) in that they are blocked by  $Mg^{2+}$  at resting membrane potentials, are highly  $Ca^{2+}$  permeable, and require co-activation by two distinct neurotransmitters: glutamate and glycine (or D-serine) (Traynelis SF et al., *Pharmacol Rev.* **2010**; 62(3):405-96). The influx of  $Ca^{2+}$  through NMDA receptors triggers signaling cascades and regulates gene expression that is critical for different forms of synaptic plasticity including both long-term potentiation of synapse efficacy (LTP) (Berberich S et al., *Neuropharmacology* **2007**; 52(1):77-86) and long-term depression (LTD) (Massey, PV et al., *J Neurosci.* **2004** Sep 8;24(36):7821-8).

The vast majority of the mammalian NMDA receptors form a heterotetramer made

of two obligatory GluN1 units and two variable GluN2 receptor subunits encoded by the GRIN1 gene and one of four GRIN2 genes, respectively. One or both GluN2 subunits can be potentially replaced by a GluN3A or a GluN3B subunit. The GRIN1 gene product has 8 splice variants while there are 4 different GRIN2 genes (GRIN2A-D) encoding four distinct  
 5 GluN2 subunits. The glycine binding site is present on the GluN1 subunit and the glutamate binding site is present on the GluN2 subunit.

The GluN2 subunits play a dominant role in determining the functional and pharmacological properties of the NMDA receptor assembly and exhibit distinct distribution in different areas of the brain. For instance, GluN2B subunits are expressed primarily in the  
 10 forebrain in the adult mammalian brain (Paoletti P et al., *Nat Rev Neurosci.* **2013**; 14(6):383-400; Watanabe M et al., *J Comp Neurol.* **1993**; 338(3):377-90) and are implicated in learning, memory processing, mood, attention, emotion and pain perception (Cull-Candy S et al., *Curr Opin Neurobiol.* **2001**; 11(3):327-35).

Compounds that modulate GluN2B-containing NMDA receptor function can be  
 15 useful in treatment of many neurological and psychiatric disorders including but not limited to bipolar disorder (Martucci L et al., *Schizophrenia Res.* **2006**; 84(2-3):214-21), major depressive disorder (Miller OH et al., *eLife.* **2014**; 3:e03581; Li N et al., *Biol Psychiatry.* **2011**; 69(8):754-61), treatment-resistant depression (Preskorn SH et al. *J Clin Psychopharmacol.* **2008**; 28(6):631-7) and other mood disorders (including schizophrenia  
 20 (Grimwood S et al., *Neuroreport.* **1999**; 10(3):461-5; Weickert CS et al. *Molecular Psychiatry* (**2013**) 18, 1185–1192), ante- and postpartum depression, seasonal affective disorder and the like), Alzheimer's disease (Hanson JE et al., *Neurobiol Dis.* **2015**; 74:254-62; Li S et al., *J Neurosci.* **2011**; 31(18):6627-38) and other dementias (Orgogozo JM et al. *Stroke* 2002, 33: 1834–1839), Parkinson's disease (Duty S, *CNS Drugs.* **2012**;  
 25 26(12):1017-32; Steece-Collier K et al., *Exp Neurol.* 2000; 163(1):239-43; Leaver KR et al. *Clin Exp Pharmacol Physiol.* **2008**; 35(11):1388-94), Huntington's chorea (Tang TS et al., *Proc Natl Acad Sci USA.* **2005**; 102(7):2602-7; Li L et al., *J Neurophysiol.* **2004**;  
 92(5):2738-46), multiple sclerosis (Grasselli G et al., *Br J Pharmacol.* **2013**; 168(2):502-17; Farjam M et al., *Iran J Pharm Res.* **2014**; 13(2):695-705), cognitive impairment (Wang D et al. **2014**, *Expert Opin Ther Targets Expert Opin Ther Targets.* **2014**; 18(10):1121-30), head  
 30 injury (Bullock MR et al., *Ann N Y Acad Sci.* **1999**; 890:51-8), spinal cord injury, stroke

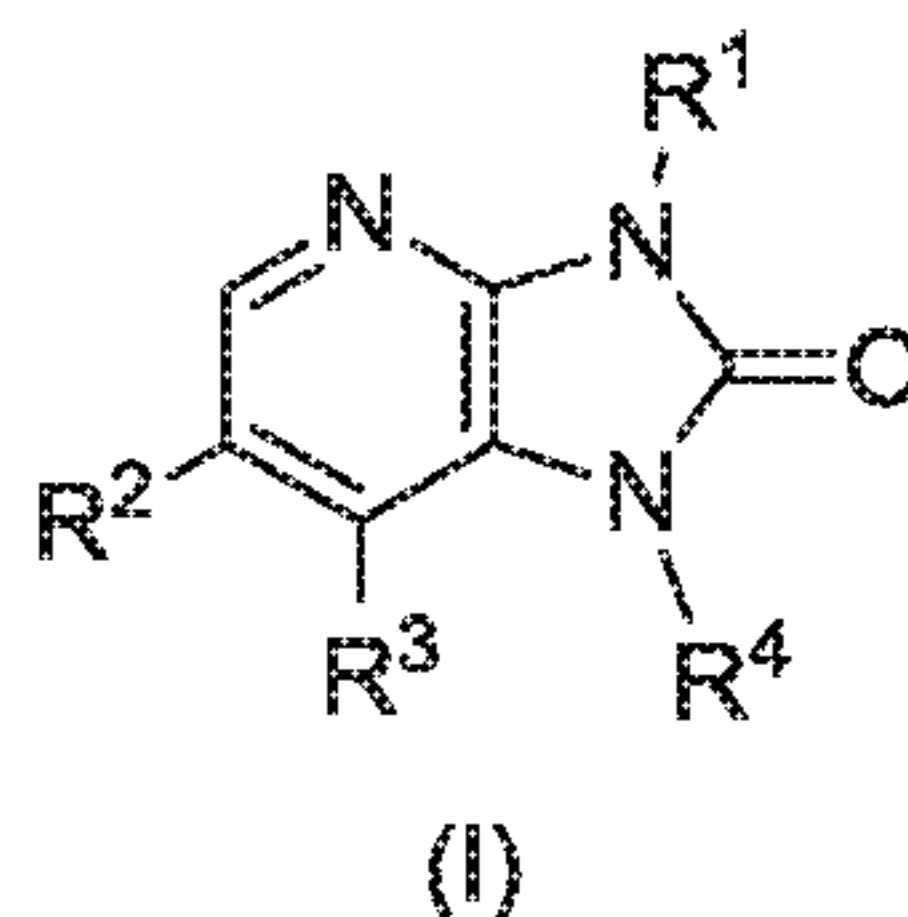
(Yang Y et al., *J Neurosurg.* **2003**; 98(2):397-403), epilepsy (Naspolini AP et al., *Epilepsy Res.* **2012** Jun;100(1-2):12-9), movement disorders (e.g. dyskinesias) (Morissette M et al., *Mov Disord.* **2006**; 21(1):9-17), various neurodegenerative diseases (e.g. amyotrophic lateral sclerosis (Fuller PI et al., *Neurosci Lett.* **2006**; 399(1-2):157-61) or  
 5 neurodegeneration associated with bacterial or chronic infections), glaucoma (Naskar R et al. *Semin Ophthalmol.* **1999** Sep;14(3):152-8 ), pain (e.g. chronic, cancer, post-operative and neuropathic pain (Wu LJ and Zhuo M, *Neurotherapeutics.* **2009**; 6(4):693-702), diabetic neuropathy, migraine (Peeters M et al., *J Pharmacol Exp Ther.* **2007**; 321(2):564-72), cerebral ischemia (Yuan H et al., *Neuron.* **2015**; 85(6):1305-18), encephalitis (Dalmau  
 10 J. et al., *Lancet Neurol.* **2008**; 7(12):1091-8.), autism and autism spectrum disorders (Won H. et al., *Nature.* **2012**; 486(7402):261-5), memory and learning disorders (Tang, Y. P. et al., *Nature.* **1999**; 401(6748):63-9), obsessive compulsive disorder (Arnold PD et al., *Psychiatry Res.* **2009**;172(2):136-9.), attention deficit hyperactivity disorder (ADHD) (Dorval KM et al., *Genes Brain Behav.* **2007**; 6(5):444-52), PTSD (Haller J et al. *Behav  
 15 Pharmacol.* 2011;22(2):113-21; Leaderbrand K et al. *Neurobiol Learn Mem.* 2014; 113:35-40), tinnitus (Guitton MJ, and Dudai Y, *Neural Plast.* 2007; 80904; Hu SS et al. **2016**; 273(2): 325-332), sleep disorders (like narcolepsy or excessive daytime sleepiness, patent WO 2009058261 A1), vertigo and nystagmus (Straube A. et al., *Curr Opin Neurol.* 2005;18(1):11-4; Starck M et al. *J Neurol.* **1997** Jan;244(1):9-16), anxiety  
 20 autoimmune disorders like neuropsychiatric systemic lupus erythematosus (Kowal C et al. *Proc. Natl. Acad. Sci. U.S.A.* **2006**; 103, 19854–19859) and addictive illnesses (e.g. alcohol addiction, drug addiction) (Nagy J, **2004**, *Curr Drug Targets CNS Neurol Disord.* **2004**; 3(3):169-79.; Shen H et al., *Proc Natl Acad Sci USA.* **2011**;108(48):19407-12).

In view of the clinical importance of NR2B, the identification of compounds that  
 25 modulate NR2B receptor function represents an attractive avenue into the development of new therapeutic agents. Such compounds are provided herein.

### Summary of the Invention

30 The invention is directed to the general and preferred embodiments defined, respectively, by the independent and dependent claims appended hereto, which are

incorporated by reference herein. One aspect of this invention concerns compounds of Formula (I):

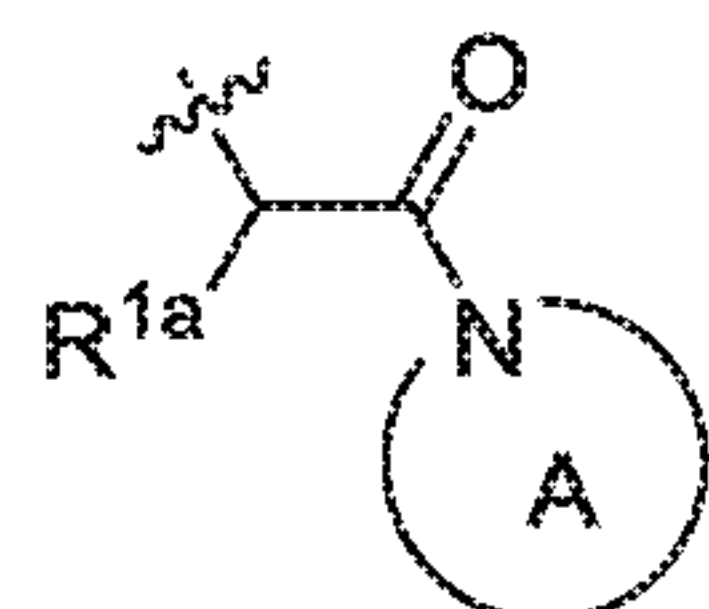


wherein

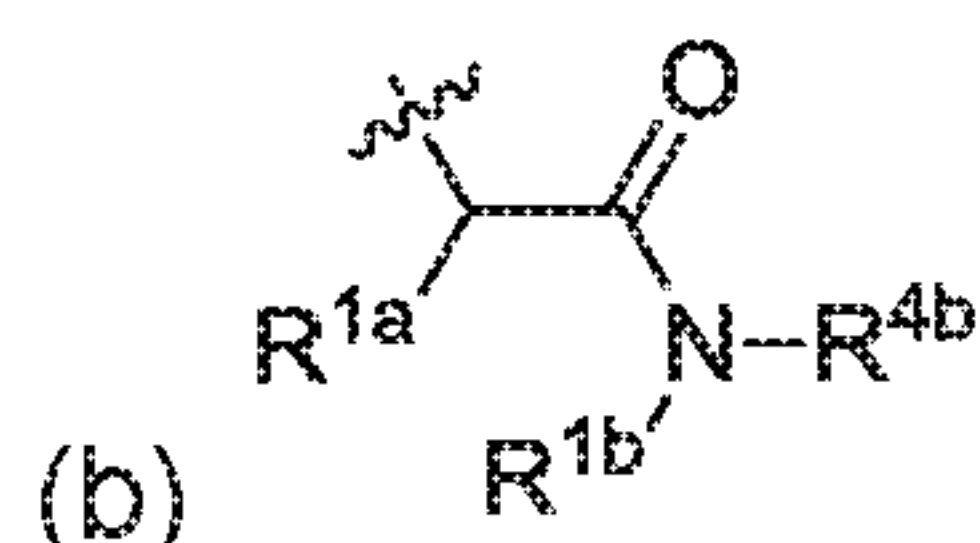
- 5  $R^1$  is H;  $\text{CH}_2\text{F}$ ; or  $\text{CH}_3$ ;  $R^2$  is selected from the group consisting of: phenyl; phenyl substituted with one, two, or three members each independently selected from the group consisting of: halo,  $\text{C}_{1-6}$ alkyl,  $\text{C}_{1-6}$ haloalkyl, CN,  $\text{OC}_{1-6}$ alkyl,  $\text{OC}_{1-6}$ haloalkyl,  $\text{N}(\text{CH}_3)_2$ , and cyclopropyl; pyridinyl; pyridinyl substituted with F,  $\text{C}_{1-4}$ alkyl, or  $\text{C}_{1-4}$ haloalkyl; thiazolyl; thiazolyl substituted with  $\text{C}_{1-6}$ alkyl or  $\text{C}_{1-6}$ haloalkyl; thienyl; and thienyl substituted with one or two members each independently selected from the group consisting of: halo,  $\text{C}_{1-6}$ alkyl,  $\text{C}_{1-6}$ haloalkyl,  $\text{CH}_2\text{OH}$ ,  $\text{CH}_2\text{OCH}_3$ , and cyclopropyl;
- 10

$R^3$  is H;

$R^4$  is selected from the group consisting of:



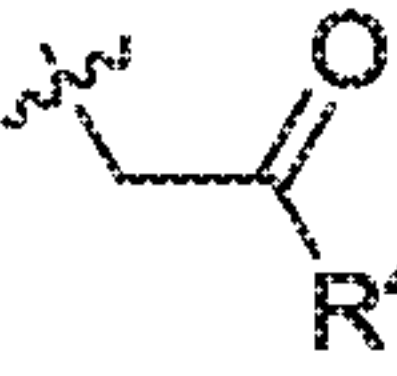
- 15 (a) wherein ring A is a 4-6 membered heterocycle optionally containing an additional oxygen heteroatom selected from the group consisting of: azetidiny; azetidiny substituted with one or two members independently selected from the group consisting of: F, OH,  $\text{C}_{1-4}$ alkyl,  $\text{C}_{1-4}$ haloalkyl,  $\text{CH}_2\text{OCH}_3$ , CN, and  $\text{OCH}_3$ ; pyrrolidiny; pyrrolidiny substituted two F members;
- 20 morpholiny; piperidiny; piperaziny substituted with  $\text{C}_{1-6}$ alkyl; and (2,6-diazaspiro[3.3]heptan-6-yl);



- (b) , wherein  $R^{4b}$  is selected from the group consisting of: H;  $\text{C}_{1-6}$ alkyl;  $\text{CH}_2\text{CH}_2\text{OCH}_3$ ;  $\text{C}_{3-6}$ cycloalkyl;  $\text{C}_{3-6}$ cycloalkyl substituted substituted with two or

three members independently selected from the group consisting of F or CH<sub>3</sub>; oxetanyl; oxetanyl substituted with CH<sub>3</sub>; and pyridinyl;

- (c)  R<sup>4c</sup> wherein R<sup>4c</sup> is selected from the group consisting of: cyclopropyl; cyclopropyl substituted with one or two F members; CH(OH)cyclopropyl; azetidiny; CH<sub>2</sub>-azetidiny; CH<sub>2</sub>-azetidiny substituted with one or two members independently selected from: F, OH, OCH<sub>3</sub>, and CF<sub>3</sub>; oxetanyl; oxetanyl substituted with F or CH<sub>3</sub>; tetrahydrofuranyl; tetrahydropyranyl; CH<sub>2</sub>pyrrolidinyl; CH<sub>2</sub>pyrrolidinyl substituted with CH<sub>3</sub>, OH, or OCH<sub>3</sub>; CH<sub>2</sub>piperidinyl; CH<sub>2</sub>piperidinyl substituted with OH, or F; morpholinyl; pyrazolyl substituted with one or two CH<sub>3</sub> members; triazolyl substituted with CH<sub>3</sub>; tetrazolyl; isoxazolyl substituted with one or two CH<sub>3</sub> members; oxadiazolyl substituted with CH<sub>3</sub>, or CH<sub>2</sub>OCH<sub>3</sub>; thiadiazolyl; pyridinyl; pyridinyl substituted with one or two members independently selected from the group consisting of: Cl, F, CH<sub>3</sub>, OCH<sub>3</sub>, and CF<sub>3</sub>; (2-oxo-1H-pyridin-3-yl); 6-oxo-1H-pyridin-3-yl; pyrimidinyl; pyrimidinyl substituted with F or CH<sub>3</sub>; pyrazinyl; pyridazinyl; pyridazinyl substituted with OCH<sub>3</sub>; phenyl; phenyl substituted with one or two members independently selected from the group consisting of: halo, CN, OCH<sub>3</sub>, C<sub>1-6</sub>alkyl, and CF<sub>3</sub>;

- (d)  R<sup>4d</sup> wherein R<sup>4d</sup> is selected from the group consisting of: OH, C<sub>1-6</sub>alkyl, O-C<sub>1-6</sub>alkyl, C<sub>3-6</sub>cycloalkyl, thienyl, and thiazolyl; and

- (e) C<sub>2-6</sub>alkyl substituted with one or two members independently selected from OH, OC<sub>1-6</sub>alkyl, or cyclopropyl; CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>1-6</sub>alkyl); CH<sub>2</sub>CH<sub>2</sub>NH(CH<sub>2</sub>CH<sub>2</sub>OH); CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>3-6</sub>cycloalkyl); and difluoro(3-pyridyl)methyl; and

R<sup>1a</sup> and R<sup>1b</sup> are each independently H or CH<sub>3</sub>;

and pharmaceutically acceptable salts, stereoisomers, isotopic variants, N-oxides, or solvates of compounds of Formula (I).

Further embodiments are provided by pharmaceutically acceptable salts of compounds of Formulas (I), pharmaceutically acceptable prodrugs of compounds of Formula (I), and pharmaceutically active metabolites of compounds of Formula (I).

In certain embodiments, the compounds of Formula (I) are compounds selected from those species described or exemplified in the detailed description below.

In a further aspect, the invention relates to enantiomers and diastereomers of the compounds of Formula (I), as well as the pharmaceutically acceptable salts.

In a further aspect, the invention relates to pharmaceutical compositions for treating a disease, disorder, or medical condition mediated by NR2B receptor activity, comprising an effective amount of at least one compound selected from compounds of Formula (I), pharmaceutically acceptable salts of compounds of Formula (I), pharmaceutically acceptable prodrugs of compounds of Formula (I), and pharmaceutically active metabolites of Formula (I).

Pharmaceutical compositions according to the invention may further comprise one or more pharmaceutically acceptable excipients.

In another aspect, the chemical embodiments of the present invention are useful as NR2B receptor modulators. Thus, the invention is directed to a method for modulating NR2B receptor activity, including when such receptor is in a subject, comprising exposing NR2B receptor to an effective amount of at least one compound selected from compounds of Formula (I), pharmaceutically acceptable salts of compounds of Formula (I), pharmaceutically acceptable prodrugs of compounds of Formula (I), and pharmaceutically active metabolites of compounds of Formula (I).

In another aspect, the invention is directed to a method of treating a subject suffering from, or diagnosed with a disease, disorder, or medical condition mediated by NR2B receptor activity, comprising administering to the subject in need of such treatment an effective amount of at least one compound selected from compounds of Formula (I), pharmaceutically acceptable salts of compounds of Formula (I), pharmaceutically acceptable prodrugs of compounds of Formula (I), and pharmaceutically active metabolites of compounds of Formula (I). Additional embodiments of methods of treatment are set forth in the detailed description.

In another aspect, the method of studying isotopically labeled compounds in metabolic studies (preferably with  $^{14}\text{C}$ ), reaction kinetic studies (with, for example  $^2\text{H}$  or  $^3\text{H}$ ), detection or imaging techniques [such as positron emission tomography (PET) or single-photon emission computed tomography (SPECT)] including drug or substrate

tissue distribution assays, or in radioactive treatment of patients. For example, an  $^{18}\text{F}$  or  $^{11}\text{C}$  labeled compound may be particularly preferred for PET or SPECT studies.

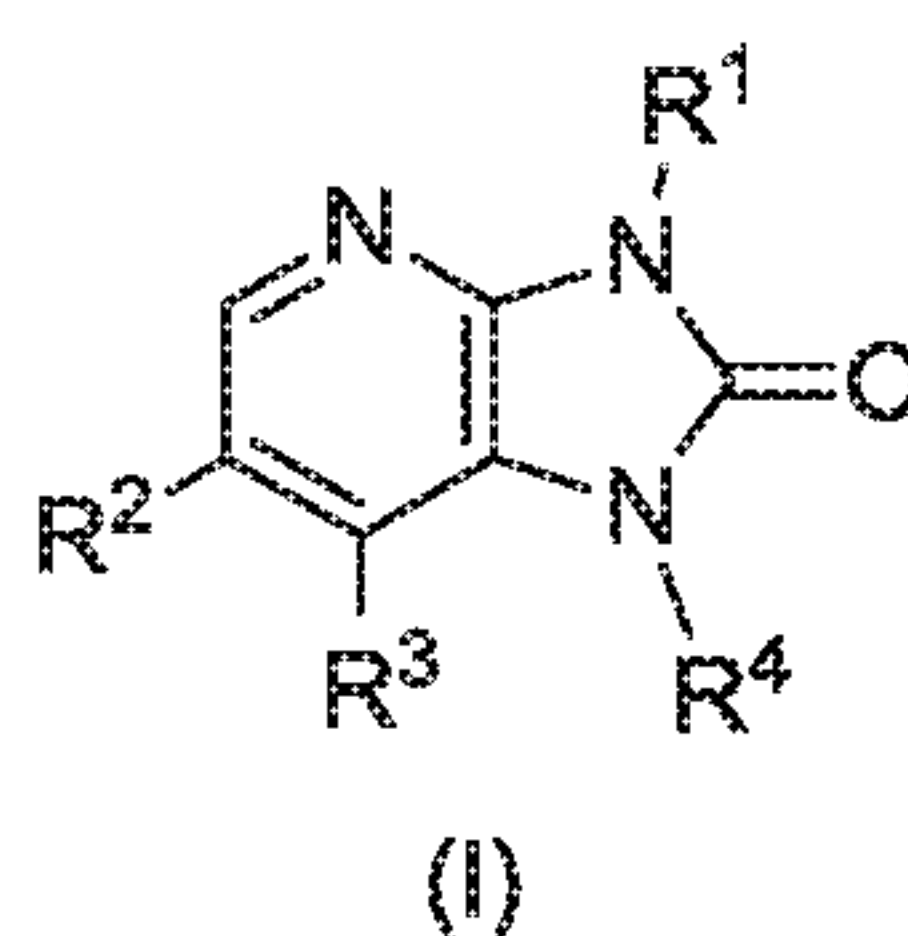
Additional embodiments of this invention include methods of making compounds of Formula (I), pharmaceutically acceptable salts of compounds of Formula (I),  
 5 pharmaceutically acceptable prodrugs of compounds of Formula (I), and pharmaceutically active metabolites of Formula (I).

An object of the present invention is to overcome or ameliorate at least one of the disadvantages of the conventional methodologies and/or prior art, or to provide a useful alternative thereto.

10 Additional embodiments, features, and advantages of the invention will be apparent from the following detailed description and through practice of the invention.

### Detailed Description of Invention

15 In one aspect, provided herein are compounds of Formula (I), and pharmaceutically acceptable salts, stereoisomers, isotopic variants, N-oxides, or solvates thereof,



20 wherein

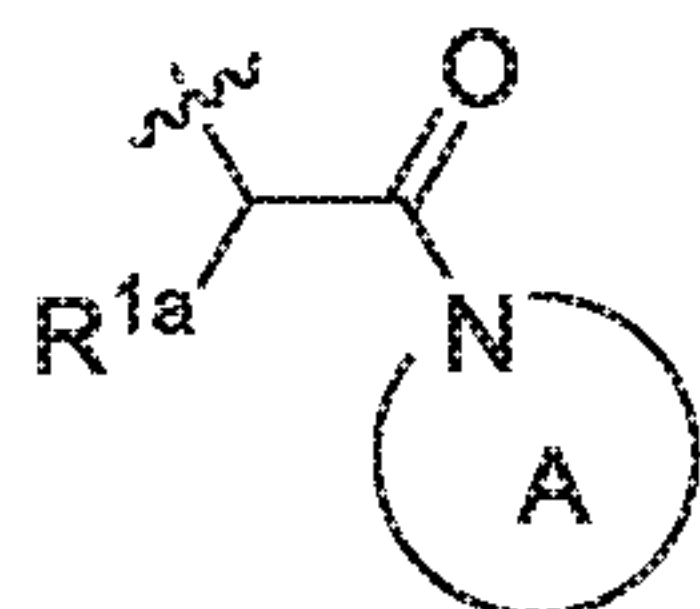
$\text{R}^1$  is H;  $\text{CH}_2\text{F}$ ; or  $\text{CH}_3$ ;

$\text{R}^2$  is selected from the group consisting of: phenyl; phenyl substituted with one, two, or three members each independently selected from the group consisting of: halo,  $\text{C}_{1-6}$ alkyl,  $\text{C}_{1-6}$ haloalkyl, CN,  $\text{OC}_{1-6}$ alkyl,  $\text{OC}_{1-6}$ haloalkyl,  $\text{N}(\text{CH}_3)_2$ , and cyclopropyl; pyridinyl; pyridinyl substituted with F,  $\text{C}_{1-4}$ alkyl, or  $\text{C}_{1-4}$ haloalkyl; thiazolyl; thiazolyl substituted with  $\text{C}_{1-6}$ alkyl or  $\text{C}_{1-6}$ haloalkyl; thienyl; and thienyl substituted with one or two members each independently selected from the

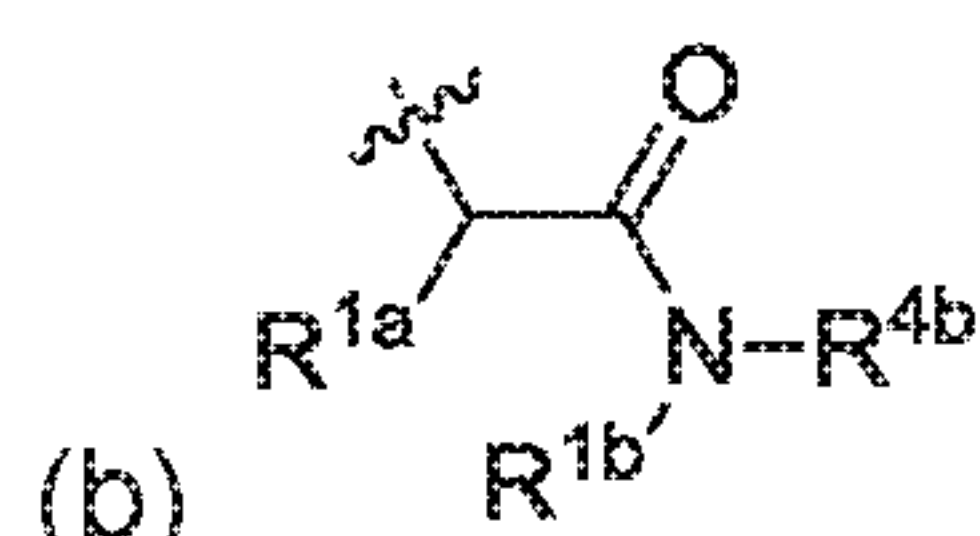
group consisting of: halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>haloalkyl, CH<sub>2</sub>OH, CH<sub>2</sub>OCH<sub>3</sub>, and cyclopropyl;

R<sup>3</sup> is H;

R<sup>4</sup> is selected from the group consisting of:



- (a) wherein ring A is a 4-6 membered heterocycle optionally containing an additional oxygen heteroatom selected from the group consisting of: azetidiny; azetidiny substituted with one or two members independently selected from the group consisting of: F, OH, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>haloalkyl, CH<sub>2</sub>OCH<sub>3</sub>, CN, and OCH<sub>3</sub>; pyrrolidiny; pyrrolidiny substituted two F members; morpholiny; piperidiny; piperaziny substituted with C<sub>1-6</sub>alkyl; and (2,6-diazaspiro[3.3]heptan-6-yl);

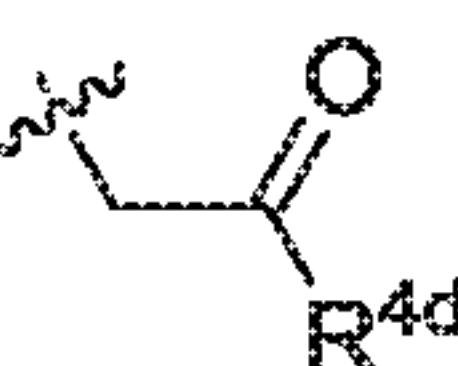


- (b) , wherein R<sup>4b</sup> is selected from the group consisting of: H; C<sub>1-6</sub>alkyl; CH<sub>2</sub>CH<sub>2</sub>OCH<sub>3</sub>; C<sub>3-6</sub>cycloalkyl; C<sub>3-6</sub>cycloalkyl substituted substituted with two or three members independently selected from the group consisting of F or CH<sub>3</sub>; oxetany; oxetany substituted with CH<sub>3</sub>; and pyridiny;



- (c) wherein R<sup>4c</sup> is selected from the group consisting of: cyclopropyl; cyclopropyl substituted with one or two F members; CH(OH)cyclopropyl; azetidiny; CH<sub>2</sub>-azetidiny; CH<sub>2</sub>-azetidiny substituted with one or two members independently selected from: F, OH, OCH<sub>3</sub>, and CF<sub>3</sub>; oxetany; oxetany substituted with F or CH<sub>3</sub>; tetrahydrofurany; tetrahydropyrany; CH<sub>2</sub>pyrrolidiny; CH<sub>2</sub>pyrrolidiny substituted with CH<sub>3</sub>, OH, or OCH<sub>3</sub>; CH<sub>2</sub>piperidiny; CH<sub>2</sub>piperidiny substituted with OH, or F; morpholiny; pyrazoly substituted with one or two CH<sub>3</sub> members; triazoly substituted with CH<sub>3</sub>; tetrazoly; isoxazoly substituted with one or two CH<sub>3</sub> members; oxadiazoly substituted with CH<sub>3</sub>, or CH<sub>2</sub>OCH<sub>3</sub>; thiadiazoly; pyridiny; pyridiny substituted with one or two members independently selected from the group consisting of: Cl, F, CH<sub>3</sub>, OCH<sub>3</sub>, and CF<sub>3</sub>; (2-oxo-1H-pyridin-3-yl); 6-oxo-1H-pyridin-3-yl; pyrimidiny; pyrimidiny

substituted with F or CH<sub>3</sub>; pyrazinyl; pyridazinyl; pyridazinyl substituted with OCH<sub>3</sub>; phenyl; phenyl substituted with one or two members independently selected from the group consisting of: halo, CN, OCH<sub>3</sub>, C<sub>1-6</sub>alkyl, and CF<sub>3</sub>;

- (d)  wherein R<sup>4d</sup> is selected from the group consisting of: OH, C<sub>1-6</sub>alkyl, O-C<sub>1-6</sub>alkyl, C<sub>3-6</sub>cycloalkyl, thienyl, and thiazolyl; and
- (e) C<sub>2-6</sub>alkyl substituted with one or two members independently selected from OH, OC<sub>1-6</sub>alkyl, or cyclopropyl; CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>1-6</sub>alkyl); CH<sub>2</sub>CH<sub>2</sub>NH(CH<sub>2</sub>CH<sub>2</sub>OH); CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>3-6</sub>cycloalkyl); and difluoro(3-pyridyl)methyl and R<sup>1a</sup> and R<sup>1b</sup> are each independently H or CH<sub>3</sub>.

An additional embodiment of the invention is a compound of Formula (I) wherein R<sup>1</sup> is H.

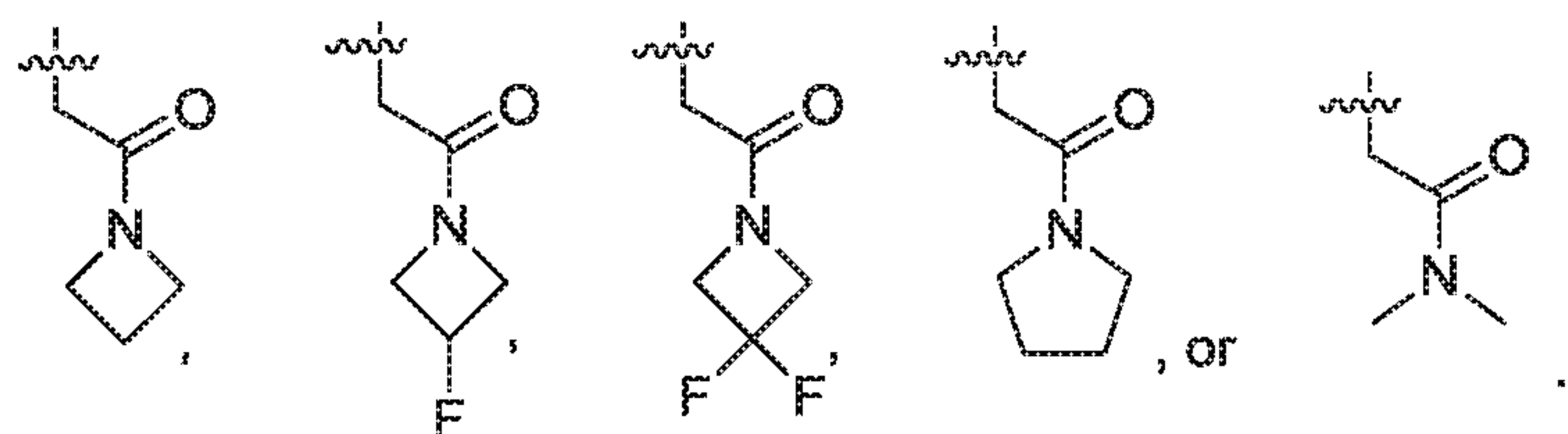
An additional embodiment of the invention is a compound of Formula (I) wherein R<sup>1</sup> is CH<sub>3</sub>.

An additional embodiment of the invention is a compound of Formula (I) wherein R<sup>1a</sup> is H.

An additional embodiment of the invention is a compound of Formula (I) wherein R<sup>2</sup> is phenyl; phenyl substituted with one, two, or three members each independently selected from the group consisting of: Cl, F, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>haloalkyl, CN, OC<sub>1-6</sub>alkyl, OC<sub>1-6</sub>haloalkyl, N(CH<sub>3</sub>)<sub>2</sub>, and cyclopropyl; pyridinyl; or pyridinyl substituted with CF<sub>3</sub>.

An additional embodiment of the invention is a compound of Formula (I) wherein R<sup>2</sup> is thiazolyl substituted with C<sub>1-6</sub>alkyl or CF<sub>3</sub>; thienyl; or thienyl substituted with one or two members each independently selected from the group consisting of: Cl, F, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>haloalkyl, CH<sub>2</sub>OH, CH<sub>2</sub>OCD<sub>3</sub>, and cyclopropyl.

An additional embodiment of the invention is a compound of Formula (I) wherein  $R^1$  is H or  $CH_3$ ,  $R^2$  is phenyl, wherein the phenyl is optionally substituted with one, two, or three members independently selected from: halo,  $C_{1-6}$ alkyl, and  $C_{1-6}$ haloalkyl; or thienyl, wherein the thienyl is optionally substituted with one or two members  
 5 independently selected from: halo,  $C_{1-6}$ alkyl, and  $C_{1-6}$ haloalkyl;  $R^3$  is H, and  $R^4$  is



An additional embodiment of the invention is a compound of Formula (I) wherein  $R^2$  is phenyl; o-tolyl; m-tolyl; p-tolyl; 4-tert-butylphenyl; 3-(trifluoromethyl)phenyl; 4-fluorophenyl; 3-fluorophenyl; 3-cyanophenyl; 3-chlorophenyl; 4-chlorophenyl; 3-(difluoromethyl)phenyl; 3-methoxyphenyl; 3-(difluoromethoxy)phenyl; 4-methoxyphenyl;  
 10 3-(trifluoromethoxy)phenyl; 2-ethoxyphenyl; 3-ethoxyphenyl; 3-cyclopropylphenyl; 3-(dimethylamino)phenyl; 2,3-dichlorophenyl; 2,3-difluorophenyl; 2,3-dimethylphenyl; 2-fluoro-3-(trifluoromethyl)phenyl; 2,4-dimethoxyphenyl; 2,3-dimethoxyphenyl; 2,4-difluorophenyl; 3,4-difluorophenyl; 3,4-dichlorophenyl; 3-(difluoromethyl)-4-fluoro-phenyl;  
 15 5-(difluoromethyl)-2-fluorophenyl; 2,6-dimethylphenyl; 3,5-dimethylphenyl; 3,5-difluorophenyl; 3-fluoro-5-(trifluoromethyl)phenyl; 2-methyl-5-(trifluoromethyl)phenyl; 2-methyl-3-(trifluoromethyl)phenyl; 4-chloro-3-methyl-phenyl; 4-fluoro-3-(trifluoromethyl)phenyl; 4-chloro-3-(trifluoromethyl)phenyl; 2-ethoxy-5-fluoro-phenyl; 3-chloro-2-fluoro-phenyl; 3-chloro-4-fluoro-phenyl; 2-chloro-4-methoxy-phenyl; 4-fluoro-2-methyl-phenyl; 4-fluoro-2-methoxy-phenyl; 2-fluoro-6-methoxy-phenyl; 3-fluoro-4-methoxy-phenyl; 3-fluoro-5-methyl-phenyl; 2-fluoro-3-methyl-phenyl; 4-fluoro-3-methyl-phenyl; 4-methoxy-3-methyl-phenyl; 4-fluoro-2,3-dimethyl-phenyl; 2,4-difluoro-3-methyl-phenyl; 2,3,4-trifluorophenyl; 3,4,5-trifluorophenyl; 3,4-difluoro-5-(trifluoromethyl)phenyl;  
 20 3-pyridyl; 2-(trifluoromethyl)-4-pyridyl; 2-thienyl; 5-methyl-2-thienyl; 5-ethyl-2-thienyl; 4-methyl-2-thienyl; 5-(trideuteriomethoxymethyl); 5-(hydroxymethyl)-2-thienyl; 5-fluoro-2-thienyl; 5-chloro-2-thienyl; 5-cyclopropyl-2-thienyl; 5-chloro-4-methyl-2-thienyl; 5-(difluoromethyl)-2-thienyl; 5-(difluoromethyl)-3-thienyl; 5-(trifluoromethyl)-2-thienyl; 5-(trifluoromethyl)-3-thienyl; 2-(trifluoromethyl)-3-thienyl; 4-(difluoromethyl)-2-thienyl; 5-

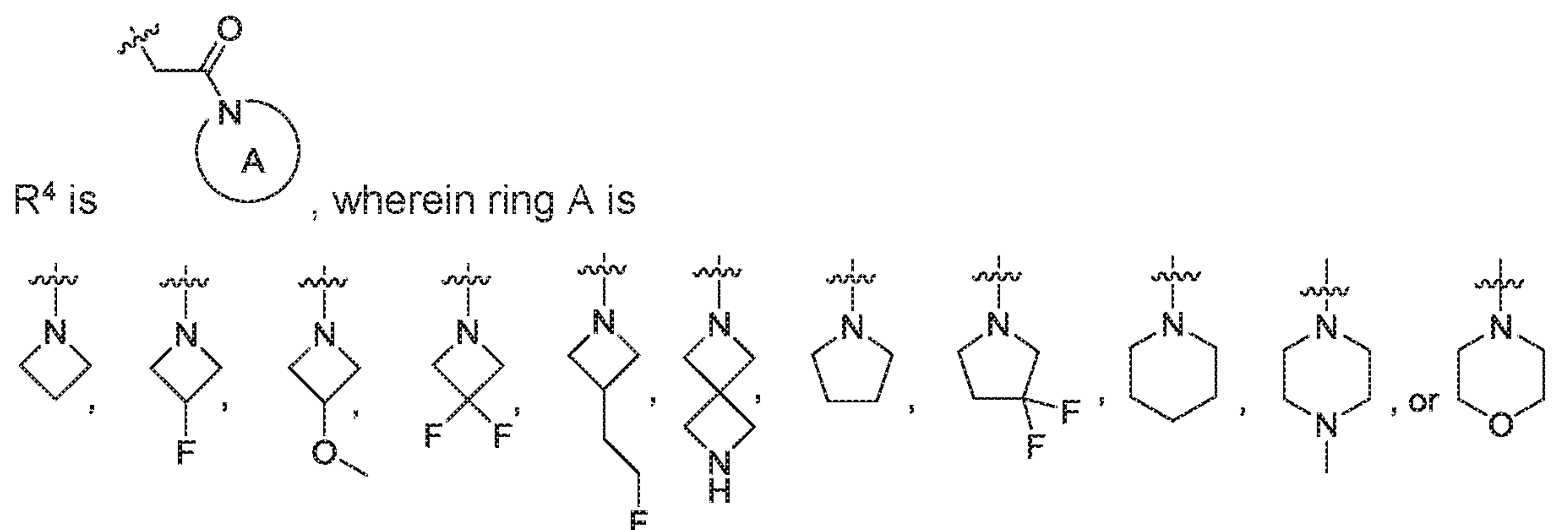
(1,1,2,2,2-pentafluoroethyl)-2-thienyl; 4-methylthiazol-2-yl; 2-methylthiazol-5-yl; 2-(trifluoromethyl)thiazol-5-yl; or 2-(trifluoromethyl)thiazol-4-yl.

An additional embodiment of the invention is a compound of Formula (I) wherein

5  $\mathbb{R}^3$  is H.

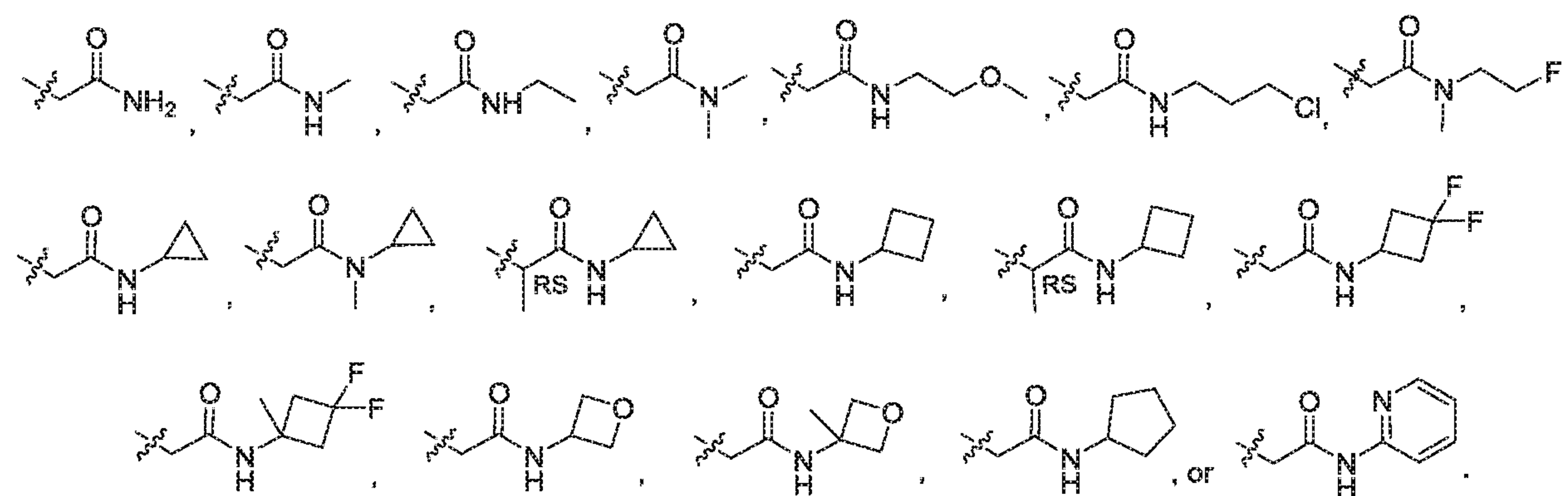
An additional embodiment of the invention is a compound of Formula (I) wherein  $R^3$  is D or T.

10           An additional embodiment of the invention is a compound of Formula (I) wherein



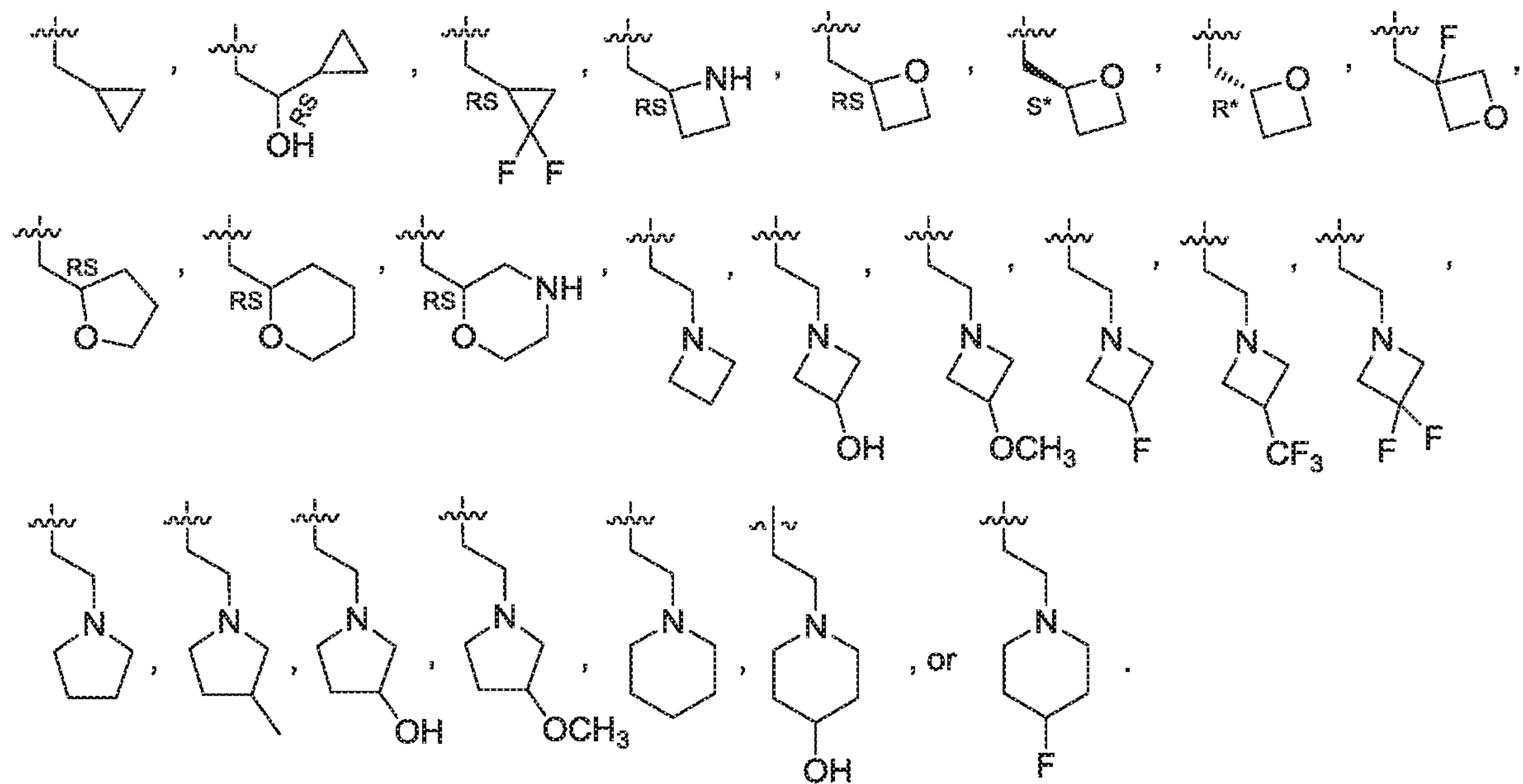
An additional embodiment of the invention is a compound of Formula (I) wherein

$\mathbb{R}^4$  is

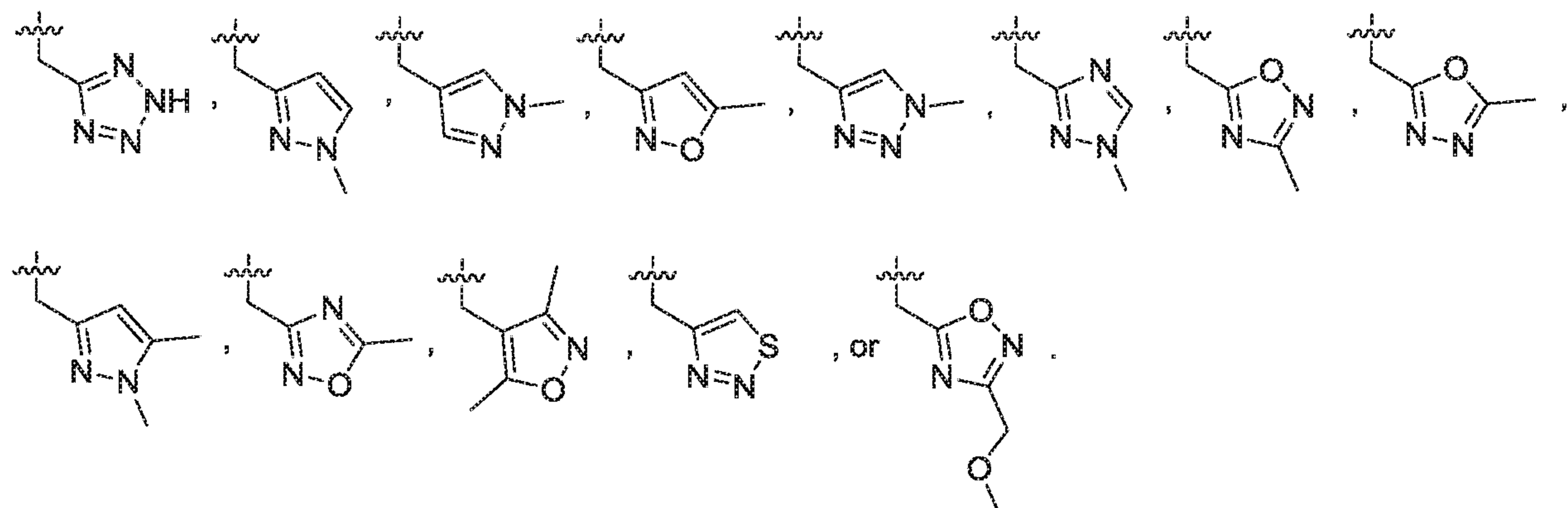


An additional embodiment of the invention is a compound of Formula (I) wherein

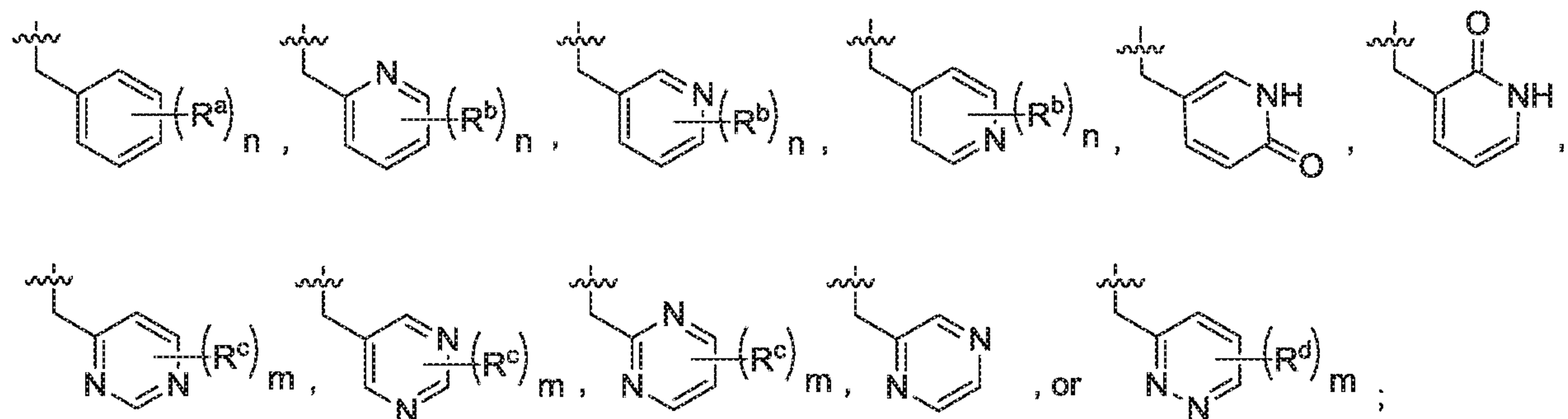
$\mathbb{R}^4$  is



An additional embodiment of the invention is a compound of Formula (I) wherein R<sup>4</sup> is



5 An additional embodiment of the invention is a compound of Formula (I) wherein R<sup>4</sup> is



wherein

$R^a$  is independently selected from: halo, CN,  $OCH_3$ ,  $C_{1-6}$ alkyl, and  $CF_3$ ;

$R^b$  is independently selected from: Cl, F,  $CH_3$ ,  $OCH_3$ , and  $CF_3$ ;

$R^c$  is F or  $CH_3$ ;

$R^d$  is  $OCH_3$ ;

5  $m$  is 0 or 1; and

$n$  is 0, 1, or 2.

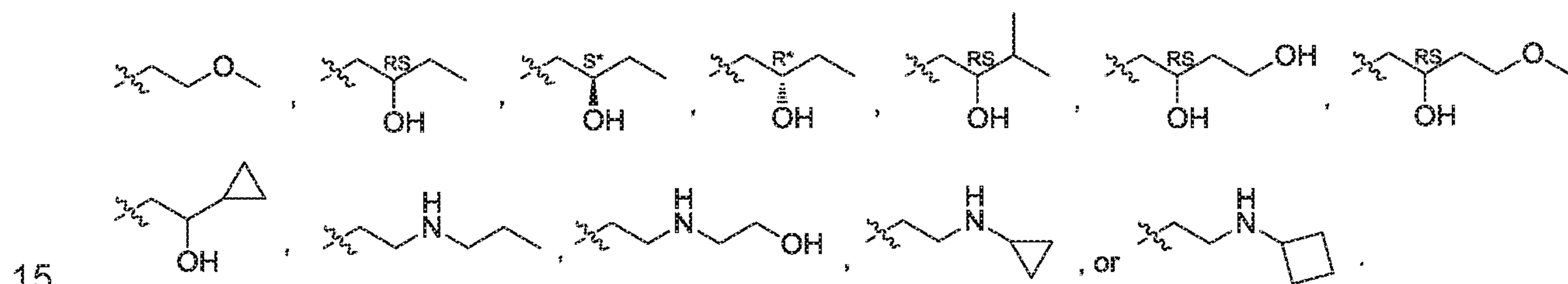
An additional embodiment of the invention is a compound of Formula (I) wherein

$R^1$  is H or  $CH_3$ ;

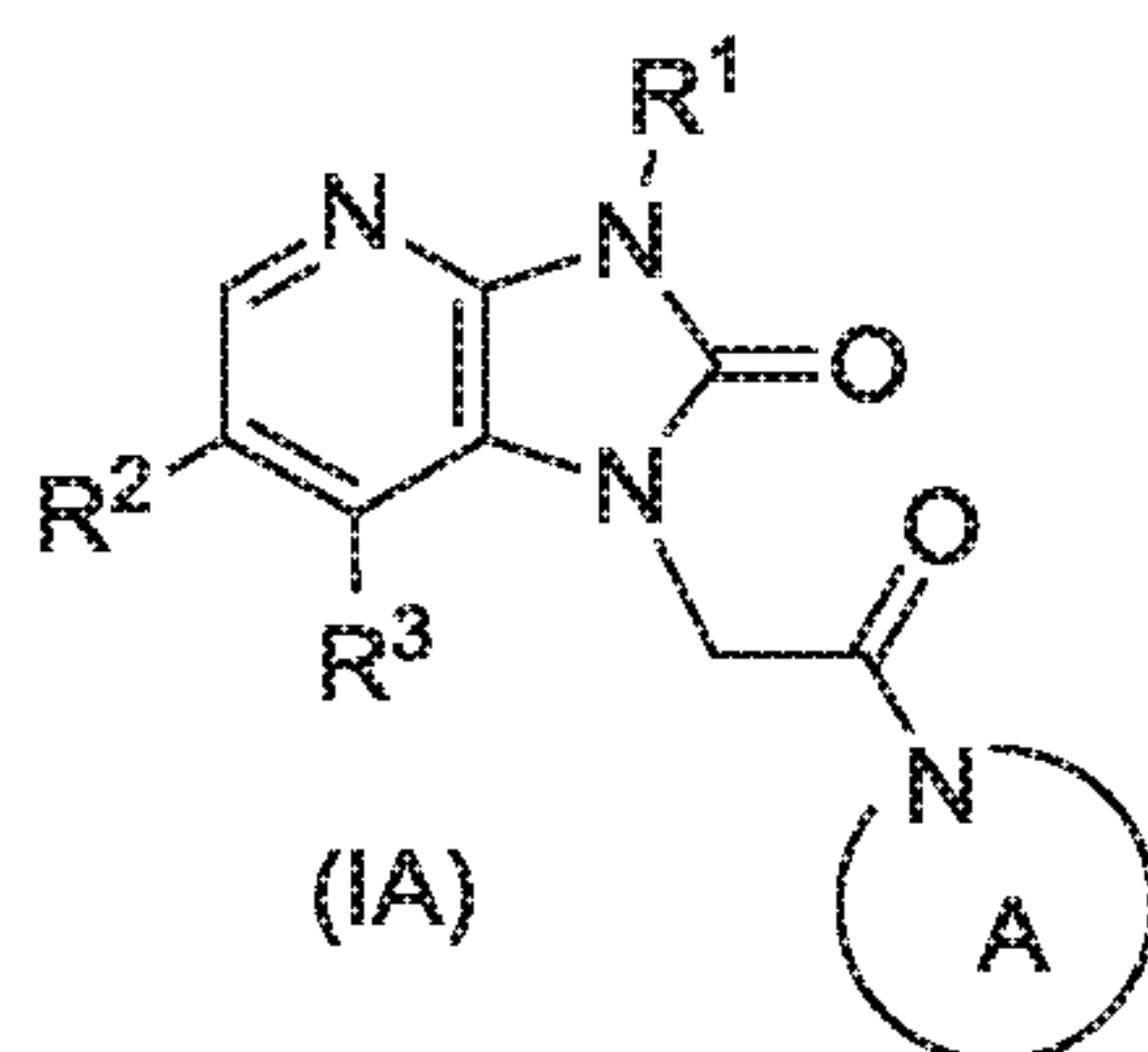
10  $R^2$  is phenyl substituted with one, two, or three members each independently selected from the group consisting of: halo,  $C_{1-6}$ alkyl,  $C_{1-6}$ haloalkyl, and  $OC_{1-6}$ alkyl;

$R^3$  is H; and

$R^4$  is



An additional embodiment of the invention is a compound of Formula (I) having the Formula (IA):



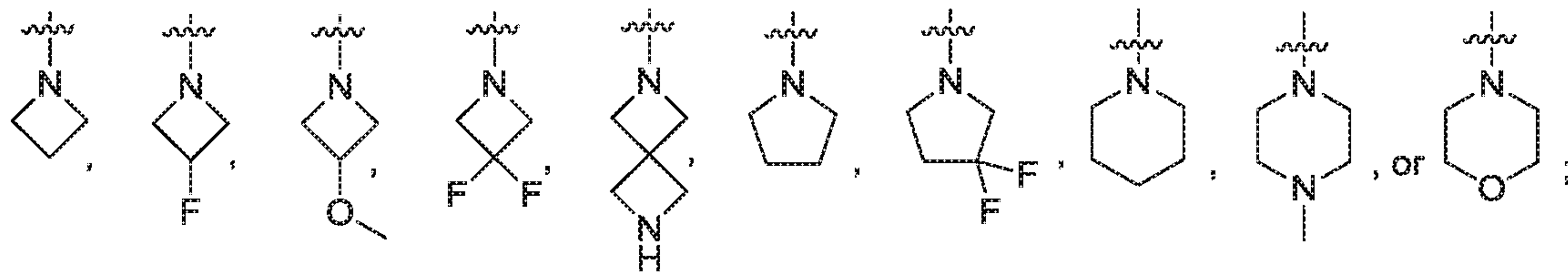
20 wherein  $R^1$  is H;  $CH_2F$ ; or  $CH_3$ ;

$R^2$  is phenyl substituted with one, two, or three members each independently selected from the group consisting of: halo,  $C_{1-6}$ alkyl,  $C_{1-6}$ haloalkyl,  $OC_{1-6}$ alkyl; thiazolyl substituted with  $C_{1-6}$ alkyl; and thienyl substituted with one or two members each

independently selected from the group consisting of: halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>haloalkyl, CH<sub>2</sub>OH, CH<sub>2</sub>OCD<sub>3</sub>, and cyclopropyl;

R<sup>3</sup> is H or T; and

ring A is

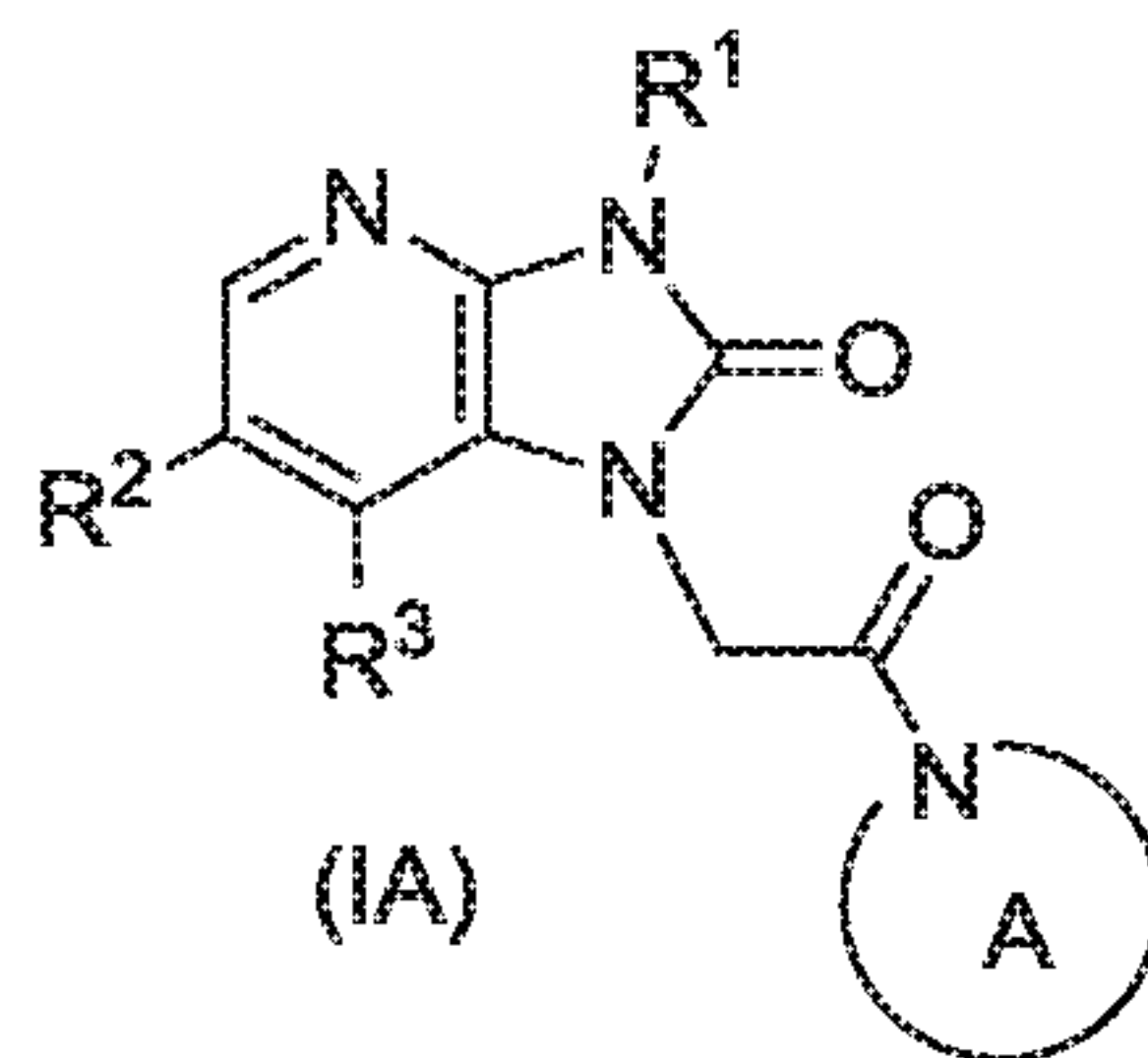


5

and pharmaceutically acceptable salts, N-oxides or solvates of compounds of Formula (IA).

An additional embodiment of the invention is a compound of Formula (I) having the Formula (IA):

10



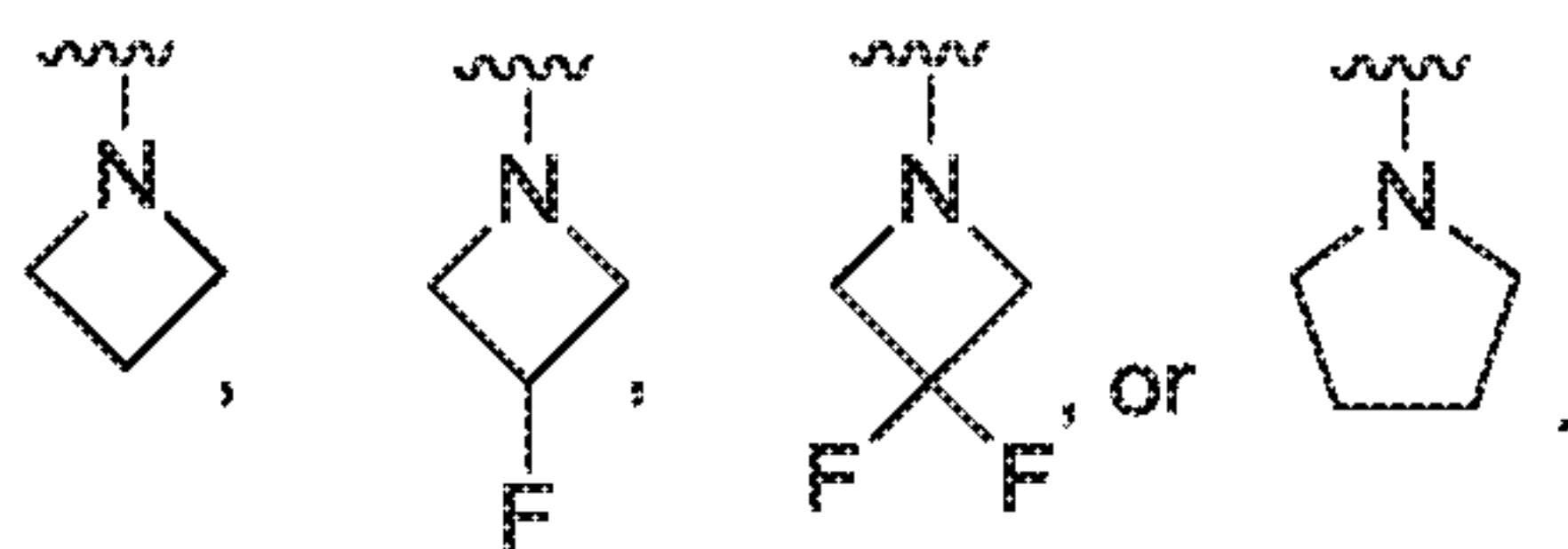
wherein

R<sup>1</sup> is H; CH<sub>2</sub>F; or CH<sub>3</sub>;

R<sup>2</sup> is 3-(trifluoromethyl)phenyl, 4-fluoro-3-methyl-phenyl, 2,4-difluoro-3-methyl-phenyl, 5-(trifluoromethyl)-2-thienyl, 5-(difluoromethyl)-2-thienyl, or 5-chloro-4-methyl-2-thienyl;

15

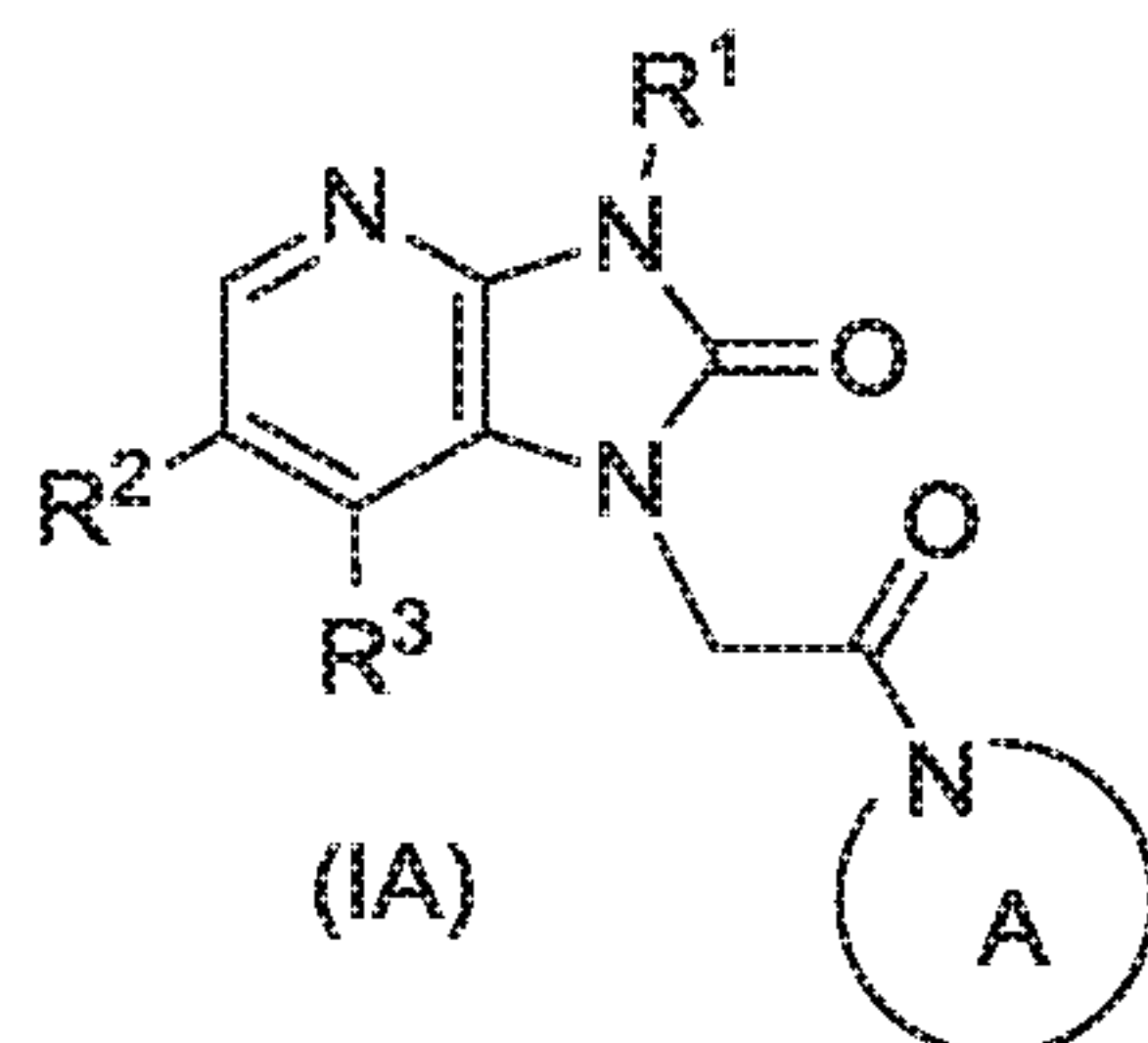
R<sup>3</sup> is H; and



ring A is

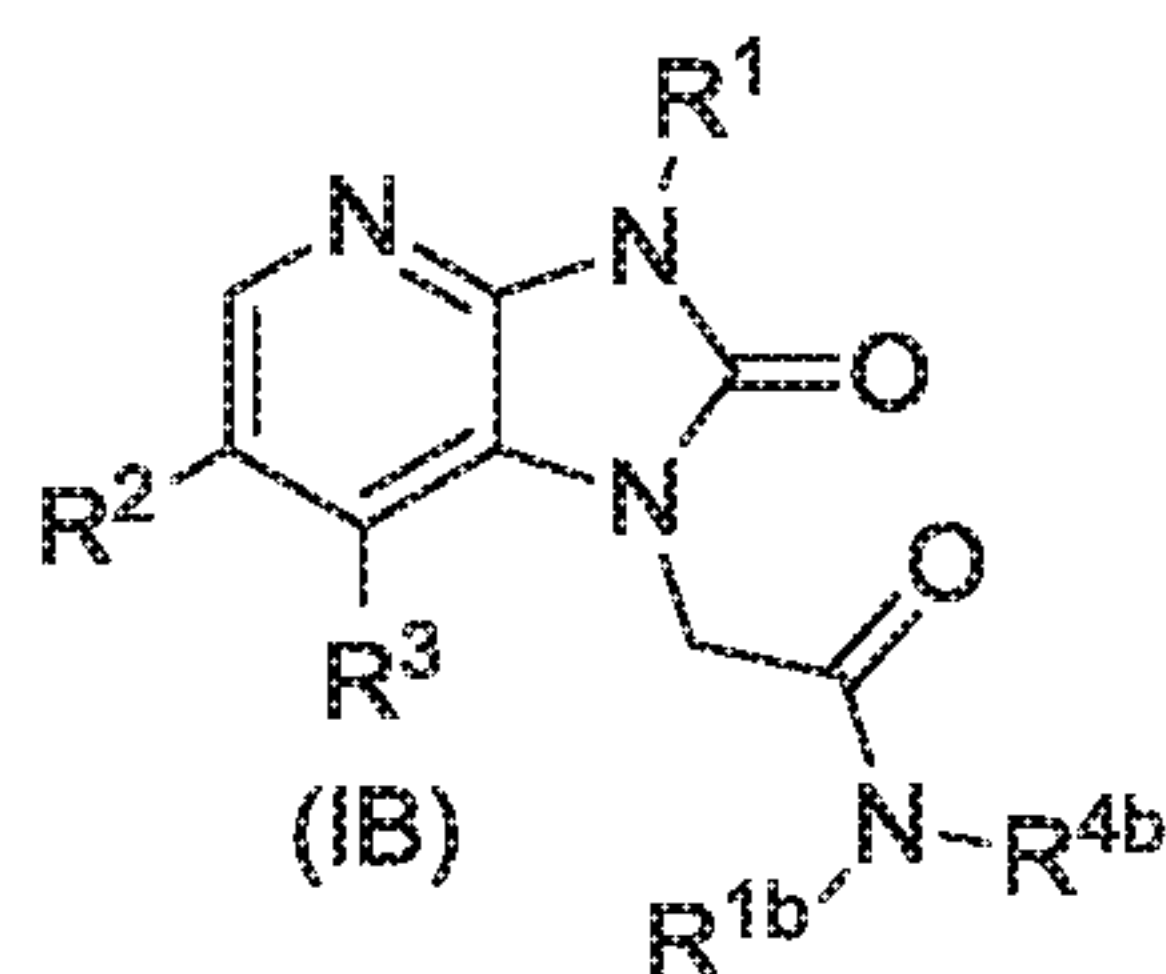
20

An additional embodiment of the invention is a compound of Formula (I) having the Formula (IA):



wherein  $R^2$  is m-tolyl, 3-fluorophenyl, 3-chlorophenyl, 3-(trifluoromethyl)phenyl, 5-methyl-2-thienyl, 5-ethyl-2-thienyl, 5-(hydroxymethyl)-2-thienyl, 5-cyclopropyl-2-thienyl, 5-(trideuteriomethoxymethyl)-2-thienyl, 5-(trifluoromethyl)-2-thienyl, 5-(trifluoromethyl)-3-thienyl, 2-(trifluoromethyl)-3-thienyl, 5-(1,1,2,2,2-pentafluoroethyl)-2-thienyl, 5-(trifluoromethyl)thiophen-2-yl, 5-fluoro-2-thienyl, 5-chloro-4-methyl-2-thienyl, 5-(difluoromethyl)-2-thienyl, 4-(difluoromethyl)-2-thienyl, 5-(difluoromethyl)-3-thienyl, 4-methylthiazol-2-yl, 2-methylthiazol-5-yl, 4-methoxyphenyl, 4-fluoro-2-methyl-phenyl, 2-fluoro-3-methyl-phenyl, 4-fluoro-3-methyl-phenyl, 3,5-difluorophenyl, 3,4-difluorophenyl, 2,4-difluoro-3-methyl-phenyl, 3,4,5-trifluorophenyl, 2-(trifluoromethyl)thiazol-5-yl, 2-(trifluoromethyl)thiazol-4-yl, 2-methyl-5-(trifluoromethyl)phenyl, 2-methyl-3-(trifluoromethyl)phenyl, 2-fluoro-3-(trifluoromethyl)phenyl, or 4-fluoro-3-(trifluoromethyl)phenyl.

An additional embodiment of the invention is a compound of Formula (I) having the Formula (IB):



wherein  $R^1$  and  $R^{1b}$  are each independently H or  $\text{CH}_3$ ;

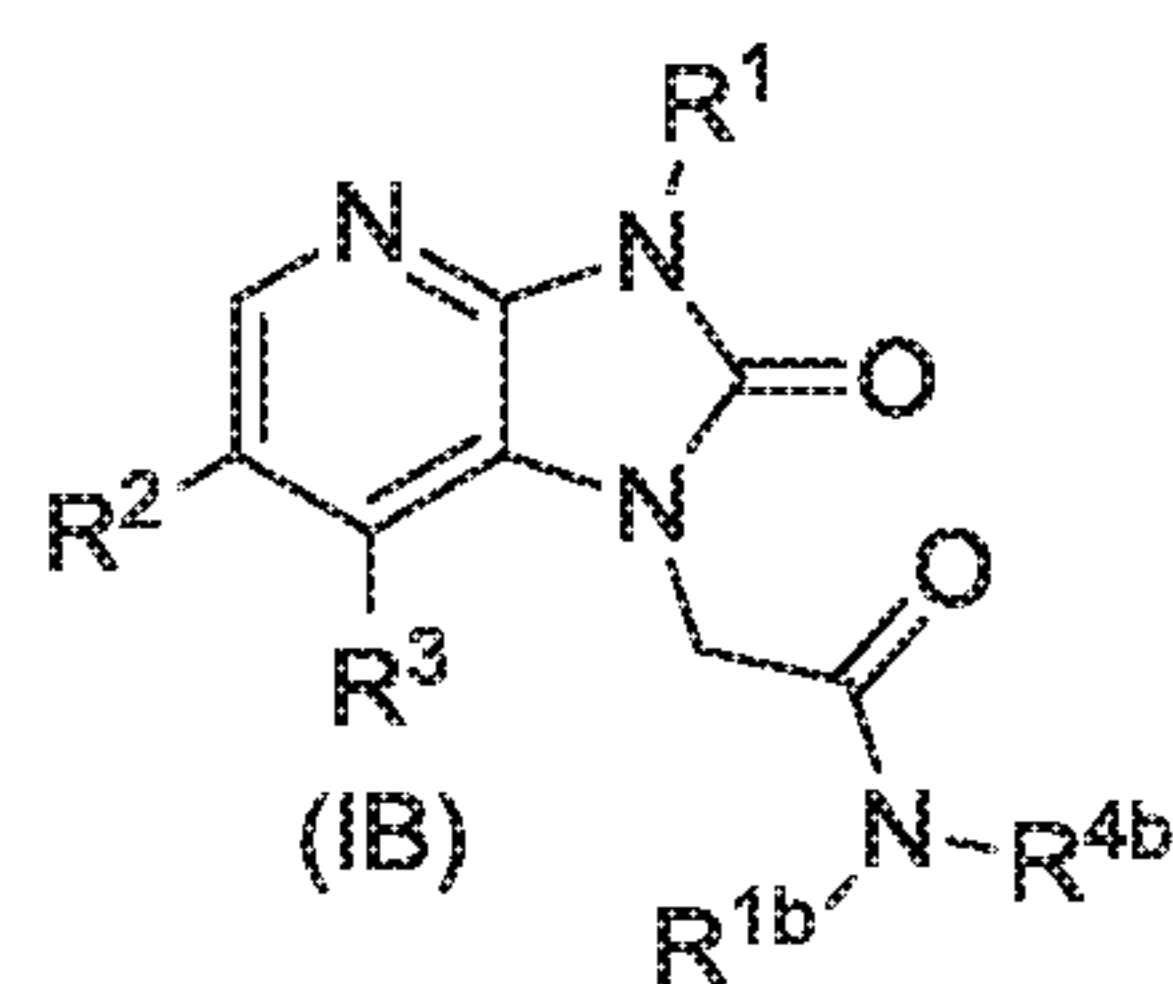
$R^2$  is selected from the group consisting of: phenyl substituted with one, two, or three members each independently selected from the group consisting of: halo,  $\text{C}_{1-6}$ alkyl,  $\text{C}_{1-6}$ haloalkyl,  $\text{OC}_{1-6}$ alkyl; pyridinyl; thiazolyl substituted with  $\text{C}_{1-6}$ alkyl; and

thienyl substituted with one or two members each independently selected from the group consisting of: halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>haloalkyl, CH<sub>2</sub>OH, and cyclopropyl;

R<sup>3</sup> is H; and

R<sup>4b</sup> is H, C<sub>1-6</sub>alkyl, 2-methoxyethyl, C<sub>3-6</sub>cycloalkyl, 3,3-difluorocyclobutyl, 3,3-difluoro-1-methyl-cyclobutyl, cyclopentyl, oxetan-3-yl, 3-methyloxetan-3-yl, or 2-pyridyl; and pharmaceutically acceptable salts, N-oxides or solvates of compounds of Formula (IB).

An additional embodiment of the invention is a compound of Formula (I) having the Formula (IB):



wherein

R<sup>1</sup> is H; CH<sub>2</sub>F; or CH<sub>3</sub>;

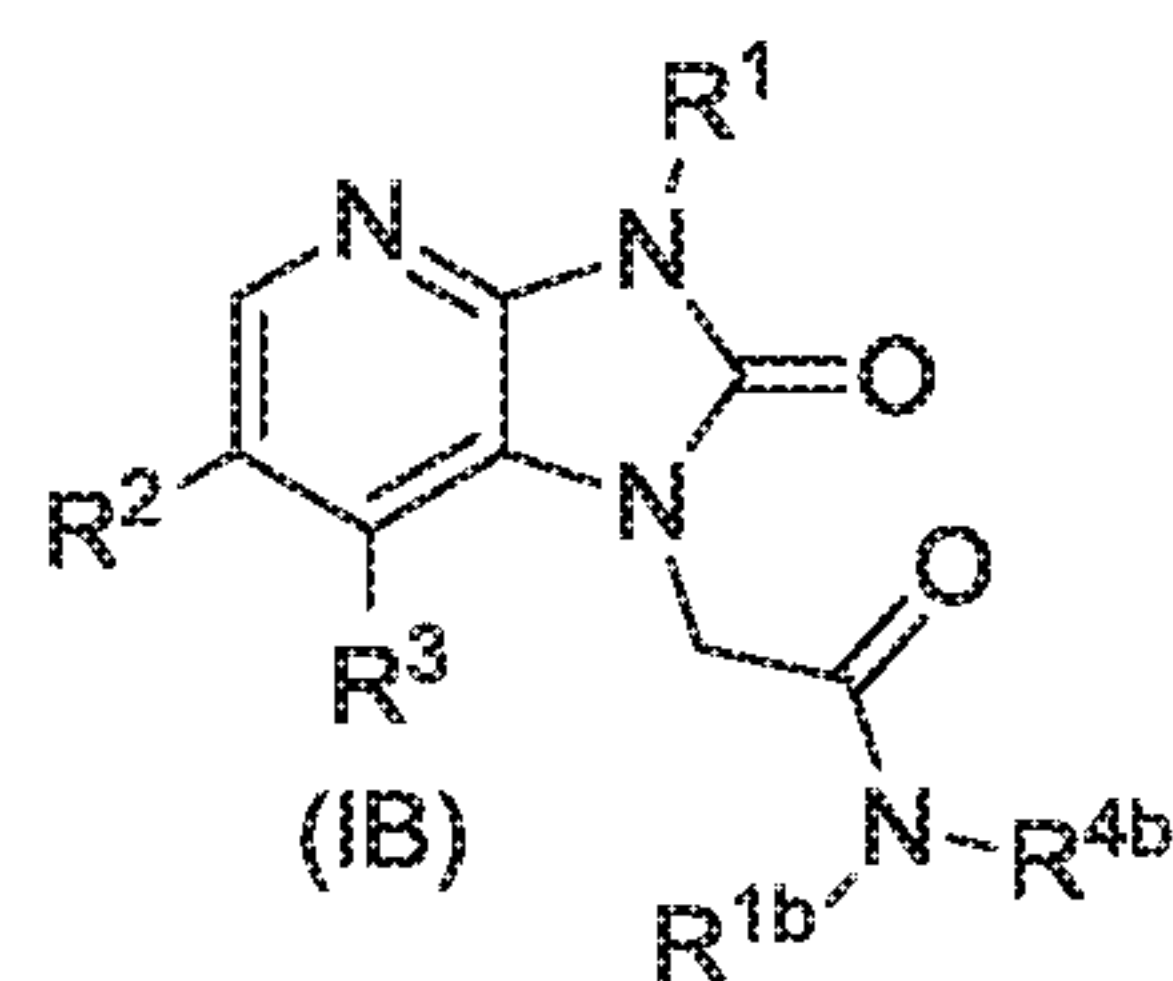
R<sup>1b</sup> is CH<sub>3</sub>;

R<sup>2</sup> is 3-(trifluoromethyl)phenyl, 4-fluoro-3-methyl-phenyl, 2,4-difluoro-3-methyl-phenyl, 5-(trifluoromethyl)-2-thienyl, 5-(difluoromethyl)-2-thienyl, or 5-chloro-4-methyl-2-thienyl;

R<sup>3</sup> is H; and

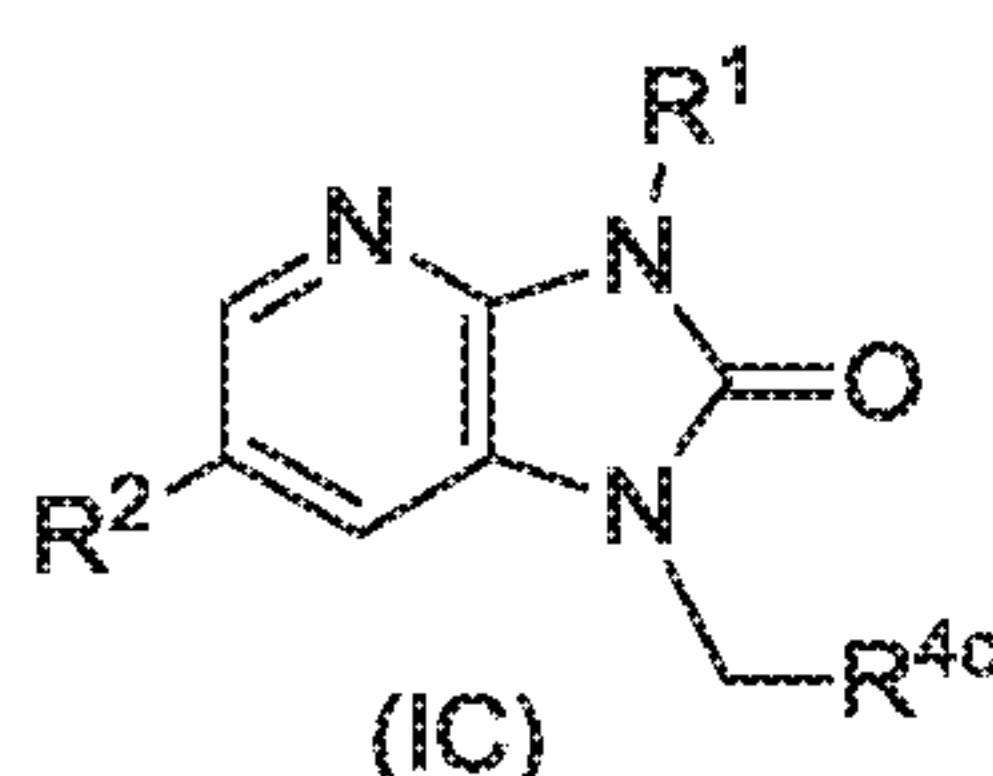
R<sup>4b</sup> is CH<sub>3</sub>.

An additional embodiment of the invention is a compound of Formula (I) having the Formula (IB):



wherein  $R^2$  is 3-pyridyl, 5-methyl-2-thienyl, 4-methyl-2-thienyl, 5-cyclopropyl-2-thienyl, 5-ethyl-2-thienyl, 5-chloro-2-thienyl, 5-(hydroxymethyl)-2-thienyl, 5-(trifluoromethyl)-2-thienyl, 5-(trifluoromethyl)-3-thienyl, 2-(trifluoromethyl)-3-thienyl, 5-(difluoromethyl)-2-thienyl, 5-(difluoromethyl)-3-thienyl, 5-chloro-4-methyl-2-thienyl, 5-fluoro-2-thienyl, 5-fluoro-2-thienyl, 2-methylthiazol-5-yl, 3,5-dimethylphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 4-fluoro-2-methyl-phenyl, 2-fluoro-3-methyl-phenyl, 4-fluoro-3-methyl-phenyl, 4-chlorophenyl, 2,3-difluorophenyl, 3,5-difluorophenyl, 3,4-difluorophenyl, 2-ethoxyphenyl, 3-ethoxyphenyl, 4-methoxy-3-methyl-phenyl, 4-fluoro-2-methoxy-phenyl, 2-fluoro-6-methoxy-phenyl, 2,4-difluoro-3-methyl-phenyl, 3-(difluoromethyl)phenyl, 3-chloro-4-fluoro-phenyl, 2,4-dimethoxyphenyl, 2-ethoxy-5-fluoro-phenyl, 2-chloro-4-methoxy-phenyl, 3-(trifluoromethyl)phenyl, 2-(trifluoromethyl)thiazol-5-yl, 2-(trifluoromethyl)thiazol-4-yl, 2-fluoro-3-(trifluoromethyl)phenyl, or 3,4-difluoro-5-(trifluoromethyl)phenyl.

An additional embodiment of the invention is a compound of Formula (I) having the Formula (IC):



wherein  $R^1$  is H or  $\text{CH}_3$ ;

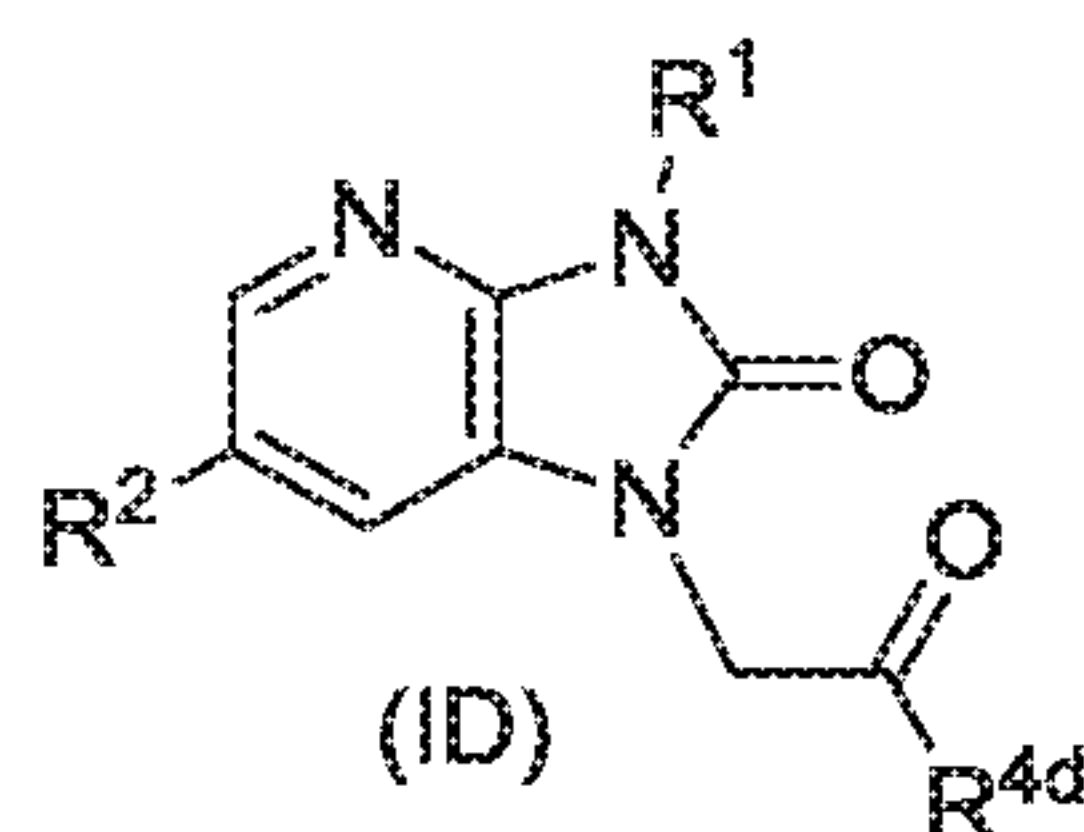
$R^2$  is selected from the group consisting of: phenyl; phenyl substituted with one, two, or three members each independently selected from the group consisting of: halo,  $\text{C}_{1-6}$ alkyl,  $\text{C}_{1-6}$ haloalkyl, CN,  $\text{OC}_{1-6}$ alkyl,  $\text{OC}_{1-6}$ haloalkyl, and  $\text{N}(\text{CH}_3)_2$ ; pyridinyl substituted with  $\text{CF}_3$ ; and thienyl substituted with one or two members each independently selected from the group consisting of: halo,  $\text{C}_{1-6}$ alkyl, and  $\text{C}_{1-6}$ haloalkyl; and

$R^{4c}$  is selected from the group consisting of: cyclopropyl; cyclopropyl substituted with one or two F members;  $\text{CH}(\text{OH})$ cyclopropyl; azetidiny;  $\text{CH}_2$ -azetidiny;  $\text{CH}_2$ -azetidiny substituted with one or two members independently selected from: F,

OH, OCH<sub>3</sub>, and CF<sub>3</sub>; oxetanyl; oxetanyl substituted with F or CH<sub>3</sub>;  
 tetrahydrofuranyl; tetrahydropyranyl; CH<sub>2</sub>pyrrolidinyl; CH<sub>2</sub>pyrrolidinyl substituted  
 with CH<sub>3</sub>, OH, or OCH<sub>3</sub>; CH<sub>2</sub>piperidinyl; CH<sub>2</sub>piperidinyl substituted with OH, or F;  
 morpholinyl; pyrazolyl substituted with one or two CH<sub>3</sub> members; triazolyl  
 5 substituted with CH<sub>3</sub>; tetrazolyl; isoxazolyl substituted with one or two CH<sub>3</sub>  
 members; oxadiazolyl substituted with CH<sub>3</sub>, or CH<sub>2</sub>OCH<sub>3</sub>; thiadiazolyl; pyridinyl;  
 pyridinyl substituted with one or two members independently selected from the  
 group consisting of: Cl, F, CH<sub>3</sub>, OCH<sub>3</sub>, and CF<sub>3</sub>; (2-oxo-1H-pyridin-3-yl); 6-oxo-  
 1H-pyridin-3-yl; pyrimidinyl; pyrimidinyl substituted with F or CH<sub>3</sub>; pyrazinyl;  
 10 pyridazinyl; pyridazinyl substituted with OCH<sub>3</sub>; phenyl; phenyl substituted with  
 one or two members independently selected from the group consisting of: halo,  
 CN, OCH<sub>3</sub>, C<sub>1-6</sub>alkyl, and CF<sub>3</sub>;

and pharmaceutically acceptable salts, N-oxides or solvates of compounds of Formula  
 (IC).

15 An additional embodiment of the invention is a compound of Formula (I) having  
 the Formula (ID):



wherein R<sup>1</sup> is H or CH<sub>3</sub>;

R<sup>2</sup> is m-tolyl, 3-(trifluoromethyl)phenyl, 4-chlorophenyl, 2,4-difluoro-3-methyl-phenyl,  
 20 3,4-difluorophenyl, 4-fluoro-3-methyl-phenyl, 3-cyclopropylphenyl, 3-fluoro-4-  
 methoxy-phenyl, 2-ethoxyphenyl, 3-ethoxyphenyl, 4-methoxyphenyl, 2-ethoxy-5-  
 fluoro-phenyl, 4-fluoro-2-methoxy-phenyl, or 3-chloro-4-fluoro-phenyl; and

R<sup>4d</sup> is OH, C<sub>1-6</sub>alkyl, C<sub>3-6</sub>cycloalkyl, OC<sub>1-6</sub>alkyl, 2-thienyl, or thiazol-2-yl;

and pharmaceutically acceptable salts, N-oxides or solvates of compounds of Formula  
 25 (ID).

A further embodiment of the current invention is a compound as shown below in  
 Table 1.

| Ex # | Compound Name                                                                                                    |
|------|------------------------------------------------------------------------------------------------------------------|
| 1    | 6-(4-Methoxyphenyl)-1-(2-morpholino-2-oxo-ethyl)-3H-imidazo[4,5-b]pyridin-2-one;                                 |
| 2    | 6-(4-Fluoro-2-methyl-phenyl)-1-(2-methoxyethyl)-3H-imidazo[4,5-b]pyridin-2-one;                                  |
| 3    | N-Ethyl-2-[6-(4-fluoro-2-methyl-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;                           |
| 4    | (S*)-1-(2-Hydroxybutyl)-6-(4-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-one;                                      |
| 5    | (R*)-1-(2-Hydroxybutyl)-6-(4-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-one;                                      |
| 6    | 6-(4-Fluoro-3-methyl-phenyl)-3-methyl-1-(2-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;                            |
| 7    | 6-(3-Fluorophenyl)-3-methyl-1-(pyrimidin-4-ylmethyl)imidazo[4,5-b]pyridin-2-one;                                 |
| 8    | 6-(3,4-Difluorophenyl)-3-methyl-1-[(5-methylisoxazol-3-yl)methyl]imidazo[4,5-b]pyridin-2-one;                    |
| 9    | 2-[6-(5-Chloro-2-thienyl)-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;                     |
| 10   | 6-[5-(Difluoromethyl)-2-thienyl]-1-[2-(3-fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-imidazo[4,5-b]pyridin-2-one; |
| 11   | 1-[(5-Methylisoxazol-3-yl)methyl]-6-phenyl-3H-imidazo[4,5-b]pyridin-2-one;                                       |
| 12   | 6-(4-Fluorophenyl)-1-[(5-methylisoxazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;                             |
| 13   | 6-(4-Fluorophenyl)-1-[(5-methyl-1,3,4-oxadiazol-2-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;                     |
| 14   | 3-Methyl-1-[(5-methylisoxazol-3-yl)methyl]-6-(4-methyl-2-thienyl)imidazo[4,5-b]pyridin-2-one;                    |
| 15   | 6-(4-Fluorophenyl)-1-[(1-methylpyrazol-4-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;                              |
| 16   | 1-[(1,5-Dimethylpyrazol-3-yl)methyl]-6-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-one;                          |
| 17   | 1-[2-(Azetidin-1-yl)ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                         |
| 18   | 1-[2-(Azetidin-1-yl)ethyl]-3-methyl-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;                    |
| 19   | 1-[(5-Methylisoxazol-3-yl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                  |
| 20   | N-Cyclopropyl-2-[2-oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;                    |

| Ex # | Compound Name                                                                                                |
|------|--------------------------------------------------------------------------------------------------------------|
| 21   | 1-[(3-Chlorophenyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                     |
| 22   | 1-[(2-Methoxy-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                |
| 23   | 1-(Pyrimidin-4-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                       |
| 24   | (R/S)-1-(Tetrahydrofuran-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;           |
| 25   | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;              |
| 26   | N,N-Dimethyl-2-[2-oxo-6-[5-(trifluoromethyl)-2-thienyl]-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;             |
| 27   | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;     |
| 28   | N,N-Dimethyl-2-[3-methyl-2-oxo-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-1-yl]acetamide;        |
| 29   | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[2-methyl-5-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;     |
| 30   | 6-(2,4-Difluoro-3-methyl-phenyl)-1-(2-oxobutyl)-3H-imidazo[4,5-b]pyridin-2-one;                              |
| 31   | (R/S)-1-(2-Cyclopropyl-2-hydroxy-ethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;        |
| 32   | 1-[(2-Oxo-1H-pyridin-3-yl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;              |
| 33   | (R/S)-6-(4-Fluoro-2-methyl-phenyl)-3-methyl-1-(oxetan-2-ylmethyl)imidazo[4,5-b]pyridin-2-one;                |
| 34   | 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one; |
| 35   | 6-(4-Methoxyphenyl)-1-(2-oxo-2-pyrrolidin-1-yl-ethyl)-3H-imidazo[4,5-b]pyridin-2-one;                        |
| 36   | N-Cyclopropyl-2-[6-(4-fluoro-2-methyl-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;                 |
| 37   | 2-[6-(2-Chloro-4-methoxy-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-cyclopropyl-acetamide;               |
| 38   | N-Cyclopropyl-2-[6-(4-methoxyphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;                          |
| 39   | N-Cyclopropyl-2-[6-(3,5-dimethylphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;                       |
| 40   | N-Cyclopropyl-2-[6-(4-fluoro-2-methyl-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-methyl-acetamide;       |

| Ex # | Compound Name                                                                                      |
|------|----------------------------------------------------------------------------------------------------|
| 41   | N-Cyclopropyl-2-[6-(4-methoxyphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-methyl-acetamide;      |
| 42   | N-Cyclopropyl-2-[6-(4-fluoro-2-methyl-phenyl)-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]acetamide; |
| 43   | (R*)-6-(4-Fluoro-2-methyl-phenyl)-1-(2-hydroxybutyl)-3H-imidazo[4,5-b]pyridin-2-one;               |
| 44   | (S*)-6-(4-Fluoro-2-methyl-phenyl)-1-(2-hydroxybutyl)-3H-imidazo[4,5-b]pyridin-2-one;               |
| 45   | 6-(4-Fluoro-3-methyl-phenyl)-3-methyl-1-(3-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;              |
| 46   | 6-(4-Fluoro-3-methyl-phenyl)-3-methyl-1-(4-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;              |
| 47   | 6-(4-Fluoro-3-methyl-phenyl)-3-methyl-1-(pyrazin-2-ylmethyl)imidazo[4,5-b]pyridin-2-one;           |
| 48   | 6-(4-Fluoro-3-methyl-phenyl)-3-methyl-1-(pyrimidin-5-ylmethyl)imidazo[4,5-b]pyridin-2-one;         |
| 49   | 6-(4-Fluoro-3-methyl-phenyl)-3-methyl-1-(pyrimidin-2-ylmethyl)imidazo[4,5-b]pyridin-2-one;         |
| 50   | 6-(4-Fluoro-3-methyl-phenyl)-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;         |
| 51   | 6-(3-Fluorophenyl)-3-methyl-1-(3-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;                        |
| 52   | 6-(3-Fluorophenyl)-3-methyl-1-(4-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;                        |
| 53   | 6-(3-Fluorophenyl)-3-methyl-1-(2-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;                        |
| 54   | 6-(3-Fluorophenyl)-3-methyl-1-(pyrimidin-5-ylmethyl)imidazo[4,5-b]pyridin-2-one;                   |
| 55   | 6-(3-Fluorophenyl)-3-methyl-1-(pyrazin-2-ylmethyl)imidazo[4,5-b]pyridin-2-one;                     |
| 56   | 6-(3-Fluorophenyl)-3-methyl-1-(pyrimidin-2-ylmethyl)imidazo[4,5-b]pyridin-2-one;                   |
| 57   | 6-(3-Fluorophenyl)-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;                   |
| 58   | 6-(3,4-Difluorophenyl)-3-methyl-1-(4-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;                    |
| 59   | 6-(3,4-Difluorophenyl)-3-methyl-1-(3-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;                    |
| 60   | 6-(3,4-Difluorophenyl)-3-methyl-1-(pyrimidin-5-ylmethyl)imidazo[4,5-b]pyridin-2-one;               |

| Ex # | Compound Name                                                                                                |
|------|--------------------------------------------------------------------------------------------------------------|
| 61   | 6-(3,4-Difluorophenyl)-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;                         |
| 62   | 6-(3,4-difluorophenyl)-3-methyl-1-(2-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;                              |
| 63   | 6-(3,4-Difluorophenyl)-3-methyl-1-(pyrazin-2-ylmethyl)imidazo[4,5-b]pyridin-2-one;                           |
| 64   | 6-(3,4-Difluorophenyl)-3-methyl-1-(pyrimidin-2-ylmethyl)imidazo[4,5-b]pyridin-2-one;                         |
| 65   | 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-(pyrimidin-2-ylmethyl)imidazo[4,5-b]pyridin-2-one;               |
| 66   | 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-(4-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;                    |
| 67   | 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;               |
| 68   | 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-(2-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;                    |
| 69   | 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-(pyrimidin-5-ylmethyl)imidazo[4,5-b]pyridin-2-one;               |
| 70   | 6-(3,4-Difluorophenyl)-3-methyl-1-(pyrimidin-4-ylmethyl)imidazo[4,5-b]pyridin-2-one;                         |
| 71   | 6-(4-Fluoro-3-methyl-phenyl)-3-methyl-1-(pyrimidin-4-ylmethyl)imidazo[4,5-b]pyridin-2-one;                   |
| 72   | 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-(pyrimidin-4-ylmethyl)imidazo[4,5-b]pyridin-2-one;               |
| 73   | 6-(3,4-Difluorophenyl)-3-methyl-1-[(5-methyl-1,3,4-oxadiazol-2-yl)methyl]imidazo[4,5-b]pyridin-2-one;        |
| 74   | 3-Methyl-1-[(5-methylisoxazol-3-yl)methyl]-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;         |
| 75   | 3-Methyl-1-[(5-methyl-1,3,4-oxadiazol-2-yl)methyl]-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one; |
| 76   | 3-Methyl-1-[(3-methyl-1,2,4-oxadiazol-5-yl)methyl]-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one; |
| 77   | 6-(3,4-Difluorophenyl)-3-methyl-1-[(3-methyl-1,2,4-oxadiazol-5-yl)methyl]imidazo[4,5-b]pyridin-2-one;        |
| 78   | N,N-Dimethyl-2-[3-methyl-6-(5-methyl-2-thienyl)-2-oxo-imidazo[4,5-b]pyridin-1-yl]acetamide;                  |
| 79   | 2-[6-(5-Ethyl-2-thienyl)-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;                  |
| 80   | N,N-Dimethyl-2-[3-methyl-6-(4-methyl-2-thienyl)-2-oxo-imidazo[4,5-b]pyridin-1-yl]acetamide;                  |

| Ex # | Compound Name                                                                                                    |
|------|------------------------------------------------------------------------------------------------------------------|
| 81   | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(5-fluoro-2-thienyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;                   |
| 82   | 2-[6-(5-Fluoro-2-thienyl)-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;                     |
| 83   | 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-6-(5-fluoro-2-thienyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;           |
| 84   | 3-Methyl-1-(pyridazin-3-ylmethyl)-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;                  |
| 85   | 6-(5-Fluoro-2-thienyl)-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;                             |
| 86   | 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-(4-methylthiazol-2-yl)imidazo[4,5-b]pyridin-2-one;          |
| 87   | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(5-ethyl-2-thienyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;                    |
| 88   | 6-(5-Ethyl-2-thienyl)-1-[2-(3-fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;            |
| 89   | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[5-(hydroxymethyl)-2-thienyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;          |
| 90   | 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-6-[5-(hydroxymethyl)-2-thienyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;  |
| 91   | 2-[6-[5-(Hydroxymethyl)-2-thienyl]-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;            |
| 92   | 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[2-(trifluoromethyl)-3-thienyl]imidazo[4,5-b]pyridin-2-one; |
| 93   | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[5-(difluoromethyl)-2-thienyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;         |
| 94   | 2-[6-[5-(Difluoromethyl)-2-thienyl]-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;           |
| 95   | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[2-(trifluoromethyl)-3-thienyl]imidazo[4,5-b]pyridin-2-one;         |
| 96   | N,N-Dimethyl-2-[3-methyl-2-oxo-6-[2-(trifluoromethyl)-3-thienyl]imidazo[4,5-b]pyridin-1-yl]acetamide;            |
| 97   | 2-[6-[5-(Difluoromethyl)-3-thienyl]-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;           |
| 98   | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[5-(difluoromethyl)-3-thienyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;         |
| 99   | 6-[5-(Difluoromethyl)-3-thienyl]-1-[2-(3-fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-imidazo[4,5-b]pyridin-2-one; |
| 100  | 6-[5-(Difluoromethyl)-2-thienyl]-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;                   |

| Ex # | Compound Name                                                                                                                  |
|------|--------------------------------------------------------------------------------------------------------------------------------|
| 101  | N,N-Dimethyl-2-[3-methyl-2-oxo-6-[5-(trifluoromethyl)-3-thienyl]imidazo[4,5-b]pyridin-1-yl]acetamide;                          |
| 102  | 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[5-(trifluoromethyl)-3-thienyl]imidazo[4,5-b]pyridin-2-one;               |
| 103  | 3-Methyl-1-(pyridazin-3-ylmethyl)-6-[5-(trifluoromethyl)-3-thienyl]imidazo[4,5-b]pyridin-2-one;                                |
| 104  | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[5-(trifluoromethyl)-3-thienyl]imidazo[4,5-b]pyridin-2-one;                       |
| 105  | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(5-cyclopropyl-2-thienyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;                            |
| 106  | 6-(5-Cyclopropyl-2-thienyl)-1-[2-(3-fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;                    |
| 107  | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[2-(trifluoromethyl)thiazol-4-yl]imidazo[4,5-b]pyridin-2-one;                     |
| 108  | N,N-Dimethyl-2-[3-methyl-2-oxo-6-[2-(trifluoromethyl)thiazol-4-yl]imidazo[4,5-b]pyridin-1-yl]acetamide;                        |
| 109  | 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[2-(trifluoromethyl)thiazol-4-yl]imidazo[4,5-b]pyridin-2-one;             |
| 110  | 2-[6-(5-Cyclopropyl-2-thienyl)-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;                              |
| 111  | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[5-(1,1,2,2,2-pentafluoroethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;            |
| 112  | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-(2-methylthiazol-5-yl)imidazo[4,5-b]pyridin-2-one;                                |
| 113  | 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-(2-methylthiazol-5-yl)imidazo[4,5-b]pyridin-2-one;                        |
| 114  | N,N-Dimethyl-2-[3-methyl-6-(2-methylthiazol-5-yl)-2-oxo-imidazo[4,5-b]pyridin-1-yl]acetamide;                                  |
| 115  | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[2-(trifluoromethyl)thiazol-5-yl]imidazo[4,5-b]pyridin-2-one;                     |
| 116  | 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[2-(trifluoromethyl)thiazol-5-yl]imidazo[4,5-b]pyridin-2-one;             |
| 117  | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[4-(difluoromethyl)-2-thienyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;                       |
| 118  | 6-[4-(Difluoromethyl)-2-thienyl]-1-[2-(3-fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;               |
| 119  | N,N-Dimethyl-2-[3-methyl-2-oxo-6-[2-(trifluoromethyl)thiazol-5-yl]imidazo[4,5-b]pyridin-1-yl]acetamide;                        |
| 120  | 1-(2-(Azetidin-1-yl)-2-oxoethyl)-3-methyl-6-(5-(trifluoromethyl)thiophen-2-yl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one-7-D; |

| Ex # | Compound Name                                                                                                                  |
|------|--------------------------------------------------------------------------------------------------------------------------------|
| 121  | N,N-Dimethyl-2-[3-methyl-2-oxo-6-[5-(trideuteriomethoxymethyl)-2-thienyl]imidazo[4,5-b]pyridin-1-yl]acetamide;                 |
| 122  | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[5-(trideuteriomethoxymethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;              |
| 123  | 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[5-(trideuteriomethoxymethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;      |
| 124  | 1-(2-(Azetidin-1-yl)-2-oxoethyl)-3-methyl-6-(5-(trifluoromethyl)thiophen-2-yl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one-7-T; |
| 125  | 1-[(5-Methylisoxazol-3-yl)methyl]-6-(4-methyl-2-thienyl)-3H-imidazo[4,5-b]pyridin-2-one;                                       |
| 126  | 1-[(5-Methylisoxazol-3-yl)methyl]-6-(o-tolyl)-3H-imidazo[4,5-b]pyridin-2-one;                                                  |
| 127  | 1-[(3-Methyl-1,2,4-oxadiazol-5-yl)methyl]-6-(4-methyl-2-thienyl)-3H-imidazo[4,5-b]pyridin-2-one;                               |
| 128  | 6-(4-Fluorophenyl)-1-[(1-methylpyrazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;                                            |
| 129  | 6-(4-Fluoro-3-methyl-phenyl)-1-[(1-methylpyrazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;                                  |
| 130  | 6-(3-Chloro-4-fluoro-phenyl)-1-[(1-methylpyrazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;                                  |
| 131  | 6-(3,4-Difluorophenyl)-1-[(1-methylpyrazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;                                        |
| 132  | 6-(2,4-Difluorophenyl)-1-[(1-methylpyrazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;                                        |
| 133  | (R/S)-3-methyl-1-(oxetan-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;                                 |
| 134  | Ethyl 2-[2-oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-yl]acetate;                                            |
| 135  | 2-[2-Oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-yl]acetic acid;                                              |
| 136  | Ethyl 2-[3-methyl-2-oxo-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-1-yl]acetate;                                       |
| 137  | 2-[3-Methyl-2-oxo-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-1-yl]acetic acid;                                         |
| 138  | 1-[2-(3,3-difluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;               |
| 139  | 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-(pyrazin-2-ylmethyl)imidazo[4,5-b]pyridin-2-one;                                   |
| 140  | 6-(4-Fluorophenyl)-1-[(3-methyl-1,2,4-oxadiazol-5-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;                                   |

| Ex # | Compound Name                                                                                             |
|------|-----------------------------------------------------------------------------------------------------------|
| 141  | 6-(4-Fluorophenyl)-1-[(1-methyl-1,2,4-triazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;                |
| 142  | 6-(4-Fluorophenyl)-1-[(1-methyltriazol-4-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;                       |
| 143  | 6-(3,4-Difluorophenyl)-1-[(3-methyl-1,2,4-oxadiazol-5-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;          |
| 144  | 6-(3,4-Difluorophenyl)-1-[(5-methyl-1,2,4-oxadiazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;          |
| 145  | 6-(3,4-Difluorophenyl)-1-[[3-(methoxymethyl)-1,2,4-oxadiazol-5-yl]methyl]-3H-imidazo[4,5-b]pyridin-2-one; |
| 146  | 1-(2-Pyrrolidin-1-ylethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                  |
| 147  | 1-[2-(3-Hydroxyazetidin-1-yl)ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;         |
| 148  | 1-[2-(Cyclopropylamino)ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;               |
| 149  | 1-[2-(3-Methoxyazetidin-1-yl)ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;         |
| 150  | 1-[2-(Cyclobutylamino)ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                |
| 151  | 1-[2-(Azetidin-1-yl)ethyl]-6-(4-fluoro-2-methyl-phenyl)-3H-imidazo[4,5-b]pyridin-2-one;                   |
| 152  | 1-[2-(Azetidin-1-yl)ethyl]-6-(o-tolyl)-3H-imidazo[4,5-b]pyridin-2-one;                                    |
| 153  | 1-[2-(Azetidin-1-yl)ethyl]-6-phenyl-3H-imidazo[4,5-b]pyridin-2-one;                                       |
| 154  | 1-[2-(Azetidin-1-yl)ethyl]-6-(m-tolyl)-3H-imidazo[4,5-b]pyridin-2-one;                                    |
| 155  | 1-[2-(Azetidin-1-yl)ethyl]-6-[2-(trifluoromethyl)-4-pyridyl]-3H-imidazo[4,5-b]pyridin-2-one;              |
| 156  | 1-[2-(Azetidin-1-yl)ethyl]-6-(4-fluoro-3-methyl-phenyl)-3H-imidazo[4,5-b]pyridin-2-one;                   |
| 157  | 1-[2-(Azetidin-1-yl)ethyl]-6-(2,6-dimethylphenyl)-3H-imidazo[4,5-b]pyridin-2-one;                         |
| 158  | 1-[2-(Azetidin-1-yl)ethyl]-6-(3-chlorophenyl)-3H-imidazo[4,5-b]pyridin-2-one;                             |
| 159  | 1-[2-(Azetidin-1-yl)ethyl]-6-(3,5-difluorophenyl)-3H-imidazo[4,5-b]pyridin-2-one;                         |
| 160  | 1-[2-(Azetidin-1-yl)ethyl]-6-[3-(trifluoromethoxy)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                 |

| Ex # | Compound Name                                                                                               |
|------|-------------------------------------------------------------------------------------------------------------|
| 161  | 1-[2-(1-Piperidyl)ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                      |
| 162  | 1-[2-(4-Fluoro-1-piperidyl)ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;             |
| 163  | 1-[2-(3-Fluoroazetidin-1-yl)ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;            |
| 164  | 1-[2-(3-Methylpyrrolidin-1-yl)ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;          |
| 165  | 1-[2-(4-Hydroxy-1-piperidyl)ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;            |
| 166  | 1-[2-[3-(Trifluoromethyl)azetidin-1-yl]ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one; |
| 167  | 1-[2-(3,3-Difluoroazetidin-1-yl)ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;        |
| 168  | 1-[2-(Azetidin-1-yl)ethyl]-6-[2-methyl-3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;           |
| 169  | 1-[2-(Azetidin-1-yl)ethyl]-6-(2,3-dimethylphenyl)-3H-imidazo[4,5-b]pyridin-2-one;                           |
| 170  | 1-[2-(Azetidin-1-yl)ethyl]-6-(3,5-dimethylphenyl)-3H-imidazo[4,5-b]pyridin-2-one;                           |
| 171  | 1-[2-(Azetidin-1-yl)ethyl]-6-(4-fluoro-2,3-dimethyl-phenyl)-3H-imidazo[4,5-b]pyridin-2-one;                 |
| 172  | 1-[2-(Azetidin-1-yl)ethyl]-6-[2-methyl-5-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;           |
| 173  | 6-(3,5-Difluorophenyl)-1-[2-(2-hydroxyethylamino)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;                     |
| 174  | 6-(3,5-Difluorophenyl)-1-(2-pyrrolidin-1-ylethyl)-3H-imidazo[4,5-b]pyridin-2-one;                           |
| 175  | 6-(3,5-Difluorophenyl)-1-[2-(3-hydroxypyrrolidin-1-yl)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;                |
| 176  | 6-(3,5-Difluorophenyl)-1-[2-(3-methoxypyrrolidin-1-yl)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;                |
| 177  | 6-(4-Fluoro-2-methyl-phenyl)-1-(2-pyrrolidin-1-ylethyl)-3H-imidazo[4,5-b]pyridin-2-one;                     |
| 178  | 6-(2,6-Dimethylphenyl)-1-(2-pyrrolidin-1-ylethyl)-3H-imidazo[4,5-b]pyridin-2-one;                           |
| 179  | 6-(o-Tolyl)-1-(2-pyrrolidin-1-ylethyl)-3H-imidazo[4,5-b]pyridin-2-one;                                      |
| 180  | 6-Phenyl-1-(2-pyrrolidin-1-ylethyl)-3H-imidazo[4,5-b]pyridin-2-one;                                         |

| Ex # | Compound Name                                                                                                             |
|------|---------------------------------------------------------------------------------------------------------------------------|
| 181  | 1-[2-(3-Fluoroazetidin-1-yl)ethyl]-6-[2-methyl-3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                 |
| 182  | 6-(2,3-Dimethylphenyl)-1-[2-(3-fluoroazetidin-1-yl)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;                                 |
| 183  | 6-(3,5-Dimethylphenyl)-1-[2-(3-fluoroazetidin-1-yl)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;                                 |
| 184  | 1-[2-(3-Fluoroazetidin-1-yl)ethyl]-6-(4-fluoro-2,3-dimethyl-phenyl)-3H-imidazo[4,5-b]pyridin-2-one;                       |
| 185  | 1-[2-(3-Fluoroazetidin-1-yl)ethyl]-6-[2-methyl-5-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                 |
| 186  | 1-[2-(3-Fluoroazetidin-1-yl)ethyl]-6-(o-tolyl)-3H-imidazo[4,5-b]pyridin-2-one;                                            |
| 187  | 1-[2-(3-Fluoroazetidin-1-yl)ethyl]-6-(4-fluoro-2-methyl-phenyl)-3H-imidazo[4,5-b]pyridin-2-one;                           |
| 188  | 1-[2-(3-Fluoroazetidin-1-yl)ethyl]-6-phenyl-3H-imidazo[4,5-b]pyridin-2-one;                                               |
| 189  | 6-(3,5-Difluorophenyl)-1-[2-(propylamino)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;                                           |
| 190  | N-Cyclobutyl-2-[2-oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;                              |
| 191  | 1-[2-(3-Methoxyazetidin-1-yl)-2-oxo-ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                  |
| 192  | N-(Oxetan-3-yl)-2-[2-oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;                           |
| 193  | 1-[2-(4-Methylpiperazin-1-yl)-2-oxo-ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                  |
| 194  | 1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;               |
| 195  | N-(3,3-Difluorocyclobutyl)-2-[2-oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;                |
| 196  | 1-[2-(3,3-Difluoropyrrolidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;        |
| 197  | 3-Methyl-1-(2-oxo-2-pyrrolidin-1-yl-ethyl)-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;                      |
| 198  | N-(3,3-Difluoro-1-methyl-cyclobutyl)-2-[3-methyl-2-oxo-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-1-yl]acetamide; |
| 199  | N-(3-Methyloxetan-3-yl)-2-[3-methyl-2-oxo-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-1-yl]acetamide;              |
| 200  | N-(3,3-Difluorocyclobutyl)-2-[3-methyl-2-oxo-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-1-yl]acetamide;           |

| Ex # | Compound Name                                                                                                        |
|------|----------------------------------------------------------------------------------------------------------------------|
| 201  | 1-(2-Oxo-2-pyrrolidin-1-yl-ethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                      |
| 202  | (R/S)-N-Cyclopropyl-2-[2-oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-yl]propanamide;                |
| 203  | (R/S)-1-[2-(Azetidin-1-yl)-1-methyl-2-oxo-ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;       |
| 204  | 1-(2-Morpholino-2-oxo-ethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                           |
| 205  | N-Cyclopentyl-2-[2-oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;                        |
| 206  | 1-[2-Oxo-2-(1-piperidyl)ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                         |
| 207  | 1-[2-(2,6-Diazaspiro[3.3]heptan-6-yl)-2-oxo-ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;     |
| 208  | 2-[2-Oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-yl]-N-(2-pyridyl)acetamide;                        |
| 209  | N-(3,3-Difluoro-1-methyl-cyclobutyl)-2-[2-oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-yl]acetamide; |
| 210  | 1-[(6-Methoxy-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                        |
| 211  | 1-(Cyclopropylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                                  |
| 212  | 3-[[2-Oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;                           |
| 213  | 2-[[2-Oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;                           |
| 214  | 1-[2-Oxo-2-(2-thienyl)ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                           |
| 215  | 1-(2-Oxo-2-thiazol-2-yl-ethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                         |
| 216  | (R/S)-1-(Oxetan-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                            |
| 217  | (R/S)-1-(Morpholin-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                         |
| 218  | (R/S)-1-(Tetrahydropyran-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                   |
| 219  | 6-[3-(Trifluoromethyl)phenyl]-1-[[4-(trifluoromethyl)phenyl]methyl]-3H-imidazo[4,5-b]pyridin-2-one;                  |
| 220  | 1-[(3-Fluoro-4-methoxy-phenyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                  |

| Ex # | Compound Name                                                                                           |
|------|---------------------------------------------------------------------------------------------------------|
| 221  | 1-[(4-Fluoro-3-methyl-phenyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;      |
| 222  | 1-[(3-Fluorophenyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                |
| 223  | (R*)-1-(Oxetan-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                |
| 224  | (S*)-1-(Oxetan-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                |
| 225  | (R/S)-1-[(2,2-Difluorocyclopropyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one; |
| 226  | 1-[(3-Fluorooxetan-3-yl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;           |
| 227  | 1-(Pyrimidin-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                  |
| 228  | 1-(2-Pyridylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                       |
| 229  | 1-(4-Pyridylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                       |
| 230  | 1-(3-Pyridylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                       |
| 231  | 1-[(2-Methylpyrimidin-5-yl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;        |
| 232  | 1-(Pyridazin-3-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                  |
| 233  | 1-[(3-Methoxy-2-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;           |
| 234  | 1-[(3-Fluoro-5-methyl-2-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;   |
| 235  | 1-[(6-Methyl-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;            |
| 236  | 1-(2H-Tetrazol-5-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                |
| 237  | 1-[Difluoro(3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;             |
| 238  | 1-[(6-Fluoro-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;            |
| 239  | 1-(2-Cyclopropyl-2-oxo-ethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;             |
| 240  | 1-(2-Oxobutyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                            |

| Ex # | Compound Name                                                                                           |
|------|---------------------------------------------------------------------------------------------------------|
| 241  | 1-(3-Methyl-2-oxo-butyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                  |
| 242  | 1-[(5-Methyl-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;            |
| 243  | 1-(Thiadiazol-4-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                 |
| 244  | 1-[(6-Oxo-1H-pyridin-3-yl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;         |
| 245  | (R/S)-1-(Azetidin-2-ylmethyl)-3-methyl-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;        |
| 246  | 3-Methyl-1-(pyrimidin-4-ylmethyl)-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;             |
| 247  | 3-Methyl-1-(pyrimidin-5-ylmethyl)-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;             |
| 248  | 3-Methyl-1-[(2-methylpyrimidin-4-yl)methyl]-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;   |
| 249  | 3-Methyl-1-(pyrazin-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;               |
| 250  | 3-Methyl-1-(4-pyridylmethyl)-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;                  |
| 251  | 3-Methyl-1-(2-pyridylmethyl)-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;                  |
| 252  | 1-[(6-Methoxypyridazin-3-yl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;       |
| 253  | 1-(Pyrazin-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                    |
| 254  | 1-[(2-Methylpyrimidin-4-yl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;        |
| 255  | 1-(Pyrimidin-5-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                  |
| 256  | 1-[(5-Fluoropyrimidin-2-yl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;        |
| 257  | 6-[3-(Trifluoromethyl)phenyl]-1-[[6-(trifluoromethyl)-3-pyridyl]methyl]-3H-imidazo[4,5-b]pyridin-2-one; |
| 258  | 1-[(5-Fluoro-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;            |
| 259  | 6-[3-(Trifluoromethyl)phenyl]-1-[[5-(trifluoromethyl)-3-pyridyl]methyl]-3H-imidazo[4,5-b]pyridin-2-one; |
| 260  | 6-[3-(Trifluoromethyl)phenyl]-1-[[4-(trifluoromethyl)-3-pyridyl]methyl]-3H-imidazo[4,5-b]pyridin-2-one; |

| Ex # | Compound Name                                                                                        |
|------|------------------------------------------------------------------------------------------------------|
| 261  | 3-Methyl-1-(pyrimidin-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;          |
| 262  | 1-(2-cyclobutyl-2-oxo-ethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;           |
| 263  | (R/S)-1-(Azetidin-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;          |
| 264  | (R/S)-1-(Azetidin-2-ylmethyl)-6-[2-fluoro-3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one; |
| 265  | (R/S)-1-(Azetidin-2-ylmethyl)-6-phenyl-3H-imidazo[4,5-b]pyridin-2-one;                               |
| 266  | (R/S)-1-(Azetidin-2-ylmethyl)-6-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-one;                     |
| 267  | (R/S)-1-(Azetidin-2-ylmethyl)-6-[4-fluoro-3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one; |
| 268  | (R/S)-1-(Azetidin-2-ylmethyl)-6-(2,3-dichlorophenyl)-3H-imidazo[4,5-b]pyridin-2-one;                 |
| 269  | 6-(4-Fluoro-3-methyl-phenyl)-1-[(5-methyl-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;          |
| 270  | 6-(2,4-Difluoro-3-methyl-phenyl)-1-[(5-methyl-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;      |
| 271  | (R/S)-6-[4-Fluoro-3-(trifluoromethyl)phenyl]-1-(oxetan-2-ylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;   |
| 272  | 6-(3,4-Difluorophenyl)-1-[(5-methyl-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;                |
| 273  | 6-(3-Chlorophenyl)-1-[(5-methyl-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;                    |
| 274  | 6-(3-Fluorophenyl)-1-[(5-methyl-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;                    |
| 275  | 6-(3,4-Difluorophenyl)-1-[(4-methyl-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;                |
| 276  | 6-(3-Fluorophenyl)-1-[(4-methyl-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;                    |
| 277  | 6-(4-Fluoro-3-methyl-phenyl)-1-[(4-methyl-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;          |
| 278  | 6-(2,4-Difluoro-3-methyl-phenyl)-1-[(4-methyl-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;      |
| 279  | 6-(3,4-Difluorophenyl)-1-(2-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;                           |
| 280  | 6-(2,4-Difluoro-3-methyl-phenyl)-1-(2-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;                 |

| Ex # | Compound Name                                                                               |
|------|---------------------------------------------------------------------------------------------|
| 281  | 6-(3-Fluorophenyl)-1-(2-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;                      |
| 282  | 6-(3-Chlorophenyl)-1-(2-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;                      |
| 283  | 6-(4-Fluoro-3-methyl-phenyl)-1-(2-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;            |
| 284  | 6-(3,4-Difluorophenyl)-1-[(3-methyl-2-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;       |
| 285  | 6-(3-Fluorophenyl)-1-[(3-methyl-2-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;           |
| 286  | 6-(4-Fluorophenyl)-1-(2-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;                      |
| 287  | 6-[3-(Difluoromethyl)phenyl]-1-(2-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;            |
| 288  | 6-(3-Methoxyphenyl)-1-(2-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;                     |
| 289  | 6-(p-Tolyl)-1-(2-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;                             |
| 290  | 6-(3-fluorophenyl)-1-(3-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;                      |
| 291  | 6-[3-(Difluoromethyl)phenyl]-1-(3-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;            |
| 292  | 6-(3,4-Difluorophenyl)-1-(3-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;                  |
| 293  | 6-(2,4-Difluoro-3-methyl-phenyl)-1-(3-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;        |
| 294  | 6-(4-Fluoro-3-methyl-phenyl)-1-(3-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;            |
| 295  | 6-(4-Fluorophenyl)-1-(3-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;                      |
| 296  | 6-(3-Chlorophenyl)-1-(3-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;                      |
| 297  | 6-(m-Tolyl)-1-(3-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;                             |
| 298  | 6-(3,4-Difluorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;       |
| 299  | 6-(4-Fluoro-3-methyl-phenyl)-1-[(5-fluoro-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one; |
| 300  | 6-[3-(Difluoromethoxy)phenyl]-1-(3-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;           |

| Ex # | Compound Name                                                                                         |
|------|-------------------------------------------------------------------------------------------------------|
| 301  | 6-(2,4-Difluoro-3-methyl-phenyl)-1-[(5-fluoro-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;       |
| 302  | 6-[3-(Difluoromethyl)phenyl]-1-[(5-fluoro-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;           |
| 303  | 6-(2,3-Difluorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;                 |
| 304  | 6-[3-(Difluoromethoxy)phenyl]-1-[(5-fluoro-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;          |
| 305  | 6-(3-Chlorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;                     |
| 306  | 6-(4-Chloro-3-methyl-phenyl)-1-[(5-fluoro-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;           |
| 307  | 1-[(5-Fluoro-3-pyridyl)methyl]-6-[3-(trifluoromethoxy)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;         |
| 308  | 1-[(5-Methyl-3-pyridyl)methyl]-6-(3,4,5-trifluorophenyl)-3H-imidazo[4,5-b]pyridin-2-one;              |
| 309  | 6-[4-Fluoro-3-(trifluoromethyl)phenyl]-1-[(5-methyl-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one; |
| 310  | 6-(2,3-Difluorophenyl)-1-[(5-methyl-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;                 |
| 311  | 6-(3,5-Difluorophenyl)-1-[(5-methyl-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;                 |
| 312  | 1-[(4-Methyl-3-pyridyl)methyl]-6-(3,4,5-trifluorophenyl)-3H-imidazo[4,5-b]pyridin-2-one;              |
| 313  | 1-[(4-Methyl-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;          |
| 314  | 6-[4-Fluoro-3-(trifluoromethyl)phenyl]-1-[(4-methyl-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one; |
| 315  | 1-[(3-Methyl-2-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;          |
| 316  | 6-(4-Fluoro-3-methyl-phenyl)-1-[(3-methyl-2-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;           |
| 317  | 6-(2,4-Difluoro-3-methyl-phenyl)-1-[(3-methyl-2-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;       |
| 318  | 6-(3,5-Difluorophenyl)-1-[(3-methyl-2-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;                 |
| 319  | 6-(2,3-Difluorophenyl)-1-[(3-methyl-2-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;                 |
| 320  | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(4-fluoro-2-methyl-phenyl)-3H-imidazo[4,5-b]pyridin-2-one;        |

| Ex # | Compound Name                                                                                                    |
|------|------------------------------------------------------------------------------------------------------------------|
| 321  | 2-[6-(5-Chloro-4-methyl-2-thienyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;                  |
| 322  | 2-[6-(5-Chloro-4-methyl-2-thienyl)-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;            |
| 323  | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[5-(trifluoromethyl)-2-thienyl]-3H-imidazo[4,5-b]pyridin-2-one;              |
| 324  | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(5-chloro-4-methyl-2-thienyl)-3H-imidazo[4,5-b]pyridin-2-one;                |
| 325  | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(5-chloro-4-methyl-2-thienyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;          |
| 326  | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-(5-methyl-2-thienyl)imidazo[4,5-b]pyridin-2-one;                    |
| 327  | 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one; |
| 328  | 3-Methyl-1-(2-oxo-2-pyrrolidin-1-yl-ethyl)-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;         |
| 329  | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[2-methyl-3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;         |
| 330  | 6-(3,4-Difluorophenyl)-1-(2-oxobutyl)-3H-imidazo[4,5-b]pyridin-2-one;                                            |
| 331  | 6-(4-Fluoro-3-methyl-phenyl)-1-(2-oxobutyl)-3H-imidazo[4,5-b]pyridin-2-one;                                      |
| 332  | 6-(m-Tolyl)-1-(2-oxobutyl)-3H-imidazo[4,5-b]pyridin-2-one;                                                       |
| 333  | (R/S)-6-(3,4-Difluorophenyl)-1-(2-hydroxybutyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;                            |
| 334  | (R/S)-6-(4-Fluoro-3-methyl-phenyl)-1-(2-hydroxybutyl)-3H-imidazo[4,5-b]pyridin-2-one;                            |
| 335  | (R/S)-1-(2-Hydroxybutyl)-6-(m-tolyl)-3H-imidazo[4,5-b]pyridin-2-one;                                             |
| 336  | (R/S)-6-(2,4-difluoro-3-methyl-phenyl)-1-(2-hydroxybutyl)-3H-imidazo[4,5-b]pyridin-2-one;                        |
| 337  | (R/S)-1-(2-Hydroxybutyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                           |
| 338  | (R/S)-1-(2-Hydroxy-3-methyl-butyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                 |
| 339  | 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-(3-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;                        |
| 340  | 6-(4-Fluoro-3-methyl-phenyl)-1-[(5-fluoro-3-pyridyl)methyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;                |

| Ex # | Compound Name                                                                                         |
|------|-------------------------------------------------------------------------------------------------------|
| 341  | 6-(2,4-Difluoro-3-methyl-phenyl)-1-[(5-fluoro-3-pyridyl)methyl]-3-methyl-imidazo[4,5-b]pyridin-2-one; |
| 342  | 6-[3-(Difluoromethoxy)phenyl]-1-[(5-fluoro-3-pyridyl)methyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;    |
| 343  | 6-(3,4-Difluorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;           |
| 344  | 1-[(5-Fluoro-3-pyridyl)methyl]-3-methyl-6-(3,4,5-trifluorophenyl)imidazo[4,5-b]pyridin-2-one;         |
| 345  | 1-[(5-Fluoro-3-pyridyl)methyl]-3-methyl-6-[3-(trifluoromethoxy)phenyl]imidazo[4,5-b]pyridin-2-one;    |
| 346  | 6-(2,3-Difluorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;           |
| 347  | 1-[(5-Fluoro-3-pyridyl)methyl]-3-methyl-6-(2,3,4-trifluorophenyl)imidazo[4,5-b]pyridin-2-one;         |
| 348  | 6-(3-Chlorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;               |
| 349  | 6-(3-Chloro-2-fluoro-phenyl)-1-[(5-fluoro-3-pyridyl)methyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;     |
| 350  | 1-[(5-Fluoro-3-pyridyl)methyl]-3-methyl-6-(m-tolyl)imidazo[4,5-b]pyridin-2-one;                       |
| 351  | 6-(3,4-Dichlorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;           |
| 352  | 6-(2-Fluoro-3-methyl-phenyl)-1-[(5-fluoro-3-pyridyl)methyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;     |
| 353  | 3-Methyl-1-(3-pyridylmethyl)-6-(3,4,5-trifluorophenyl)imidazo[4,5-b]pyridin-2-one;                    |
| 354  | 6-(3,5-Difluorophenyl)-3-methyl-1-(3-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;                       |
| 355  | 6-(3-Chloro-4-fluoro-phenyl)-3-methyl-1-(3-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;                 |
| 356  | 3-Methyl-6-(m-tolyl)-1-(3-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;                                  |
| 357  | 6-(2-Fluoro-3-methyl-phenyl)-3-methyl-1-(3-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;                 |
| 358  | 6-[2-Fluoro-3-(trifluoromethyl)phenyl]-3-methyl-1-(3-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;       |
| 359  | 6-(3-Chloro-2-fluoro-phenyl)-3-methyl-1-(3-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;                 |
| 360  | 6-[4-Fluoro-3-(trifluoromethyl)phenyl]-3-methyl-1-(3-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;       |

| Ex # | Compound Name                                                                                         |
|------|-------------------------------------------------------------------------------------------------------|
| 361  | 3-Methyl-1-(3-pyridylmethyl)-6-(2,3,4-trifluorophenyl)imidazo[4,5-b]pyridin-2-one;                    |
| 362  | 3-Methyl-1-(3-pyridylmethyl)-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;                |
| 363  | 6-[3-(Difluoromethyl)phenyl]-3-methyl-1-(3-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;                 |
| 364  | 3-Methyl-1-(3-pyridylmethyl)-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;            |
| 365  | 6-(5-Chloro-4-methyl-2-thienyl)-3-methyl-1-(3-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;              |
| 366  | 1-[(5-Chloro-3-pyridyl)methyl]-3-methyl-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;     |
| 367  | 1-[(5-Chloro-3-pyridyl)methyl]-6-(4-fluoro-3-methyl-phenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;     |
| 368  | 1-[(5-Chloro-3-pyridyl)methyl]-6-(2,4-difluoro-3-methyl-phenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one; |
| 369  | 1-[(5-Chloro-3-pyridyl)methyl]-6-(3,4-difluorophenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;           |
| 370  | 1-[(5-Chloro-3-pyridyl)methyl]-3-methyl-6-(3,4,5-trifluorophenyl)imidazo[4,5-b]pyridin-2-one;         |
| 371  | 1-[(5-Chloro-3-pyridyl)methyl]-6-(2-fluoro-3-methyl-phenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;     |
| 372  | 6-(5-Chloro-4-methyl-2-thienyl)-1-[(5-chloro-3-pyridyl)methyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;  |
| 373  | 1-[(5-Chloro-3-pyridyl)methyl]-3-methyl-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one; |
| 374  | 1-[(5-Chloro-3-pyridyl)methyl]-3-methyl-6-(m-tolyl)imidazo[4,5-b]pyridin-2-one;                       |
| 375  | 1-[(5-Chloro-3-pyridyl)methyl]-6-(2,3-difluorophenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;           |
| 376  | 6-(3-Chlorophenyl)-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;                      |
| 377  | 6-[3-(Difluoromethyl)phenyl]-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;            |
| 378  | 3-Methyl-1-(pyridazin-3-ylmethyl)-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;           |
| 379  | 3-Methyl-6-(m-tolyl)-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;                             |
| 380  | 6-(3-Chloro-4-fluoro-phenyl)-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;            |

| Ex # | Compound Name                                                                                                    |
|------|------------------------------------------------------------------------------------------------------------------|
| 381  | 6-(3-Fluoro-5-methyl-phenyl)-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;                       |
| 382  | 6-[4-Fluoro-3-(trifluoromethyl)phenyl]-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;             |
| 383  | 6-[3-Fluoro-5-(trifluoromethyl)phenyl]-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;             |
| 384  | 6-[4-Chloro-3-(trifluoromethyl)phenyl]-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;             |
| 387  | 6-[3,4-Difluoro-5-(trifluoromethyl)phenyl]-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;         |
| 388  | 3-Methyl-1-(2-oxobutyl)-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;                                |
| 389  | 6-(4-Fluoro-3-methyl-phenyl)-3-methyl-1-(2-oxobutyl)imidazo[4,5-b]pyridin-2-one;                                 |
| 390  | 6-(3,4-Difluorophenyl)-3-methyl-1-(2-oxobutyl)imidazo[4,5-b]pyridin-2-one;                                       |
| 391  | 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-(2-oxobutyl)imidazo[4,5-b]pyridin-2-one;                             |
| 392  | 6-(3-Cyclopropylphenyl)-3-methyl-1-(2-oxobutyl)imidazo[4,5-b]pyridin-2-one;                                      |
| 393  | (R/S)-6-(4-Fluoro-3-methyl-phenyl)-1-(2-hydroxy-4-methoxy-butyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;           |
| 394  | (R/S)-6-[3-(Difluoromethyl)phenyl]-3-methyl-1-(oxetan-2-ylmethyl)imidazo[4,5-b]pyridin-2-one;                    |
| 395  | (R/S)-6-(4-Fluoro-3-methyl-phenyl)-3-methyl-1-(oxetan-2-ylmethyl)imidazo[4,5-b]pyridin-2-one;                    |
| 396  | (R/S)-6-[2-Fluoro-3-(trifluoromethyl)phenyl]-3-methyl-1-(oxetan-2-ylmethyl)imidazo[4,5-b]pyridin-2-one;          |
| 397  | (R/S)-6-(3-Chlorophenyl)-3-methyl-1-(oxetan-2-ylmethyl)imidazo[4,5-b]pyridin-2-one;                              |
| 398  | (R/S)-3-Methyl-6-[2-methyl-3-(trifluoromethyl)phenyl]-1-(oxetan-2-ylmethyl)imidazo[4,5-b]pyridin-2-one;          |
| 399  | (R/S)-1-(2,4-Dihydroxybutyl)-3-methyl-6-[2-methyl-3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;         |
| 400  | 6-(2,4-Difluoro-3-methyl-phenyl)-1-[2-(3-fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-imidazo[4,5-b]pyridin-2-one; |
| 401  | 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-6-(4-fluoro-3-methyl-phenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;     |
| 402  | 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-(3,4,5-trifluorophenyl)imidazo[4,5-b]pyridin-2-one;         |

| Ex # | Compound Name                                                                                                              |
|------|----------------------------------------------------------------------------------------------------------------------------|
| 403  | 6-(3,4-Difluorophenyl)-1-[2-(3-fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;                     |
| 404  | 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-(m-tolyl)imidazo[4,5-b]pyridin-2-one;                                 |
| 405  | 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-6-(2-fluoro-3-methyl-phenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;               |
| 406  | 6-(3-Chlorophenyl)-1-[2-(3-fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;                         |
| 407  | 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-6-[4-fluoro-3-(trifluoromethyl)phenyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;     |
| 408  | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;                       |
| 409  | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(2,4-difluoro-3-methyl-phenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;                   |
| 410  | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(4-fluoro-3-methyl-phenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;                       |
| 411  | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-(3,4,5-trifluorophenyl)imidazo[4,5-b]pyridin-2-one;                           |
| 412  | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(3,5-difluorophenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;                             |
| 413  | 1-(2-(3,3-Difluoroazetidin-1-yl)-2-oxoethyl)-6-(4-fluoro-3-methylphenyl)-3-methyl-1H-imidazo[4,5-b]pyridin-2(3H)-one;      |
| 414  | 1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]-6-(2,4-difluoro-3-methyl-phenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;       |
| 415  | 1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]-6-[2-fluoro-3-(trifluoromethyl)phenyl]-3-methyl-imidazo[4,5-b]pyridin-2-one; |
| 416  | 1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]-6-(3,4-difluorophenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;                 |
| 417  | 1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]-6-(3-fluorophenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;                     |
| 418  | 1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]-6-(2-fluoro-3-methyl-phenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;           |
| 419  | N,N-Dimethyl-2-[3-methyl-2-oxo-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-1-yl]acetamide;                          |
| 420  | 2-[6-(4-Fuoro-3-methyl-phenyl)-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;                          |
| 421  | 2-[6-(3,4-Difluorophenyl)-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;                               |
| 422  | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(3,4-difluorophenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;                             |

| Ex # | Compound Name                                                                                                        |
|------|----------------------------------------------------------------------------------------------------------------------|
| 423  | 2-[6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;               |
| 424  | 2-[6-[2-Fluoro-3-(trifluoromethyl)phenyl]-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;         |
| 425  | 2-[6-(2,3-Difluorophenyl)-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;                         |
| 426  | 2-[6-[3-(Difluoromethyl)phenyl]-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;                   |
| 427  | 2-[6-(2-Fluoro-3-methyl-phenyl)-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;                   |
| 428  | 2-[6-(3,5-Difluorophenyl)-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;                         |
| 429  | N,N-Dimethyl-2-[3-methyl-2-oxo-6-(3-pyridyl)imidazo[4,5-b]pyridin-1-yl]acetamide;                                    |
| 430  | 1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one; |
| 431  | 2-[6-[3,4-Difluoro-5-(trifluoromethyl)phenyl]-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;     |
| 432  | 2-[2-Oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;                                      |
| 433  | 2-[6-(4-Fluoro-2-methoxy-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;                                      |
| 434  | 2-[6-(3-Chloro-4-fluoro-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;                                       |
| 435  | N-Methyl-2-[2-oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;                             |
| 436  | 2-[6-(4-Chlorophenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-methyl-acetamide;                                       |
| 437  | 2-[6-(4-Fluoro-2-methyl-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-methyl-acetamide;                             |
| 438  | 2-[6-(3,5-Dimethylphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-methyl-acetamide;                                   |
| 439  | 2-[6-(4-Methoxy-3-methyl-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-methyl-acetamide;                            |
| 440  | 2-[6-(4-Fluoro-2-methoxy-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-methyl-acetamide;                            |
| 441  | 2-[6-(2-Ethoxyphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-methyl-acetamide;                                       |
| 442  | N-(2-Methoxyethyl)-2-[2-oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;                   |

| Ex # | Compound Name                                                                                      |
|------|----------------------------------------------------------------------------------------------------|
| 443  | 2-[6-(2-Ethoxy-5-fluoro-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-(2-methoxyethyl)acetamide;  |
| 444  | N-(2-Methoxyethyl)-2-[6-(4-methoxyphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;           |
| 445  | N-(2-Methoxyethyl)-2-[2-oxo-6-(3-pyridyl)-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;                 |
| 446  | 2-[6-(4-Fluoro-2-methoxy-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-(2-methoxyethyl)acetamide; |
| 447  | N-Cyclopropyl-2-[6-(3,5-difluorophenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;             |
| 448  | 2-[6-(3-Chloro-4-fluoro-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-cyclopropyl-acetamide;      |
| 449  | N-Cyclopropyl-2-[6-(3-ethoxyphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;                 |
| 450  | N-Cyclopropyl-2-[6-(3-methoxyphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;                |
| 451  | N-Cyclopropyl-2-[6-(4-methoxy-3-methyl-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;      |
| 452  | N-Cyclopropyl-2-[6-(4-fluoro-2-methoxy-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;      |
| 453  | 2-[6-(4-Chlorophenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-cyclopropyl-acetamide;                |
| 454  | N-Cyclopropyl-2-[6-(2,4-dimethoxyphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;            |
| 455  | N-Cyclopropyl-2-[6-(2-fluoro-6-methoxy-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;      |
| 456  | N-Cyclopropyl-2-[6-(2-ethoxyphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;                 |
| 457  | 6-(3-Fluoro-4-methoxy-phenyl)-1-[2-oxo-2-(2-thienyl)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;         |
| 458  | 6-(2-Ethoxyphenyl)-1-[2-oxo-2-(2-thienyl)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;                    |
| 459  | 6-(4-Chlorophenyl)-1-[2-oxo-2-(2-thienyl)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;                    |
| 460  | 6-(2-Ethoxy-5-fluoro-phenyl)-1-[2-oxo-2-(2-thienyl)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;          |
| 461  | 6-(4-Methoxyphenyl)-1-[2-oxo-2-(2-thienyl)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;                   |
| 462  | 6-(4-Fluoro-2-methoxy-phenyl)-1-[2-oxo-2-(2-thienyl)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;         |

| Ex # | Compound Name                                                                              |
|------|--------------------------------------------------------------------------------------------|
| 463  | 6-(3-Ethoxyphenyl)-1-[2-oxo-2-(2-thienyl)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;            |
| 464  | 6-(3-Chloro-4-fluoro-phenyl)-1-[2-oxo-2-(2-thienyl)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;  |
| 465  | 1-(Cyclopropylmethyl)-6-(2,4-dimethoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-one;              |
| 466  | 1-(Cyclopropylmethyl)-6-(2-ethoxy-5-fluoro-phenyl)-3H-imidazo[4,5-b]pyridin-2-one;         |
| 467  | 1-(Cyclopropylmethyl)-6-(4-fluoro-2-methoxy-phenyl)-3H-imidazo[4,5-b]pyridin-2-one;        |
| 468  | 1-(Cyclopropylmethyl)-6-(4-methoxy-3-methyl-phenyl)-3H-imidazo[4,5-b]pyridin-2-one;        |
| 469  | 1-(Cyclopropylmethyl)-6-(3-fluoro-4-methoxy-phenyl)-3H-imidazo[4,5-b]pyridin-2-one;        |
| 470  | 1-(Cyclopropylmethyl)-6-(3,5-difluorophenyl)-3H-imidazo[4,5-b]pyridin-2-one;               |
| 471  | 1-(Cyclopropylmethyl)-6-(4-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-one;                  |
| 472  | 1-(Cyclopropylmethyl)-6-(2-thienyl)-3H-imidazo[4,5-b]pyridin-2-one;                        |
| 473  | 1-(Cyclopropylmethyl)-6-[3-(dimethylamino)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;          |
| 474  | 1-(Cyclopropylmethyl)-6-(3,5-dimethylphenyl)-3H-imidazo[4,5-b]pyridin-2-one;               |
| 475  | 6-(3-Methoxyphenyl)-1-(tetrahydrofuran-2-ylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;         |
| 476  | 4-[[6-(4-Methoxyphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;           |
| 477  | 3-[[6-(4-Methoxyphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;           |
| 478  | 3-[[6-(4-Fluoro-2-methoxy-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile; |
| 479  | 3-[[6-(4-Fluoro-2-methyl-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;  |
| 480  | 3-[[6-(3-Chloro-4-fluoro-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;  |
| 481  | 2-[[6-(2-Fluoro-6-methoxy-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile; |
| 482  | 2-[[6-(4-Chlorophenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;            |

| Ex # | Compound Name                                                                              |
|------|--------------------------------------------------------------------------------------------|
| 483  | 2-[[6-(4-Fluoro-2-methyl-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;  |
| 484  | 2-[[6-(2-Ethoxyphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;            |
| 485  | 2-[[6-(3-Methoxyphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;           |
| 486  | 2-[[6-(3-Cyanophenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;             |
| 487  | 2-[[6-(2,4-Dimethoxyphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;       |
| 488  | 2-[[6-(3,5-Dimethylphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;        |
| 489  | 2-[[6-(2-Ethoxy-5-fluoro-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;  |
| 490  | 2-[[6-(4-Fluoro-2-methoxy-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile; |
| 491  | 2-[[6-(3-Fluoro-4-methoxy-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile; |
| 492  | 6-(4-Fluoro-2-methyl-phenyl)-1-[(4-fluorophenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;    |
| 493  | 6-(2,3-Dimethoxyphenyl)-1-[(4-fluorophenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;         |
| 494  | 6-(2-Ethoxy-5-fluoro-phenyl)-1-[(3-fluorophenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;    |
| 495  | 6-(3,5-Dimethylphenyl)-1-[(3-fluorophenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;          |
| 496  | 6-(2,4-Dimethoxyphenyl)-1-[(3-fluorophenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;         |
| 497  | 6-(2-Ethoxyphenyl)-1-[(3-fluorophenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;              |
| 498  | 1-[(3-Fluorophenyl)methyl]-6-(4-methoxy-3-methyl-phenyl)-3H-imidazo[4,5-b]pyridin-2-one;   |
| 499  | 6-(4-Fluoro-2-methoxy-phenyl)-1-[(3-fluorophenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;   |
| 500  | 6-[3-(Dimethylamino)phenyl]-1-[(3-fluorophenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;     |
| 501  | 6-(4-Fluoro-2-methoxy-phenyl)-1-[(4-fluorophenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;   |
| 502  | 6-(3-Chloro-4-fluoro-phenyl)-1-[(4-fluorophenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;    |

| Ex # | Compound Name                                                                                      |
|------|----------------------------------------------------------------------------------------------------|
| 503  | 6-(2-Ethoxyphenyl)-1-[(2-fluorophenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;                      |
| 504  | 1-[(3-Chlorophenyl)methyl]-6-(3,5-difluorophenyl)-3H-imidazo[4,5-b]pyridin-2-one;                  |
| 505  | 6-(4-Fluoro-2-methoxy-phenyl)-1-[(3-methoxyphenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;          |
| 506  | 1-[(3-Methoxyphenyl)methyl]-6-(3-pyridyl)-3H-imidazo[4,5-b]pyridin-2-one;                          |
| 507  | 1-[(3-Methoxyphenyl)methyl]-6-(4-methyl-2-thienyl)-3H-imidazo[4,5-b]pyridin-2-one;                 |
| 508  | 6-(3,5-Difluorophenyl)-1-[(4-methoxyphenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;                 |
| 509  | 1-[(3,5-Dimethoxyphenyl)methyl]-6-(2-fluoro-6-methoxy-phenyl)-3H-imidazo[4,5-b]pyridin-2-one;      |
| 510  | 1-[(3,5-Dimethoxyphenyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;      |
| 511  | 6-(4-Chlorophenyl)-1-[(4-isopropylphenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;                   |
| 512  | 6-(4-tert-Butylphenyl)-1-[(3,4-dimethoxy-2-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;         |
| 513  | 3-[1-[(3,5-Dimethylisoxazol-4-yl)methyl]-2-oxo-3H-imidazo[4,5-b]pyridin-6-yl]benzonitrile;         |
| 514  | 1-[(3,5-Dimethylisoxazol-4-yl)methyl]-6-(2-ethoxy-5-fluoro-phenyl)-3H-imidazo[4,5-b]pyridin-2-one; |
| 515  | 6-(4-Methoxy-3-methyl-phenyl)-1-[(5-methylisoxazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;    |
| 516  | 6-(3,5-Dimethylphenyl)-1-[(5-methylisoxazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;           |
| 517  | 6-(2-Ethoxyphenyl)-1-[(5-methylisoxazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;               |
| 518  | 6-(2,4-Dimethoxyphenyl)-1-[(5-methylisoxazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;          |
| 519  | 6-(3-Fluoro-4-methoxy-phenyl)-1-[(5-methylisoxazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;    |
| 520  | 6-(4-Fluoro-2-methoxy-phenyl)-1-[(5-methylisoxazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;    |
| 521  | 6-(2-Ethoxy-5-fluoro-phenyl)-1-[(5-methylisoxazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;     |
| 522  | 6-(4-Fluoro-2-methyl-phenyl)-1-[(5-methylisoxazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;     |

| Ex # | Compound Name                                                                                                                    |
|------|----------------------------------------------------------------------------------------------------------------------------------|
| 523  | 6-(3,5-Difluorophenyl)-1-[(5-methylisoxazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;                                         |
| 532  | N-(3-Chloropropyl)-2-[3-methyl-2-oxo-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-1-yl]acetamide;                      |
| 533  | 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;                     |
| 534  | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-(fluoromethyl)-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;                 |
| 535  | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-(2-fluoroethyl)-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;                |
| 536  | 1-[2-[3-(2-Fluoroethyl)azetidin-1-yl]-2-oxo-ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;                 |
| 537  | 6-(6-Fluoro-2-pyridyl)-1-(2-oxobutyl)-3H-imidazo[4,5-b]pyridin-2-one;                                                            |
| 538  | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[4-(2-fluoroethoxy)-3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;               |
| 539  | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[3-(2-fluoroethoxy)-5-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;               |
| 540  | 1-[2-(3- <sup>18</sup> F-Fluoranylazetidin-1-yl)-2-oxo-ethyl]-6-(4-fluoro-3-methyl-phenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one; |
| 541  | 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;                             |
| 542  | 6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;                            |
| 543  | 6-[4-Chloro-3-(difluoromethoxy)phenyl]-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;                             |
| 544  | 6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-[(5-fluoro-3-pyridyl)methyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;                      |
| 545  | 6-(3,4-Difluorophenyl)-3-methyl-1-(thiadiazol-4-ylmethyl)imidazo[4,5-b]pyridin-2-one;                                            |
| 546  | 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-fluoro-3-pyridyl)methyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;                      |
| 547  | 6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(5-fluoro-3-pyridyl)methyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;                     |
| 548  | 3-Methyl-1-(thiadiazol-4-ylmethyl)-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;                                     |
| 549  | 6-(3,4-Difluorophenyl)-3-methyl-1-[(1-methyltriazol-4-yl)methyl]imidazo[4,5-b]pyridin-2-one;                                     |
| 550  | 6-(3,4-Difluorophenyl)-3-methyl-1-[(1-methylpyrazol-4-yl)methyl]imidazo[4,5-b]pyridin-2-one;                                     |

| Ex # | Compound Name                                                                                                    |
|------|------------------------------------------------------------------------------------------------------------------|
| 551  | 3-Methyl-1-[(1-methylpyrazol-4-yl)methyl]-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;              |
| 552  | 3-Methyl-1-[(1-methyltriazol-4-yl)methyl]-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;              |
| 553  | 3-Methyl-6-(5-methyl-2-thienyl)-1-[(1-methyltriazol-4-yl)methyl]imidazo[4,5-b]pyridin-2-one;                     |
| 554  | 3-Methyl-1-[(5-methyl-1,3,4-oxadiazol-2-yl)methyl]-6-(5-methyl-2-thienyl)imidazo[4,5-b]pyridin-2-one;            |
| 555  | 3-Methyl-1-[(1-methylpyrazol-4-yl)methyl]-6-(5-methyl-2-thienyl)imidazo[4,5-b]pyridin-2-one;                     |
| 556  | 3-Methyl-6-(5-methyl-2-thienyl)-1-(thiadiazol-4-ylmethyl)imidazo[4,5-b]pyridin-2-one;                            |
| 557  | 3-Methyl-1-[(3-methyl-1,2,4-oxadiazol-5-yl)methyl]-6-(5-methyl-2-thienyl)imidazo[4,5-b]pyridin-2-one;            |
| 558  | 3-Methyl-1-[(5-methylisoxazol-3-yl)methyl]-6-(5-methyl-2-thienyl)imidazo[4,5-b]pyridin-2-one;                    |
| 559  | 6-[5-(Difluoromethyl)-2-thienyl]-3-methyl-1-[(1-methyltriazol-4-yl)methyl]imidazo[4,5-b]pyridin-2-one;           |
| 560  | 6-[5-(Difluoromethyl)-2-thienyl]-3-methyl-1-[(5-methyl-1,3,4-oxadiazol-2-yl)methyl]imidazo[4,5-b]pyridin-2-one;  |
| 561  | 6-[5-(Difluoromethyl)-2-thienyl]-3-methyl-1-[(1-methylpyrazol-4-yl)methyl]imidazo[4,5-b]pyridin-2-one;           |
| 562  | 6-[5-(Difluoromethyl)-2-thienyl]-3-methyl-1-(thiadiazol-4-ylmethyl)imidazo[4,5-b]pyridin-2-one;                  |
| 563  | 6-[5-(Difluoromethyl)-2-thienyl]-3-methyl-1-[(3-methyl-1,2,4-oxadiazol-5-yl)methyl]imidazo[4,5-b]pyridin-2-one;  |
| 564  | 6-[5-(Difluoromethyl)-2-thienyl]-3-methyl-1-[(5-methylisoxazol-3-yl)methyl]imidazo[4,5-b]pyridin-2-one;          |
| 565  | 3-Methyl-1-[(1-methylpyrazol-4-yl)methyl]-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;          |
| 566  | 3-Methyl-1-[(1-methyltriazol-4-yl)methyl]-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;          |
| 567  | 3-Methyl-1-[(5-methyl-1,3,4-oxadiazol-2-yl)methyl]-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one; |
| 568  | 3-Methyl-1-(thiadiazol-4-ylmethyl)-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;                 |
| 569  | 3-Methyl-1-[(3-methyl-1,2,4-oxadiazol-5-yl)methyl]-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one; |
| 570  | 3-Methyl-1-[(5-methylisoxazol-3-yl)methyl]-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;         |

| Ex # | Compound Name                                                                                                               |
|------|-----------------------------------------------------------------------------------------------------------------------------|
| 571  | 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-[(5-methylisoxazol-3-yl)methyl]imidazo[4,5-b]pyridin-2-one;                     |
| 572  | 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-[(1-methylpyrazol-4-yl)methyl]imidazo[4,5-b]pyridin-2-one;                      |
| 573  | 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-[(3-methyl-1,2,4-oxadiazol-5-yl)methyl]imidazo[4,5-b]pyridin-2-one;             |
| 574  | 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-[(1-methyltriazol-4-yl)methyl]imidazo[4,5-b]pyridin-2-one;                      |
| 575  | 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-[(5-methyl-1,3,4-oxadiazol-2-yl)methyl]imidazo[4,5-b]pyridin-2-one;             |
| 576  | 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-(thiadiazol-4-ylmethyl)imidazo[4,5-b]pyridin-2-one;                             |
| 577  | N-(2-Fluoroethyl)-N-methyl-2-[3-methyl-2-oxo-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-1-yl]acetamide;         |
| 578  | 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-6-[5-(trifluoromethyl)-2-thienyl]-3H-imidazo[4,5-b]pyridin-2-one;                 |
| 579  | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(2,4-difluoro-3-methyl-phenyl)-3H-imidazo[4,5-b]pyridin-2-one;                          |
| 580  | 1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]-6-(m-tolyl)-3H-imidazo[4,5-b]pyridin-2-one;                                   |
| 581  | 1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-(m-tolyl)imidazo[4,5-b]pyridin-2-one;                              |
| 582  | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[3-(2-fluoroethoxy)-5-(trifluoromethyl)phenyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;    |
| 583  | N,N-Dimethyl-2-[3-methyl-6-(m-tolyl)-2-oxo-imidazo[4,5-b]pyridin-1-yl]acetamide;                                            |
| 584  | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[3-(difluoromethyl)-4-fluoro-phenyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;              |
| 585  | 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[2-(3-fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;      |
| 586  | 1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]-6-[3-(difluoromethyl)-4-fluoro-phenyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;  |
| 587  | 2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;               |
| 588  | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[3-(difluoromethoxy)-4-fluoro-phenyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;             |
| 589  | 6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[2-(3-fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;     |
| 590  | 1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]-6-[3-(difluoromethoxy)-4-fluoro-phenyl]-3-methyl-imidazo[4,5-b]pyridin-2-one; |

| Ex # | Compound Name                                                                                                              |
|------|----------------------------------------------------------------------------------------------------------------------------|
| 591  | 2-[6-[4-Chloro-3-(difluoromethoxy)phenyl]-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;               |
| 592  | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[4-chloro-3-(difluoromethoxy)phenyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;             |
| 593  | 6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-[2-(3-fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;     |
| 594  | 6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-[2-(3,3-difluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-imidazo[4,5-b]pyridin-2-one; |
| 595  | 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(2,4-difluoro-3-methyl-phenyl)-3-(fluoromethyl)imidazo[4,5-b]pyridin-2-one;            |
| 596  | 2-[3-(Fluoromethyl)-2-oxo-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;             |
| 597  | 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-3-(fluoromethyl)-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;   |
| 598  | 3-(Fluoromethyl)-1-(2-oxo-2-pyrrolidin-1-yl-ethyl)-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;           |
| 599  | 2-[6-(2,4-Difluoro-3-methyl-phenyl)-3-(fluoromethyl)-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;             |
| 600  | 6-(2,4-Difluoro-3-methyl-phenyl)-1-[2-(3-fluoroazetidin-1-yl)-2-oxo-ethyl]-3-(fluoromethyl)imidazo[4,5-b]pyridin-2-one;    |
| 601  | 1-(3,3-Dimethyl-2-oxo-butyl)-6-(4-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-one;                                           |
| 602  | 6-(3-Methoxyphenyl)-1-[2-oxo-2-(2-thienyl)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;                                           |
| 603  | 1-(3,3-Dimethyl-2-oxo-butyl)-6-(4-methoxy-3-methyl-phenyl)-3H-imidazo[4,5-b]pyridin-2-one;                                 |
| 604  | 1-Isobutyl-6-(4-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-one;                                                             |
| 605  | 6-(2-Ethoxyphenyl)-1-[(3-methoxyphenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;                                             |
| 606  | 6-(2-Ethoxyphenyl)-1-[(4-fluorophenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;                                              |
| 607  | N-Cyclopropyl-2-[6-(2-ethoxy-5-fluoro-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;                               |
| 608  | 2-[[6-(4-Methoxy-3-methyl-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;                                 |
| 609  | 1-(3,3-Dimethyl-2-oxo-butyl)-6-(3-fluoro-4-methoxy-phenyl)-3H-imidazo[4,5-b]pyridin-2-one;                                 |
| 610  | 2-[6-(3,5-Difluorophenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-(2-methoxyethyl)acetamide;                                |

| Ex # | Compound Name                                                                                     |
|------|---------------------------------------------------------------------------------------------------|
| 611  | 1-(3,3-Dimethyl-2-oxo-butyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one; and    |
| 612  | 2-[6-(3-Chloro-4-fluoro-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-(2-methoxyethyl)acetamide; |

and pharmaceutically acceptable salts, N-oxides, or solvates thereof.

A further embodiment of the current invention is a compound selected from the group consisting of:

1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;

N,N-Dimethyl-2-[3-methyl-2-oxo-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-1-yl]acetamide;

1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[5-(trifluoromethyl)-2-thienyl]-3H-imidazo[4,5-b]pyridin-2-one;

1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(5-chloro-4-methyl-2-thienyl)-3H-imidazo[4,5-b]pyridin-2-one;

1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-6-(4-fluoro-3-methyl-phenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;

1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(2,4-difluoro-3-methyl-phenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;

1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(4-fluoro-3-methyl-phenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;

1-(2-(3,3-Difluoroazetidin-1-yl)-2-oxoethyl)-6-(4-fluoro-3-methylphenyl)-3-methyl-1H-imidazo[4,5-b]pyridin-2(3H)-one;

1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]-6-(2,4-difluoro-3-methyl-phenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one; and

2-[6-(4-Fuoro-3-methyl-phenyl)-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

and pharmaceutically acceptable salts, solvates, or N-oxides thereof.

A further embodiment of the current invention is a compound selected from the group consisting of:

- 6-(5-(Difluoromethyl)-2-fluorophenyl)-3-methyl-1-(pyridazin-3-ylmethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one;
- 5 6-(5-(Difluoromethyl)-2-fluorophenyl)-3-methyl-1-(pyridin-3-ylmethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one;
- N-(3-Chloropropyl)-2-[3-methyl-2-oxo-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-1-yl]acetamide;
- 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
- 10 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-(fluoromethyl)-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;
- 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-(2-fluoroethyl)-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;
- 15 1-[2-[3-(2-Fluoroethyl)azetidin-1-yl]-2-oxo-ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(6-Fluoro-2-pyridyl)-1-(2-oxobutyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[4-(2-fluoroethoxy)-3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 20 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[3-(2-fluoroethoxy)-5-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 1-[2-(3-<sup>18</sup>F-Fluoranylazetidin-1-yl)-2-oxo-ethyl]-6-(4-fluoro-3-methyl-phenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one
- 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 25 6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-[4-Chloro-3-(difluoromethoxy)phenyl]-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 30 6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-[(5-fluoro-3-pyridyl)methyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;

- 6-(3,4-Difluorophenyl)-3-methyl-1-(thiadiazol-4-ylmethyl)imidazo[4,5-b]pyridin-2-one;  
 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-fluoro-3-pyridyl)methyl]-3-methyl-  
 imidazo[4,5-b]pyridin-2-one;  
 6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(5-fluoro-3-pyridyl)methyl]-3-methyl-  
 5 imidazo[4,5-b]pyridin-2-one;  
 3-Methyl-1-(thiadiazol-4-ylmethyl)-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-  
 2-one;  
 6-(3,4-Difluorophenyl)-3-methyl-1-[(1-methyltriazol-4-yl)methyl]imidazo[4,5-b]pyridin-  
 2-one;  
 10 6-(3,4-Difluorophenyl)-3-methyl-1-[(1-methylpyrazol-4-yl)methyl]imidazo[4,5-  
 b]pyridin-2-one;  
 3-Methyl-1-[(1-methylpyrazol-4-yl)methyl]-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-  
 b]pyridin-2-one;  
 3-Methyl-1-[(1-methyltriazol-4-yl)methyl]-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-  
 15 b]pyridin-2-one;  
 3-Methyl-6-(5-methyl-2-thienyl)-1-[(1-methyltriazol-4-yl)methyl]imidazo[4,5-b]pyridin-  
 2-one;  
 3-Methyl-1-[(5-methyl-1,3,4-oxadiazol-2-yl)methyl]-6-(5-methyl-2-thienyl)imidazo[4,5-  
 b]pyridin-2-one;  
 20 3-Methyl-1-[(1-methylpyrazol-4-yl)methyl]-6-(5-methyl-2-thienyl)imidazo[4,5-  
 b]pyridin-2-one;  
 3-Methyl-6-(5-methyl-2-thienyl)-1-(thiadiazol-4-ylmethyl)imidazo[4,5-b]pyridin-2-one;  
 3-Methyl-1-[(3-methyl-1,2,4-oxadiazol-5-yl)methyl]-6-(5-methyl-2-thienyl)imidazo[4,5-  
 b]pyridin-2-one;  
 25 3-Methyl-1-[(5-methylisoxazol-3-yl)methyl]-6-(5-methyl-2-thienyl)imidazo[4,5-  
 b]pyridin-2-one;  
 6-[5-(Difluoromethyl)-2-thienyl]-3-methyl-1-[(1-methyltriazol-4-yl)methyl]imidazo[4,5-  
 b]pyridin-2-one;  
 6-[5-(Difluoromethyl)-2-thienyl]-3-methyl-1-[(5-methyl-1,3,4-oxadiazol-2-  
 30 yl)methyl]imidazo[4,5-b]pyridin-2-one;

- 6-[5-(Difluoromethyl)-2-thienyl]-3-methyl-1-[(1-methylpyrazol-4-yl)methyl]imidazo[4,5-b]pyridin-2-one;
- 6-[5-(Difluoromethyl)-2-thienyl]-3-methyl-1-(thiadiazol-4-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 5 6-[5-(Difluoromethyl)-2-thienyl]-3-methyl-1-[(3-methyl-1,2,4-oxadiazol-5-yl)methyl]imidazo[4,5-b]pyridin-2-one;
- 6-[5-(Difluoromethyl)-2-thienyl]-3-methyl-1-[(5-methylisoxazol-3-yl)methyl]imidazo[4,5-b]pyridin-2-one;
- 3-Methyl-1-[(1-methylpyrazol-4-yl)methyl]-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;
- 10 3-Methyl-1-[(1-methyltriazol-4-yl)methyl]-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;
- 3-Methyl-1-[(5-methyl-1,3,4-oxadiazol-2-yl)methyl]-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;
- 15 3-Methyl-1-(thiadiazol-4-ylmethyl)-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;
- 3-Methyl-1-[(3-methyl-1,2,4-oxadiazol-5-yl)methyl]-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;
- 3-Methyl-1-[(5-methylisoxazol-3-yl)methyl]-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;
- 20 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-[(5-methylisoxazol-3-yl)methyl]imidazo[4,5-b]pyridin-2-one;
- 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-[(1-methylpyrazol-4-yl)methyl]imidazo[4,5-b]pyridin-2-one;
- 25 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-[(3-methyl-1,2,4-oxadiazol-5-yl)methyl]imidazo[4,5-b]pyridin-2-one;
- 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-[(1-methyltriazol-4-yl)methyl]imidazo[4,5-b]pyridin-2-one;
- 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-[(5-methyl-1,3,4-oxadiazol-2-yl)methyl]imidazo[4,5-b]pyridin-2-one;
- 30

- 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-(thiadiazol-4-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- N-(2-Fluoroethyl)-N-methyl-2-[3-methyl-2-oxo-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-1-yl]acetamide;
- 5 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-6-[5-(trifluoromethyl)-2-thienyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(2,4-difluoro-3-methyl-phenyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]-6-(m-tolyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 10 one;
- 1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-(m-tolyl)imidazo[4,5-b]pyridin-2-one;
- 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[3-(2-fluoroethoxy)-5-(trifluoromethyl)phenyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 15 N,N-Dimethyl-2-[3-methyl-6-(m-tolyl)-2-oxo-imidazo[4,5-b]pyridin-1-yl]acetamide;
- 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[3-(difluoromethyl)-4-fluoro-phenyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[2-(3-fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 20 1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]-6-[3-(difluoromethyl)-4-fluoro-phenyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
- 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[3-(difluoromethoxy)-4-fluoro-phenyl]-3-methyl-
- 25 imidazo[4,5-b]pyridin-2-one;
- 6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[2-(3-fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]-6-[3-(difluoromethoxy)-4-fluoro-phenyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 30 2-[6-[4-Chloro-3-(difluoromethoxy)phenyl]-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

- 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[4-chloro-3-(difluoromethoxy)phenyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-[2-(3-fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 5 6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-[2-(3,3-difluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(2,4-difluoro-3-methyl-phenyl)-3-(fluoromethyl)imidazo[4,5-b]pyridin-2-one;
- 2-[3-(Fluoromethyl)-2-oxo-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-1-yl]-
- 10 N,N-dimethyl-acetamide;
- 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-3-(fluoromethyl)-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;
- 3-(Fluoromethyl)-1-(2-oxo-2-pyrrolidin-1-yl-ethyl)-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;
- 15 2-[6-(2,4-Difluoro-3-methyl-phenyl)-3-(fluoromethyl)-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
- 6-(2,4-Difluoro-3-methyl-phenyl)-1-[2-(3-fluoroazetidin-1-yl)-2-oxo-ethyl]-3-(fluoromethyl)imidazo[4,5-b]pyridin-2-one;
- 1-(3,3-Dimethyl-2-oxo-butyl)-6-(4-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 20 6-(3-Methoxyphenyl)-1-[2-oxo-2-(2-thienyl)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 1-(3,3-Dimethyl-2-oxo-butyl)-6-(4-methoxy-3-methyl-phenyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 1-Isobutyl-6-(4-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(2-Ethoxyphenyl)-1-[(3-methoxyphenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 25 6-(2-Ethoxyphenyl)-1-[(4-fluorophenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- N-Cyclopropyl-2-[6-(2-ethoxy-5-fluoro-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;
- 2-[[6-(4-Methoxy-3-methyl-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;
- 30 1-(3,3-Dimethyl-2-oxo-butyl)-6-(3-fluoro-4-methoxy-phenyl)-3H-imidazo[4,5-b]pyridin-2-one;

2-[6-(3,5-Difluorophenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-(2-methoxyethyl)acetamide;

1-(3,3-Dimethyl-2-oxo-butyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one; and

5 2-[6-(3-Chloro-4-fluoro-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-(2-methoxyethyl)acetamide;

and pharmaceutically acceptable salts, solvates, or N-oxides thereof.

10 A further embodiment of the current invention is a compound selected from the group consisting of:

and pharmaceutically acceptable salts, solvates, or N-oxides thereof.

1-(2-Oxo-2-(pyrrolidin-1-yl)ethyl)-6-(thiazol-5-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one;

1-(2-(3-hydroxy-3-methylazetidin-1-yl)-2-oxoethyl)-6-(5-methylpyridin-3-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one;

15 1-(2-(Azetidin-1-yl)-2-oxoethyl)-6-(6-fluoropyridin-3-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one;

1-(2-(2-Oxo-6-(3-(trifluoromethyl)phenyl)-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetyl)azetidine-3-carbonitrile;

1-Benzyl-6-(4-fluoro-3-(trifluoromethyl)phenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one;

20 1-(2-(3-Methylazetidin-1-yl)-2-oxoethyl)-6-(3-(trifluoromethyl)phenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one;

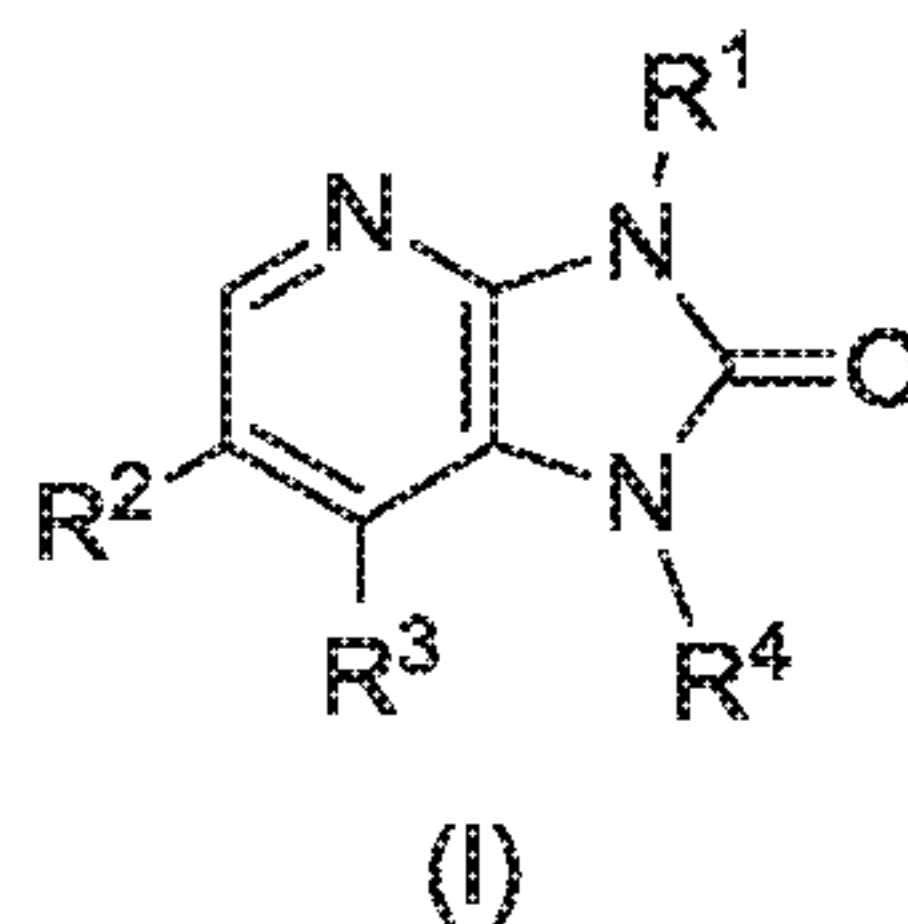
1-(2-(3-(Methoxymethyl)azetidin-1-yl)-2-oxoethyl)-6-(3-(trifluoromethyl)phenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one; and

25 6-(2-Fluoro-3-methylphenyl)-1-(2-oxo-2-(3-(trifluoromethyl)azetidin-1-yl)ethyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one; and

pharmaceutically acceptable salts, solvates, or N-oxides thereof.

An additional embodiment of the invention is a pharmaceutical composition comprising:

30 (A) an effective amount of at least one compound selected from compounds of Formula (I):



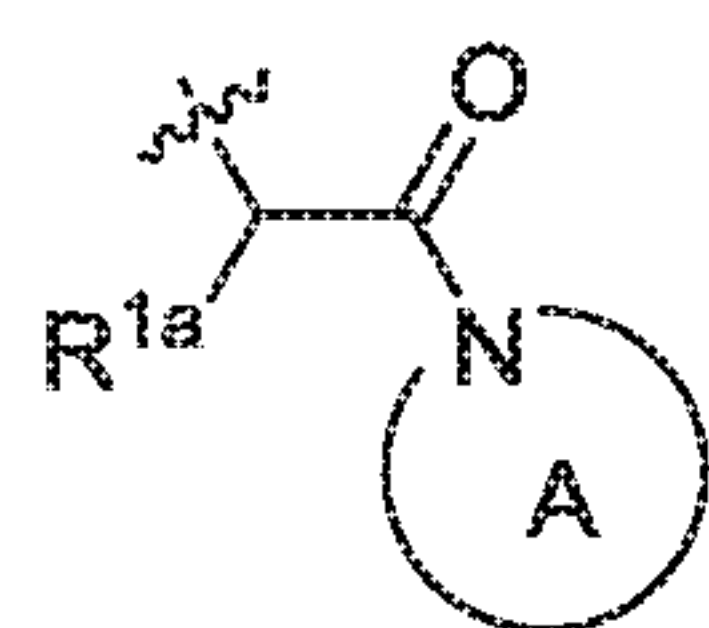
wherein

$R^1$  is H;  $\text{CH}_2\text{F}$ ; or  $\text{CH}_3$ ;

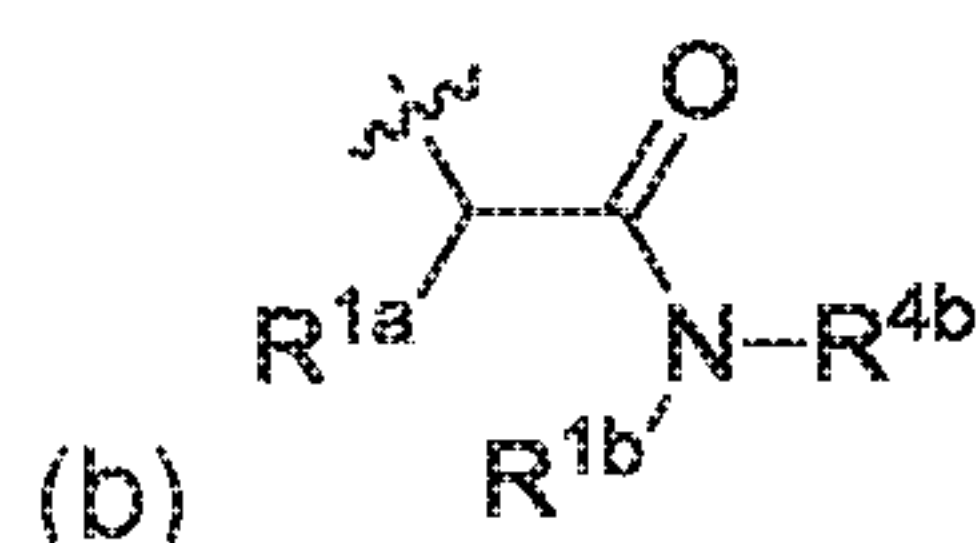
$R^2$  is selected from the group consisting of: phenyl; phenyl substituted with one, two, or three members each independently selected from the group consisting of: halo,  $\text{C}_{1-6}$ alkyl,  $\text{C}_{1-6}$ haloalkyl, CN,  $\text{OC}_{1-6}$ alkyl,  $\text{OC}_{1-6}$ haloalkyl,  $\text{N}(\text{CH}_3)_2$ , and cyclopropyl; pyridinyl; pyridinyl substituted with F,  $\text{C}_{1-4}$ alkyl, or  $\text{C}_{1-4}$ haloalkyl; thiazolyl; thiazolyl substituted with  $\text{C}_{1-6}$ alkyl or  $\text{C}_{1-6}$ haloalkyl; thienyl; and thienyl substituted with one or two members each independently selected from the group consisting of: halo,  $\text{C}_{1-6}$ alkyl,  $\text{C}_{1-6}$ haloalkyl,  $\text{CH}_2\text{OH}$ ,  $\text{CH}_2\text{OCH}_3$ , and cyclopropyl;

$R^3$  is H;

$R^4$  is selected from the group consisting of:



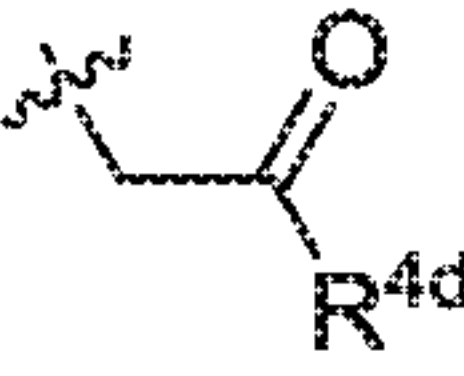
(a) wherein ring A is a 4-6 membered heterocycle optionally containing an additional oxygen heteroatom selected from the group consisting of: azetidiny; azetidiny substituted with one or two members independently selected from the group consisting of: F, OH,  $\text{C}_{1-4}$ alkyl,  $\text{C}_{1-4}$ haloalkyl,  $\text{CH}_2\text{OCH}_3$ , CN, and  $\text{OCH}_3$ ; pyrrolidiny; pyrrolidiny substituted two F members; morpholiny; piperidiny; piperaziny substituted with  $\text{C}_{1-6}$ alkyl; and (2,6-diazaspiro[3.3]heptan-6-yl);



(b) , wherein  $R^{4b}$  is selected from the group consisting of: H;  $\text{C}_{1-6}$ alkyl;  $\text{CH}_2\text{CH}_2\text{OCH}_3$ ;  $\text{C}_{3-6}$ cycloalkyl;  $\text{C}_{3-6}$ cycloalkyl substituted with two or

three members independently selected from the group consisting of F or CH<sub>3</sub>; oxetanyl; oxetanyl substituted with CH<sub>3</sub>; and pyridinyl;

- (c)  R<sup>4c</sup> wherein R<sup>4c</sup> is selected from the group consisting of: cyclopropyl; cyclopropyl substituted with one or two F members; CH(OH)cyclopropyl; azetidiny; CH<sub>2</sub>-azetidiny; CH<sub>2</sub>-azetidiny substituted with one or two members independently selected from: F, OH, OCH<sub>3</sub>, and CF<sub>3</sub>; oxetanyl; oxetanyl substituted with F or CH<sub>3</sub>; tetrahydrofuranyl; tetrahydropyranyl; CH<sub>2</sub>pyrrolidinyl; CH<sub>2</sub>pyrrolidinyl substituted with CH<sub>3</sub>, OH, or OCH<sub>3</sub>; CH<sub>2</sub>piperidinyl; CH<sub>2</sub>piperidinyl substituted with OH, or F; morpholinyl; pyrazolyl substituted with one or two CH<sub>3</sub> members; triazolyl substituted with CH<sub>3</sub>; tetrazolyl; isoxazolyl substituted with one or two CH<sub>3</sub> members; oxadiazolyl substituted with CH<sub>3</sub>, or CH<sub>2</sub>OCH<sub>3</sub>; thiadiazolyl; pyridinyl; pyridinyl substituted with one or two members independently selected from the group consisting of: Cl, F, CH<sub>3</sub>, OCH<sub>3</sub>, and CF<sub>3</sub>; (2-oxo-1H-pyridin-3-yl); 6-oxo-1H-pyridin-3-yl; pyrimidinyl; pyrimidinyl substituted with F or CH<sub>3</sub>; pyrazinyl; pyridazinyl; pyridazinyl substituted with OCH<sub>3</sub>; phenyl; phenyl substituted with one or two members independently selected from the group consisting of: halo, CN, OCH<sub>3</sub>, C<sub>1-6</sub>alkyl, and CF<sub>3</sub>;

- (d)  R<sup>4d</sup> wherein R<sup>4d</sup> is selected from the group consisting of: OH, C<sub>1-6</sub>alkyl, O-C<sub>1-6</sub>alkyl, C<sub>3-6</sub>cycloalkyl, thienyl, and thiazolyl; and

- (e) C<sub>2-6</sub>alkyl substituted with one or two members independently selected from OH, OC<sub>1-6</sub>alkyl, or cyclopropyl; CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>1-6</sub>alkyl); CH<sub>2</sub>CH<sub>2</sub>NH(CH<sub>2</sub>CH<sub>2</sub>OH); CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>3-6</sub>cycloalkyl); and difluoro(3-pyridyl)methyl; and

R<sup>1a</sup> and R<sup>1b</sup> are each independently H or CH<sub>3</sub>;

and pharmaceutically acceptable salts, stereoisomers, isotopic variants, N-oxides or solvates of compounds of Formula (I);

and (B) at least one pharmaceutically acceptable excipient.

An additional embodiment of the invention is a pharmaceutical composition comprising an effective amount of at least one compound of Formula (IA), as well as pharmaceutically acceptable salts, N-oxides or solvates of compounds of Formula (IA),

pharmaceutically acceptable prodrugs of compounds of Formula (IA), and pharmaceutically active metabolites of Formula (IA); and at least one pharmaceutically acceptable excipient.

An additional embodiment of the invention is a pharmaceutical composition comprising an effective amount of at least one compound of Formula (IB), as well as pharmaceutically acceptable salts, N-oxides or solvates of compounds of Formula (IB), pharmaceutically acceptable prodrugs of compounds of Formula (IB), and pharmaceutically active metabolites of Formula (IB); and at least one pharmaceutically acceptable excipient.

An additional embodiment of the invention is a pharmaceutical composition comprising an effective amount of at least one compound of Formula (IC), as well as pharmaceutically acceptable salts, N-oxides or solvates of compounds of Formula (IC), pharmaceutically acceptable prodrugs of compounds of Formula (IC), and pharmaceutically active metabolites of Formula (IC); and at least one pharmaceutically acceptable excipient.

An additional embodiment of the invention is a pharmaceutical composition comprising an effective amount of at least one compound of Formula (ID), as well as pharmaceutically acceptable salts, N-oxides or solvates of compounds of Formula (ID), pharmaceutically acceptable prodrugs of compounds of Formula (ID), and pharmaceutically active metabolites of Formula (ID); and at least one pharmaceutically acceptable excipient.

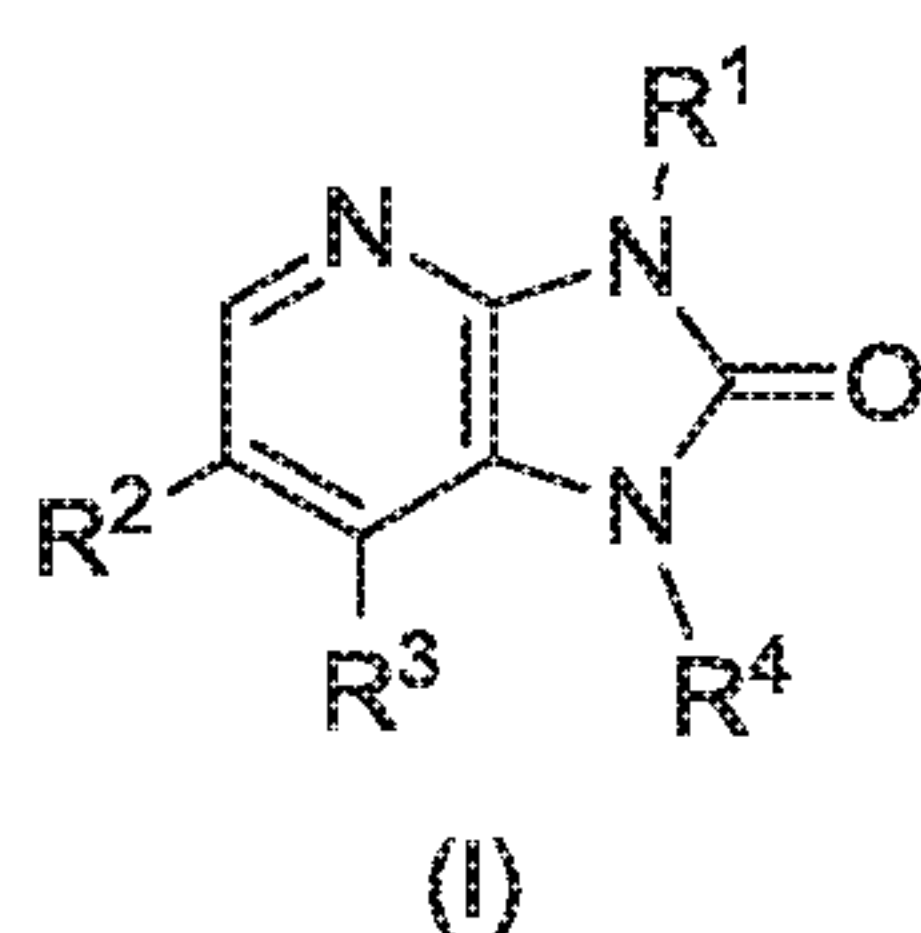
An additional embodiment of the invention is a pharmaceutical composition comprising an effective amount of at least one compound in Table 1, as well as pharmaceutically acceptable salts, N-oxides or solvates of compounds of Table 1, pharmaceutically acceptable prodrugs of compounds of Table 1, and pharmaceutically active metabolites of Table 1; and at least one pharmaceutically acceptable excipient.

Also within the scope of the invention are enantiomers and diastereomers of the compounds of Formula (I) (as well as Formulas (IA), (IB), (IC), and (ID)). Also within the scope of the invention are the pharmaceutically acceptable salts, N-oxides or solvates of the compounds of Formula (I) (as well as Formulas (IA), (IB), (IC), and (ID)). Also  
5 within the scope of the invention are the pharmaceutically acceptable prodrugs of

compounds of Formula (I) (as well as Formulas (IA), (IB), (IC), and (ID)), and pharmaceutically active metabolites of the compounds of Formula (I) (as well as Formulas (IA), (IB), (IC), and (ID)).

Also within the scope of the invention are isotopic variations of compounds of Formula (I) (as well as Formulas (IA), (IB), (IC), and (ID)), such as, e.g., deuterated compounds of Formula (I). Also within the scope of the invention are the pharmaceutically acceptable salts, N-oxides or solvates of the isotopic variations of the compounds of Formula (I) (as well as Formulas (IA), (IB), (IC), and (ID)). Also within the scope of the invention are the pharmaceutically acceptable prodrugs of the isotopic variations of the compounds of Formula (I) (as well as Formulas (IA), (IB), (IC), and (ID)), and pharmaceutically active metabolites of the isotopic variations of the compounds of Formula (I) (as well as Formulas (IA), (IB), (IC), and (ID)).

An additional embodiment of the invention is a method of treating a subject suffering from or diagnosed with a disease, disorder, or medical condition mediated by NR2B receptor activity, comprising administering to a subject in need of such treatment an effective amount of at least one compound selected from compounds of Formula (I):



wherein

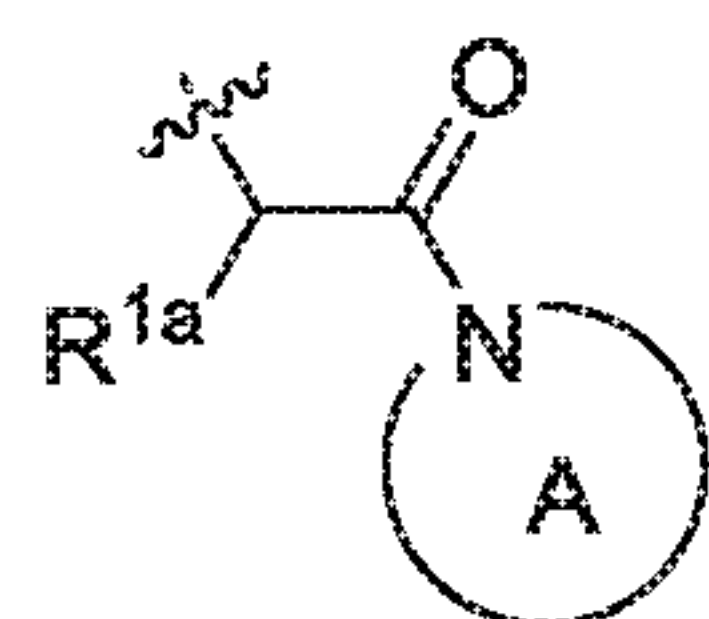
R<sup>1</sup> is H; CH<sub>2</sub>F; or CH<sub>3</sub>;

R<sup>2</sup> is selected from the group consisting of: phenyl; phenyl substituted with one, two, or three members each independently selected from the group consisting of: halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>haloalkyl, CN, OC<sub>1-6</sub>alkyl, OC<sub>1-6</sub>haloalkyl, N(CH<sub>3</sub>)<sub>2</sub>, and cyclopropyl; pyridinyl; pyridinyl substituted with F, C<sub>1-4</sub>alkyl, or C<sub>1-4</sub>haloalkyl; thiazolyl; thiazolyl substituted with C<sub>1-6</sub>alkyl or C<sub>1-6</sub>haloalkyl; thienyl; and thienyl substituted with one or two members each independently selected from the

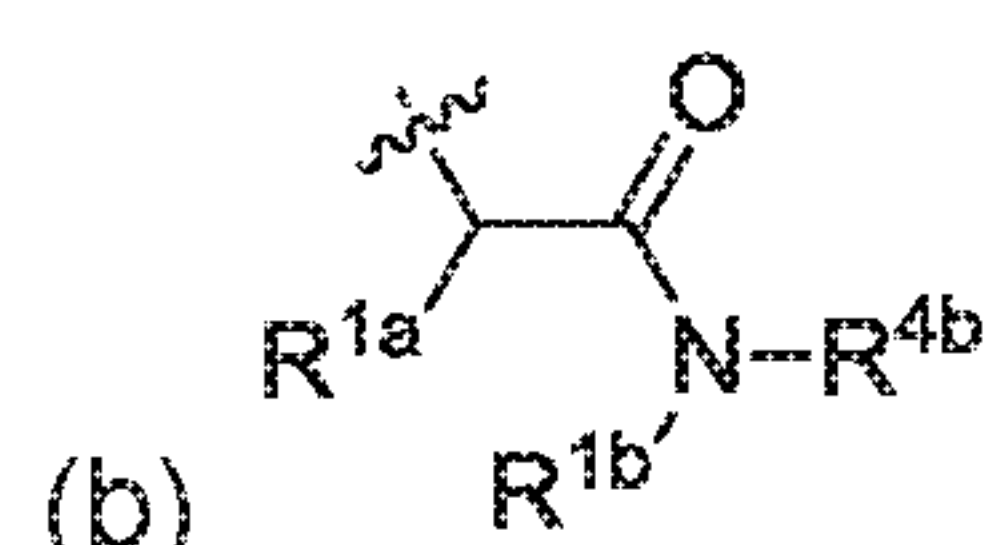
group consisting of: halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>haloalkyl, CH<sub>2</sub>OH, CH<sub>2</sub>OCH<sub>3</sub>, and cyclopropyl;

R<sup>3</sup> is H;

R<sup>4</sup> is selected from the group consisting of:



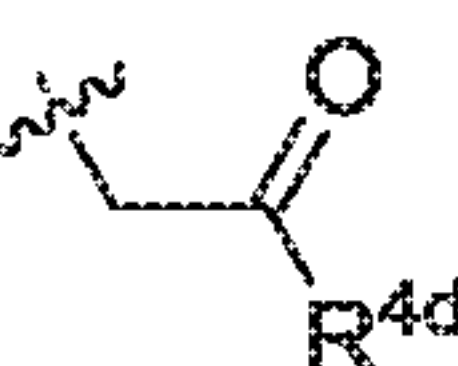
- (a) wherein ring A is a 4-6 membered heterocycle optionally containing an additional oxygen heteroatom selected from the group consisting of: azetidiny; azetidiny substituted with one or two members independently selected from the group consisting of: F, OH, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>haloalkyl, CH<sub>2</sub>OCH<sub>3</sub>, CN, and OCH<sub>3</sub>; pyrrolidiny; pyrrolidiny substituted two F members; morpholiny; piperidiny; piperaziny substituted with C<sub>1-6</sub>alkyl; and (2,6-diazaspiro[3.3]heptan-6-yl);



- (b) , wherein R<sup>4b</sup> is selected from the group consisting of: H; C<sub>1-6</sub>alkyl; CH<sub>2</sub>CH<sub>2</sub>OCH<sub>3</sub>; C<sub>3-6</sub>cycloalkyl; C<sub>3-6</sub>cycloalkyl substituted substituted with two or three members independently selected from the group consisting of F or CH<sub>3</sub>; oxetany; oxetany substituted with CH<sub>3</sub>; and pyridiny;

- (c) wherein R<sup>4c</sup> is selected from the group consisting of: cyclopropyl; cyclopropyl substituted with one or two F members; CH(OH)cyclopropyl; azetidiny; CH<sub>2</sub>-azetidiny; CH<sub>2</sub>-azetidiny substituted with one or two members independently selected from: F, OH, OCH<sub>3</sub>, and CF<sub>3</sub>; oxetany; oxetany substituted with F or CH<sub>3</sub>; tetrahydrofurany; tetrahydropyrany; CH<sub>2</sub>pyrrolidiny; CH<sub>2</sub>pyrrolidiny substituted with CH<sub>3</sub>, OH, or OCH<sub>3</sub>; CH<sub>2</sub>piperidiny; CH<sub>2</sub>piperidiny substituted with OH, or F; morpholiny; pyrazoly substituted with one or two CH<sub>3</sub> members; triazoly substituted with CH<sub>3</sub>; tetrazoly; isoxazoly substituted with one or two CH<sub>3</sub> members; oxadiazoly substituted with CH<sub>3</sub>, or CH<sub>2</sub>OCH<sub>3</sub>; thiadiazoly; pyridiny; pyridiny substituted with one or two members independently selected from the group consisting of: Cl, F, CH<sub>3</sub>, OCH<sub>3</sub>, and CF<sub>3</sub>; (2-oxo-1H-pyridin-3-yl); 6-oxo-1H-pyridin-3-yl; pyrimidiny; pyrimidiny

substituted with F or CH<sub>3</sub>; pyrazinyl; pyridazinyl; pyridazinyl substituted with OCH<sub>3</sub>; phenyl; phenyl substituted with one or two members independently selected from the group consisting of: halo, CN, OCH<sub>3</sub>, C<sub>1-6</sub>alkyl, and CF<sub>3</sub>;

(d)  wherein R<sup>4d</sup> is selected from the group consisting of: OH, C<sub>1-6</sub>alkyl, O-

C<sub>1-6</sub>alkyl, C<sub>3-6</sub>cycloalkyl, thienyl, and thiazolyl; and

(e) C<sub>2-6</sub>alkyl substituted with one or two members independently selected from OH, OC<sub>1-6</sub>alkyl, or cyclopropyl; CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>1-6</sub>alkyl); CH<sub>2</sub>CH<sub>2</sub>NH(CH<sub>2</sub>CH<sub>2</sub>OH); CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>3-6</sub>cycloalkyl); and difluoro(3-pyridyl)methyl; and

R<sup>1a</sup> and R<sup>1b</sup> are each independently H or CH<sub>3</sub>;

and pharmaceutically acceptable salts, stereoisomers, isotopic variants, N-oxides, or solvates thereof, to a subject in need thereof.

An additional embodiment of the invention is a method of treating a subject suffering from or diagnosed with a disease, disorder, or medical condition mediated by NR2B receptor activity, comprising administering to a subject in need of such treatment an effective amount of at least one compound selected from compounds of Formula (I) (as well as Formulas (IA), (IB), (IC), and (ID)), enantiomers and diastereomers of the compounds of Formula (I), isotopic variations of the compounds of Formula (I), and pharmaceutically acceptable salts of all of the foregoing.

In preferred embodiments of the inventive method, the disease, disorder, or medical condition is selected from: neurologic and psychiatric disorders including, but not limited to: (1) mood disorders and mood affective disorders; (2) neurotic, stress-related and somatoform disorders including anxiety disorders; (3) disorders of psychological development; (4) behavioral syndromes associated with physiological disturbances and physical factors; (5) extrapyramidal and movement disorders; (6) episodic and paroxysmal disorders, epilepsy; (7) pain; (8) forms of neurodegeneration; (9) cerebrovascular diseases, acute and chronic; and any sequelae of cerebrovascular diseases.

Examples of mood disorders and mood affective disorders that can be treated according to the present invention include, but are not limited to, bipolar disorder I depressed, hypomanic, manic and mixed form; bipolar disorder II; depressive disorders,

such as single depressive episode or recurrent major depressive disorder, minor depressive disorder, treatment-resistant depression, depressive disorder with postpartum onset, depressive disorders with psychotic symptoms; persistent mood disorders, such as cyclothymia, dysthymia, euthymia; and premenstrual dysphoric disorder. In specific embodiments, the mood disorders and mood affective disorders that can be treated according to the present invention are major depressive disorder, treatment-resistant depression and bipolar disorder.

Examples of disorders belonging to the neurotic, stress-related and somatoform disorders that can be treated according to the present invention include, but are not limited to, anxiety disorders, general anxiety disorder, panic disorder with or without agoraphobia, specific phobia, social anxiety disorder, chronic anxiety disorders; obsessive compulsive disorder; reaction to severe stress and adjustment disorders, such as post-traumatic stress disorder (PTSD); other neurotic disorders such as depersonalisation-derealisation syndrome.

Examples of disorders of psychological development that can be treated according to the present invention include, but are not limited to pervasive developmental disorders, including but not limited to Asperger's syndrome and Rett's syndrome, autistic disorders, childhood autism and overactive disorder associated with mental retardation and stereotyped movements, specific developmental disorder of motor function, specific developmental disorders of scholastic skills.

Examples of behavioral syndromes associated with physiological disturbances and physical factors according to the present invention include, but are not limited to mental and behavioural disorders associated with childbirth, including but not limited to postnatal (postpartum) and prenatal depression; eating disorders, including but not limited to anorexia nervosa, bulimia nervosa, pica and binge eating disorder.

Examples of extrapyramidal and movement disorders that can be treated according to the present invention include, but are not limited to Parkinson's disease; second Parkinsonism, such as postencephalitic Parkinsonism; Parkinsonism comprised in other disorders; Lewis body disease; degenerative diseases of the basal ganglia; other extrapyramidal and movement disorders including but not limited to tremor, essential tremor and drug-induced tremor, myoclonus, chorea and drug-induced chorea,

drug-induced tics and tics of organic origin, drug-induced acute dystonia, drug-induced tardive dyskinesia, L-dopa-induced dyskinesia; neuroleptic-induced movement disorders including but not limited to neuroleptic malignant syndrome (NMS), neuroleptic induced parkinsonism, neuroleptic-induced early onset or acute dyskinesia, neuroleptic-induced acute dystonia, neuroleptic-induced acute akathisia, neuroleptic-induced tardive dyskinesia, neuroleptic-induced tremor; restless leg syndrome, Stiff-man syndrome.

Further examples of movement disorders with malfunction and/or degeneration of basal ganglia that can be treated according to the present invention include, but are not limited to dystonia including but not limited to focal dystonia, multiple-focal or segmental dystonia, torsion dystonia, hemispheric, generalised and tardive dystonia (induced by psychopharmacological drugs). Focal dystonia include cervical dystonia (torticollis), blepharospasm (cramp of the eyelid), appendicular dystonia (cramp in the extremities, like the writer's cramp), oromandibular dystonia and spasmodic dysphonia (cramp of the vocal cord);

Examples for episodic and paroxysmal disorders that can be treated according to the present invention include, but are not limited to epilepsy, including localization-related (focal)(partial) idiopathic epilepsy and epileptic syndromes with seizures of localized onset, localization-related (focal)(partial) symptomatic epilepsy and epileptic syndromes with simple partial seizures, localization-related (focal)(partial) symptomatic epilepsy and epileptic syndromes with complex partial seizures, generalized idiopathic epilepsy and epileptic syndromes including but not limited to myoclonic epilepsy in infancy, neonatal convulsions (familial), childhood absence epilepsy (pyknolepsy), epilepsy with grand mal seizures on awakening, absence epilepsy, myoclonic epilepsy (impulsive petit mal) and nonspecific atonic, clonic, myoclonic, tonic, tonic-clonic epileptic seizures.

Further examples of epilepsy that can be treated according to the present invention include, but are not limited to epilepsy with myoclonic absences, myoclonic-astatic seizures, infantile spasms, Lennox-Gastaut syndrome, Salaam attacks, symptomatic early myoclonic encephalopathy, West's syndrome, petit and grand mal seizures; status epilepticus.

Examples of pain include, but are not limited to pain disorders related to psychological factors, such as persistent somatoform disorders; acute, chronic and chronic intractable pain, headache; acute and chronic pain related to physiological processes and physical disorders including but not limited to back pain, tooth pain, abdominal pain, low back pain, pain in joints; acute and chronic pain that is related to diseases of the musculoskeletal system and connective tissue including, but not limited to rheumatism, myalgia, neuralgia and fibromyalgia; acute and chronic pain that is related to nerve, nerve root and plexus disorders, such as trigeminal pain, postzoster neuralgia, phantom limb syndrome with pain, carpal tunnel syndrome, lesion of sciatic nerve, diabetic mononeuropathy; acute and chronic pain that is related to polyneuropathies and other disorders of the peripheral nervous system, such as hereditary and idiopathic neuropathy, inflammatory polyneuropathy, polyneuropathy induced by drugs, alcohol or toxic agents, polyneuropathy in neoplastic disease, diabetic polyneuropathy.

Examples of diseases that include forms of neurodegeneration include, but are not limited to, acute neurodegeneration, such as intracranial brain injuries, such as stroke, diffuse and local brain injuries, epidural, subdural and subarachnoid haemorrhage, and chronic neurodegeneration, such as Alzheimer's disease, Huntington's disease, multiple sclerosis and ALS.

Examples of cerebrovascular diseases include, but are not limited to, subarachnoid haemorrhage, intracerebral haemorrhage and other nontraumatic intracranial haemorrhage, cerebral infarction, stroke, occlusion and stenosis or precerebral and cerebral arteries, not resulting in cerebral infarction, dissection of cerebral arteries, cerebral aneurysm, cerebral atherosclerosis, progressive vascular leukoencephalopathy, hypertensive encephalopathy, nonpyogenic thrombosis of intracranial venous system, cerebral arteritis, cerebral amyloid angiopathy and sequelae of cerebrovascular diseases.

In some embodiments, administration of a compound of the invention, or pharmaceutically acceptable salt thereof, is effective in preventing the disease; for example, preventing a disease, condition or disorder in an individual who may be

predisposed to the disease, condition or disorder but does not yet experience or display the pathology or symptomatology of the disease.

Additional embodiments, features, and advantages of the invention will be apparent from the following detailed description and through practice of the invention.

5 The invention may be more fully appreciated by reference to the following description, including the following glossary of terms and the concluding examples. For the sake of brevity, the disclosures of the publications, including patents, cited in this specification are herein incorporated by reference.

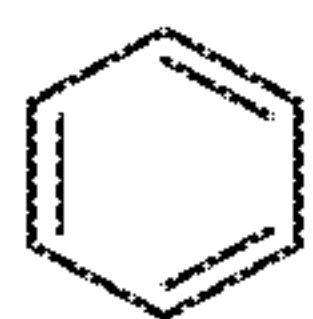
10 As used herein, the terms "including", "containing" and "comprising" are used herein in their open, non-limiting sense.

The term "alkyl" refers to a straight- or branched-chain alkyl group having from 1 to 12 carbon atoms in the chain. Examples of alkyl groups include methyl (Me, which also may be structurally depicted by the symbol, "/"), ethyl (Et), n-propyl, isopropyl, butyl, isobutyl, sec-butyl, tert-butyl (tBu), pentyl, isopentyl, tert-pentyl, hexyl, isohexyl, and groups that in light of the ordinary skill in the art and the teachings provided herein would be considered equivalent to any one of the foregoing examples. The term C<sub>1-4</sub>alkyl as used here refers to a straight- or branched-chain alkyl group having from 1 to 4 carbon atoms in the chain. The term C<sub>1-6</sub>alkyl as used here refers to a straight- or branched-chain alkyl group having from 1 to 6 carbon atoms in the chain.

20 The term "alkoxy" includes a straight chain or branched alkyl group with a terminal oxygen linking the alkyl group to the rest of the molecule. Alkoxy includes methoxy, ethoxy, propoxy, isopropoxy, butoxy, t-butoxy, pentoxy and so on.

The term "aryl" refers to a monocyclic, aromatic carbocycle (ring structure having ring atoms that are all carbon) having 6 atoms per ring. (Carbon atoms in the aryl groups are sp<sup>2</sup> hybridized.)

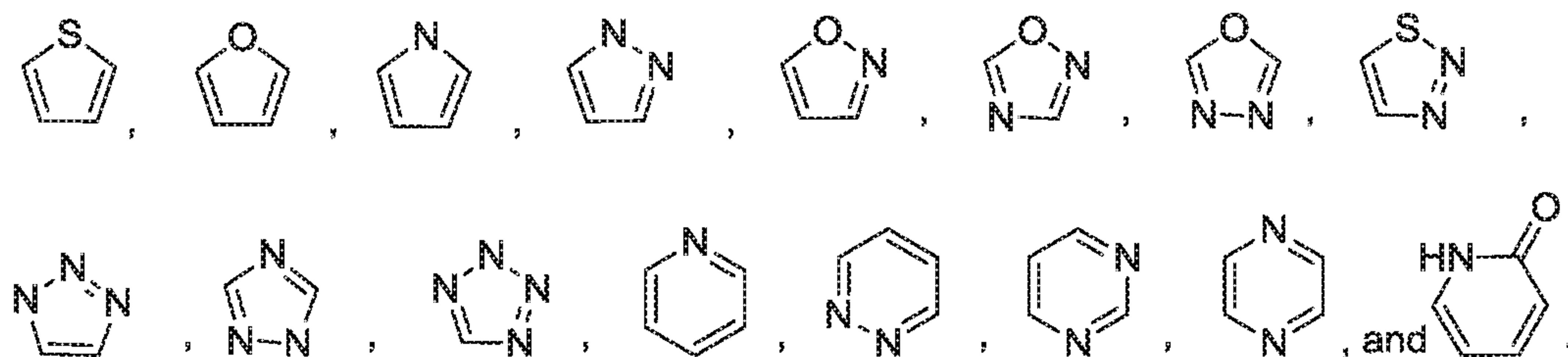
The term "phenyl" represents the following moiety:



The term "thienyl" represents the following moiety:

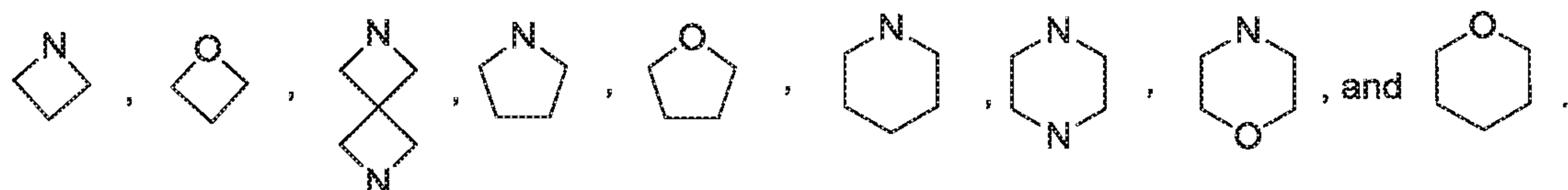


The term “heteroaryl” refers to a monocyclic or fused bicyclic heterocycle (ring structure having ring atoms selected from carbon atoms and up to four heteroatoms selected from nitrogen, oxygen, and sulfur) having from 3 to 9 ring atoms per heterocycle. Illustrative examples of heteroaryl groups include the following entities, in the form of properly bonded moieties:



Those skilled in the art will recognize that the species of heteroaryl, cycloalkyl, aryl and heterocycloalkyl groups listed or illustrated above are not exhaustive, and that additional species within the scope of these defined terms may also be selected.

A “heterocycloalkyl” refers to a monocyclic ring structure that is saturated or partially saturated and has from 4 to 7 ring atoms per ring structure selected from carbon atoms and up to two heteroatoms selected from nitrogen, oxygen, and sulfur. The ring structure may optionally contain up to two oxo groups on sulfur ring members. Illustrative entities, in the form of properly bonded moieties, include:

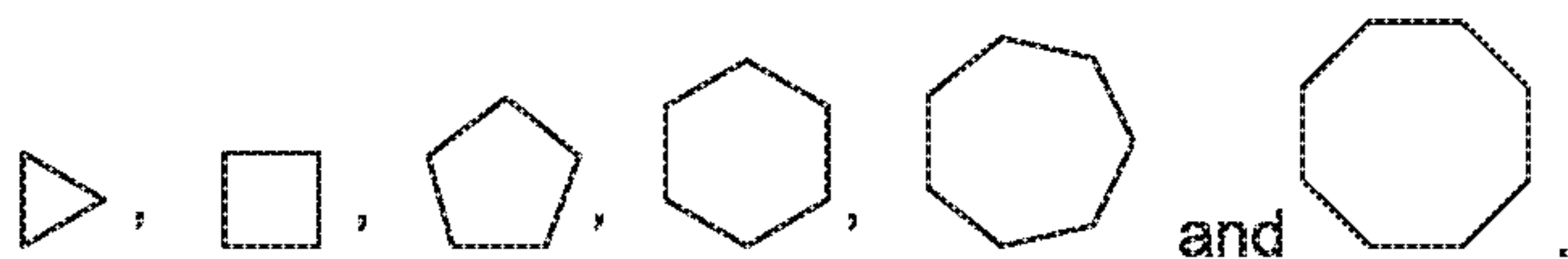


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The term “cyano” refers to the group -CN.

The term “cycloalkyl” refers to a saturated or partially saturated, monocyclic, fused polycyclic, or spiro polycyclic carbocycle having from 3 to 12 ring atoms per carbocycle. Illustrative examples of cycloalkyl groups include the following entities, in the form of properly bonded moieties:

10



The term “halo” represents chloro, fluoro, bromo or iodo.

The term “perhaloalkyl” or “haloalkyl” refers to a straight- or branched-chain alkyl group having from 1 to 6 carbon atoms in the chain optionally substituting hydrogens

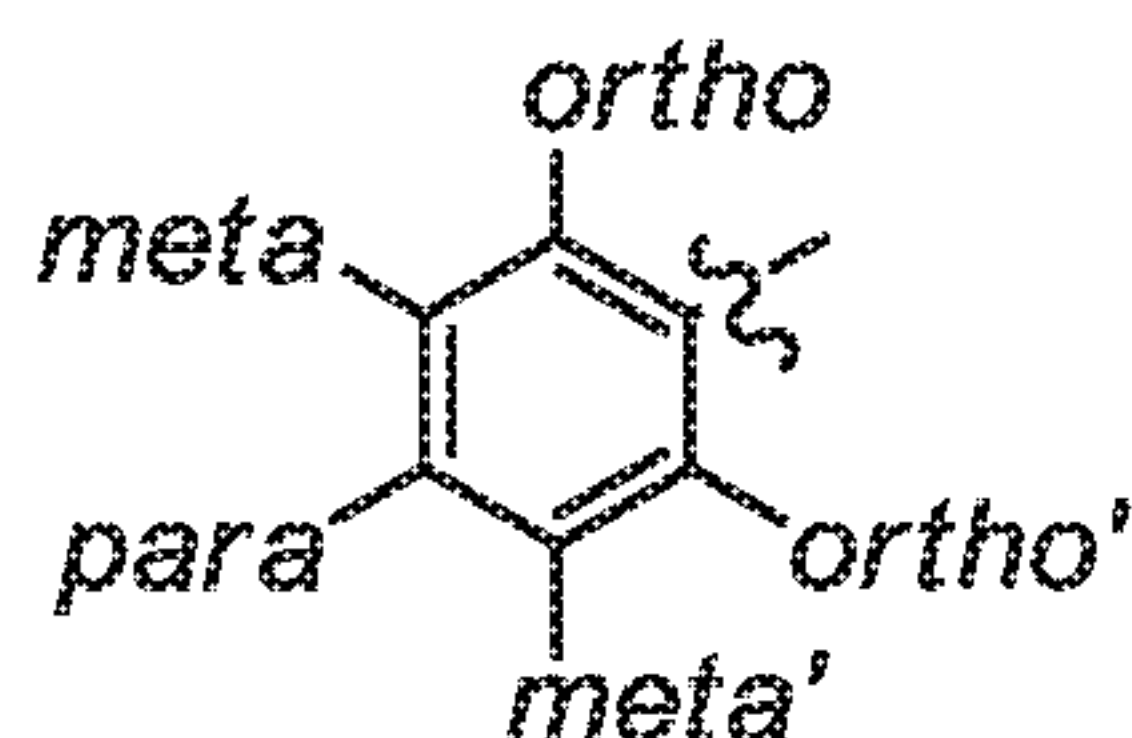
with halogens. The term "C<sub>1-4</sub>haloalkyl" as used here refers to a straight- or branched-chain alkyl group having from 1 to 4 carbon atoms in the chain, optionally substituting hydrogens with halogens. The term "C<sub>1-6</sub>haloalkyl" as used here refers to a straight- or branched-chain alkyl group having from 1 to 6 carbon atoms in the chain, optionally substituting hydrogens with halogens. Examples of "perhaloalkyl", "haloalkyl" groups include trifluoromethyl (CF<sub>3</sub>), difluoromethyl (CF<sub>2</sub>H), monofluoromethyl (CH<sub>2</sub>F), pentafluoroethyl (CF<sub>2</sub>CF<sub>3</sub>), tetrafluoroethyl (CHFCH<sub>2</sub>CF<sub>3</sub>), monofluoroethyl (CH<sub>2</sub>CH<sub>2</sub>F), trifluoroethyl (CH<sub>2</sub>CF<sub>3</sub>), tetrafluorotrifluoromethylethyl (-CF(CF<sub>3</sub>)<sub>2</sub>), and groups that in light of the ordinary skill in the art and the teachings provided herein would be considered equivalent to any one of the foregoing examples.

The term "perhaloalkoxy" or "haloalkoxy" refers to a straight- or branched-chain alkoxy group having from 1 to 6 carbon atoms in the chain optionally substituting hydrogens with halogens. Examples of perhaloalkoxy groups include trifluoromethoxy (OCF<sub>3</sub>), difluoromethoxy (OCF<sub>2</sub>H), monofluoromethoxy (OCH<sub>2</sub>F), monofluoroethoxy (OCH<sub>2</sub>CH<sub>2</sub>F), pentafluoroethoxy (OCF<sub>2</sub>CF<sub>3</sub>), tetrafluoroethoxy (OCHFCH<sub>2</sub>CF<sub>3</sub>), trifluoroethoxy (OCH<sub>2</sub>CF<sub>3</sub>), tetrafluorotrifluoromethylethoxy (-OCF(CF<sub>3</sub>)<sub>2</sub>), and groups that in light of the ordinary skill in the art and the teachings provided herein would be considered equivalent to any one of the foregoing examples.

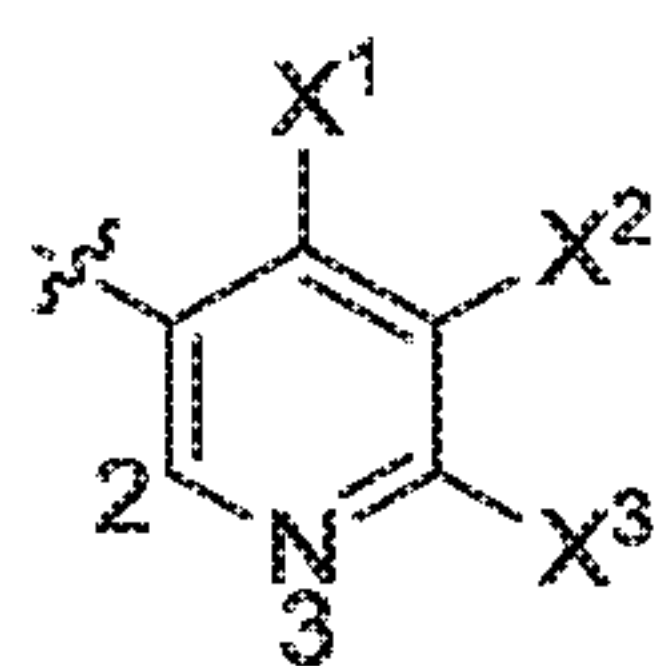
The term "substituted" means that the specified group or moiety bears one or more substituents. The term "unsubstituted" means that the specified group bears no substituents. The term "optionally substituted" means that the specified group is unsubstituted or substituted by one or more substituents. Where the term "substituted" is used to describe a structural system, the substitution is meant to occur at any valency-allowed position on the system. In cases where a specified moiety or group is not expressly noted as being optionally substituted or substituted with any specified substituent, it is understood that such a moiety or group is intended to be unsubstituted.

The terms "para", "meta", and "ortho" have the meanings as understood in the art. Thus, for example, a fully substituted phenyl group has substituents at both "ortho"(*o*) positions adjacent to the point of attachment of the phenyl ring, both "meta"(*m*) positions, and the one "para"(*p*) position across from the point of attachment. To further clarify the position of substituents on the phenyl ring, the 2 different ortho

positions will be designated as ortho and ortho' and the 2 different meta positions as meta and meta' as illustrated below.



When referring to substituents on a pyridyl group, the terms "para", "meta", and  
 5 "ortho" refer to the placement of a substituent relative to the point of attachment of the pyridyl ring. For example the structure below is described as 3-pyridyl with the X<sup>1</sup> substituent in the ortho position, the X<sup>2</sup> substituent in the meta position, and X<sup>3</sup> substituent in the para position:



10 To provide a more concise description, some of the quantitative expressions given herein are not qualified with the term "about". It is understood that, whether the term "about" is used explicitly or not, every quantity given herein is meant to refer to the actual given value, and it is also meant to refer to the approximation to such given value that would reasonably be inferred based on the ordinary skill in the art, including  
 15 equivalents and approximations due to the experimental and/or measurement conditions for such given value. Whenever a yield is given as a percentage, such yield refers to a mass of the entity for which the yield is given with respect to the maximum amount of the same entity that could be obtained under the particular stoichiometric conditions. Concentrations that are given as percentages refer to mass ratios, unless  
 20 indicated differently.

The terms "buffered" solution or "buffer" solution are used herein interchangeably according to their standard meaning. Buffered solutions are used to control the pH of a medium, and their choice, use, and function is known to those of ordinary skill in the art. See, for example, G.D. Considine, ed., Van Nostrand's Encyclopedia of Chemistry, p.  
 25 261, 5<sup>th</sup> ed. (2005), describing, inter alia, buffer solutions and how the concentrations of the buffer constituents relate to the pH of the buffer. For example, a buffered solution is

obtained by adding  $\text{MgSO}_4$  and  $\text{NaHCO}_3$  to a solution in a 10:1 w/w ratio to maintain the pH of the solution at about 7.5.

Any formula given herein is intended to represent compounds having structures depicted by the structural formula as well as certain variations or forms. In particular, compounds of any formula given herein may have asymmetric centers and therefore exist in different enantiomeric forms. All optical isomers of the compounds of the general formula, and mixtures thereof, are considered within the scope of the formula. Thus, any formula given herein is intended to represent a racemate, one or more enantiomeric forms, one or more diastereomeric forms, one or more atropisomeric forms, and mixtures thereof. Furthermore, certain structures may exist as geometric isomers (i.e., *cis* and *trans* isomers), as tautomers, or as atropisomers.

It is also to be understood that compounds that have the same molecular formula but differ in the nature or sequence of bonding of their atoms or the arrangement of their atoms in space are termed "isomers."

Stereoisomers that are not mirror images of one another are termed "diastereomers" and those that are non-superimposable mirror images of each other are termed "enantiomers." When a compound has an asymmetric center, for example, it is bonded to four different groups, and a pair of enantiomers is possible. An enantiomer can be characterized by the absolute configuration of its asymmetric center and is described by the R-and S-sequencing rules of Cahn and Prelog, or by the manner in which the molecule rotates the plane of polarized light and designated as dextrorotatory or levorotatory (i.e., as (+)- or (-)-isomers respectively). A chiral compound can exist as either an individual enantiomer or as a mixture thereof. A mixture containing equal proportions of the enantiomers is called a "racemic mixture."

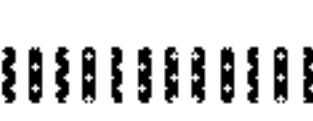
"Tautomers" refer to compounds that are interchangeable forms of a particular compound structure, and that vary in the displacement of hydrogen atoms and electrons. Thus, two structures may be in equilibrium through the movement of  $\pi$  electrons and an atom (usually H). For example, enols and ketones are tautomers because they are rapidly interconverted by treatment with either acid or base. Another example of tautomerism is the aci-and nitro-forms of phenyl nitromethane, that are likewise formed by treatment with acid or base.

Tautomeric forms may be relevant to the attainment of the optimal chemical reactivity and biological activity of a compound of interest.

The compounds of this invention may possess one or more asymmetric centers; such compounds can therefore be produced as individual (*R*)- or (*S*)-stereoisomers or  
5 as mixtures thereof.

Unless indicated otherwise, the description or naming of a particular compound in the specification and claims is intended to include both individual enantiomers and mixtures, racemic or otherwise, thereof. The methods for the determination of stereochemistry and the separation of stereoisomers are well-known in the art.

10 Certain examples contain chemical structures that are depicted as an absolute enantiomer but are intended to indicate enantiopure material that is of unknown configuration. In these cases (*R*<sup>\*</sup>) or (*S*<sup>\*</sup>) is used in the name to indicate that the absolute stereochemistry of the corresponding stereocenter is unknown. Thus, a compound designated as (*R*<sup>\*</sup>) refers to an enantiopure compound with an absolute  
15 configuration of either (*R*) or (*S*). In cases where the absolute stereochemistry has been confirmed, the structures are named using (*R*) and (*S*).

The symbols  and  are used as meaning the same spatial arrangement in chemical structures shown herein. Analogously, the symbols  and  are used as meaning the same spatial arrangement in chemical structures  
20 shown herein.

Additionally, any formula given herein is intended to refer also to hydrates, solvates, and polymorphs of such compounds, and mixtures thereof, even if such forms are not listed explicitly. Certain compounds of Formula (I) (as well as Formulas (IA), (IB), (IC), and (ID)), or pharmaceutically acceptable salts of compounds of Formula (I)  
25 (as well as Formulas (IA), (IB), (IC), and (ID)) may be obtained as solvates. Solvates include those formed from the interaction or complexation of compounds of the invention with one or more solvents, either in solution or as a solid or crystalline form. In some embodiments, the solvent is water and the solvates are hydrates. In addition, certain crystalline forms of compounds of Formula (I) (as well as Formulas (IA), (IB),  
30 (IC), and (ID)) or pharmaceutically acceptable salts of compounds of Formula (I) (as well as Formulas (IA), (IB), (IC), and (ID)) may be obtained as co-crystals. In certain

embodiments of the invention, compounds of Formula (I) were obtained in a crystalline form. In other embodiments, crystalline forms of compounds of Formula (I) were cubic in nature. In other embodiments, pharmaceutically acceptable salts of compounds of Formula (I) were obtained in a crystalline form. In still other embodiments, compounds  
5 of Formula (I) were obtained in one of several polymorphic forms, as a mixture of crystalline forms, as a polymorphic form, or as an amorphous form. In other embodiments, compounds of Formula (I) convert in solution between one or more crystalline forms and/or polymorphic forms.

Reference to a compound herein stands for a reference to any one of: (a) the  
10 actually recited form of such compound, and (b) any of the forms of such compound in the medium in which the compound is being considered when named. For example, reference herein to a compound such as R-COOH, encompasses reference to any one of, for example, R-COOH<sub>(s)</sub>, R-COOH<sub>(sol)</sub>, and R-COO<sup>-</sup><sub>(sol)</sub>. In this example, R-COOH<sub>(s)</sub> refers to the solid compound, as it could be for example in a tablet or some other solid  
15 pharmaceutical composition or preparation; R-COOH<sub>(sol)</sub> refers to the undissociated form of the compound in a solvent; and R-COO<sup>-</sup><sub>(sol)</sub> refers to the dissociated form of the compound in a solvent, such as the dissociated form of the compound in an aqueous environment, whether such dissociated form derives from R-COOH, from a salt thereof, or from any other entity that yields R-COO<sup>-</sup> upon dissociation in the medium being  
20 considered. In another example, an expression such as “exposing an entity to compound of formula R-COOH” refers to the exposure of such entity to the form, or forms, of the compound R-COOH that exists, or exist, in the medium in which such exposure takes place. In still another example, an expression such as “reacting an entity with a compound of formula R-COOH” refers to the reacting of (a) such entity in  
25 the chemically relevant form, or forms, of such entity that exists, or exist, in the medium in which such reacting takes place, with (b) the chemically relevant form, or forms, of the compound R-COOH that exists, or exist, in the medium in which such reacting takes place. In this regard, if such entity is for example in an aqueous environment, it is understood that the compound R-COOH is in such same medium, and therefore the  
30 entity is being exposed to species such as R-COOH<sub>(aq)</sub> and/or R-COO<sup>-</sup><sub>(aq)</sub>, where the subscript “(aq)” stands for “aqueous” according to its conventional meaning in chemistry

and biochemistry. A carboxylic acid functional group has been chosen in these nomenclature examples; this choice is not intended, however, as a limitation but it is merely an illustration. It is understood that analogous examples can be provided in terms of other functional groups, including but not limited to hydroxyl, basic nitrogen members, such as those in amines, and any other group that interacts or transforms according to known manners in the medium that contains the compound. Such interactions and transformations include, but are not limited to, dissociation, association, tautomerism, solvolysis, including hydrolysis, solvation, including hydration, protonation, and deprotonation. No further examples in this regard are provided herein because these interactions and transformations in a given medium are known by any one of ordinary skill in the art.

In another example, a zwitterionic compound is encompassed herein by referring to a compound that is known to form a zwitterion, even if it is not explicitly named in its zwitterionic form. Terms such as zwitterion, zwitterions, and their synonyms zwitterionic compound(s) are standard IUPAC-endorsed names that are well known and part of standard sets of defined scientific names. In this regard, the name zwitterion is assigned the name identification CHEBI:27369 by the Chemical Entities of Biological Interest (ChEBI) dictionary of molecular entities. As generally well known, a zwitterion or zwitterionic compound is a neutral compound that has formal unit charges of opposite sign. Sometimes these compounds are referred to by the term "inner salts". Other sources refer to these compounds as "dipolar ions", although the latter term is regarded by still other sources as a misnomer. As a specific example, aminoethanoic acid (the amino acid glycine) has the formula  $\text{H}_2\text{NCH}_2\text{COOH}$ , and it exists in some media (in this case in neutral media) in the form of the zwitterion  $^+\text{H}_3\text{NCH}_2\text{COO}^-$ . Zwitterions, zwitterionic compounds, inner salts and dipolar ions in the known and well established meanings of these terms are within the scope of this invention, as would in any case be so appreciated by those of ordinary skill in the art. Because there is no need to name each and every embodiment that would be recognized by those of ordinary skill in the art, no structures of the zwitterionic compounds that are associated with the compounds of this invention are given explicitly herein. They are, however, part of the embodiments of this invention. No further examples in this regard are provided herein because the

interactions and transformations in a given medium that lead to the various forms of a given compound are known by any one of ordinary skill in the art.

Any formula given herein is also intended to represent unlabeled forms as well as isotopically labeled forms of the compounds. Isotopically labeled compounds have  
5 structures depicted by the formulas given herein except that one or more atoms are replaced by an atom having a selected atomic mass or mass number. Examples of isotopes that can be incorporated into compounds of the invention include isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorus, sulfur, fluorine, chlorine, and iodine such as  $^2\text{H}$ ,  $^3\text{H}$ ,  $^{11}\text{C}$ ,  $^{13}\text{C}$ ,  $^{14}\text{C}$ ,  $^{15}\text{N}$ ,  $^{18}\text{O}$ ,  $^{17}\text{O}$ ,  $^{31}\text{P}$ ,  $^{32}\text{P}$ ,  $^{35}\text{S}$ ,  $^{18}\text{F}$ ,  $^{36}\text{Cl}$ ,  $^{125}\text{I}$ , respectively.

10 Such isotopically labeled compounds are useful in metabolic studies (preferably with  $^{14}\text{C}$ ), reaction kinetic studies (with, for example deuterium (i.e., D or  $^2\text{H}$ ); or tritium (i.e., T or  $^3\text{H}$ )), detection or imaging techniques [such as positron emission tomography (PET) or single-photon emission computed tomography (SPECT)] including drug or substrate tissue distribution assays, or in radioactive treatment of patients. In particular, an  $^{18}\text{F}$  or  
15  $^{11}\text{C}$  labeled compound may be particularly preferred for PET or SPECT studies. Further, substitution with heavier isotopes such as deuterium (i.e.,  $^2\text{H}$ ) may afford certain therapeutic advantages resulting from greater metabolic stability, for example increased *in vivo* half-life or reduced dosage requirements. Isotopically labeled compounds of this invention and prodrugs thereof can generally be prepared by carrying out the  
20 procedures disclosed in the schemes or in the examples and preparations described below by substituting a readily available isotopically labeled reagent for a non-isotopically labeled reagent.

When referring to any formula given herein, the selection of a particular moiety from a list of possible species for a specified variable is not intended to define the same  
25 choice of the species for the variable appearing elsewhere. In other words, where a variable appears more than once, the choice of the species from a specified list is independent of the choice of the species for the same variable elsewhere in the formula, unless stated otherwise.

According to the foregoing interpretive considerations on assignments and  
30 nomenclature, it is understood that explicit reference herein to a set implies, where chemically meaningful and unless indicated otherwise, independent reference to

embodiments of such set, and reference to each and every one of the possible embodiments of subsets of the set referred to explicitly.

By way of a first example on substituent terminology, if substituent  $S^1_{\text{example}}$  is one of  $S_1$  and  $S_2$ , and substituent  $S^2_{\text{example}}$  is one of  $S_3$  and  $S_4$ , then these assignments refer to embodiments of this invention given according to the choices  $S^1_{\text{example}}$  is  $S_1$  and  $S^2_{\text{example}}$  is  $S_3$ ;  $S^1_{\text{example}}$  is  $S_1$  and  $S^2_{\text{example}}$  is  $S_4$ ;  $S^1_{\text{example}}$  is  $S_2$  and  $S^2_{\text{example}}$  is  $S_3$ ;  $S^1_{\text{example}}$  is  $S_2$  and  $S^2_{\text{example}}$  is  $S_4$ ; and equivalents of each one of such choices. The shorter terminology " $S^1_{\text{example}}$  is one of  $S_1$  and  $S_2$ , and  $S^2_{\text{example}}$  is one of  $S_3$  and  $S_4$ " is accordingly used herein for the sake of brevity, but not by way of limitation. The foregoing first example on substituent terminology, which is stated in generic terms, is meant to illustrate the various substituent assignments described herein. The foregoing convention given herein for substituents extends, when applicable, to members such as  $R^1$ ,  $R^{1a}$ ,  $R^{1b}$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^{4b}$ ,  $R^{4c}$ ,  $R^{4d}$ ,  $R^a$ ,  $R^b$ ,  $R^c$ ,  $\text{Het}^1$ ,  $\text{HAL}^1$ , PG, Y, and ring A, and any other generic substituent symbol used herein.

Furthermore, when more than one assignment is given for any member or substituent, embodiments of this invention comprise the various groupings that can be made from the listed assignments, taken independently, and equivalents thereof. By way of a second example on substituent terminology, if it is herein described that substituent  $S_{\text{example}}$  is one of  $S_1$ ,  $S_2$ , and  $S_3$ , this listing refers to embodiments of this invention for which  $S_{\text{example}}$  is  $S_1$ ;  $S_{\text{example}}$  is  $S_2$ ;  $S_{\text{example}}$  is  $S_3$ ;  $S_{\text{example}}$  is one of  $S_1$  and  $S_2$ ;  $S_{\text{example}}$  is one of  $S_1$  and  $S_3$ ;  $S_{\text{example}}$  is one of  $S_2$  and  $S_3$ ;  $S_{\text{example}}$  is one of  $S_1$ ,  $S_2$  and  $S_3$ ; and  $S_{\text{example}}$  is any equivalent of each one of these choices. The shorter terminology " $S_{\text{example}}$  is one of  $S_1$ ,  $S_2$ , and  $S_3$ " is accordingly used herein for the sake of brevity, but not by way of limitation. The foregoing second example on substituent terminology, which is stated in generic terms, is meant to illustrate the various substituent assignments described herein. The foregoing convention given herein for substituents extends, when applicable, to members such as  $R^1$ ,  $R^{1a}$ ,  $R^{1b}$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^{4b}$ ,  $R^{4c}$ ,  $R^{4d}$ ,  $R^a$ ,  $R^b$ ,  $R^c$ ,  $\text{Het}^1$ ,  $\text{HAL}^1$ , PG, Y, and ring A, and any other generic substituent symbol used herein.

The nomenclature " $C_{i-j}$ " with  $j > i$ , when applied herein to a class of substituents, is meant to refer to embodiments of this invention for which each and every one of the

number of carbon members, from i to j including i and j, is independently realized. By way of example, the term C<sub>1-4</sub> refers independently to embodiments that have one carbon member (C<sub>1</sub>), embodiments that have two carbon members (C<sub>2</sub>), embodiments that have three carbon members (C<sub>3</sub>), and embodiments that have four carbon members (C<sub>4</sub>).

The term C<sub>n-m</sub>alkyl refers to an aliphatic chain, whether straight or branched, with a total number N of carbon members in the chain that satisfies  $n \leq N \leq m$ , with  $m > n$ . Any disubstituent referred to herein is meant to encompass the various attachment possibilities when more than one of such possibilities are allowed. For example, reference to disubstituent –A-B–, where  $A \neq B$ , refers herein to such disubstituent with A attached to a first substituted member and B attached to a second substituted member, and it also refers to such disubstituent with A attached to the second substituted member and B attached to the first substituted member.

The invention includes also pharmaceutically acceptable salts of the compounds of Formula (I) (as well as Formulas (IA), (IB), (IC), and (ID)), preferably of those described above and of the specific compounds exemplified herein, and methods of treatment using such salts.

The term “pharmaceutically acceptable” means approved or approvable by a regulatory agency of Federal or a state government or the corresponding agency in countries other than the United States, or that is listed in the U. S. Pharmacopoeia or other generally recognized pharmacopoeia for use in animals, and more particularly, in humans.

A “pharmaceutically acceptable salt” is intended to mean a salt of a free acid or base of compounds represented by Formula (I) (as well as Formulas (IA), (IB), (IC), and (ID)) that are non-toxic, biologically tolerable, or otherwise biologically suitable for administration to the subject. It should possess the desired pharmacological activity of the parent compound. See, generally, G.S. Paulekuhn, et al., “Trends in Active Pharmaceutical Ingredient Salt Selection based on Analysis of the Orange Book Database”, *J. Med. Chem.*, **2007**, 50:6665–72, S.M. Berge, et al., “Pharmaceutical Salts”, *J Pharm Sci.*, **1977**, 66:1-19, and *Handbook of Pharmaceutical Salts, Properties, Selection, and Use*, Stahl and Wermuth, Eds., Wiley-VCH and VHCA, Zurich, **2002**.

Examples of pharmaceutically acceptable salts are those that are pharmacologically effective and suitable for contact with the tissues of patients without undue toxicity, irritation, or allergic response. A compound of Formula (I) (as well as Formulas (IA), (IB), (IC), and (ID)) may possess a sufficiently acidic group, a sufficiently basic group, or both types of functional groups, and accordingly react with a number of inorganic or organic bases, and inorganic and organic acids, to form a pharmaceutically acceptable salt.

Examples of pharmaceutically acceptable salts include sulfates, pyrosulfates, bisulfates, sulfites, bisulfites, phosphates, monohydrogen-phosphates, dihydrogenphosphates, metaphosphates, pyrophosphates, chlorides, bromides, iodides, acetates, propionates, decanoates, caprylates, acrylates, formates, isobutyrate, caproates, heptanoates, propiolates, oxalates, malonates, succinates, suberates, sebacates, fumarates, maleates, butyne-1,4-dioates, hexyne-1,6-dioates, benzoates, chlorobenzoates, methylbenzoates, dinitrobenzoates, hydroxybenzoates, methoxybenzoates, phthalates, sulfonates, xylenesulfonates, phenylacetates, phenylpropionates, phenylbutyrates, citrates, lactates,  $\gamma$ -hydroxybutyrates, glycolates, tartrates, methane-sulfonates, propanesulfonates, naphthalene-1-sulfonates, naphthalene-2-sulfonates, and mandelates.

When the compounds of Formula (I) (as well as Formulas (IA), (IB), (IC), and (ID)) contain a basic nitrogen, the desired pharmaceutically acceptable salt may be prepared by any suitable method available in the art. For example, treatment of the free base with an inorganic acid, such as hydrochloric acid, hydrobromic acid, sulfuric acid, sulfamic acid, nitric acid, boric acid, phosphoric acid, and the like, or with an organic acid, such as acetic acid, phenylacetic acid, propionic acid, stearic acid, lactic acid, ascorbic acid, maleic acid, hydroxymaleic acid, isethionic acid, succinic acid, valeric acid, fumaric acid, malonic acid, pyruvic acid, oxalic acid, glycolic acid, salicylic acid, oleic acid, palmitic acid, lauric acid, a pyranosidyl acid, such as glucuronic acid or galacturonic acid, an  $\alpha$ -hydroxy acid, such as mandelic acid, citric acid, or tartaric acid, an amino acid, such as aspartic acid, glutaric acid or glutamic acid, an aromatic acid, such as benzoic acid, 2-acetoxybenzoic acid, naphthoic acid, or cinnamic acid, a sulfonic acid, such as laurylsulfonic acid, *p*-toluenesulfonic acid, methanesulfonic acid,

ethanesulfonic acid, any compatible mixture of acids such as those given as examples herein, and any other acid and mixture thereof that are regarded as equivalents or acceptable substitutes in light of the ordinary level of skill in this technology.

When the compound of Formula (I) (as well as Formulas (IA), (IB), (IC), and (ID)) is an acid, such as a carboxylic acid or sulfonic acid, the desired pharmaceutically acceptable salt may be prepared by any suitable method, for example, treatment of the free acid with an inorganic or organic base, such as an amine (primary, secondary or tertiary), an alkali metal hydroxide, alkaline earth metal hydroxide, any compatible mixture of bases such as those given as examples herein, and any other base and mixture thereof that are regarded as equivalents or acceptable substitutes in light of the ordinary level of skill in this technology. Illustrative examples of suitable salts include organic salts derived from amino acids, such as *N*-methyl-D-glucamine, lysine, choline, glycine and arginine, ammonia, carbonates, bicarbonates, primary, secondary, and tertiary amines, and cyclic amines, such as tromethamine, benzylamines, pyrrolidines, piperidine, morpholine, and piperazine, and inorganic salts derived from sodium, calcium, potassium, magnesium, manganese, iron, copper, zinc, aluminum, and lithium.

The invention also relates to pharmaceutically acceptable prodrugs of the compounds of Formula (I) (as well as Formulas (IA), (IB), (IC), and (ID)), and treatment methods employing such pharmaceutically acceptable prodrugs. The term "prodrug" means a precursor of a designated compound that, following administration to a subject, yields the compound *in vivo* via a chemical or physiological process such as solvolysis or enzymatic cleavage, or under physiological conditions (e.g., a prodrug on being brought to physiological pH is converted to the compound of Formula (I). A "pharmaceutically acceptable prodrug" is a prodrug that is non-toxic, biologically tolerable, and otherwise biologically suitable for administration to the subject. Illustrative procedures for the selection and preparation of suitable prodrug derivatives are described, for example, in "*Design of Prodrugs*", ed. H. Bundgaard, Elsevier, **1985**.

Exemplary prodrugs include compounds having an amino acid residue, or a polypeptide chain of two or more (e.g., two, three or four) amino acid residues, covalently joined through an amide or ester bond to a free amino, hydroxyl, or carboxylic acid group of a compound of Formula (I) (as well as Formulas (IA), (IB), (IC),

and (ID)). Examples of amino acid residues include the twenty naturally occurring amino acids, commonly designated by three letter symbols, as well as 4-hydroxyproline, hydroxylysine, demosine, isodemosine, 3-methylhistidine, norvalin, beta-alanine, gamma-aminobutyric acid, citrulline homocysteine, homoserine, ornithine and  
5 methionine sulfone.

Additional types of prodrugs may be produced, for instance, by derivatizing free carboxyl groups of structures of Formula (I) (as well as Formulas (IA), (IB), (IC), and (ID)) as amides or alkyl esters. Examples of amides include those derived from ammonia, primary C<sub>1-6</sub>alkyl amines and secondary di(C<sub>1-6</sub>alkyl) amines. Secondary  
10 amines include 5- or 6-membered heterocycloalkyl or heteroaryl ring moieties.

Examples of amides include those that are derived from ammonia, C<sub>1-3</sub>alkyl primary amines, and di(C<sub>1-2</sub>alkyl)amines. Examples of esters of the invention include C<sub>1-7</sub>alkyl, C<sub>5-7</sub>cycloalkyl, phenyl, and phenyl(C<sub>1-6</sub>alkyl) esters. Preferred esters include methyl

esters. Prodrugs may also be prepared by derivatizing free hydroxy groups using  
15 groups including hemisuccinates, phosphate esters, dimethylaminoacetates, and phosphoryloxymethyloxycarbonyls, following procedures such as those outlined in

Fleisher et al., *Adv. Drug Delivery Rev.* **1996**, 19, 115-130. Carbamate derivatives of hydroxy and amino groups may also yield prodrugs. Carbonate derivatives, sulfonate esters, and sulfate esters of hydroxy groups may also provide prodrugs. Derivatization  
20 of hydroxy groups as (acyloxy)methyl and (acyloxy)ethyl ethers, wherein the acyl group may be an alkyl ester, optionally substituted with one or more ether, amine, or carboxylic acid functionalities, or where the acyl group is an amino acid ester as described above, is also useful to yield prodrugs. Prodrugs of this type may be prepared as described in Robinson et al., *J Med Chem.* **1996**, 39 (1), 10-18. Free amines can  
25 also be derivatized as amides, sulfonamides or phosphoramides. All of these prodrug moieties may incorporate groups including ether, amine, and carboxylic acid functionalities.

The present invention also relates to pharmaceutically active metabolites of the compounds of Formula (I) (as well as Formulas (IA), (IB), (IC), and (ID)), which may  
30 also be used in the methods of the invention. A "pharmaceutically active metabolite" means a pharmacologically active product of metabolism in the body of a compound of

Formula (I) (as well as Formulas (IA), (IB), (IC), and (ID) as applicable) or salt thereof. Prodrugs and active metabolites of a compound may be determined using routine techniques known or available in the art. See, e.g., Bertolini, et al., *J Med Chem.* **1997**, 40, 2011-2016; Shan, et al., *J Pharm Sci.* **1997**, 86 (7), 765-767; Bagshawe, *Drug Dev*  
5 *Res.* **1995**, 34, 220-230; Bodor, *Adv Drug Res.* **1984**, 13, 224-331; Bundgaard, *Design of Prodrugs* (Elsevier Press, **1985**); and Larsen, *Design and Application of Prodrugs, Drug Design and Development* (Krogsgaard-Larsen, et al., eds., Harwood Academic Publishers, **1991**).

The compounds of Formula (I) (as well as Formulas (IA), (IB), (IC), and (ID)) and  
10 their pharmaceutically acceptable salts, pharmaceutically acceptable prodrugs, and pharmaceutically active metabolites of the present invention are useful as modulators of the NR2B receptor in the methods of the invention. As such modulators, the compounds may act as antagonists, agonists, or inverse agonists. The term "modulators" include both inhibitors and activators, where "inhibitors" refer to compounds that decrease,  
15 prevent, inactivate, desensitize, or down-regulate the NR2B receptor expression or activity, and "activators" are compounds that increase, activate, facilitate, sensitize, or up-regulate NR2B receptor expression or activity.

The term "treat", "treatment" or "treating", as used herein, is intended to refer to administration of an active agent or composition of the invention to a subject for the  
20 purpose of affecting a therapeutic or prophylactic benefit through modulation of NR2B receptor activity. Treating includes reversing, ameliorating, alleviating, inhibiting the progress of, lessening the severity of, or preventing a disease, disorder, or condition, or one or more symptoms of such disease, disorder or condition mediated through modulation of NR2B receptor activity. The term "subject" refers to a mammalian patient  
25 in need of such treatment, such as a human.

Accordingly, the invention relates to methods of using the compounds described herein to treat subjects diagnosed with or suffering from a disease, disorder, or condition mediated by NR2B receptor activity, such as: bipolar disorder I depressed, hypomanic, manic and mixed form; bipolar disorder II; depressive disorders, such as  
30 single depressive episode or recurrent major depressive disorder, minor depressive disorder, treatment-resistant depression, depressive disorder with postpartum onset,

disruptive mood dysregulation disorder, depressive disorders with psychotic symptoms;  
 persistent mood disorders, such as cyclothymia, dysthymia, euthymia; and  
 premenstrual dysphoric disorder; anxiety disorders, general anxiety disorder, panic  
 disorder with or without agoraphobia, specific phobia, social anxiety disorder, chronic  
 5 anxiety disorders; obsessive compulsive disorder; reaction to severe stress and  
 adjustment disorders, such as post traumatic stress disorder (PTSD); other neurotic  
 disorders such as depersonalisation-derealisation syndrome; pervasive developmental  
 disorders, including but not limited to Asperger's syndrome and Rett's syndrome,  
 autistic disorders, childhood autism and overactive disorder associated with mental  
 10 retardation and stereotyped movements, specific developmental disorder of motor  
 function, specific developmental disorders of scholastic skills; postnatal (postpartum)  
 and prenatal depression; eating disorders, including but not limited to anorexia nervosa,  
 bulimia nervosa, pica and binge eating disorder; Parkinson's disease; second  
 Parkinsonism, such as postencephalitic Parkinsonism; Parkinsonism comprised in other  
 15 disorders; Lewis body disease; degenerative diseases of the basal ganglia; other  
 extrapyramidal and movement disorders including but not limited to tremor, essential  
 tremor and drug-induced tremor, myoclonus, chorea and drug-induced chorea, drug-  
 induced tics and tics of organic origin, drug-induced acute dystonia, drug-induced  
 tardive dyskinesia, L-dopa-induced dyskinesia; neuroleptic-induced movement  
 20 disorders including but not limited to neuroleptic malignant syndrome (NMS),  
 neuroleptic induced parkinsonism, neuroleptic-induced early onset or acute dyskinesia,  
 neuroleptic-induced acute dystonia, neuroleptic-induced acute akathisia, neuroleptic-  
 induced tardive dyskinesia, neuroleptic-induced tremor; restless leg syndrome, Stiff-  
 man syndrome; dystonia including but not limited to focal dystonia, multiple-focal or  
 25 segmental dystonia, torsion dystonia, hemispheric, generalised and tardive dystonia  
 (induced by psychopharmacological drugs). Focal dystonia include cervical dystonia  
 (torticollis), blepharospasm (cramp of the eyelid), appendicular dystonia (cramp in the  
 extremities, like the writer's cramp), oromandibular dystonia and spasmodic dysphonia  
 (cramp of the vocal cord); epilepsy, including localization-related (focal)(partial)  
 30 idiopathic epilepsy and epileptic syndromes with seizures of localized onset,  
 localization-related (focal)(partial) symptomatic epilepsy and epileptic syndromes with

simple partial seizures, localization-related (focal)(partial) symptomatic epilepsy and  
 epileptic syndromes with complex partial seizures, generalized idiopathic epilepsy and  
 epileptic syndromes including but not limited to myoclonic epilepsy in infancy, neonatal  
 convulsions (familial), childhood absence epilepsy (pyknolepsy), epilepsy with grand  
 5 mal seizures on awakening, absence epilepsy, myoclonic epilepsy (impulsive petit mal)  
 and nonspecific atonic, clonic, myoclonic, tonic, tonic-clonic epileptic seizures; epilepsy  
 with myoclonic absences, myoclonic-astatic seizures, infantile spasms, Lennox-Gastaut  
 syndrome, Salaam attacks, symptomatic early myoclonic encephalopathy, West's  
 syndrome, petit and grand mal seizures; status epilepticus; persistent somatoform  
 10 disorders; acute, chronic and chronic intractable pain, headache; acute and chronic pain  
 related to physiological processes and physical disorders including but not limited to  
 back pain, tooth pain, abdominal pain, low back pain, pain in joints; acute and chronic  
 pain that is related to diseases of the musculoskeletal system and connective tissue  
 including, but not limited to rheumatism, myalgia, neuralgia and fibromyalgia; acute and  
 15 chronic pain that is related to nerve, nerve root and plexus disorders, such as trigeminal  
 pain, postzoster neuralgia, phantom limb syndrome with pain, carpal tunnel syndrome,  
 lesion of sciatic nerve, diabetic mononeuropathy; acute and chronic pain that is related  
 to polyneuropathies and other disorders of the peripheral nervous system, such as  
 hereditary and idiopathic neuropathy, inflammatory polyneuropathy, polyneuropathy  
 20 induced by drugs, alcohol or toxic agents, polyneuropathy in neoplastic disease,  
 diabetic polyneuropathy; and acute neurodegeneration, such as intracranial brain  
 injuries, such as stroke, diffuse and local brain injuries, epidural, subdural and  
 subarachnoid haemorrhage, and chronic neurodegeneration, such as Alzheimer's  
 disease, Huntington's disease, multiple sclerosis, and ALS; subarachnoid haemorrhage,  
 25 intracerebral haemorrhage and other nontraumatic intracranial haemorrhage, cerebral  
 infarction, stroke, occlusion and stenosis or precerebral and cerebral arteries, not  
 resulting in cerebral infarction, dissection of cerebral arteries, cerebral aneurysm,  
 cerebral atherosclerosis, progressive vascular leukoencephalopathy, hypertensive  
 encephalopathy, nonpyogenic thrombosis of intracranial venous system, cerebral  
 30 arteritis, cerebral amyloid angiopathy and sequelae of cerebrovascular diseases;  
 glaucoma and other neuropathies; dementias, vascular demensia, Lewy body dementia,

frontotemporal dementia, and HIV-dementia; vertigo and nystagmus; tinnitus; neuropsychiatric systemic lupus erythematosus; disruptive mood dysregulation disorder; schizophrenia spectrum disorder; and sleep/wake disorders. In specific embodiments, subjects that can be treated according to the present invention are diagnosed with or suffering from major depressive disorder, treatment-resistant depression and bipolar disorder.

In treatment methods according to the invention, an effective amount of a pharmaceutical agent according to the invention is administered to a subject suffering from or diagnosed as having such a disease, disorder, or condition. An "effective amount" means an amount or dose sufficient to generally bring about the desired therapeutic or prophylactic benefit in patients in need of such treatment for the designated disease, disorder, or condition. Effective amounts or doses of the compounds of the present invention may be ascertained by routine methods such as modeling, dose escalation studies or clinical trials, and by taking into consideration routine factors, e.g., the mode or route of administration or drug delivery, the pharmacokinetics of the compound, the severity and course of the disease, disorder, or condition, the subject's previous or ongoing therapy, the subject's health status and response to drugs, and the judgment of the treating physician. An example of a dose is in the range of from about 0.001 to about 200 mg of compound per kg of subject's body weight per day, preferably about 0.05 to 100 mg/kg/day, or about 1 to 35 mg/kg/day, in single or divided dosage units (e.g., BID, TID, QID). For a 70-kg human, an illustrative range for a suitable dosage amount is from about 0.05 to about 7 g/day, or about 0.2 to about 2.5 g/day.

Once improvement of the patient's disease, disorder, or condition has occurred, the dose may be adjusted for preventative or maintenance treatment. For example, the dosage or the frequency of administration, or both, may be reduced as a function of the symptoms, to a level at which the desired therapeutic or prophylactic effect is maintained. Of course, if symptoms have been alleviated to an appropriate level, treatment may cease. Patients may, however, require intermittent treatment on a long-term basis upon any recurrence of symptoms.

In addition, the active agents of the invention may be used in combination with additional active ingredients in the treatment of the above conditions. The additional active ingredients may be co-administered separately with an active agent of compounds of Table 1 or included with such an agent in a pharmaceutical composition according to the invention. In an exemplary embodiment, additional active ingredients are those that are known or discovered to be effective in the treatment of conditions, disorders, or diseases mediated by NR2B activity, such as another NR2B modulator or a compound active against another target associated with the particular condition, disorder, or disease. The combination may serve to increase efficacy (e.g., by including in the combination a compound potentiating the potency or effectiveness of an active agent according to the invention), decrease one or more side effects, or decrease the required dose of the active agent according to the invention.

The active agents of the invention are used, alone or in combination with one or more additional active ingredients, to formulate pharmaceutical compositions of the invention. A pharmaceutical composition of the invention comprises: (a) an effective amount of at least one active agent in accordance with the invention; and (b) a pharmaceutically acceptable excipient.

A "pharmaceutically acceptable excipient" refers to a substance that is non-toxic, biologically tolerable, and otherwise biologically suitable for administration to a subject, such as an inert substance, added to a pharmacological composition or otherwise used as a vehicle, carrier, or diluent to facilitate administration of an agent and that is compatible therewith. Examples of excipients include calcium carbonate, calcium phosphate, various sugars and types of starch, cellulose derivatives, gelatin, vegetable oils, and polyethylene glycols.

Delivery forms of the pharmaceutical compositions containing one or more dosage units of the active agents may be prepared using suitable pharmaceutical excipients and compounding techniques known or that become available to those skilled in the art. The compositions may be administered in the inventive methods by a suitable route of delivery, e.g., oral, parenteral, rectal, topical, or ocular routes, or by inhalation.

The preparation may be in the form of tablets, capsules, sachets, dragees, powders, granules, lozenges, powders for reconstitution, liquid preparations, or suppositories. Preferably, the compositions are formulated for intravenous infusion, topical administration, or oral administration.

5 For oral administration, the compounds of the invention can be provided in the form of tablets or capsules, or as a solution, emulsion, or suspension. To prepare the oral compositions, the compounds may be formulated to yield a dosage of, e.g., from about 0.05 to about 100 mg/kg daily, or from about 0.05 to about 35 mg/kg daily, or from about 0.1 to about 10 mg/kg daily. For example, a total daily dosage of about 5 mg to 5 g daily  
10 may be accomplished by dosing once, twice, three, or four times per day.

Oral tablets may include a compound according to the invention mixed with pharmaceutically acceptable excipients such as inert diluents, disintegrating agents, binding agents, lubricating agents, sweetening agents, flavoring agents, coloring agents and preservative agents. Suitable inert fillers include sodium and calcium carbonate,  
15 sodium and calcium phosphate, lactose, starch, sugar, glucose, methyl cellulose, magnesium stearate, mannitol, sorbitol, and the like. Exemplary liquid oral excipients include ethanol, glycerol, water, and the like. Starch, polyvinyl-pyrrolidone (PVP), sodium starch glycolate, microcrystalline cellulose, and alginic acid are suitable disintegrating agents. Binding agents may include starch and gelatin. The lubricating  
20 agent, if present, may be magnesium stearate, stearic acid or talc. If desired, the tablets may be coated with a material such as glyceryl monostearate or glyceryl distearate to delay absorption in the gastrointestinal tract, or may be coated with an enteric coating.

Capsules for oral administration include hard and soft gelatin capsules. To prepare hard gelatin capsules, compounds of the invention may be mixed with a solid,  
25 semi-solid, or liquid diluent. Soft gelatin capsules may be prepared by mixing the compound of the invention with water, an oil such as peanut oil or olive oil, liquid paraffin, a mixture of mono and di-glycerides of short chain fatty acids, polyethylene glycol 400, or propylene glycol.

Liquids for oral administration may be in the form of suspensions, solutions,  
30 emulsions or syrups or may be lyophilized or presented as a dry product for reconstitution with water or other suitable vehicle before use. Such liquid compositions

may optionally contain: pharmaceutically-acceptable excipients such as suspending agents (for example, sorbitol, methyl cellulose, sodium alginate, gelatin, hydroxyethylcellulose, carboxymethylcellulose, aluminum stearate gel and the like); non-aqueous vehicles, e.g., oil (for example, almond oil or fractionated coconut oil),  
5 propylene glycol, ethyl alcohol, or water; preservatives (for example, methyl or propyl p-hydroxybenzoate or sorbic acid); wetting agents such as lecithin; and, if desired, flavoring or coloring agents.

The active agents of this invention may also be administered by non-oral routes. For example, the compositions may be formulated for rectal administration as a  
10 suppository. For parenteral use, including intravenous, intramuscular, intraperitoneal, or subcutaneous routes, the compounds of the invention may be provided in sterile aqueous solutions or suspensions, buffered to an appropriate pH and isotonicity or in parenterally acceptable oil. Suitable aqueous vehicles include Ringer's solution and isotonic sodium chloride. Such forms will be presented in unit-dose form such as  
15 ampules or disposable injection devices, in multi-dose forms such as vials from which the appropriate dose may be withdrawn, or in a solid form or pre-concentrate that can be used to prepare an injectable formulation. Illustrative infusion doses may range from about 1 to 1000 µg/kg/minute of compound, admixed with a pharmaceutical carrier over a period ranging from several minutes to several days.

For topical administration, the compounds may be mixed with a pharmaceutical carrier at a concentration of about 0.1% to about 10% of drug to vehicle. Another mode of administering the compounds of the invention may utilize a patch formulation to affect transdermal delivery.

20 Compounds of the invention may alternatively be administered in methods of this invention by inhalation, via the nasal or oral routes, e.g., in a spray formulation also containing a suitable carrier.

Exemplary compounds useful in methods of the invention will now be described by reference to the illustrative synthetic schemes for their general preparation below and the specific examples that follow. Artisans will recognize that, to obtain the various compounds herein, starting materials may be suitably selected so that the ultimately desired substituents will be carried through the reaction scheme with or without

protection as appropriate to yield the desired product. Alternatively, it may be necessary or desirable to employ, in the place of the ultimately desired substituent, a suitable group that may be carried through the reaction scheme and replaced as appropriate with the desired substituent. Unless otherwise specified, the variables are as defined above in reference to Formula (I). Reactions may be performed between the melting point and the reflux temperature of the solvent, and preferably between 0 °C and the reflux temperature of the solvent. Reactions may be heated employing conventional heating or microwave heating. Reactions may also be conducted in sealed pressure vessels above the normal reflux temperature of the solvent.

Abbreviations and acronyms used herein include the following:

Table 2:

| Term                                                                    | Acronym                |
|-------------------------------------------------------------------------|------------------------|
| Acetonitrile                                                            | ACN                    |
| Aqueous                                                                 | aq                     |
| Atmosphere                                                              | atm                    |
| Gold(III) chloride                                                      | Au(III)Cl <sub>3</sub> |
| tert-Butylcarbamoyl                                                     | Boc                    |
| Benzotriazol-1-yloxy-tris(dimethylamino)phosphonium hexafluorophosphate | BOP                    |
| Broad                                                                   | br                     |
| 1,1'-Carbonyldiimidazole                                                | CDI                    |
| Diatomaceous Earth                                                      | Celite®                |
| Diethylaminosulfur trifluoride                                          | DAST                   |
| 1,8-Diazabicyclo[5.4.0]undec-7-ene                                      | DBU                    |

| Term                                                                                          | Acronym                      |
|-----------------------------------------------------------------------------------------------|------------------------------|
| N,N'-Dicyclohexylcarbodiimide                                                                 | DCC                          |
| Dichloroethane                                                                                | DCE                          |
| Dichloromethane                                                                               | DCM                          |
| Bis(2-methoxyethyl)aminosulfur trifluoride                                                    | Deoxo-Fluor®                 |
| Diisopropylethylamine                                                                         | DIPEA, DIEA, or Hunig's base |
| 4-Dimethylaminopyridine                                                                       | DMAP                         |
| 1,2-Dimethoxyethane                                                                           | DME                          |
| N,N-Dimethylformamide                                                                         | DMF                          |
| Dimethylsulfoxide                                                                             | DMSO                         |
| 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide                                                 | EDCI, EDAC, or EDC           |
| Diethyl ether                                                                                 | Ether, Et <sub>2</sub> O     |
| Ethyl Acetate                                                                                 | EtOAc, or EA                 |
| Ethanol                                                                                       | EtOH                         |
| Electrospray ionization                                                                       | ESI                          |
| Normal-phase silica gel chromatography                                                        | FCC                          |
| Grams                                                                                         | g                            |
| Hours                                                                                         | h                            |
| 1-[Bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxid hexafluorophosphate | HATU                         |

| Term                                                                      | Acronym    |
|---------------------------------------------------------------------------|------------|
| N,N,N',N'-Tetramethyl-O-(1H-benzotriazol-1-yl)uronium hexafluorophosphate | HBTU       |
| Hydroxybenzotriazole                                                      | HOBT       |
| High-pressure liquid chromatography                                       | HPLC       |
| Hertz                                                                     | Hz         |
| Isopropyl alcohol                                                         | iPrOH, IPA |
| Liquid chromatography and mass spectrometry                               | LCMS       |
| Lithium bis(trimethylsilyl)amide                                          | LHMDS      |
| Molar                                                                     | M          |
| Mass to charge ratio                                                      | m/z        |
| meta-Chloroperoxybenzoic acid                                             | mCPBA      |
| Methyl Iodide                                                             | Mel        |
| Methanol                                                                  | MeOH       |
| Milligrams                                                                | mg         |
| Minute                                                                    | min        |
| Milliliter                                                                | mL         |
| Microliter                                                                | μL         |
| Millimoles                                                                | mmol       |
| Mass spectrometry                                                         | MS         |

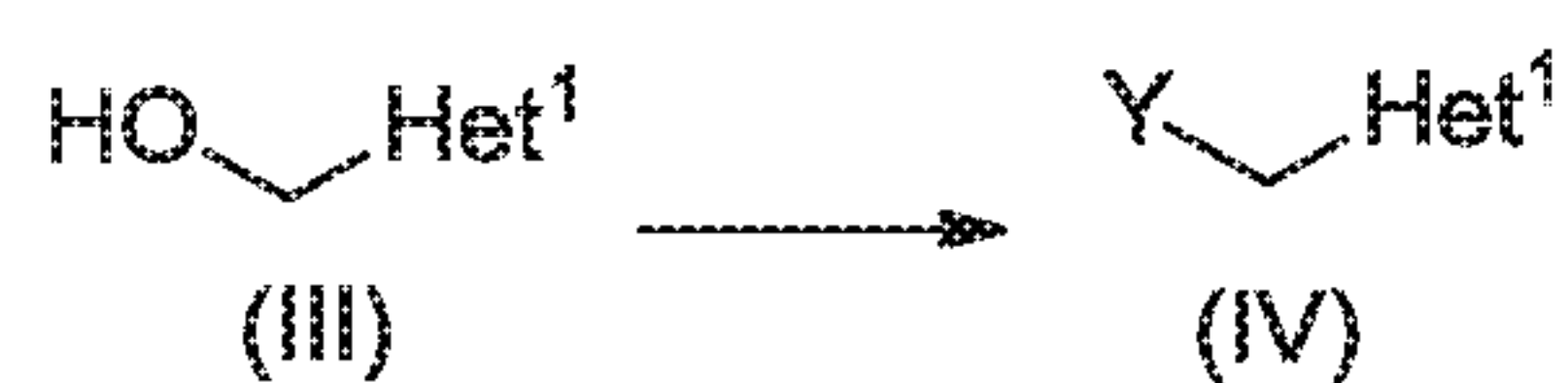
| Term                                                             | Acronym                                                             |
|------------------------------------------------------------------|---------------------------------------------------------------------|
| Normal                                                           | N                                                                   |
| N-Bromosuccinimide                                               | NBS                                                                 |
| N-Chlorosuccinimide                                              | NCS                                                                 |
| N-Iodosuccinimide                                                | NIS                                                                 |
| Nuclear magnetic resonance                                       | NMR                                                                 |
| CF <sub>3</sub> SO <sub>3</sub> <sup>-</sup> or triflate         | OTf                                                                 |
| Palladium(II)bis(triphenylphosphine) dichloride                  | Pd(PPh <sub>3</sub> ) <sub>2</sub> Cl <sub>2</sub>                  |
| Tetrakis(triphenylphosphine)palladium(0)                         | Pd(PPh <sub>3</sub> ) <sub>4</sub>                                  |
| [1,1'-Bis(di-tert-butylphosphino)ferrocene]dichloropalladium(II) | PdCl <sub>2</sub> (dtbpf) or Pd(dtbpf) <sub>2</sub> Cl <sub>2</sub> |
| [1,1'-Bis(diphenylphosphino)ferrocene]dichloropalladium(II)      | PdCl <sub>2</sub> (dppf) or Pd(dppf) <sub>2</sub> Cl <sub>2</sub>   |
| Parts per million                                                | ppm                                                                 |
| Precipitate                                                      | ppt                                                                 |
| Polytetrafluoroethylene                                          | PTFE                                                                |
| Bromotripyrrolidinophosphonium hexafluorophosphate               | PyBroP®                                                             |
| Retention time                                                   | R <sub>t</sub>                                                      |
| Room temperature                                                 | rt                                                                  |
| Saturated                                                        | sat                                                                 |

| Term                                                                            | Acronym          |
|---------------------------------------------------------------------------------|------------------|
| 1-Chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) | Selectfluor®     |
| [2-(Trimethylsilyl)ethoxy]methyl acetal                                         | SEM              |
| Supercritical Fluid Chromatography                                              | SFC              |
| Temperature                                                                     | T                |
| Triphenylmethyl                                                                 | Trityl           |
| Tetra-n-butylammonium fluoride                                                  | TBAF             |
| Triethylamine                                                                   | TEA              |
| Trifluoroacetic acid                                                            | TFA              |
| 2,4,6-Tripropyl-1,3,5,2,4,6-trioxatriphosphorinane-2,4,6-trioxide               | T <sub>3</sub> P |
| Tetrahydrofuran                                                                 | THF              |
| Thin layer chromatography                                                       | TLC              |
| Volume in milliliters of solvent per gram of substrate                          | V, or volumes    |

## PREPARATIVE EXAMPLES

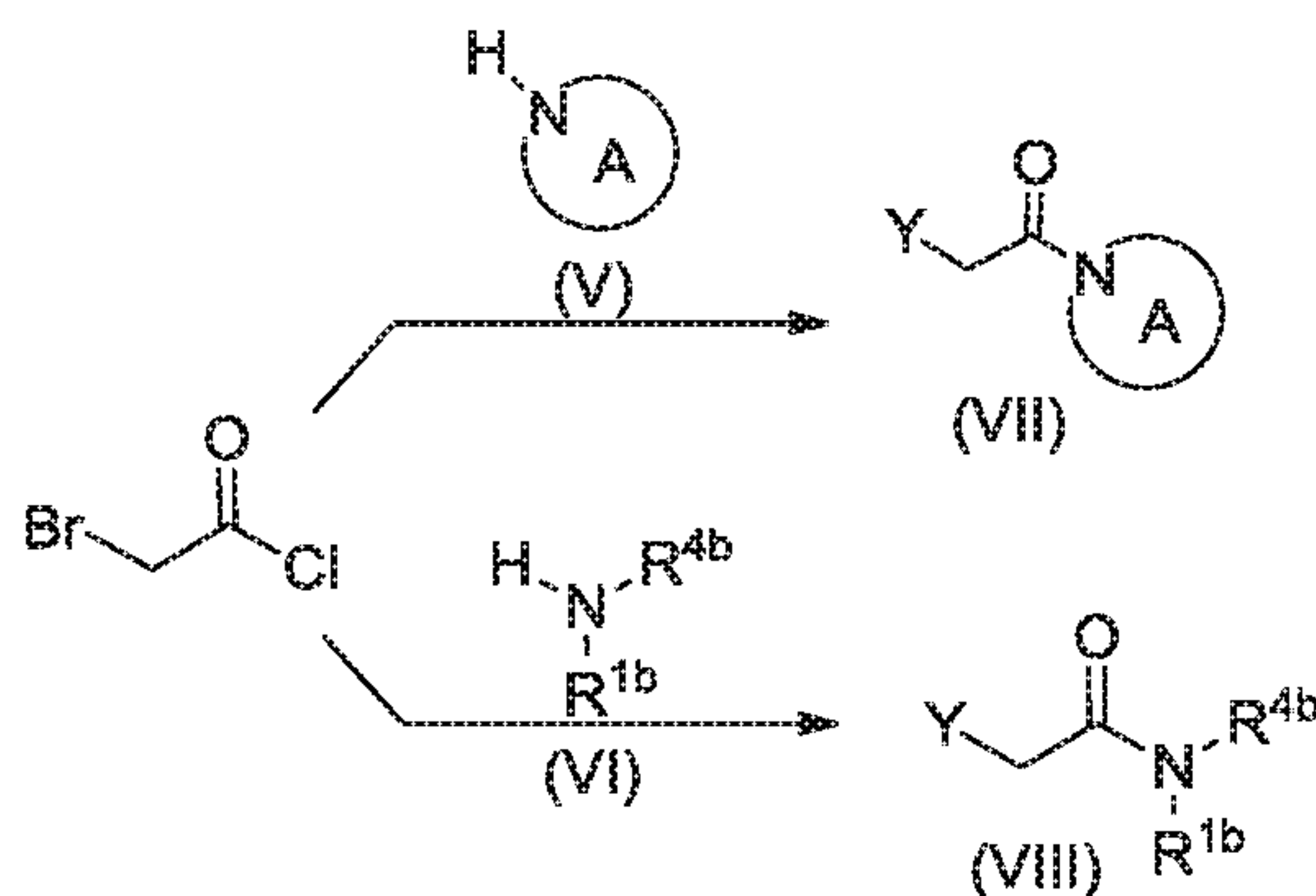
Exemplary compounds useful in methods of the invention will now be described  
 5 by reference to the illustrative synthetic schemes for their general preparation below  
 and the specific examples to follow.

SCHEME 1



According to SCHEME 1, a compound of formula (IV), where Y is a suitable leaving group such as Cl or -OSO<sub>2</sub>CH<sub>3</sub> and Het<sup>1</sup> is a suitably substituted heteroaryl such as pyrimidinyl, pyrazinyl, pyridinyl, is prepared from a compound of formula (III), under conditions known to one skilled in the art. For example, a compound of formula (III) is  
 5 reacted with a base such as TEA, methanesulfonyl chloride, in a solvent such as DCM, at temperatures ranging from 0°C to rt, to afford a compound of formula (IV), where Y is -OSO<sub>2</sub>CH<sub>3</sub>. A compound of formula (III), where Het<sup>1</sup> is pyrazinyl, pyridazinyl, pyrimidinyl and the like, is reacted under chlorination conditions, for example, reaction with thionyl chloride, and the like, in a solvent such as DCM, at temperatures ranging from 0°C to rt,  
 10 to afford a compound of formula (IV), where Y is Cl.

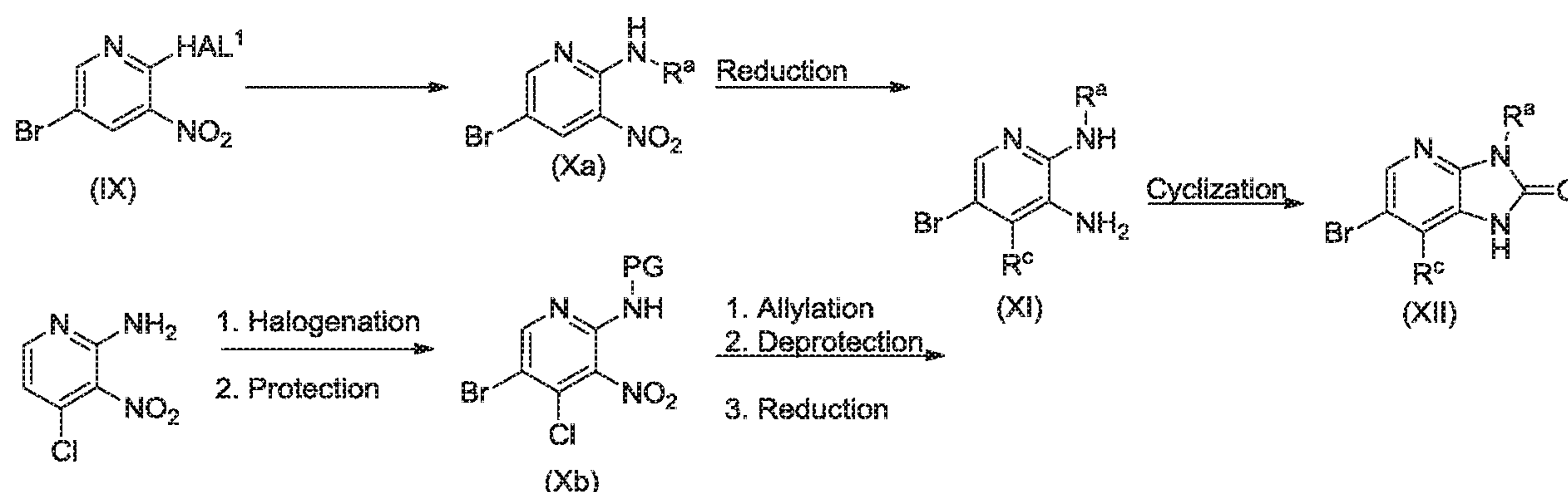
SCHEME 2



According to SCHEME 2, 2-bromoacetyl chloride is reacted with a commercially available or synthetically accessible suitably substituted heterocycloalkylamine of formula (V), where A is a fully saturated or partially saturated 3-6 membered ring optionally containing additional S, N, or O atoms, or suitably substituted amine of  
 15 formula (VI), where R<sup>4b</sup> and R<sup>1b</sup> are as defined in Formula (I), in the presence of a suitable base such as Et<sub>3</sub>N (TEA), in a solvent such as acetonitrile (ACN), at temperatures ranging from -78 °C to rt, to provide a compound of formula (VII) or (VIII).

20

SCHEME 3



According to SCHEME 3, a compound of formula (Xa) is prepared from a compound of formula (IX), where HAL<sup>1</sup> is Cl or Br, by reaction with an amine such as methylamine, benzhydrylamine and the like, with or without a base such as DIPEA, in a solvent such as THF, EtOH, and the like, at temperatures ranging from 0 °C to the reflux temperature of the solvent, for a period of 3 to 24 h to provide a compound of formula (Xa), where R<sup>a</sup> is CH<sub>3</sub> or benzhydryl. Reduction of the nitro compound of formula (Xa), where R<sup>a</sup> is H, CH<sub>3</sub>, or a suitable nitrogen protecting group such as benzhydryl, employing conditions known to one skilled in the art, provides a diamine compound of formula (XI). For example, reduction with zinc in the presence of NH<sub>4</sub>Cl, in a solvent such as acetone/water, for a period of 24 to 72 h; or reduction with Pt/C, aq. H<sub>3</sub>PO<sub>2</sub>, NH<sub>4</sub>VO<sub>3</sub>, under H<sub>2</sub>, at temperatures ranging from 20 to 45 °C, for a period of 1-3 h; or reduction with Na<sub>2</sub>S<sub>2</sub>O<sub>4</sub>, NH<sub>3</sub> in H<sub>2</sub>O, in a solvent such as THF, water, or a mixture thereof, provides a compound of formula (XI), where R<sup>a</sup> is H, CH<sub>3</sub> or benzhydryl and R<sup>c</sup> is H.

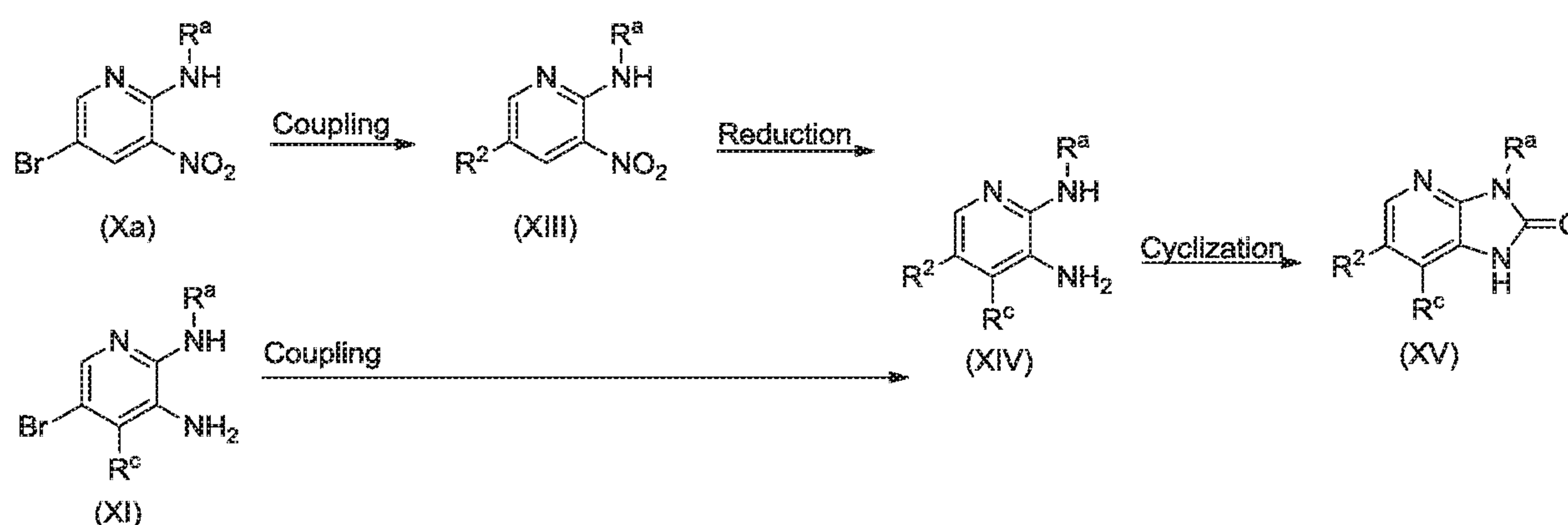
A compound of formula (Xb) is prepared from in two steps from 4-chloro-3-nitropyridin-2-amine. In the first step, 4-chloro-3-nitropyridin-2-amine is halogenated with a halogenating agent such as N-bromosuccinimide (NBS), in a solvent such as ACN, at temperatures ranging from rt to 80 °C. In the second step, 5-bromo-4-chloro-3-nitropyridin-2-amine is protected with a suitable nitrogen protecting group (PG) such as BOC, and the like, under conditions known to one skilled in the art, to provide a compound of formula (Xb).

A compound of formula (XI), where R<sup>a</sup> is CH<sub>3</sub> and R<sup>c</sup> is Cl, is prepared in three steps from a compound of formula (Xb). In the first step, alkylation with an alkylating agent such as MeI, in a solvent such as DMF, THF and the like, at temperatures

ranging from 0 °C to rt, for a period of 3 to 16 h. In the second step, deprotection of the *tert*-butylcarbamate protecting group (PG), is achieved by reaction with an acid such as TFA, in a solvent such as DCM, and the like, at rt. In the third step, reduction of the nitro group employing reduction conditions previously described, affords a compound of formula (XI), where R<sup>a</sup> is CH<sub>3</sub> and R<sup>c</sup> is Cl.

Cyclization of a commercially available or synthetically accessible compound of formula (XI), where R<sup>a</sup> is H; a suitable nitrogen protecting group such as benzhydryl; or CH<sub>3</sub>; and R<sup>c</sup> is H or Cl, in the presence of CDI, in a solvent such as ACN, DMF, THF and the like, at a temperature ranging from 5 °C to 60 °C, for a period of 1-16 h, provides a compound of formula (XII), where R<sup>a</sup> is H, a suitable nitrogen protecting group such as benzhydryl, or CH<sub>3</sub>.

SCHEME 4

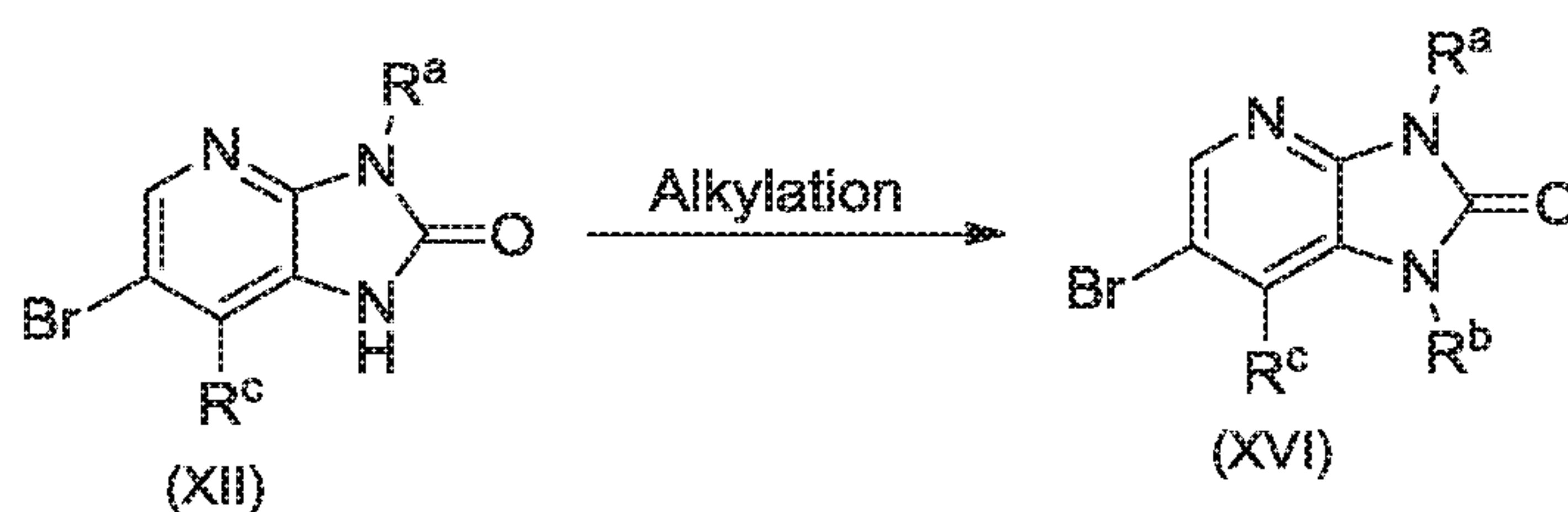


According to SCHEME 4, a compound of formula (Xa), where R<sup>a</sup> is H, CH<sub>3</sub> or a suitable nitrogen protecting group such as BOC, benzhydryl, and the like, is reacted in a metal mediated cross coupling reaction to provide a compound of formula (XIII), where R<sup>2</sup> is a suitably substituted phenyl, pyridinyl, or thienyl. For example, a compound of formula (Xa), where R<sup>a</sup> is H, CH<sub>3</sub>, or BOC, is reacted with a suitably substituted commercially available or synthetically accessible aryl or heteroaryl boronic acid, boronate ester, and the like, in the presence of a palladium catalyst such as PdCl<sub>2</sub>(dtbpf), Pd(PPh<sub>3</sub>)<sub>4</sub>, PdCl<sub>2</sub>(dppf), Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub>, and the like, a base such as K<sub>3</sub>PO<sub>4</sub>, aq. Na<sub>2</sub>CO<sub>3</sub>, Na<sub>2</sub>CO<sub>3</sub>, Cs<sub>2</sub>CO<sub>3</sub>, and the like, in a suitable solvent such as 1,2-dimethoxyethane, 1,4-dioxane, DMF, water, or a mixture thereof, at a temperature ranging from 60 to 180 °C, employing microwave or conventional heating, for a period of

about 30 min to 16 h, to provide a compound of formula (XIII). Reduction of the nitro group, under hydrogenation conditions, for example, Pd/C, in a solvent such as EtOH, and the like, at a temperature ranging from 25-35 °C, under an atmosphere of H<sub>2</sub>, provides a compound of formula (XIV).

5 A compound of formula (XIV) is also prepared from a compound of formula (XI), where R<sup>a</sup> and R<sup>c</sup> are H, employing a metal mediated cross coupling reaction as previously described. Cyclization of a compound of formula (XIV), employing CDI conditions previously described provides a compound of formula (XV).

SCHEME 5

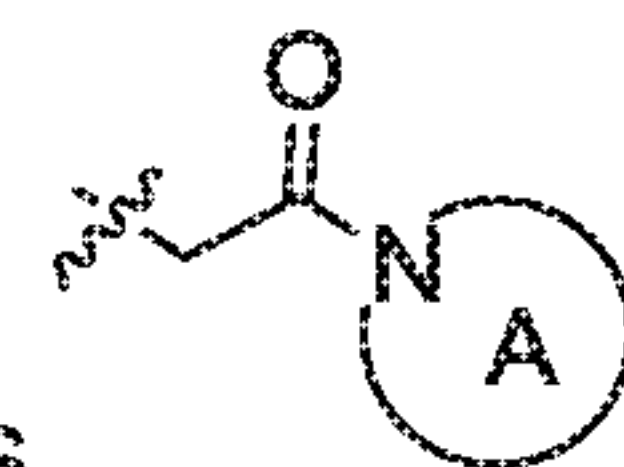


10

According to SCHEME 5, a compound of formula (XII), where R<sup>a</sup> is H, CH<sub>3</sub>, or a suitable nitrogen protecting group such as 4-methoxybenzyl, benzhydryl, trityl, and the like, is alkylated with a suitable alkylating agent, employing a base such as NaH, K<sub>2</sub>CO<sub>3</sub>, Na<sub>2</sub>CO<sub>3</sub>, TEA, and the like, in a suitable solvent such as DMF, ACN, DCM, at  
 15 temperatures ranging from 0 °C to 85 °C, to afford a compound of formula (XVI).

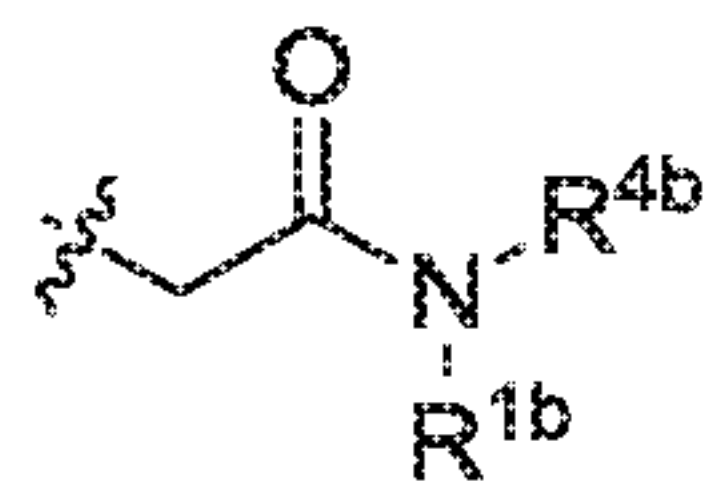
Alkylation with a compound of formula (IV); where Y is Cl, Br or OSO<sub>2</sub>CH<sub>3</sub> and Het<sup>1</sup> is an appropriately substituted heteroaryl, or heterocycloalkyl such as pyridazinyl, pyrimidinyl, pyrazinyl, isoxazolyl, oxadiazolyl, oxetanyl, and the like, affords a compound of formula (XVI), where R<sup>b</sup> is -CH<sub>2</sub>R<sup>4c</sup>.

20 Alkylation with a compound of formula (VII); where Y is Cl, and ring A is a suitably substituted heterocycloalkylamine such as azetidin-1-yl, 3-fluoroazetidin-1-yl, pyrrolidinyl, and the like, affords a compound of formula (XVI), where R<sup>b</sup> is

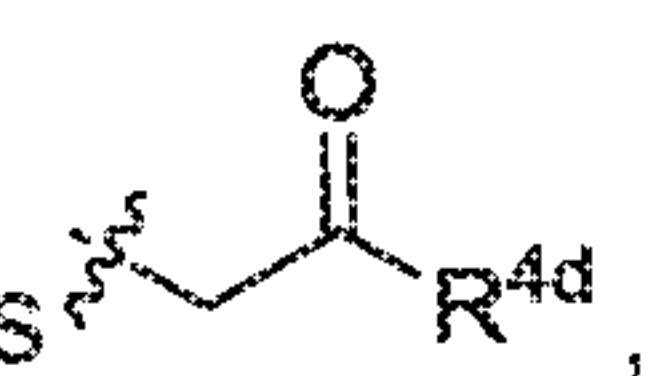


pyrrolidinyl, and the like, affords a compound of formula (XVI), where R<sup>b</sup> is

Alkylation with a compound of formula (VIII); where Y is Cl, R<sup>1b</sup> is H or CH<sub>3</sub>, and R<sup>4b</sup> is as defined in Formula (I) affords a compound of formula (XVI), where R<sup>b</sup> is



Alkylation with 2-bromo-1-cyclopropylethanone, tert-butyl bromoacetate, ethyl

5 bromoacetate, and the like, affords a compound of formula (XVI), where R<sup>b</sup> is , where R<sup>4d</sup> is C<sub>1-6</sub>alkyl, OC<sub>1-6</sub>alkyl, or C<sub>3-6</sub>cycloalkyl. Further reduction of a compound of formula (XVI), where R<sup>4d</sup> is C<sub>1-6</sub>alkyl or C<sub>3-6</sub>cycloalkyl, with a reducing agent such as NaBH<sub>4</sub>, in a suitable solvent such as EtOH, provides a compound of formula (XVI) where R<sup>b</sup> is CH<sub>2</sub>CH(OH)C<sub>1-6</sub>alkyl or CH<sub>2</sub>CH(OH)C<sub>3-6</sub>cycloalkyl. Reduction of a  
10 compound of formula (XVI), where R<sup>4d</sup> is OC<sub>1-6</sub>alkyl, with a reducing agent such as LiBH<sub>4</sub>, provides a compound of formula (XVI), where R<sup>b</sup> is CH<sub>2</sub>CH<sub>2</sub>OH. Subsequent oxidation, employing an oxidizing agent such as Dess-Martin Periodinane, provides a compound of formula (XVI), where R<sup>b</sup> is CH<sub>2</sub>(C=O)H.

A compound of formula (XVI), where R<sup>b</sup> is CH<sub>2</sub>(C=O)H, is reacted under  
15 reductive amination conditions, for example, reaction with a suitably substituted amine such as azetidine, pyrrolidine, piperidine, cyclopropylamine, cyclobutyl amine, ethanolamine, and the like, a reducing agent such as NaBH(OAc)<sub>3</sub>, NaCNBH<sub>3</sub>, NaBH<sub>4</sub>, and the like, in a suitable solvent such as DCM, and the like, for a period of 12-24 h.

Alkylation of a compound of formula (XII) with an alkylating agent such as ethyl  
20 pyridin-2-yl carbonate provides a compound of formula (XVI), where R<sup>a</sup> is H, R<sup>b</sup> is CO<sub>2</sub>Et. Alkylation with 1-bromo-2-methoxyethane provides a compound of formula (XVI), where R<sup>a</sup> is trityl, and R<sup>b</sup> is CH<sub>2</sub>CH<sub>2</sub>OCH<sub>3</sub>.

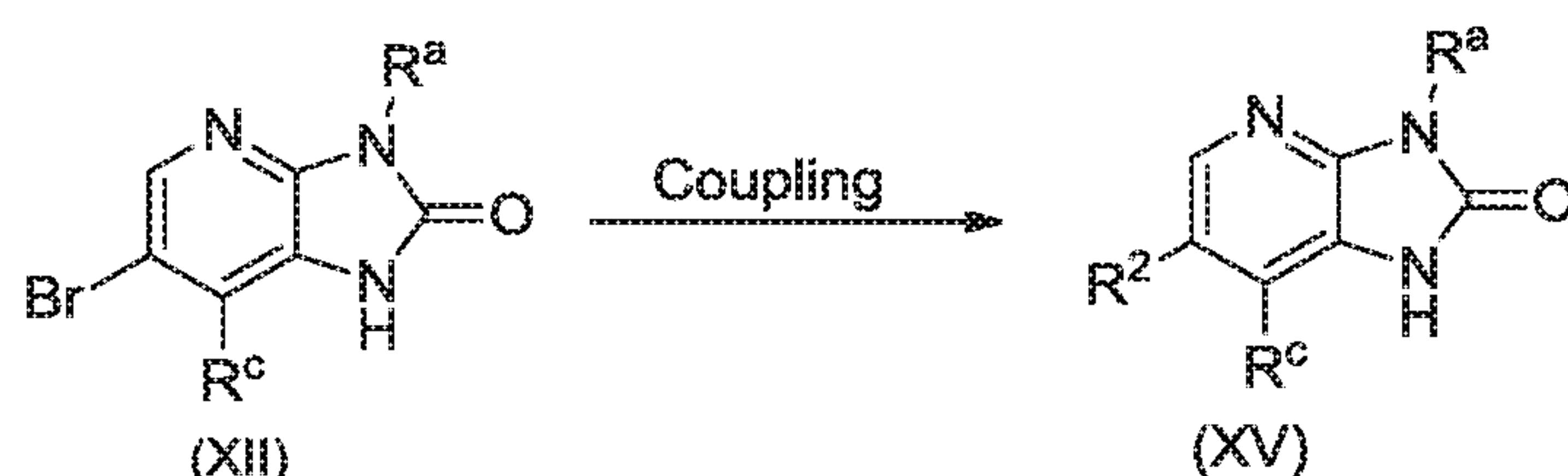
A compound of formula (XVI), where R<sup>a</sup> is H, and R<sup>b</sup> is CO<sub>2</sub>Et, is further alkylated with an alkylating agent such as trityl chloride, under conditions previously described,  
25 for a period of 24-28 h, at rt, to provide a compound of formula (XVI), where R<sup>a</sup> is the trityl protecting group. Subsequent removal of the carboxylate, with isopropylamine, in THF, affords a compound of formula (XVI), where R<sup>a</sup> is trityl and R<sup>b</sup> is H. A compound of

formula (XVI), where  $R^a$  is trityl and  $R^b$  is H, is alkylated under conditions described for SCHEME 5.

A compound of formula (XVI), where  $R^a$  is trityl and  $R^b$  is  $\text{CH}_2\text{CO}_2\text{C}_{1-6}\text{alkyl}$ , is saponified, employing conditions known to one skilled in the art, to provide an acid compound formula (XVI), where  $R^a$  is trityl and  $R^b$  is  $\text{CH}_2\text{CO}_2\text{H}$ .

Deprotection of protecting group on a compound of formula (XVI), where  $R^a$  is benzhydryl, is achieved in TFA, in the presence of thioanisole, at  $80^\circ\text{C}$ , for a period of 1 h, to afford a compound of formula (XVI), where  $R^a$  is H.

SCHEME 7

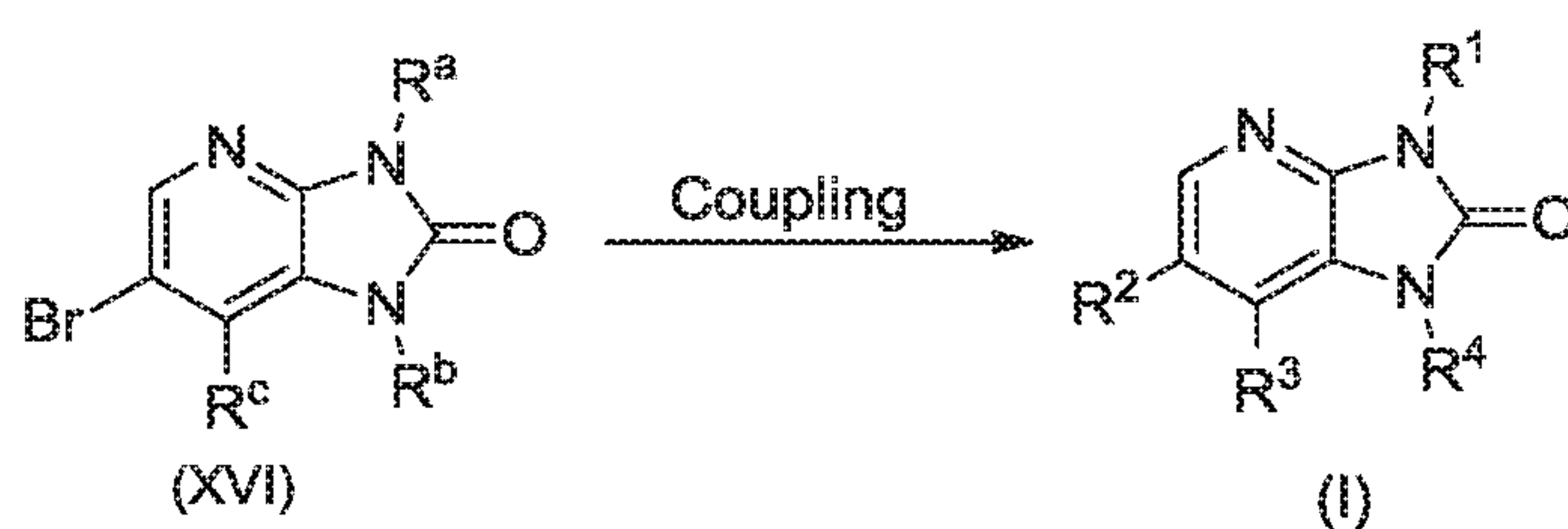


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According to Scheme 7, a compound of formula (XII), where  $R^a$  is a suitable nitrogen protecting group such as 4-methoxybenzyl, trityl, and the like, is coupled in a metal mediated cross coupling reaction using conditions previously described, to provide a compound of formula (XV), where  $R^2$  is a suitably substituted phenyl or pyridyl.

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SCHEME 8



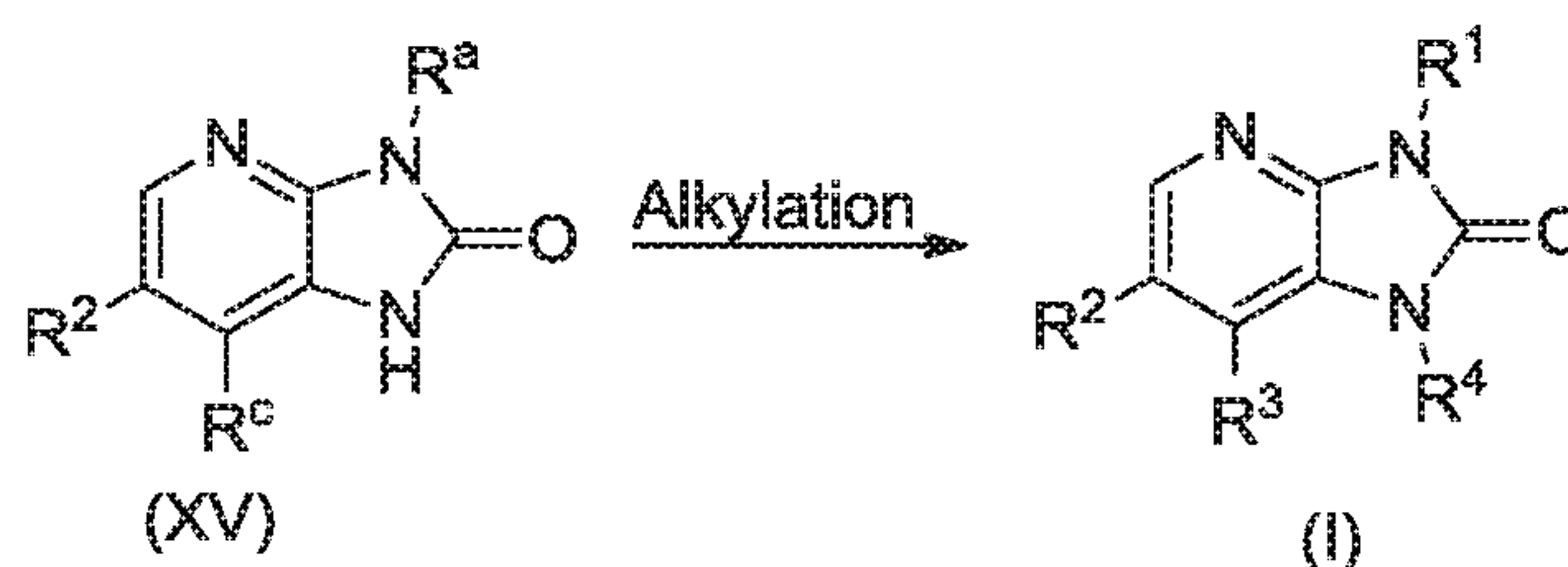
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According to SCHEME 8, a compound of formula (XVI), where  $R^a$  is H,  $\text{CH}_3$ , or a suitable nitrogen protecting group such as trityl, is reacted in a metal mediated cross coupling reaction with a commercially available or synthetically accessible boronic acid or boronate ester, as previously described to provide a compound of Formula (I), where  $R^2$  is suitably substituted phenyl, pyridinyl or thienyl. Boronate esters are also prepared *in-situ*, under conditions known to one skilled in the art, in a one pot coupling reaction.

When  $R^a$  is a protecting group such as trityl, a deprotection step, employing an acid such as TFA, in a solvent such as DCM, provides a compound of Formula (I), where  $R^1$  is H.

A compound of Formula (I) is also prepared from a compound of formula (XVI) in two steps. In a first step, a compound of formula (XVI) is converted into the boronate ester, by reaction with bis(pinacolato)diboron, KOAc, and  $\text{PdCl}_2(\text{dppf})$ , in a suitable solvent such as 1,4-dioxane, at a temperature of about 130 °C, for period of about 2 h. In a second step, the boronate ester is reacted in a metal mediated cross coupling reaction, as previously described, with suitably substituted phenyl, to provide a compound of Formula (I).

SCHEME 9



According to SCHEME 9, a compound of Formula (I), is prepared from a compound of formula (XV). A compound of formula (XV) where  $R^a$  is H,  $\text{CH}_3$ , or a protecting group such as 4-methoxybenzyl or trityl,  $R^c$  is H, and  $R^2$  is a suitably substituted phenyl or thienyl, is alkylated according to methods described in SCHEME 5. For example, alkylation with an electrophile such as ethyl 2-bromoacetate, tert-butyl 2-bromoacetate, 2-(chloromethyl)pyridine, 3-(chloromethyl)-5-methylisoxazole, 2-(chloromethyl)-5-methyl-1,3,4-oxadiazole, 1-(bromomethyl)-3-chlorobenzene, pyrimidin-4-ylmethyl methanesulfonate, 2-bromo-1-cyclopropylethanone, and the like, a base such as NaH,  $\text{K}_2\text{CO}_3$ , and the like, in a suitable solvent such as ACN, DMF, and the like, at temperatures ranging from 0 to 85 °C, provides a compound of Formula (I), where  $R^4$  is  $\text{CH}_2\text{CO}_2\text{C}_{1-6}\text{alkyl}$ ,  $\text{CH}_2\text{pyridine}$ , and the like. Where  $R^a$  is a protecting group such as 4-methoxybenzyl, or trityl, a deprotection step is employed to provide a compound of Formula (I), where  $R^1$  is H.

A compound of formula (XII) is reacted under Mitsunobu conditions to form a compound of Formula (I), where  $R^4$  is  $\text{CH}_2\text{-R}^{4c}$ , where  $\text{R}^{4c}$  is pyrimidinyl. For example,

a compound of formula (XII), where  $R^2$  is a suitably substituted phenyl or thienyl,  $R^a$  is  $CH_3$ , and  $R^c$  is H, is reacted with a compound of formula (III), where Het<sup>1</sup> is pyrimidinyl, using triphenylphosphine and di-*tert*-butyl azodicarboxylate, in a solvent such as ACN, and the like, at a temperature ranging from 90 to 110 °C, to provide a compound of

5 Formula (I), where  $R^4$  is  $CH_2-R^{4c}$ , where  $R^{4c}$  is pyrimidinyl,  $R^1$  is  $CH_3$  and  $R^2$  is H.

Saponification of an ester compound of Formula (I) under basic conditions such as LiOH, and the like, in a solvent such as THF and water, at a temperature of about rt, affords a compound of Formula (I), where  $R^4$  is  $CH_2CO_2H$ .

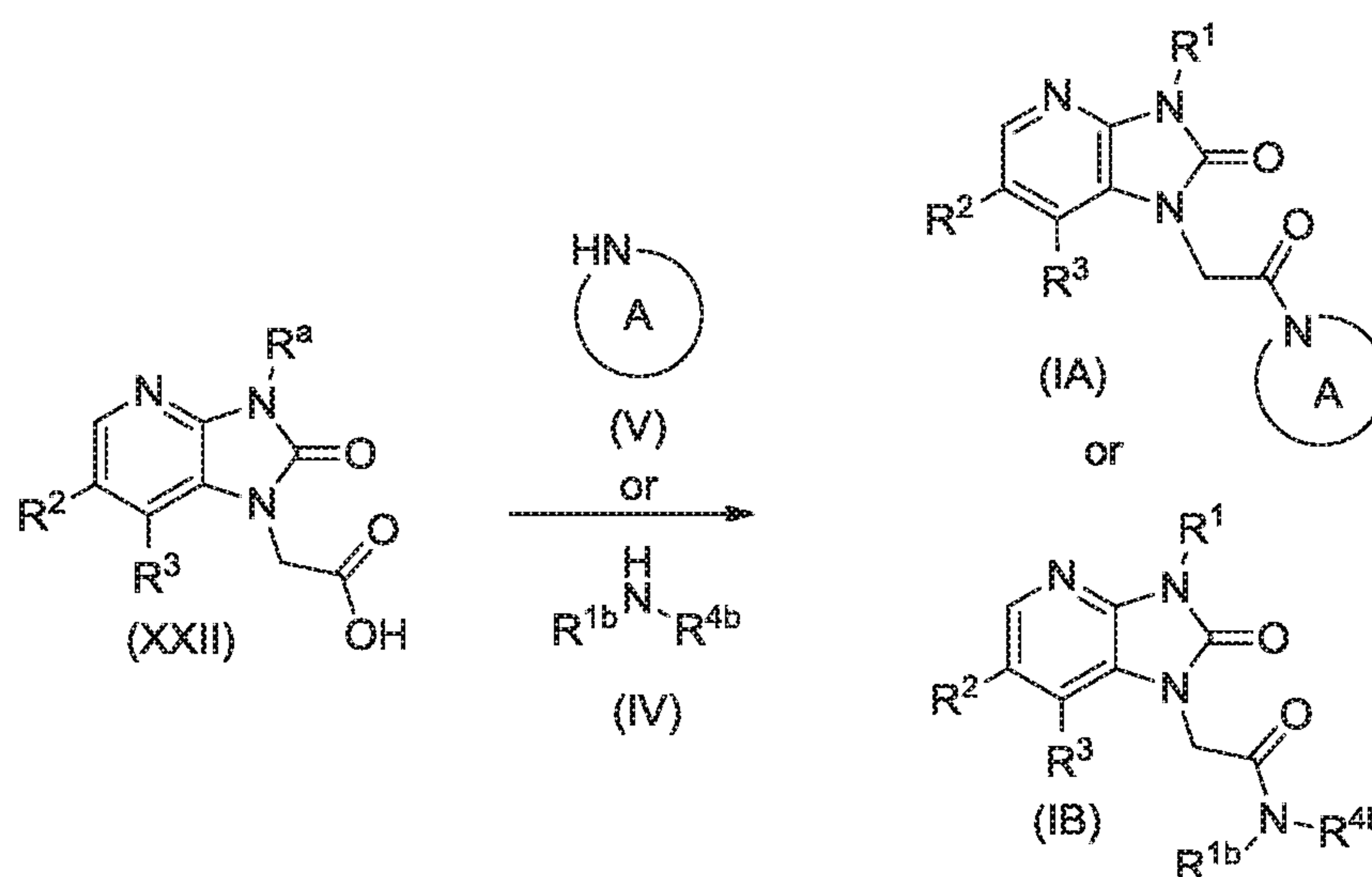
Alkylation of a compound of Formula (I), where  $R^1$  is H, with a base such as NaH, an alkylating agent such as MeI, in a suitable solvent such as DMF, affords a compound of Formula (I) where  $R^1$  is  $CH_3$ .

10

Reduction of a compound of Formula (I), where  $R^1$  is H,  $R^2$  is a suitably substituted phenyl or thienyl,  $R^3$  is H and  $R^4$  is  $CH_2C(=O)cyclopropyl$ ,  $CH_2C(=O)C_{1-6}alkyl$ , and the like, using a reducing agent such as  $NaBH_4$ , in a suitable solvent such as MeOH, provides a compound of Formula (I), where  $R^4$  is  $C_{1-6}alkyl$  substituted with one or two members independently selected from OH or cyclopropyl.

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SCHEME 10

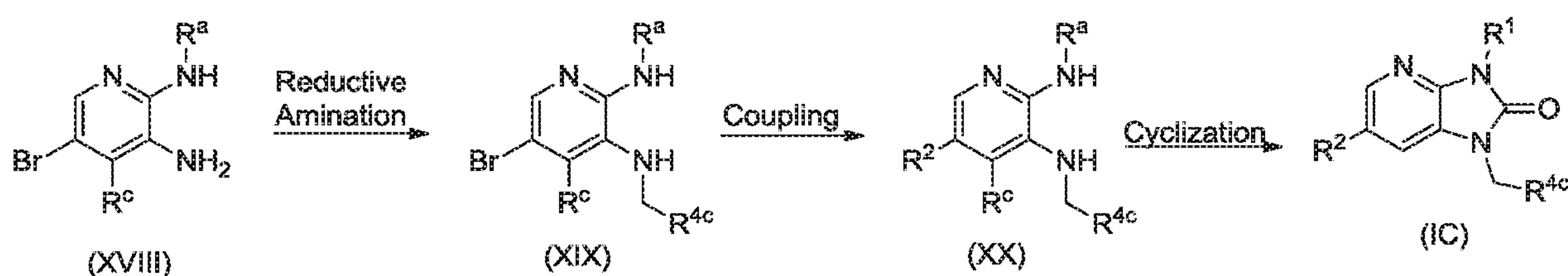


According to SCHEME 10, a compound of Formula (IA) or (IB), where  $R^a$  is H,  $CH_3$ , or a suitable nitrogen protecting group such as trityl, and  $R^2$  is a suitably substituted phenyl or thienyl, is prepared by conventional amide bond forming techniques such as coupling reactions which are well known to those skilled in the art.

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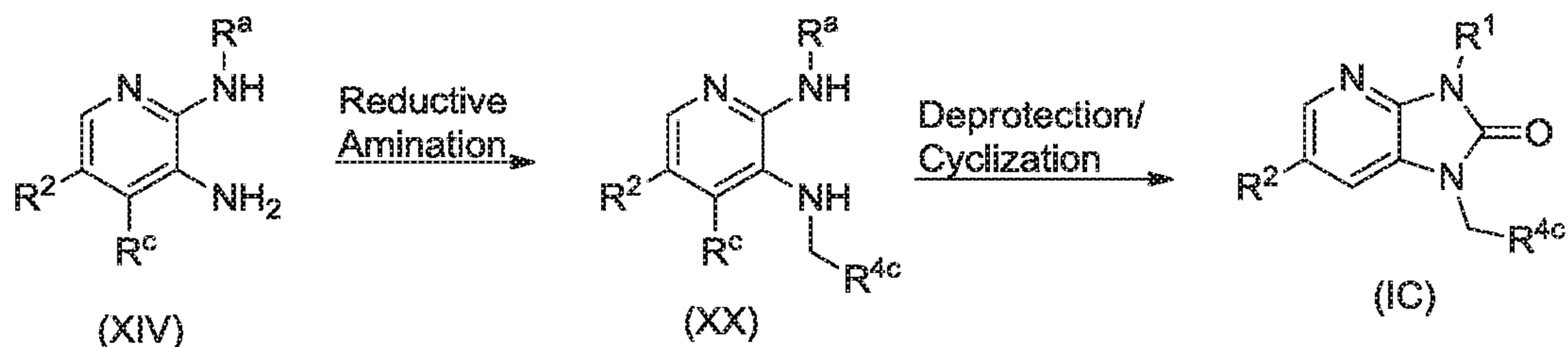
For example, reaction of a suitably substituted heterocycloalkyl amine of formula (V) or amine of formula (IV) where  $R^{1b}$  is H or  $CH_3$  and  $R^{4b}$  is  $C_{1-6}$ alkyl,  $C_{3-6}$ cycloalkyl, with an acid compound of formula (XXII), where the acid is activated with an appropriate activating reagent, for example a carbodiimide, such as DCC or EDCI optionally in the presence of HOBt and/or a catalyst such as DMAP; a halotrisaminophosphonium salt such as BOP, or PyBroP; a suitable pyridinium salt such as 2-chloro-1-methylpyridinium chloride; or another suitable coupling agent such as HBTU, HATU, 2,4,6-tripropyl-1,3,5,2,4,6-trioxatriphosphorinane-2,4,6-trioxide (T3P®) and the like. Coupling reactions are conducted in a suitable solvent such as DCM, THF, DMF and the like, optionally in the presence of a tertiary amine such as N-methylmorpholine, N-ethyldiisopropylamine (DIEA, DIPEA), or triethylamine (TEA), at a temperature ranging from about 0 °C to rt, to provide compound a of Formula (IA) or Formula (IB). Deprotection, in instances where  $R^a$  is a protecting group, employing conditions known to one skilled in the art provides a compound of Formula (IA) or Formula (IB).

SCHEME 11



According to SCHEME 11, a compound of formula (XVIII) where  $R^a$  and  $R^c$  are H, is reacted under a two step reductive amination reaction, with a suitably substituted aldehyde such as 5-methylisoxazole-3-carbaldehyde. In a first step, the imine is formed by reaction of the aldehyde with an amine compound of formula (XVIII), in the presence of molecular sieves, at a temperature of about 70 °C, for a period of 16-24 h. In a second step, reduction of the imine, with a reducing agent such as  $NaBH_4$ , in a suitable solvent such as EtOH, and the like, provides a compound of formula (XIX), where  $R^{4c}$  is a suitably substituted heteroaryl such as 5-methylisoxazole. Coupling of a compound of formula (XIX), under conditions previously described provides a compound of formula (XX). Cyclization of a compound of formula (XX), under conditions previously described, such as reaction with CDI, provides a compound of Formula (IC).

SCHEME 12



According to SCHEME 12, an amine compound of formula (XIV), where  $R^a$  is a protecting group such as BOC, and  $R^c$  is H, and  $R^2$  is an appropriately substituted phenyl, is reacted under reductive amination conditions with an aldehyde such as 1,5-dimethyl-1h-pyrazole-3-carbaldehyde, AcOH, in a solvent such as DCE, and a reducing agent such as  $\text{NaBH}(\text{OAc})_3$ , to provide a compound of formula (XX). Deprotection of a compound of formula (XX), where  $R^a$  is BOC, and  $R^c$  is H, with an acid such as TFA, in a solvent such as DCM, at room temperature, afforded the cyclized compound of Formula (IC).

A compound of formula (XXI), where  $R^a$  is H, and  $R^{4c}$  is 5-methylisoxazol-3-yl, and the like, is cyclized under CDI conditions previously described, to provide a compound of Formula (IC).

Compounds of Formula (I) may be converted to their corresponding salts using methods known to one of ordinary skill in the art. For example, an amine of Formula (I) is treated with trifluoroacetic acid, HCl, or citric acid in a solvent such as  $\text{Et}_2\text{O}$ ,  $\text{CH}_2\text{Cl}_2$ , THF, MeOH, chloroform, or isopropanol to provide the corresponding salt form. Alternately, trifluoroacetic acid or formic acid salts are obtained as a result of reverse phase HPLC purification conditions. Crystalline forms of pharmaceutically acceptable salts of compounds of Formula (I) may be obtained in crystalline form by recrystallization from polar solvents (including mixtures of polar solvents and aqueous mixtures of polar solvents) or from non-polar solvents (including mixtures of non-polar solvents).

Where the compounds according to this invention have at least one chiral center, they may accordingly exist as enantiomers. Where the compounds possess two or more chiral centers, they may additionally exist as diastereomers. It is to be understood that all such isomers and mixtures thereof are encompassed within the scope of the present invention.

Compounds prepared according to the schemes described above may be obtained as single forms, such as single enantiomers, by form-specific synthesis, or by resolution. Compounds prepared according to the schemes above may alternately be obtained as mixtures of various forms, such as racemic (1:1) or non-racemic (not 1:1) mixtures. Where racemic and non-racemic mixtures of enantiomers are obtained, single enantiomers may be isolated using conventional separation methods known to one of ordinary skill in the art, such as chiral chromatography, recrystallization, diastereomeric salt formation, derivatization into diastereomeric adducts, biotransformation, or enzymatic transformation. Where regioisomeric or diastereomeric mixtures are obtained, as applicable, single isomers may be separated using conventional methods such as chromatography or crystallization.

The following specific examples are provided to further illustrate the invention and various preferred embodiments.

## EXAMPLES

In obtaining the compounds described in the examples below and the corresponding analytical data, the following experimental and analytical protocols were followed unless otherwise indicated.

Unless otherwise stated, reaction mixtures were magnetically stirred at room temperature (rt) under a nitrogen atmosphere. Where solutions were "dried," they were generally dried over a drying agent such as Na<sub>2</sub>SO<sub>4</sub> or MgSO<sub>4</sub>. Where mixtures, solutions, and extracts were "concentrated", they were typically concentrated on a rotary evaporator under reduced pressure. Reactions under microwave irradiation conditions were carried out in a Biotage Initiator or CEM (Microwave Reactor) Discover instrument.

For the reactions conducted under continuous flow conditions, "flowed through a LTF-VS mixer" refers to the use of a Chemyx Fusion 100 Touch Syringe Pump that is in line via 1/16" PTFE tubing to a LTF-VS mixer (Little Things Factory GmbH (<http://www.ltf-gmbh.com>), unless otherwise indicated.

Normal-phase silica gel chromatography (FCC) was performed on silica gel (SiO<sub>2</sub>) using prepacked cartridges.

Preparative reverse-phase high performance liquid chromatography (RP HPLC) was performed on either:

METHOD A. An Agilent HPLC with an Xterra Prep RP18 column (5  $\mu$ M, 30 x 100 or 50 x 150mm) or an XBridge C18 OBD column (5  $\mu$ M, 30 x 100 or 50 x 150mm), and a mobile phase of 5% ACN in 20mM NH<sub>4</sub>OH was held for 2 min, then a gradient of 5-99% ACN over 15 min, then held at 99% ACN for 5 min, with a flow rate of 40 or 80 mL/min.

or

METHOD B. A Shimadzu LC-8A Series HPLC with an Inertsil ODS-3 column (3  $\mu$ m, 30 x 100mm, T = 45 °C), mobile phase of 5% ACN in H<sub>2</sub>O (both with 0.05% TFA) was held for 1 min, then a gradient of 5-99% ACN over 6 min, then held at 99% ACN for 3 min, with a flow rate of 80 mL/min.

or

METHOD C. A Shimadzu LC-8A Series HPLC with an XBridge C18 OBD column (5  $\mu$ m, 50 x 100mm), mobile phase of 5% ACN in H<sub>2</sub>O (both with 0.05% TFA) was held for 1 min, then a gradient of 5-99% ACN over 14 min, then held at 99% ACN for 10 min, with a flow rate of 80 mL/min.

or

METHOD D. A Gilson HPLC with an XBridge C18 column (5 $\mu$ m, 100 x 50mm), mobile phase of 5-99% ACN in 20 mM NH<sub>4</sub>OH over 10 min and then hold at 99 ACN for 2 min, at a flow rate of 80 mL/min.

Preparative supercritical fluid high performance liquid chromatography (SFC) was performed either on a Jasco preparative SFC system, an APS 1010 system from Berger instruments, or a SFC-PICLAB-PREP 200 (PIC SOLUTION, Avignon, France). The separations were conducted at 100 to 150 bar with a flow rate ranging from 40 to 60 mL/min. The column was heated to 35 to 40 °C.

Mass spectra (MS) were obtained on an Agilent series 1100 MSD using electrospray ionization (ESI) in positive mode unless otherwise indicated. Calculated (calcd.) mass corresponds to the exact mass.

Nuclear magnetic resonance (NMR) spectra were obtained on Bruker model DRX spectrometers. Definitions for multiplicity are as follows: s = singlet, d = doublet, t =

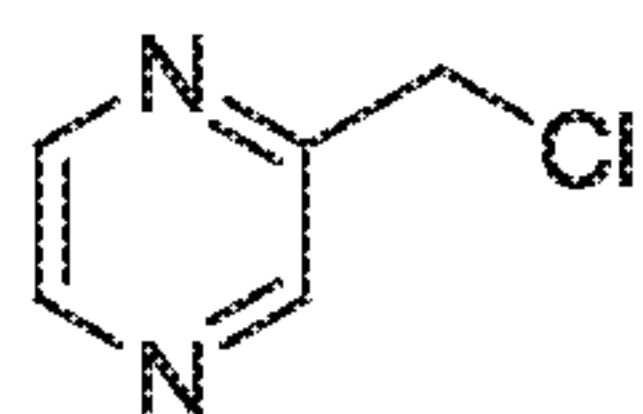
triplet, q = quartet, m = multiplet, br = broad. It will be understood that for compounds comprising an exchangeable proton, said proton may or may not be visible on an NMR spectrum depending on the choice of solvent used for running the NMR spectrum and the concentration of the compound in the solution.

5 Chemical names were generated using ChemDraw Ultra 12.0, ChemDraw Ultra 14.0 (CambridgeSoft Corp., Cambridge, MA) or ACD/Name Version 10.01 (Advanced Chemistry).

Compounds designated as R\* or S\* are enantiopure compounds where the absolute configuration was not determined.

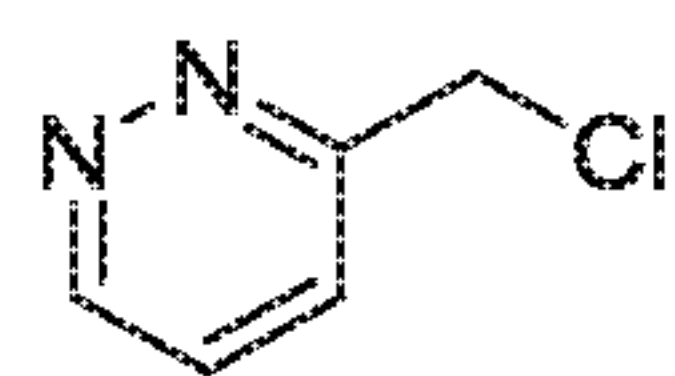
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Intermediate 1: 2-(Chloromethyl)pyrazine.



To a solution of 2-pyrazinylmethanol (500 mg, 4.54 mmol) in DCM (15 mL) at 0 °C was added thionyl chloride (0.66 mL, 9.1 mmol). The reaction mixture was stirred at 0 °C for 3 h. The reaction mixture was concentrated in vacuo. The crude reaction mixture was trituated with Et<sub>2</sub>O to yield the title compound as a black solid (749 mg, 4.54 mmol, 99.9%), which was used without further purification. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 4.87 (s, 2 H), 8.63 - 8.69 (m, 2 H), 8.82 (d, *J* = 1.39 Hz, 1 H).

20 Intermediate 2: 3-(Chloromethyl)pyridazine hydrochloride.

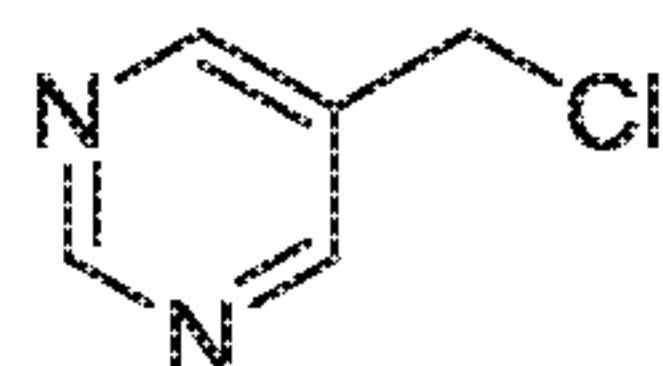


Method A: 3-(Chloromethyl)pyridazine hydrochloride. The title compound was prepared in a manner analogous to Intermediate 1. MS (ESI): mass calcd. for C<sub>5</sub>H<sub>5</sub>ClN<sub>2</sub>, 128.0; *m/z* found, 129.0 [M+H]<sup>+</sup>.

25 Method B: 3-(Chloromethyl)pyridazine. Trichloroisocyanuric acid (148 mg, 0.6 mmol) was added in portions to a mixture of 3-methylpyridazine (145 μL, 1.6 mmol) in CHCl<sub>3</sub> at reflux. The mixture was stirred at reflux overnight. After cooling, the mixture was filtered, and the filtrate was diluted with DCM, washed with an aqueous solution of 1M NaOH followed by brine, dried (MgSO<sub>4</sub>) and concentrated under reduced pressure to yield title

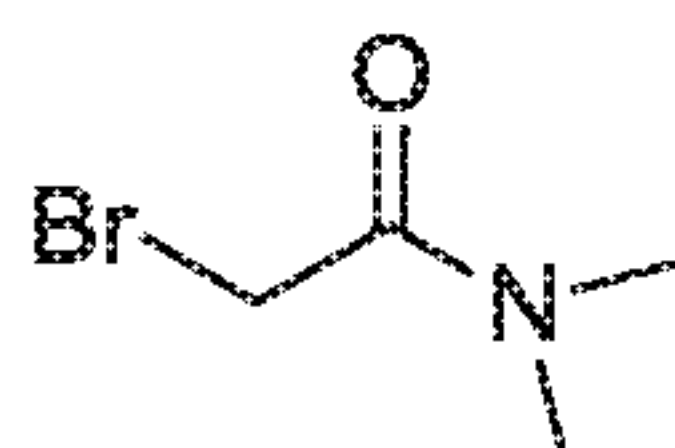
compound (205 mg, 80%). MS (ESI): mass calcd. for  $C_5H_5ClN_2$ , 128.0;  $m/z$  found, 129  $[M+H]^+$ .

Intermediate 3: 5-(Chloromethyl)pyrimidine hydrochloride.



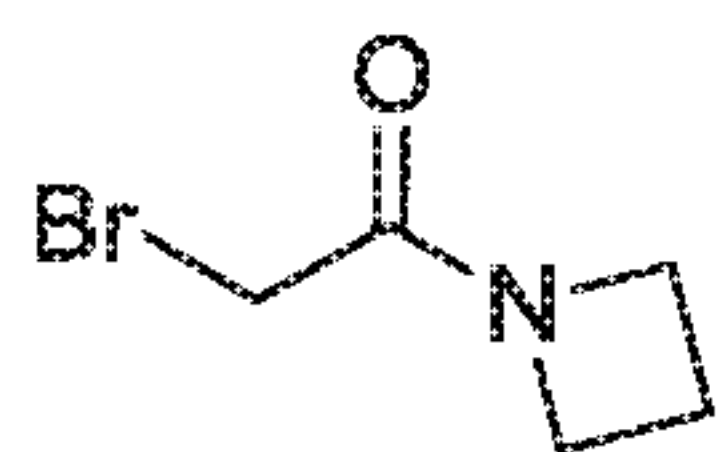
The title compound was prepared in a manner analogous to Intermediate 1.  $^1H$  NMR (400 MHz,  $DMSO-d_6$ )  $\delta$  4.85 (s, 2 H) 8.90 (s, 2 H) 9.16 (s, 1 H).

Intermediate 4: 2-Bromo-N,N-dimethylacetamide.



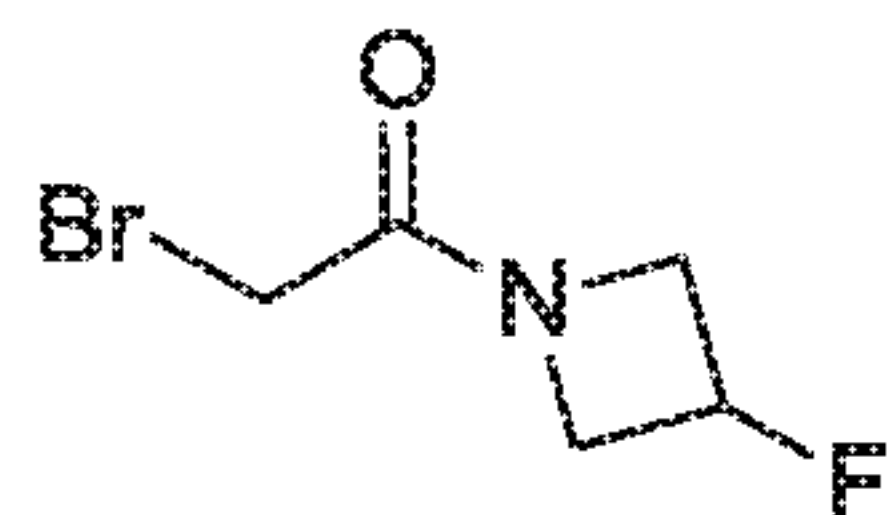
Under an atmosphere of nitrogen, 2-bromoacetyl chloride (1.3 mL, 16 mmol) was added to a mixture of TEA (2.2 mL, 16 mmol) and dimethylamine (8 mL, 16 mmol) in MeCN (20 mL) at  $-78^\circ C$ . The stirred reaction mixture was then allowed to slowly warm to room temperature. After stirring for 2 hours, water was added (30 mL) and the mixture was extracted with DCM (3 x 40 mL). The combined organic layers were dried, and concentrated under vacuum to afford the desired product (2.03 g, 76%) which was carried forward as crude material. MS (ESI): mass calcd. for  $C_4H_8BrNO$ , 166.1.  $^1H$  NMR (500 MHz,  $DMSO-d_6$ )  $\delta$  4.35 (s, 2H), 2.99 (s, 3H), 2.85 (s, 3H).

Intermediate 5: 1-(Azetidin-1-yl)-2-bromoethan-1-one.



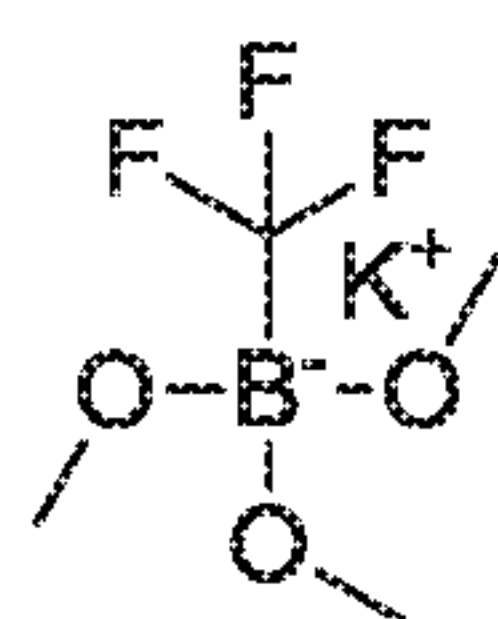
The title compound was prepared in a manner analogous to 2-bromo-N,N-dimethylacetamide (Intermediate 4), using azetidine. MS (ESI): mass calcd. for  $C_5H_8BrNO$ , 178.1.  $^1H$  NMR (500 MHz,  $CDCl_3$ )  $\delta$  4.35 – 4.29 (m, 2H), 4.14 – 4.09 (m, 2H), 3.91 – 3.88 (s, 2H), 2.38 – 2.31 (m, 2H).

Intermediate 6: 2-Bromo-1-(3-fluoroazetidin-1-yl)ethan-1-one.



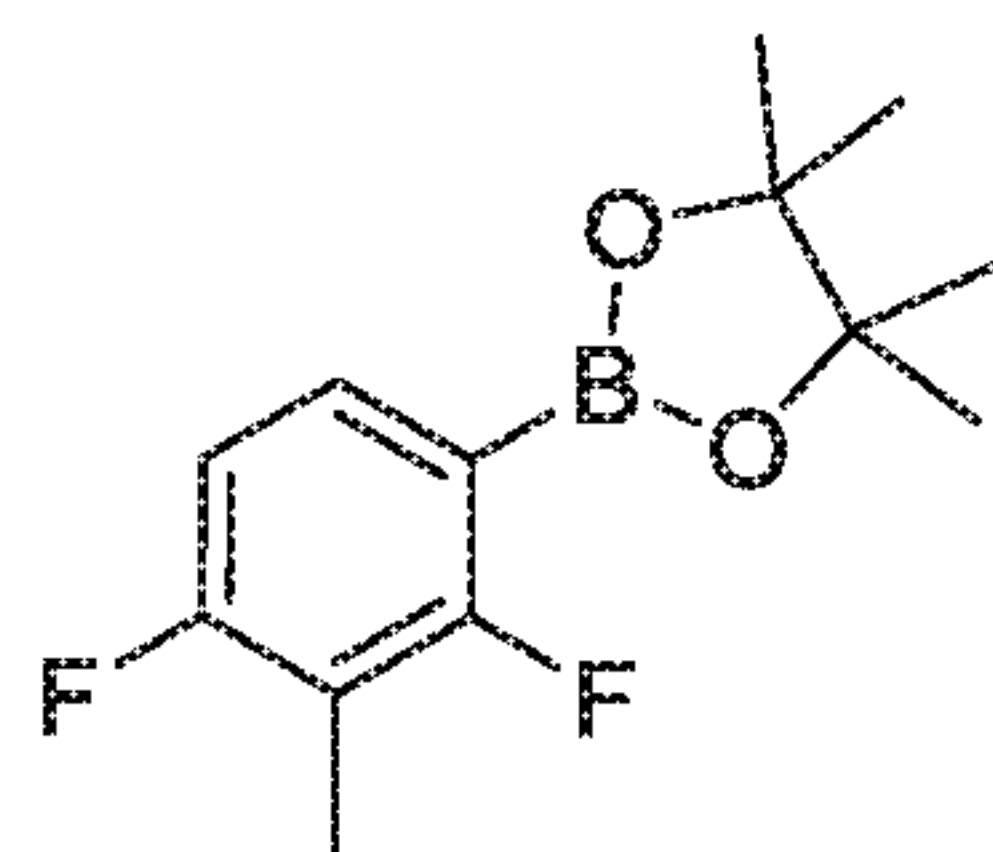
The title compound was prepared in a manner analogous to 2-bromo-N,N-dimethylacetamide (Intermediate 4) using 3-fluoroazetidine.HCl. MS (ESI): mass calcd. for C<sub>5</sub>H<sub>7</sub>BrFNO, 196.1. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 5.50 – 5.29 (m, 1H), 4.57 – 4.45 (m, 1H), 4.32 – 4.14 (m, 2H), 4.01 – 3.86 (m, 3H).

Intermediate 7: Potassium trimethoxy(trifluoromethyl)borate.



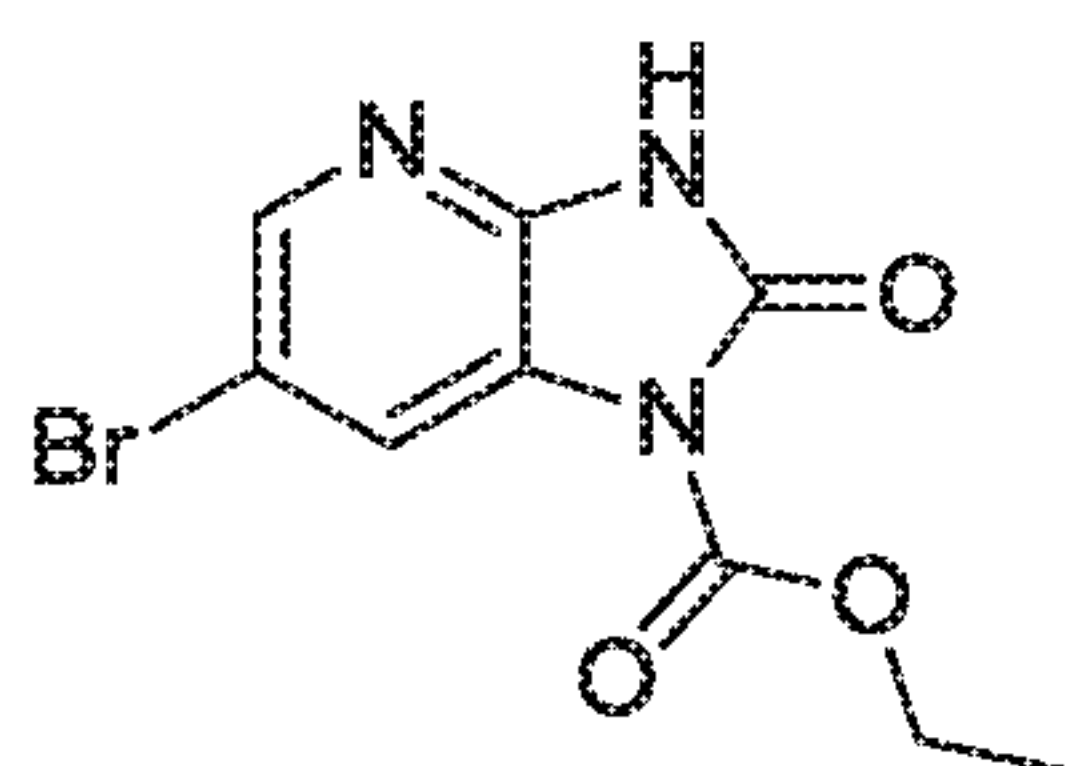
To a three-necked round-bottom flask equipped with a thermometer and nitrogen inlet/outlet adapter were added KF (1000 g, 17.2 mol, 1.0 equiv.) and anhydrous THF (15 L). The mixture was stirred at 23±2°C under a nitrogen flow. B(OMe)<sub>3</sub> (1860 g, 17.9 mol, 1.04 equiv.) was added to the mixture while a slight temperature drop was observed. F<sub>3</sub>CTMS (2690 g, 18.9 mol, 1.1 equiv.) was added to the mixture while a slight temperature drop was observed. The mixture was stirred at 23±2°C for 20 hours under a nitrogen flow until the solid was completely dissolved. The resulting mixture was concentrated to 6L under reduced pressure, then hexane 12L was added to the mixture and the mixture was stirred for 20 min. The precipitated solid was collected by filtration followed by washing with hexane 2L×2. The wet solid was dried under vacuum to give the title compound (3840 g, 94.5%). <sup>1</sup>H NMR (400 MHz, D<sub>2</sub>O) 3.22 (s, 9H). <sup>19</sup>F NMR (376 MHz, D<sub>2</sub>O) δ -74.83 (dd, *J* = 59.1, 28.5 Hz).

Intermediate 8: 2-(2,4-difluoro-3-methylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.



To a solution a 3-bromo-2,6-difluorotoluene (0.95 mL, 7.2 mmol), 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi-1,3,2-dioxaborolane (3.68 g, 14.5 mmol) and KOAc (1.07 g, 10.9 mmol) in 1,4-dioxane (38 mL) was added PdCl<sub>2</sub>(dppf) (265 mg, 0.362 mmol). The reaction mixture was stirred at 120 °C for 16 h. Then, the crude reaction mixture was cooled, filtered through Celite® and concentrated in vacuo. The crude product was purified (FCC, SiO<sub>2</sub>, 0 -20% EtOAc in hexanes) to yield the title compound (1.8 g, 98%).

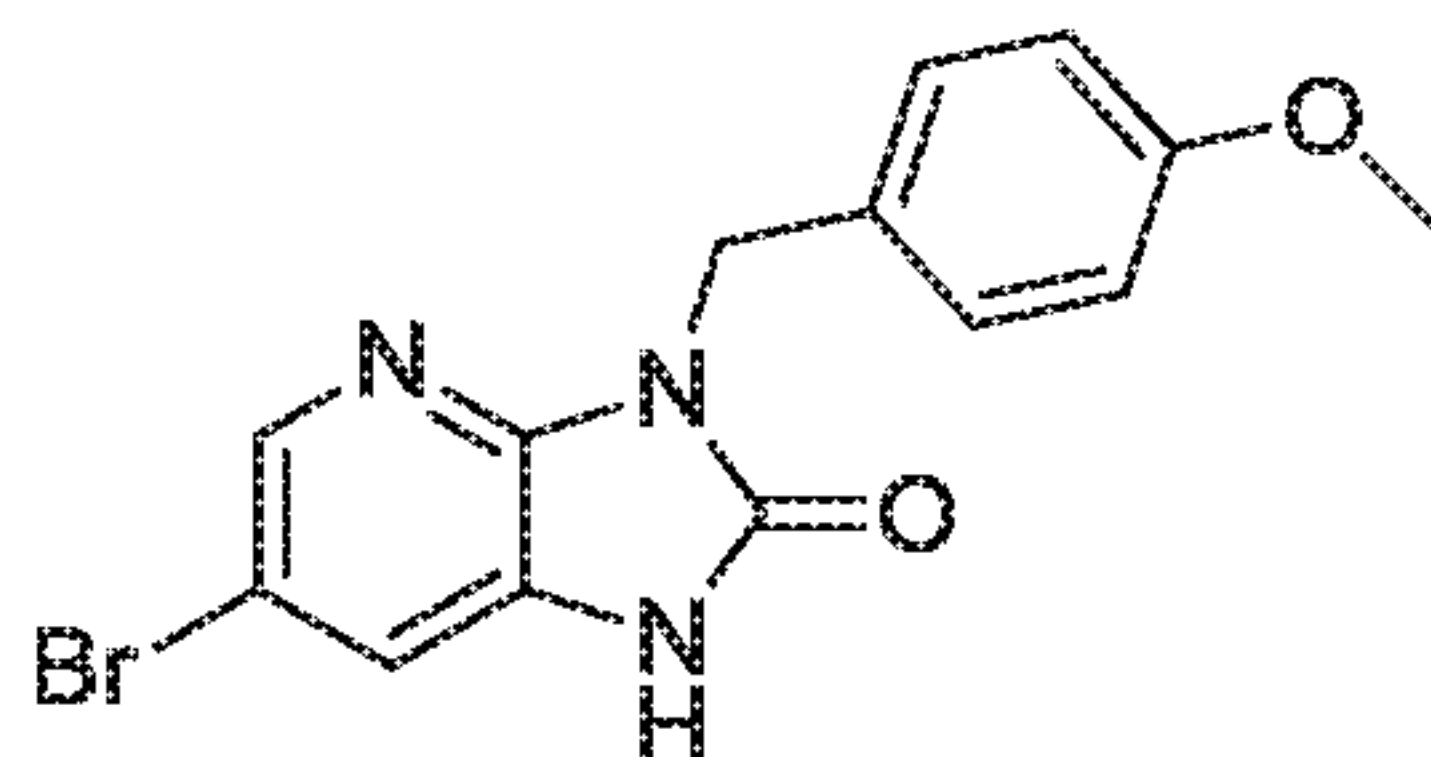
Intermediate 9: Ethyl 6-bromo-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridine-1-carboxylate.



Step A: 6-Bromo-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. To a solution of 2,3-diamino-5-bromopyridine (5 g, 27 mmol) in THF (87 mL) was added CDI (3.02 g, 18.6 mmol), and the reaction mixture was stirred at 80 °C for 16 h. Then, water was added, and the mixture was filtered. The solids were collected by filtration, washed with water and Et<sub>2</sub>O, and dried under vacuum to afford the title compound (5.3 g, 25 mmol, 93%), which was used in the next step without further purification. MS (ESI): mass calcd. for C<sub>6</sub>H<sub>4</sub>BrN<sub>3</sub>O, 212.95; m/z found, 214 [M+H]<sup>+</sup>.

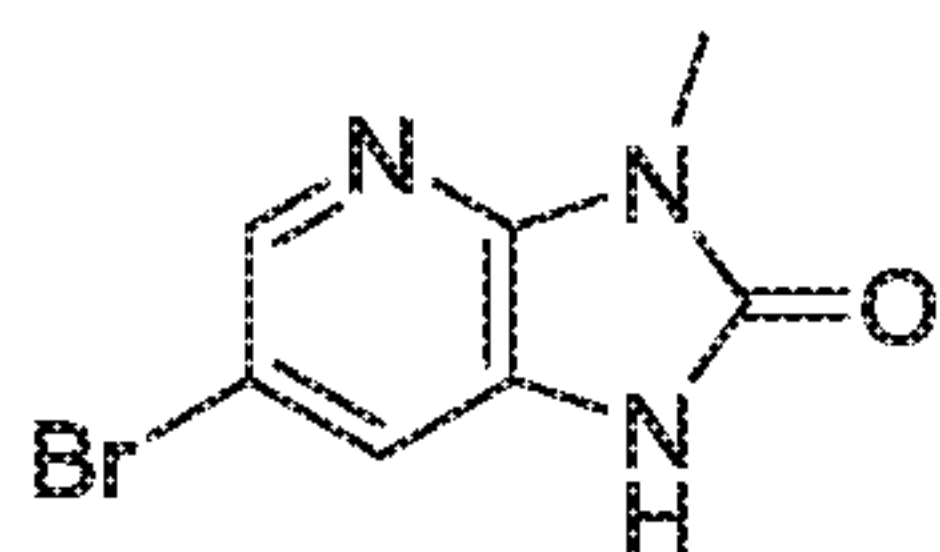
Step B: Ethyl 6-bromo-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridine-1-carboxylate. A mixture of 6-bromo-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (5.3 g, 25 mmol), ethyl pyridin-2-yl carbonate (5.36 g, 27.2 mmol) and K<sub>2</sub>CO<sub>3</sub> (3.77 g, 27.2 mmol) in DMF (245 mL) was heated to 75 °C for 3 h. The crude reaction mixture was concentrated in vacuo and diluted with water and 1 M HCl until the mixture reached pH 1. The solution was filtered and triturated with Et<sub>2</sub>O to afford the title compound (6.6 g, 23 mmol, 93%), which was used in the next step without further purification. MS (ESI): mass calcd. for C<sub>9</sub>H<sub>8</sub>BrN<sub>3</sub>O<sub>3</sub>, 284.97; m/z found, 286 [M+H]<sup>+</sup>.

Intermediate 10: 6-Bromo-3-(4-methoxybenzyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one.



To a solution of ethyl 6-bromo-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridine-1-carboxylate (11.48 g, 40.21 mmol), and  $K_2CO_3$  (6.65 g, 48.1 mmol), in DMF (120 mL) was added 4-methoxybenzylchloride (6.01 mL, 44.1 mmol) dropwise. The reaction mixture was heated to 50 °C for 6 h. The reaction mixture was cooled to rt, and isopropylamine (3.4 mL, 40.1 mmol) was added, the reaction mixture was stirred at rt for 1 h. Water and EtOAc were added. The organic layer was separated, dried ( $MgSO_4$ ), filtered and concentrated under reduced pressure. Purification (FCC,  $SiO_2$ , EtOAc in DCM from 0% to 35%) afforded the title compound as a cream solid. Trituration with  $Et_2O$  to afforded the title compound (6.9 g, 51%). MS (ESI): m/z found  $[M+H] = 334$ .

Intermediate 11: 6-Bromo-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.



Method A:

Step A: 5-Bromo-N-methyl-3-nitropyridin-2-amine. To a solution of 5-bromo-2-chloro-3-nitropyridine (15 g, 63 mmol) in THF (570 mL) at 0 °C was added a solution of methylamine (40% in  $H_2O$ , 10.9 mL, 126 mmol). The reaction mixture was stirred at room temperature for 16 h. Upon completion, the reaction mixture was extracted with EtOAc (3 x 500 mL). The combined organic layers were dried ( $Na_2SO_4$ ), filtered and concentrated under reduced pressure to yield the title compound as a yellow solid (14.6 g, 62.7 mmol, 99%), which was used in the next step without further purification. MS (ESI): mass calcd. for  $C_6H_5BrN_3O_2$ , 230.96; m/z found, 232  $[M+H]^+$ .  $^1H$  NMR (500 MHz,  $DMSO-d_6$ )  $\delta$  8.54 (d,  $J = 2.3$  Hz, 1H), 8.46 (d,  $J = 2.3$  Hz, 1H), 8.17 (br s, 1H), 3.16 (d,  $J = 4.9$  Hz, 3H).

Step B: 5-Bromo-N<sup>2</sup>-methylpyridine-2,3-diamine.

To a stirred suspension of 5-bromo-N-methyl-3-nitropyridin-2-amine (14.6 g, 62.7 mmol) and zinc (41 g, 627 mmol) in a mixture of water (29 mL) and acetone (291 mL) was added  $\text{NH}_4\text{Cl}$  (33.6 g, 627 mmol). The reaction mixture was stirred at room temperature for 72 h. Upon completion the mixture was filtered through Celite® and rinsed with DCM. The filtrate was washed with water and the aqueous layer was extracted with DCM (3X). The combined organic layers were dried ( $\text{Na}_2\text{SO}_4$ ), filtered and concentrated under reduced pressure to yield the title compound as an oil (12.7 g, 69.3 mmol), which was used in the next step without further purification. MS (ESI): mass calcd. for  $\text{C}_6\text{H}_8\text{BrN}_3$ , 200.99; m/z found, 202  $[\text{M}+\text{H}]^+$ .

Step C: 6-Bromo-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. To a solution of 5-bromo-N<sup>2</sup>-methylpyridine-2,3-diamine (14 g, 69 mmol) in DMF (702 mL) at room temperature was added CDI (29 g, 180 mmol). The reaction mixture was stirred for 16 h. LCMS analysis of the crude reaction mixture showed that the reaction was not complete, and the resultant residue was re-dissolved in THF and CDI (11.2, 69 mmol) was added. The reaction mixture was stirred at 60 °C for 16 h. The reaction mixture was quenched with water and diluted with  $\text{Et}_2\text{O}$ . The suspension was filtered and the resulting solid was washed with  $\text{Et}_2\text{O}$  and dried under vacuum to yield the title compound as a black solid (15.8 g, 35.7 mmol), which was used in the next step without further purification. MS (ESI): mass calcd. for  $\text{C}_7\text{H}_8\text{BrN}_3\text{O}$ , 226.97; m/z found, 227.0  $[\text{M}+\text{H}]^+$ .

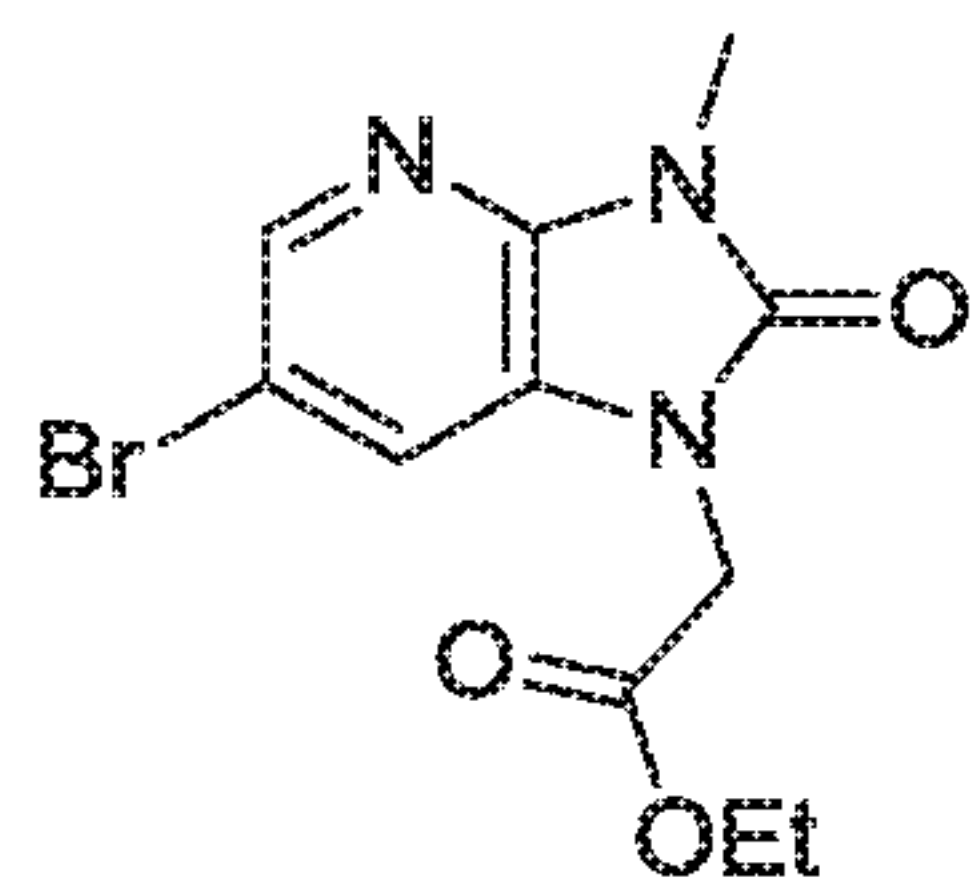
#### Method B:

Step A: 5-Bromo-N-methyl-3-nitropyridin-2-amine. Into a 20 L four-necked flask were charged with EtOH (10.5 L) and 2,5-dibromo-3-nitropyridine (1500 g, 5.32 mol). The mixture was heated to 50 °C followed by addition of aq.  $\text{MeNH}_2$  (40% w/w, 1032.5 g, 13.3 mol) during 1 h. After stirring at 55 to 65 °C for 2 h, the reaction mixture was cooled to 20 °C and filtered. The cake was washed with EtOH/ $\text{H}_2\text{O}$  (V/V = 1/1, 1 L) followed by slurring in water (8 L) at room temperature for 1.5 h. Then the suspension was filtered and the cake was washed with water (1 L). The cake was collected and dried at room temperature overnight to give the title compound (1198 g, 97%).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.55 (d,  $J$  = 2.3 Hz, 1H), 8.48 (d,  $J$  = 2.3 Hz, 1H), 8.20 (bs, 1H), 3.18 (d,  $J$  = 8.0 Hz, 3H).

Step B: 5-Bromo-N<sup>2</sup>-methylpyridine-2,3-diamine. Into a pressure reactor was charged with Pt/C (5% wt, 78.7 g, 10.6% w/w), aq. H<sub>3</sub>PO<sub>2</sub> (50 % wt, 5.8 g), NH<sub>4</sub>VO<sub>3</sub> (2.1 g), THF/EtOH (V/V = 1/1, 12.1 L) and 5-bromo-N-methyl-3-nitropyridin-2-amine (740 g, 3.19 mol). The reactor was purged with hydrogen and pressurized to 20 atm followed by stirring at 20 to 30 °C for about 0.5 h. Then the mixture was re-pressurized to 20 atm with hydrogen and stirred at 30 to 45 °C for 1 h. The reaction mixture was cooled to room temperature and filtered through a pad of Celite® followed by washing the cake with THF (1 L). The combined filtrate was concentrated at 40 to 45 °C under vacuum. Solvent chasing distillation by *n*-heptane (1 L × 2) and dilution with ACN (3 L) afforded a dark solution of the title compound in ACN which was used in the next step without further purification.

Step C: 6-Bromo-3-methyl-1H-imidazo[4,5-b]pyridin-2(3H)-one. Into a 5 L three-necked flask was charged with a solution of 5-bromo-N<sup>2</sup>-methylpyridine-2,3-diamine (in ACN (3.05 L). The mixture was cooled to 5 °C followed by addition of CDI (564.55 g, 3.48 mol) in portions. The mixture was stirred at 5 to 25 °C for 3 h followed by concentration until about 2 L of solvent was left. The resulting mixture was filtered and the cake was slurried with H<sub>2</sub>O (3.5 L) at 20 to 25 °C for 3 h. The suspension was filtered and the cake was dried at 20 to 25 °C for 48 h to give the title compound (680 g, 87.9%, over two steps). <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ 11.30 (s, 1H), 8.06 (d, *J* = 3.0 Hz, 1H), 7.49 (d, *J* = 3.0 Hz, 1H), 3.29 (s, 3H).

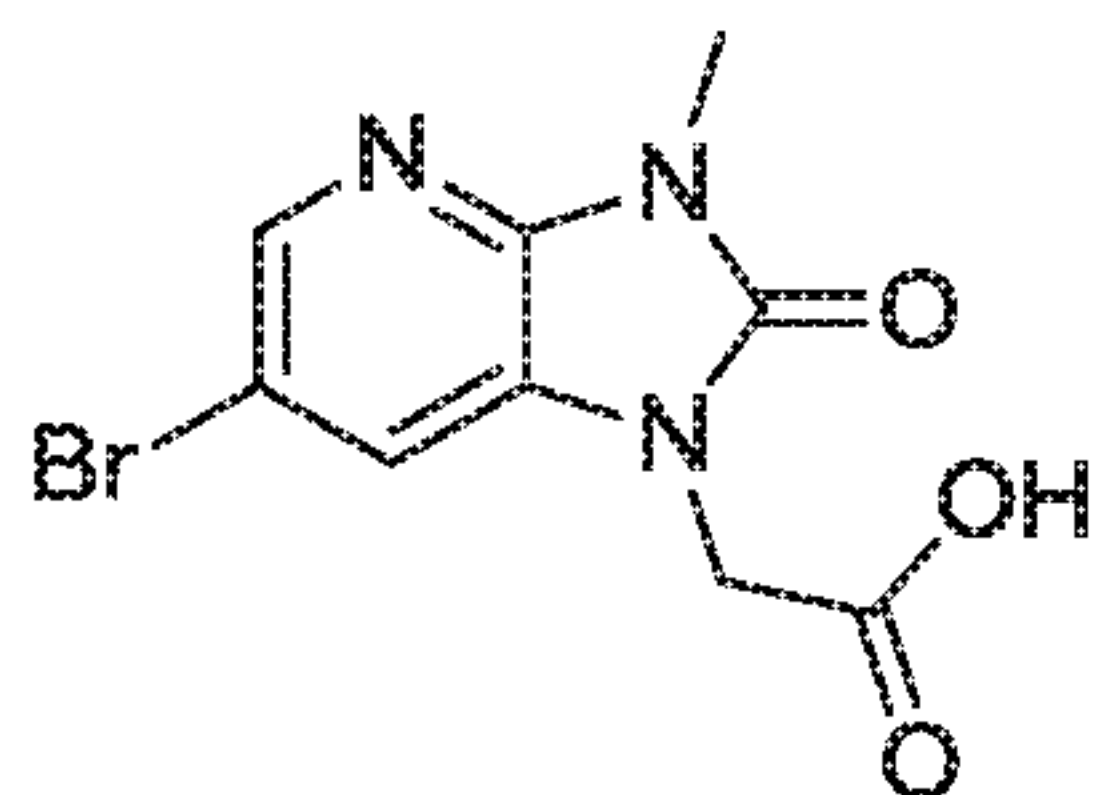
Intermediate 12: Ethyl 2-(6-bromo-3-methyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetate.



To a mixture of 6-bromo-3-methyl-1H-imidazo[4,5-b]pyridin-2(3H)-one (Intermediate 11, 350.0 g, 1.535 mol) and ACN (4800 mL) was charged with K<sub>2</sub>CO<sub>3</sub> (318.2 g). The resulting mixture was warmed to 45 to 50 °C followed by dropwise addition of ethyl 2-bromoacetate (281.9 g, 1.688 mol) at 50 to 60 °C. Then the reaction mixture was

warmed to 80 to 85 °C and kept at this temperature for 7.5 h. Additional ethyl 2-bromoacetate (25.6 g, 0.153 mol) was charged into the reaction mixture. After stirring at 80 to 85 °C for 3 h, the mixture was cooled to room temperature naturally and stirred overnight. The mixture was warmed to 80 to 85 °C followed by addition of ethyl 2-bromoacetate (51.2 g, 0.306 mmol) and K<sub>2</sub>CO<sub>3</sub> (42.4 g). Another portion of K<sub>2</sub>CO<sub>3</sub> (106.0 g) was added into the mixture after stirring for 3.5 h. The reaction was cooled to 65 to 70 °C followed by filtration. The cake was washed with ACN (1400 mL) and the combined filtrate was concentrated at 40 to 45 °C until about 2.8 volume of ACN was left. HCl (0.08 N, 2500 mL) was poured into the residue and the resulting suspension was stirred at 20 to 25 °C for 30 min followed by filtration. The cake was collected and dried at 45 °C vacuum oven for 14 h to give the title compound (438 g, 91%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.12 (d, *J* = 1.9 Hz, 1H), 7.23 (d, *J* = 1.9 Hz, 1H), 4.61 (s, 2H), 4.25 (q, *J* = 7.5 Hz, 2H), 3.49 (s, 3H), 1.30 (t, *J* = 7.5 Hz, 3H).

15 Intermediate 13: 2-(6-Bromo-3-methyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetic acid. Lithium salt.

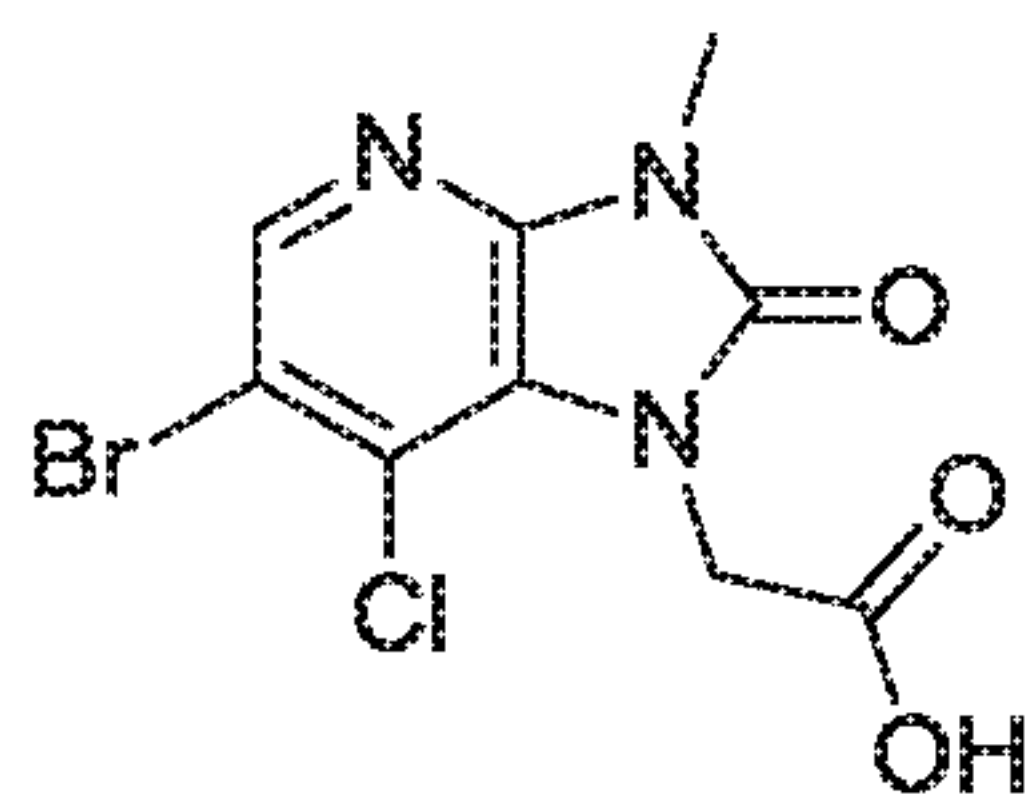


Step A: Ethyl 2-(6-bromo-3-methyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetate.

Under a nitrogen atmosphere was added 6-bromo-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 11, 5 g, 21.9 mmol) to a suspension of sodium hydride (60% dispersion in mineral oil, 1.3 g, 32.9 mmol) in DMF (171 mL) at room temperature. After 10 minutes ethyl bromoacetate (3.2 mL, 28.5 mmol) was added and the reaction was stirred at room temperature. After 4 h, complete conversion was observed. The reaction was cooled to 0 °C and water was added (200 mL). The precipitates were collected by filtration and washed with water to give the title compound (6.1 g, 88%). MS (ESI): mass calcd. for C<sub>11</sub>H<sub>12</sub>BrN<sub>3</sub>O<sub>3</sub>, 313.0; *m/z* found, 313.9 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 8.14 (d, *J* = 2.0 Hz, 1H), 7.92 (d, *J* = 2.0 Hz, 1H), 4.76 (s, 2H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.35 (s, 3H), 1.22 (t, *J* = 7.1 Hz, 3H).

Step B: 2-(6-bromo-3-methyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetic acid. Lithium hydroxide (2M, 1.2 mL, 2.3 mmol) was added to a mixture of ethyl 2-(6-bromo-3-methyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetate (612 mg, 1.9 mmol) in THF (23 mL) at room temperature. The precipitates were collected by filtration  
 5 and washed with THF to give the title compound (465 mg, 83%). MS (ESI): mass calcd. for C<sub>9</sub>H<sub>8</sub>BrN<sub>3</sub>O<sub>3</sub>, 285.0; m/z found, 286.0 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 8.02 (d, J = 2.0 Hz, 1H), 7.46 (d, J = 2.0 Hz, 1H), 4.03 (s, 2H), 3.31 (s, 3H).

Intermediate 14: 2-(6-Bromo-7-chloro-3-methyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetic acid and its trifluoroacetic acid salt.  
 10



Step A: 5-Bromo-4-chloro-3-nitropyridin-2-amine. A solution of 4-chloro-3-nitropyridin-2-amine (2 g, 11.5 mmol) and N-bromosuccinimide (2.5 g, 13.8 mmol) in ACN (125 mL) was heated at 80 °C. After 1h, the reaction mixture was cooled to room  
 15 temperature and volatiles were removed under reduced pressure. Purification (FCC, SiO<sub>2</sub>, 0-5% EtOAc in DCM), afforded the title compound (2.9 g, 99%). MS (ESI): mass calcd. for C<sub>5</sub>H<sub>3</sub>BrClN<sub>3</sub>O<sub>2</sub>, 250.9; m/z found, 251.8 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 8.42 (s, 1H), 7.37 (br s, 2H).

Step B: *tert*-Butyl (5-bromo-4-chloro-3-nitropyridin-2-yl)carbamate. To a mixture of 5-bromo-4-chloro-3-nitropyridin-2-amine (2.9 g, 11.4 mmol) in THF (200 mL) at room  
 20 temperature, under a nitrogen atmosphere was added sodium hydride (60% dispersion in mineral oil, 1.1 g, 27.4 mmol) in small batches. After 30 minutes, BOC-anhydride (2.4 mL, 11.4 mmol) was added to the reaction mixture. After 16 h, water (5 mL) was added to the reaction mixture and volatiles were removed. The residue was partitioned  
 25 between water (100 mL) and EtOAc (150 mL). The organic layer was collected. The aqueous layer was washed with EtOAc (3 x 150 mL). The combined organics were dried (MgSO<sub>4</sub>), filtered and concentrated under vacuum. Purification (FCC, SiO<sub>2</sub>, 0-5% EtOAc in DCM), afforded the title compound (3.0 g, 75%). MS (ESI): mass calcd. for

$C_{10}H_{11}BrClN_3O_4$ , 351.0; m/z found, 295.9  $[M-tBu]^+$ .  $^1H$  NMR (500 MHz, DMSO- $d_6$ )  $\delta$  10.62 (s, 1H), 8.89 (s, 1H), 1.42 (s, 9H).

Step C: *tert*-Butyl (5-bromo-4-chloro-3-nitropyridin-2-yl)(methyl)carbamate. To a mixture of *tert*-butyl (5-bromo-4-chloro-3-nitropyridin-2-yl)carbamate (3.0 g, 8.6 mmol) in DMF (140 mL) at room temperature, under a nitrogen atmosphere was added sodium hydride (60% dispersion in mineral oil, 445 mg, 11.1 mmol) in small batches. After 30 minutes, iododmethane (0.64 mL, 10.3 mmol) was added to the reaction mixture at 0 °C. After 16 h, EtOAc (200 mL) was added to the reaction mixture. The mixture was washed with brine (1 x 350 mL). The organic was dried ( $MgSO_4$ ), filtered and concentrated under vacuum to give the title compound (3.1 g, 99 %). MS (ESI): mass calcd. for  $C_{11}H_{13}BrClN_3O_4$ , 365.0; m/z found, 309.9  $[M-tBu]^+$ .

Step D: 5-Bromo-4-chloro-N-methyl-3-nitropyridin-2-amine, TFA Salt. To a solution of *tert*-butyl (5-bromo-4-chloro-3-nitropyridin-2-yl)(methyl)carbamate (3.1 g, 8.6 mmol) in DCM (100 mL) at room temperature was added TFA (13 mL, 171 mmol). After completion, volatiles were removed. The solid was dissolved in EtOAc (200 mL). The mixture was washed with brine (2 x 300 mL). The organic was dried over  $MgSO_4$ , filtered and concentrated under vacuum to give the title compound (2.3 g, 99 %). MS (ESI): mass calcd. for  $C_8H_5BrClN_3O_2$ , 265.0; m/z found, 265.8  $[M+H]^+$ .  $^1H$  NMR (400 MHz, DMSO- $d_6$ )  $\delta$  8.53 (s, 1H), 7.60 – 7.52 (m, 1H), 2.86 (d,  $J$  = 4.5 Hz, 3H).

Step E: 5-Bromo-4-chloro-N<sup>2</sup>-methylpyridine-2,3-diamine. To a stirred suspension of 5-bromo-4-chloro-N-methyl-3-nitropyridin-2-amine (500 mg, 1.9 mmol) and zinc (1.2 g, 18.8 mmol) in a mixture of water (0.9 mL) and acetone (8.7 mL) was slowly added ammonium chloride (1g, 18.8 mmol) at 0 °C. Upon completion, the mixture was filtered through Celite® and rinsed with MeOH. The volatiles were removed and the material was partitioned between water (40 mL) and EtOAc (40 mL). The organic layer was collected. The aqueous layer was washed with EtOAc (3 x 60 mL). The combined organics were dried ( $MgSO_4$ ), filtered and concentrated under vacuum. Purification (FCC,  $SiO_2$ , 0-10% MeOH in DCM), afforded the title compound (280 mg, 63%). MS (ESI): mass calcd. for  $C_8H_7BrClN_3$ , 235.0; m/z found, 235.8  $[M+H]^+$ .

Step F: 6-Bromo-7-chloro-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. To a mixture of 5-bromo-4-chloro-N<sup>2</sup>-methylpyridine-2,3-diamine (210 mg, 0.9 mmol) in DMF

(7 mL), under a nitrogen atmosphere, at room temperature was added CDI (432 mg, 2.7 mmol). After 16 h, additional CDI (432 mg, 2.7 mmol) was added to the reaction mixture. The reaction mixture was heated at 70 °C. Upon complete conversion, the reaction mixture was slowly poured into ice. The resulting mixture was extracted using EtOAc (3 x). The combined organics were washed with 1N HCl (1 x), dried (MgSO<sub>4</sub>), filtered and concentrated under vacuum to afford title product which was used crude without further purification. MS (ESI): mass calcd. for C<sub>7</sub>H<sub>5</sub>BrClN<sub>3</sub>O, 260.9; m/z found, 261.8 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 11.98 (s, 1H), 8.21 (s, 1H), 3.28 (s, 3H).

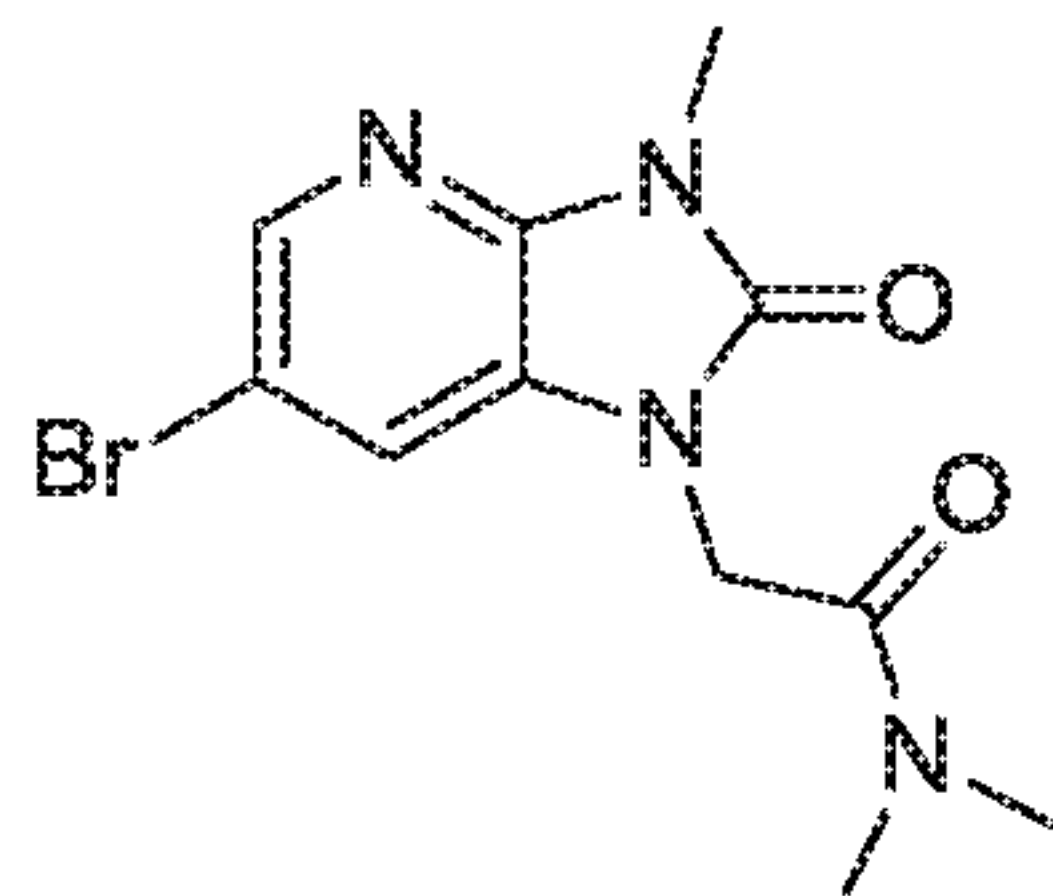
Step G: *tert*-Butyl 2-(6-bromo-7-chloro-3-methyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-

b]pyridin-1-yl)acetate. To a suspension of sodium hydride (60% dispersion in mineral oil, 38 mg, 1.0 mmol) in DMF (5 mL), under a nitrogen atmosphere, at room temperature was added 6-bromo-7-chloro-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (170 mg, 0.6 mmol). After 10 min, *tert*-butyl bromoacetate (0.12 mL, 0.84 mmol) was added to the reaction mixture. After 16 h, water (50 mL) was added to the mixture. After 30 minutes, the resulting precipitates were filtered off and washed with water to give title compound, which was used crude without further purification. MS (ESI): mass calcd. for C<sub>13</sub>H<sub>15</sub>BrClN<sub>3</sub>O<sub>3</sub>, 375.0; m/z found, 375.8 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 8.33 (s, 1H), 4.80 (s, 2H), 3.37 (s, 3H), 1.43 (s, 9H).

Step H: 2-(6-Bromo-7-chloro-3-methyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-

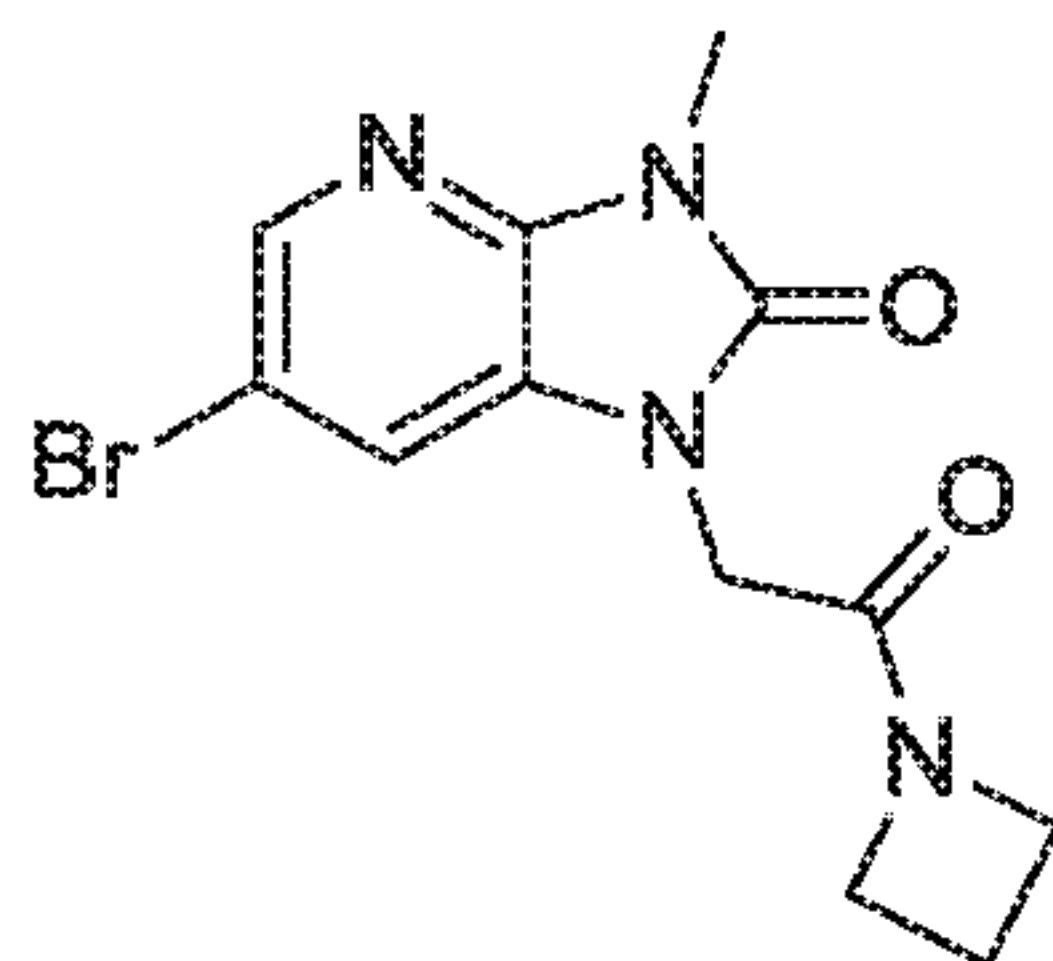
yl)acetic acid and its trifluoroacetic acid salt. To a solution of *tert*-butyl 2-(6-bromo-7-chloro-3-methyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetate (126 mg, 0.3 mmol) in DCM (3.8 mL) at room temperature was added TFA (0.26 mL, 3.3 mmol). After completion, volatiles were removed. The resulting solid was triturated in MeOH. The solids were collected by filtration and washed with MeOH to give the title compound (112 mg, 77 %). MS (ESI): mass calcd. for C<sub>9</sub>H<sub>7</sub>BrClN<sub>3</sub>O<sub>3</sub>, 318.9; m/z found, 319.8 [M+H]<sup>+</sup>.

Intermediate 15: 2-(6-bromo-3-methyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)-N,N-dimethylacetamide.



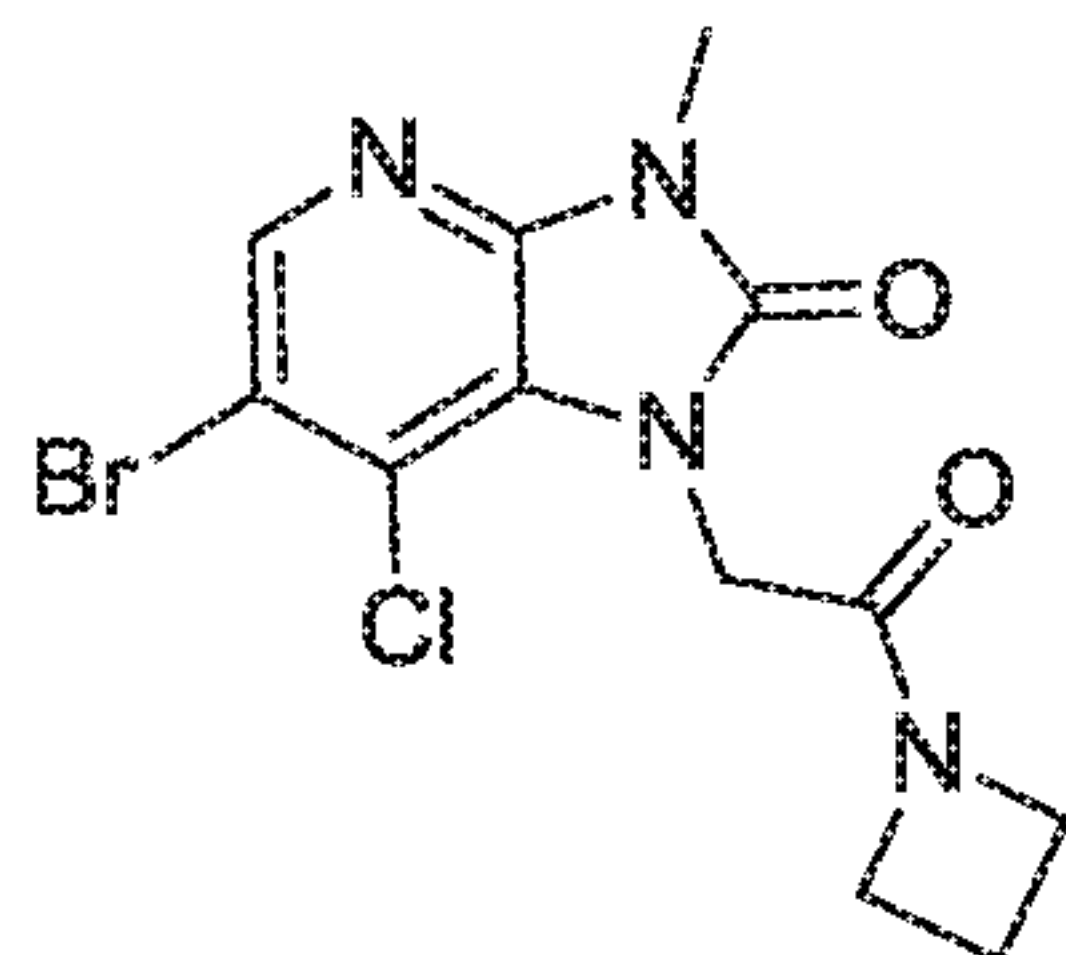
To a solution of 6-bromo-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 11, 600 mg, 2.6 mmol) in DMF (20 mL) was added NaH (72 mg, 3.2 mmol). Upon addition of NaH vigorous bubbling occurred. After 30 min of stirring at  
 5 room temperature, bubbling had ceased and 2-bromo-N,N-dimethylacetamide (Intermediate 4, 618 mg, 3.7 mmol) was added. The resulting reaction mixture was stirred at room temperature then diluted with ethyl acetate and quenched with water. The combined organic layers were dried using Mg<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure to yield a yellow oil which was purified (FCC, SiO<sub>2</sub>, 0-7% 2M  
 10 NH<sub>3</sub>/MeOH in DCM) to provide the title compound (504 mg, 61%) as a beige solid. MS (ESI): mass calcd. for C<sub>11</sub>H<sub>13</sub>BrN<sub>4</sub>O<sub>2</sub>, 313.1; m/z found, 314.1 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 8.12 – 8.08 (d, *J* = 2.0 Hz, 1H), 7.81 – 7.77 (d, *J* = 2.0 Hz, 1H), 4.83 – 4.75 (s, 2H), 3.35 – 3.33 (s, 3H), 3.08 – 3.06 (s, 3H), 2.85 – 2.83 (s, 3H).

15 Intermediate 16: 1-(2-(Azetidin-1-yl)-2-oxoethyl)-6-bromo-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.



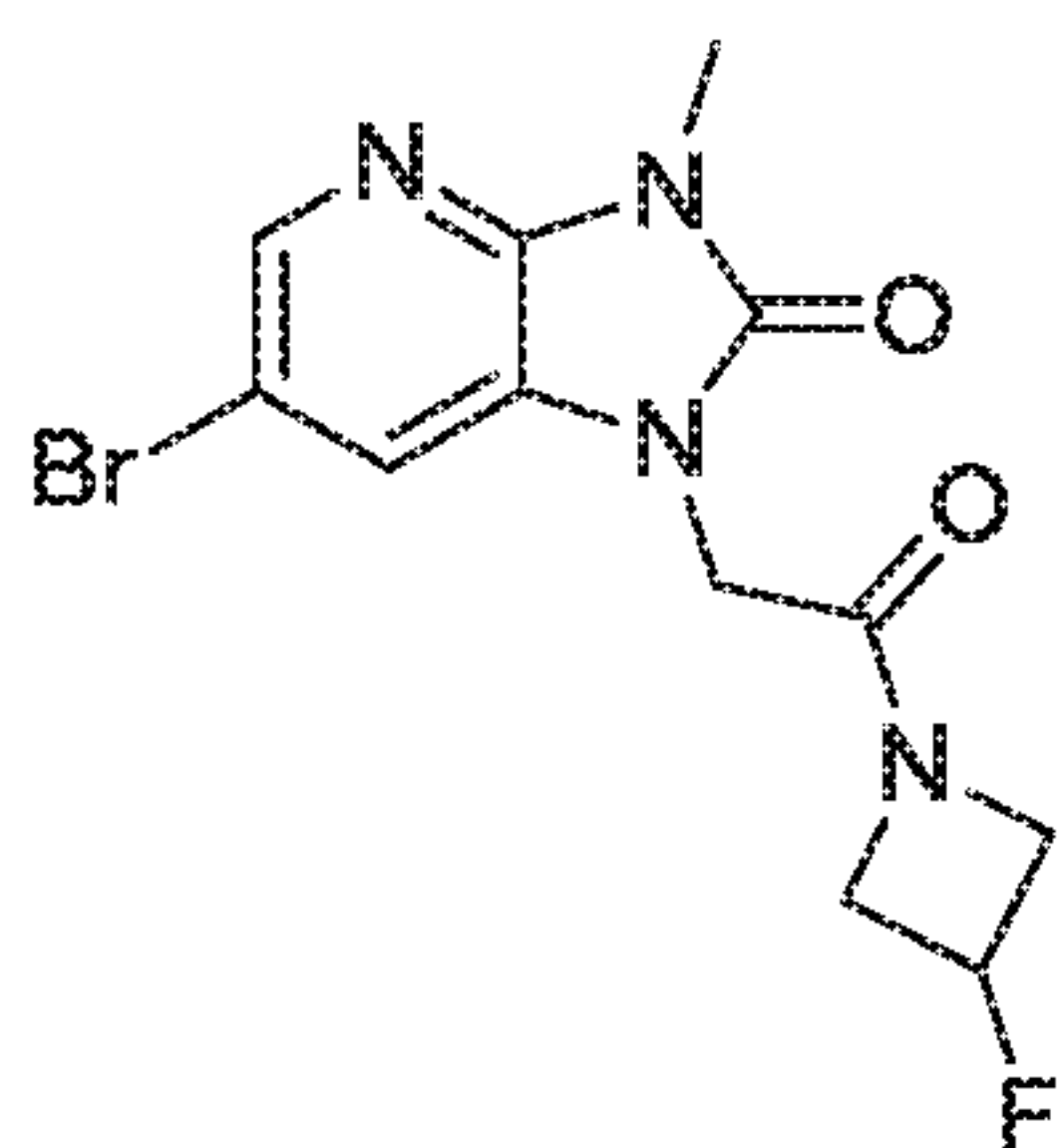
The title compound was prepared in a manner analogous to 2-(6-bromo-3-methyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)-N,N-dimethylacetamide (Intermediate 15),  
 20 using 1-(azetidin-1-yl)-2-bromoethan-1-one (Intermediate 5). MS (ESI): mass calcd. for C<sub>11</sub>H<sub>13</sub>BrN<sub>4</sub>O<sub>2</sub>, 325.1; m/z found, 326.1 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 8.10 (d, *J* = 2.0 Hz, 1H), 7.78 (d, *J* = 2.0 Hz, 1H), 4.55 (s, 2H), 4.27 (t, *J* = 7.6 Hz, 2H), 3.91 (t, *J* = 7.7 Hz, 2H), 3.33 (s, 3H), 2.32 – 2.24 (m, 2H).

Intermediate 17: 1-(2-(Azetidin-1-yl)-2-oxoethyl)-6-bromo-7-chloro-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one and its trifluoroacetic acid salt.



A mixture of 2-(6-bromo-7-chloro-3-methyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetic acid TFA salt (Intermediate 14, 112 mg, 0.3 mmol), azetidine (0.03 mL, 0.5 mmol), DIPEA (0.15 mL, 0.9 mmol) and 2,4,6-tripropyl-1,3,5,2,4,6-trioxatriphosphorinane-2,4,6-trioxide (50% solution in DCM, 0.7 mL, 1.2 mmol) in DMF (3.4 mL) was stirred at room temperature. After 3 days, azetidine (0.03 mL, 0.5 mmol), DIPEA (0.15 mL, 0.9 mmol) and 2,4,6-tripropyl-1,3,5,2,4,6-trioxatriphosphorinane-2,4,6-trioxide (50% solution in DCM, 0.7 mL, 1.2 mmol) were added again. After 16 h, a saturated aqueous solution NaHCO<sub>3</sub> (20 mL) was added. The mixture was extracted using DCM (3 x 30 mL). The combined organics were dried over MgSO<sub>4</sub>, filtered and concentrated under vacuum to give the title compound (92 mg, 0.3 mmol, 99 %) which was used crude without further purification. MS (ESI): mass calcd. for C<sub>12</sub>H<sub>12</sub>BrClN<sub>4</sub>O<sub>2</sub>, 358.0; m/z found, 358.8 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (400 MHz, DMSO) δ 8.10 (s, 1H), 4.54 (s, 2H), 4.08 (t, J = 7.6 Hz, 2H), 3.71 (t, J = 7.7 Hz, 2H), 3.17 (s, 3H), 2.15 – 2.05 (m, 2H).

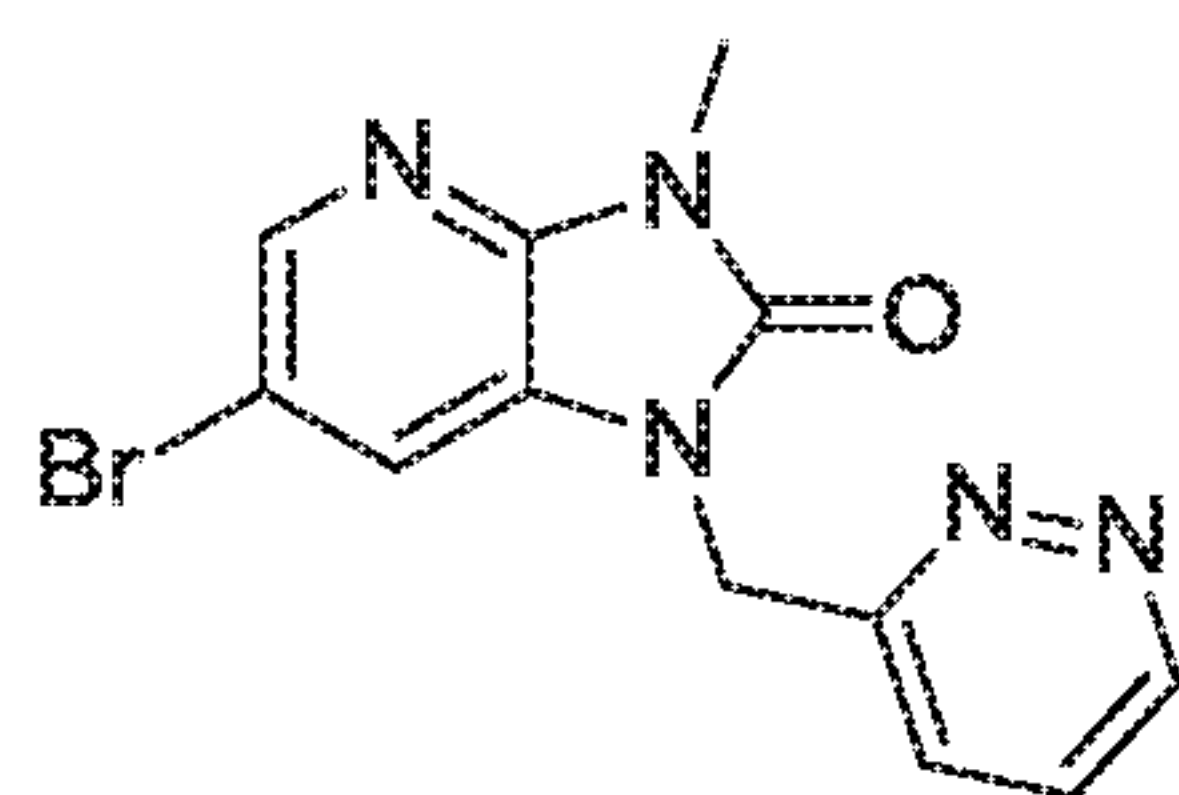
Intermediate 18: 6-Bromo-1-(2-(3-fluoroazetidin-1-yl)-2-oxoethyl)-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.



The title compound was prepared in a manner analogous to 2-(6-bromo-3-methyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)-N,N-dimethylacetamide (Intermediate 15), using 2-bromo-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 6). MS (ESI): mass

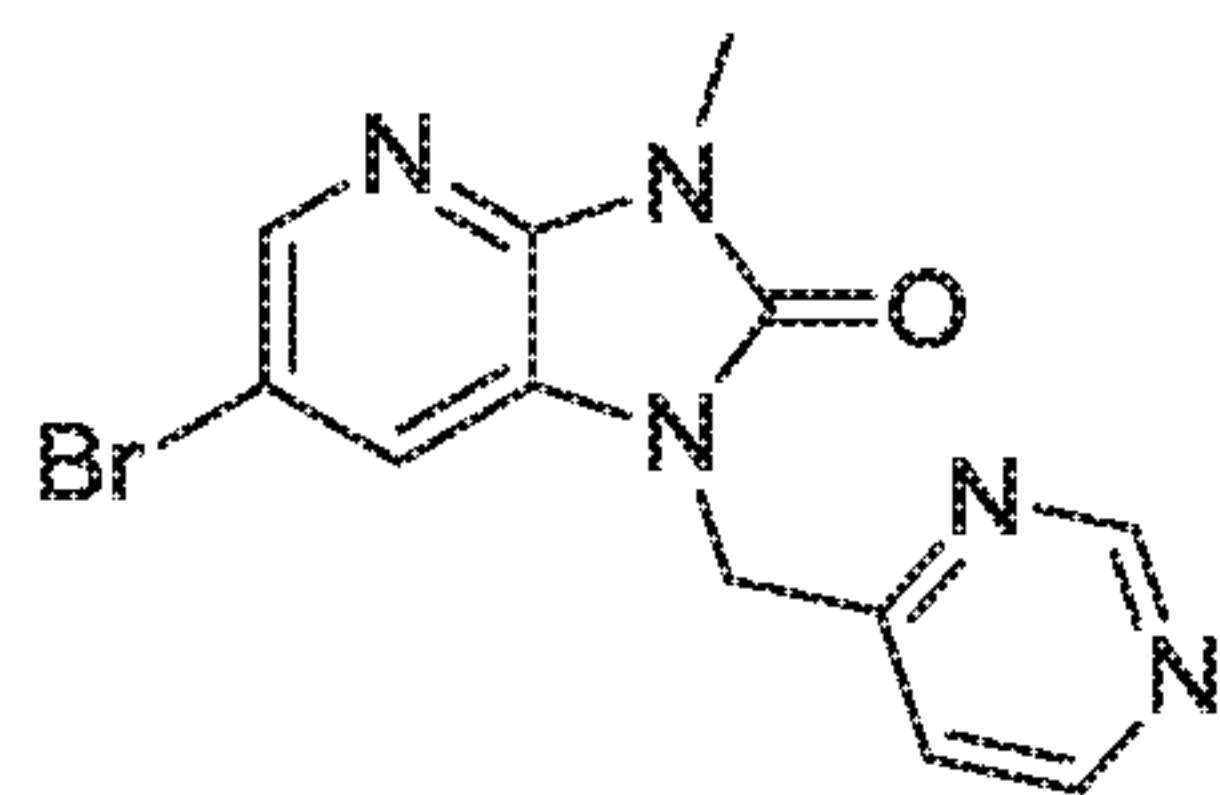
calcd. for  $C_{12}H_{12}BrFN_4O_2$ , 343.1; m/z found, 344.1  $[M+H]^+$ .  $^1H$  NMR (500 MHz, DMSO- $d_6$ )  $\delta$  8.11 (d,  $J = 2.0$  Hz, 1H), 7.79 (d,  $J = 2.0$  Hz, 1H), 5.55 – 5.37 (m, 1H), 4.68 – 4.56 (m, 3H), 4.45 – 4.34 (m, 1H), 4.30 – 4.19 (m, 1H), 4.02 – 3.91 (m, 1H), 3.34 (s, 3H).

5 Intermediate 19: 6-Bromo-3-methyl-1-(pyridazin-3-ylmethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.



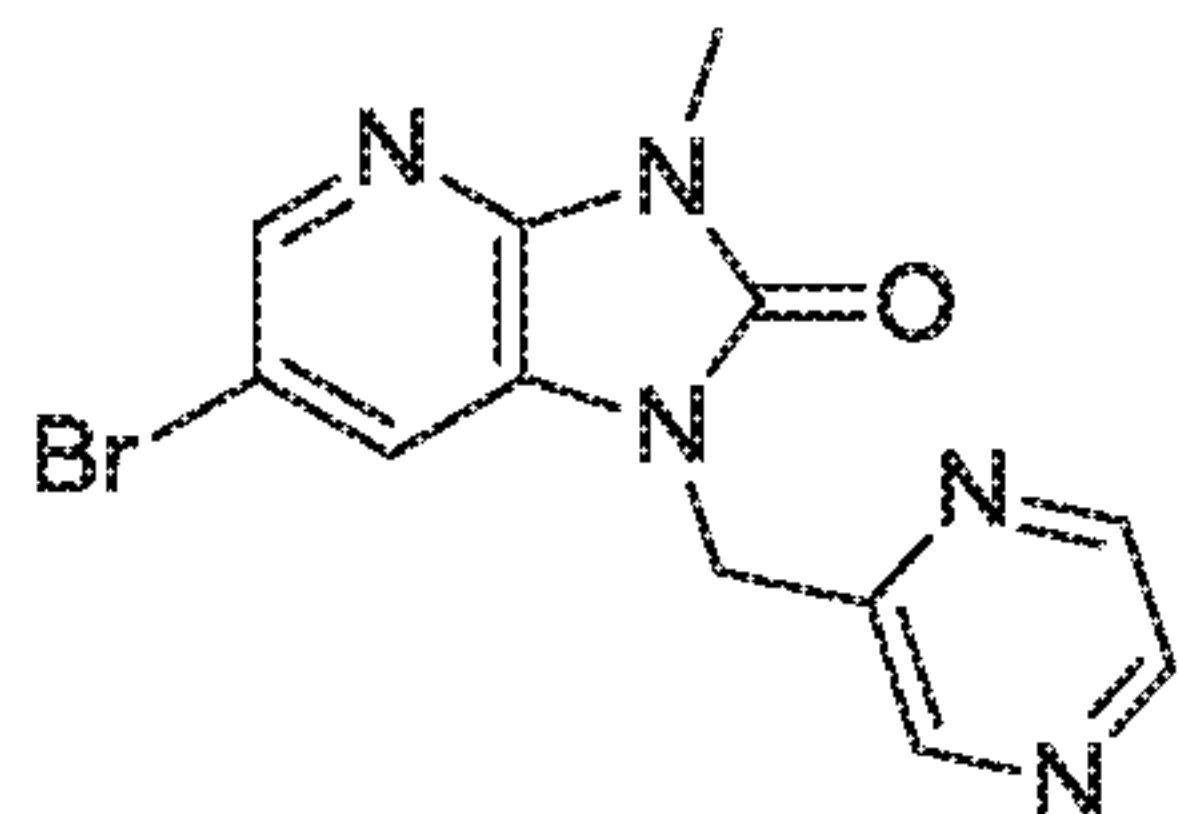
The title compound was prepared in a manner analogous to Intermediate 15, using 3-(chloromethyl)pyridazine (Intermediate 2). MS (ESI): mass calcd. for  $C_{12}H_{10}BrN_5O$ ,  
 10 320.1; m/z found, 321.1  $[M+H]^+$ .  $^1H$  NMR (500 MHz, DMSO- $d_6$ )  $\delta$  9.16 (dd,  $J = 4.6, 2.0$  Hz, 1H), 8.13 (d,  $J = 1.9$  Hz, 1H), 7.82 (d,  $J = 2.0$  Hz, 1H), 7.72 – 7.65 (m, 2H), 5.41 (s, 2H), 3.36 (s, 3H).

15 Intermediate 20: 6-Bromo-3-methyl-1-(pyrimidin-4-ylmethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.



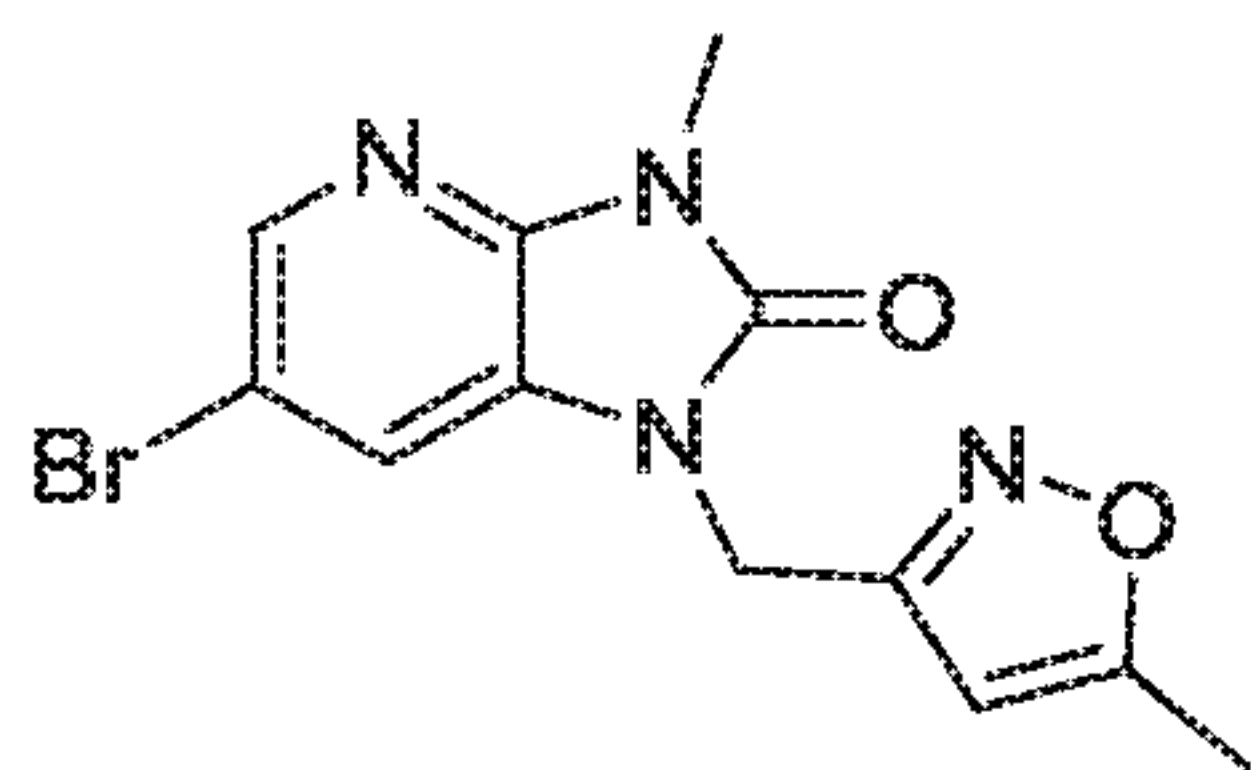
To a cooled (0 °C) solution of 6-bromo-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 11, 65 mg, 0.28 mmol), triphenylphosphine (149 mg, 0.57 mmol), and pyrimidin-4-ylmethanol (31 mg, 0.28 mmol) in ACN (1.6 mL) was added (E)-di-tert-butyl diazene-1,2-dicarboxylate (98 mg, 0.43 mmol). The reaction mixture was heated  
 20 under microwave irradiation at 110 °C for 15 minutes. The reaction mixture was cooled to rt, and concentrated under reduced pressure. Purification (Reverse phase HPLC; Stationary phase: C18 XBridge 30 x 100 mm 5  $\mu$ m; gradient 81% 10mM  $NH_4CO_3H$  pH 9 solution in Water, 19%  $CH_3CN$  to 64% 10mM  $NH_4CO_3H$  pH 9 solution in  
 25 Water, 36%  $CH_3CN$ ) afforded the title compound as a white solid (28 mg, 31%).

Intermediate 21: 6-Bromo-3-methyl-1-(pyrazin-2-ylmethyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one.



- 5 The title compound was prepared in a manner analogous to Intermediate 20, using pyrazin-2-ylmethanol.

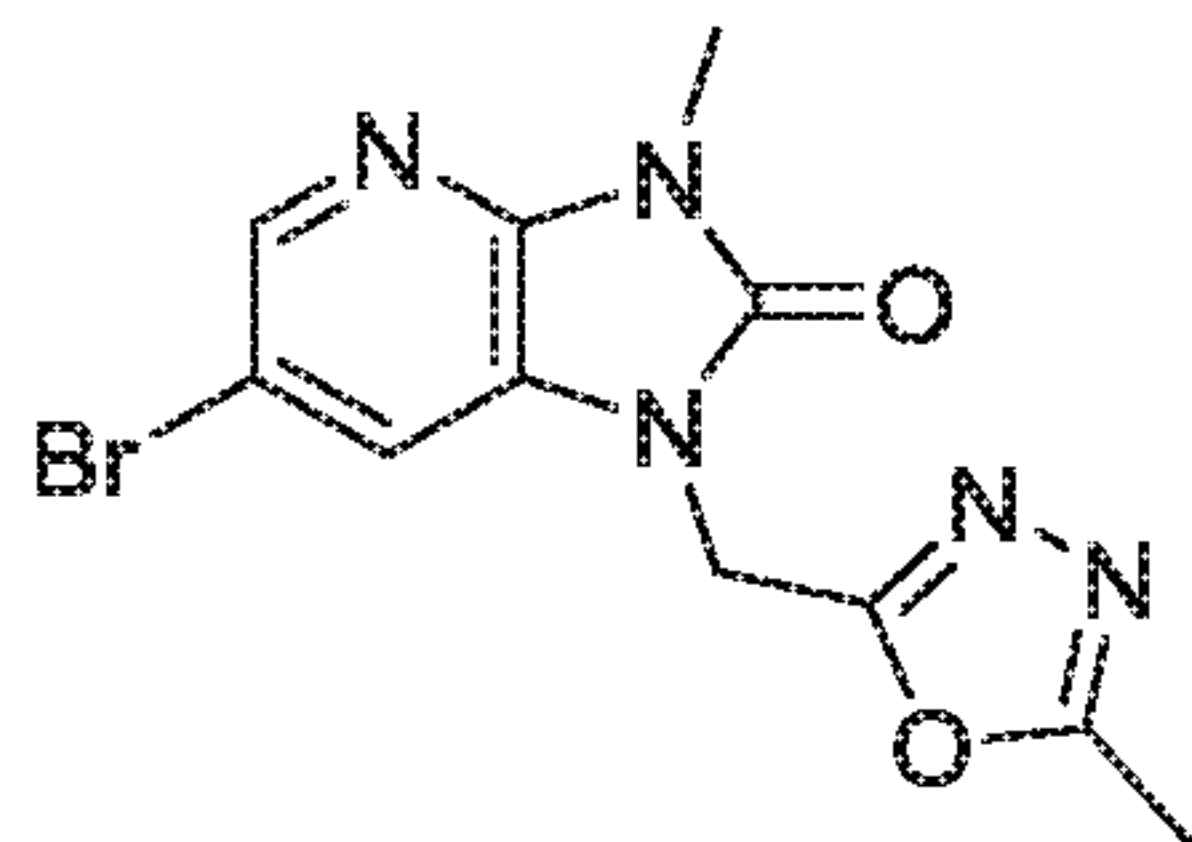
Intermediate 22: 6-Bromo-3-methyl-1-((5-methylisoxazol-3-yl)methyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.



10

- To a solution of 6-bromo-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 11, 600 mg, 2.63 mmol) in DMF (8 mL) at 0 °C was added NaH (60% dispersion in mineral oil, 137 mg, 3.42 mmol), and the reaction mixture was stirred at room temperature for 10 min. Then, 3-chloromethyl-5-methylisoxazole (288 µL, 2.63 mmol) was added at 0 °C, and the mixture was stirred at room temperature overnight. The crude reaction mixture was quenched with water and extracted with EtOAc. The combined organic layers were dried (MgSO<sub>4</sub>), filtered and concentrated under reduced pressure. The residue was purified (FCC, SiO<sub>2</sub>, 0-40% EtOAc in heptanes) to yield the title compound (850 mg, 83%). MS (ESI): mass calcd. for C<sub>12</sub>H<sub>11</sub>BrN<sub>4</sub>O<sub>2</sub>, 322.0; m/z found, 323 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ 8.12 (d, *J* = 1.2 Hz, 1H), 7.79 (d, *J* = 1.3 Hz, 1H), 6.18 (s, 1H), 5.14 (s, 2H), 3.34 (s, 3H), 2.35 (s, 3H).
- 15
- 20

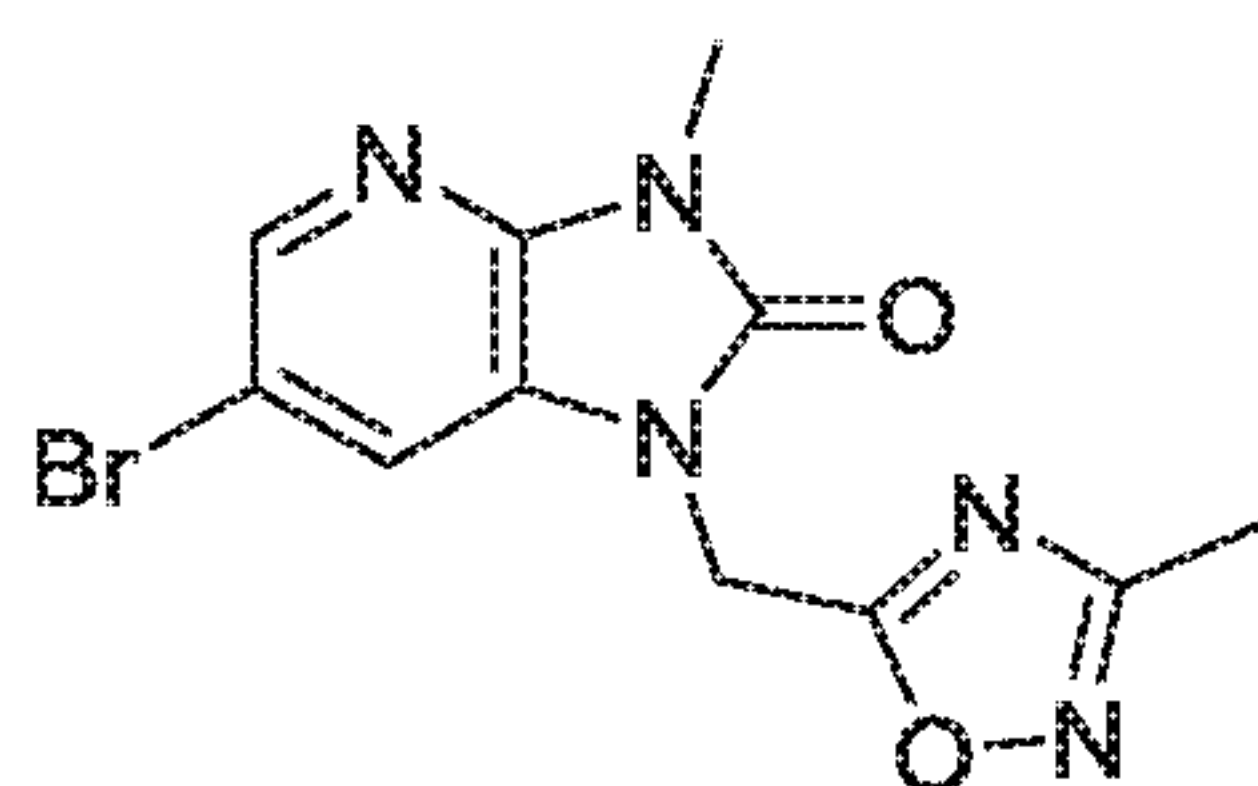
Intermediate 23: 6-Bromo-3-methyl-1-((5-methyl-1,3,4-oxadiazol-2-yl)methyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.



The title compound was prepared in a manner analogous to Intermediate 22: 6-bromo-3-methyl-1-((5-methylisoxazol-3-yl)methyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one using 2-(chloromethyl)-5-methyl-1,3,4-oxadiazole.

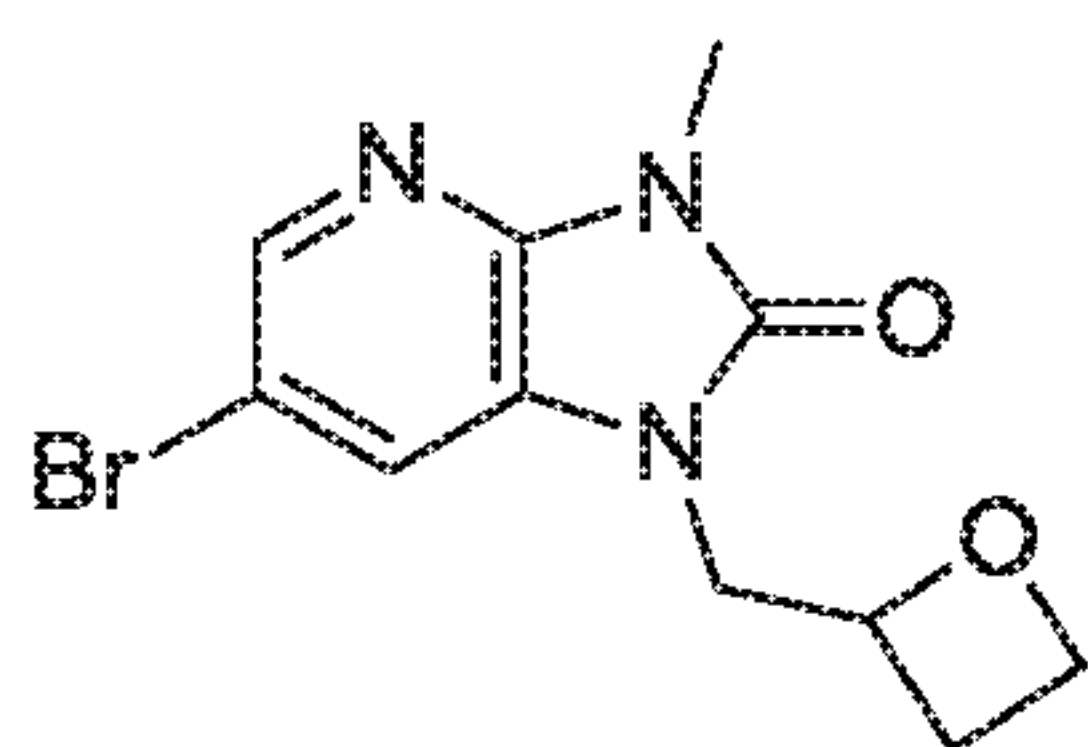
5

Intermediate 24: 6-Bromo-3-methyl-1-((3-methyl-1,2,4-oxadiazol-5-yl)methyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.



The title compound was prepared in a manner analogous to Intermediate 22: 6-bromo-3-methyl-1-((5-methylisoxazol-3-yl)methyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one using 5-(chloromethyl)-3-methyl-1,2,4-oxadiazole. MS (ESI): m/z found, 325.9 [M+H], <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ 8.17 (d, J = 1.7 Hz, 1H), 7.96 (d, J = 1.7 Hz, 1H), 5.48 (s, 2H), 3.36 (s, 3H), 2.29 (s, 3H).

15 Intermediate 25: 6-Bromo-3-methyl-1-(oxetan-2-ylmethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.

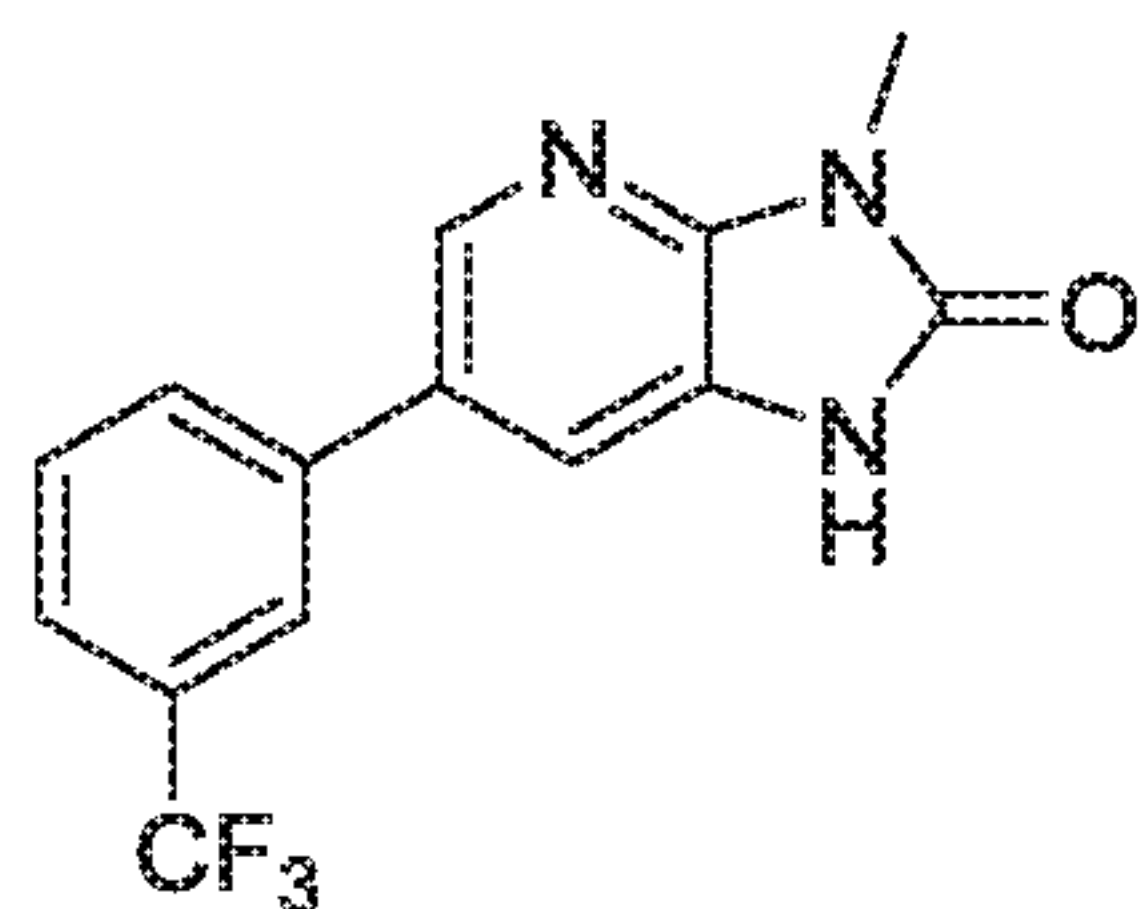


The title compound was prepared in a manner analogous to Intermediate 22, using 6-bromo-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 11) and 2-(bromomethyl)oxetane. MS (ESI): mass calcd. for C<sub>11</sub>H<sub>12</sub>BrN<sub>3</sub>O<sub>2</sub>, 297.0; m/z found, 298.1 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 8.10 (d, J = 2.0 Hz, 1H), 7.83 (d, J = 2.0

20

Hz, 1H), 5.02 – 4.96 (m, 1H), 4.45 (ddd, J = 8.6, 7.1, 5.7 Hz, 1H), 4.32 (dt, J = 9.0, 6.0 Hz, 1H), 4.19 – 4.01 (m, 2H), 3.34 (s, 3H), 2.69 – 2.61 (m, 1H), 2.46 – 2.38 (m, 1H).

Intermediate 26: 3-Methyl-6-(3-(trifluoromethyl)phenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.



Step A: N-Methyl-3-nitro-5-(3-(trifluoromethyl)phenyl)pyridin-2-amine.

A mixture of 5-bromo-N-methyl-3-nitropyridin-2-amine (Intermediate 11, product from Step A, 2.2 g, 9.5 mmol), 3-(trifluoromethyl)phenylboronic acid (2.7 g, 14.2 mmol), 1,1'-bis(diphenylphosphino)ferrocene palladium(II)dichloride dichloromethane complex (542 mg, 0.66 mmol), Cs<sub>2</sub>CO<sub>3</sub> (6.2 g, 19.0 mmol), dioxane (87 mL) and H<sub>2</sub>O (17 mL) was heated to 90 °C using an oil bath. After 16 h, the reaction mixture was cooled to room temperature and volatiles were removed. The crude material was purified (FCC, SiO<sub>2</sub>, 0-100% EtOAc in hexanes), to give the title compound (2.6 g, 91%).

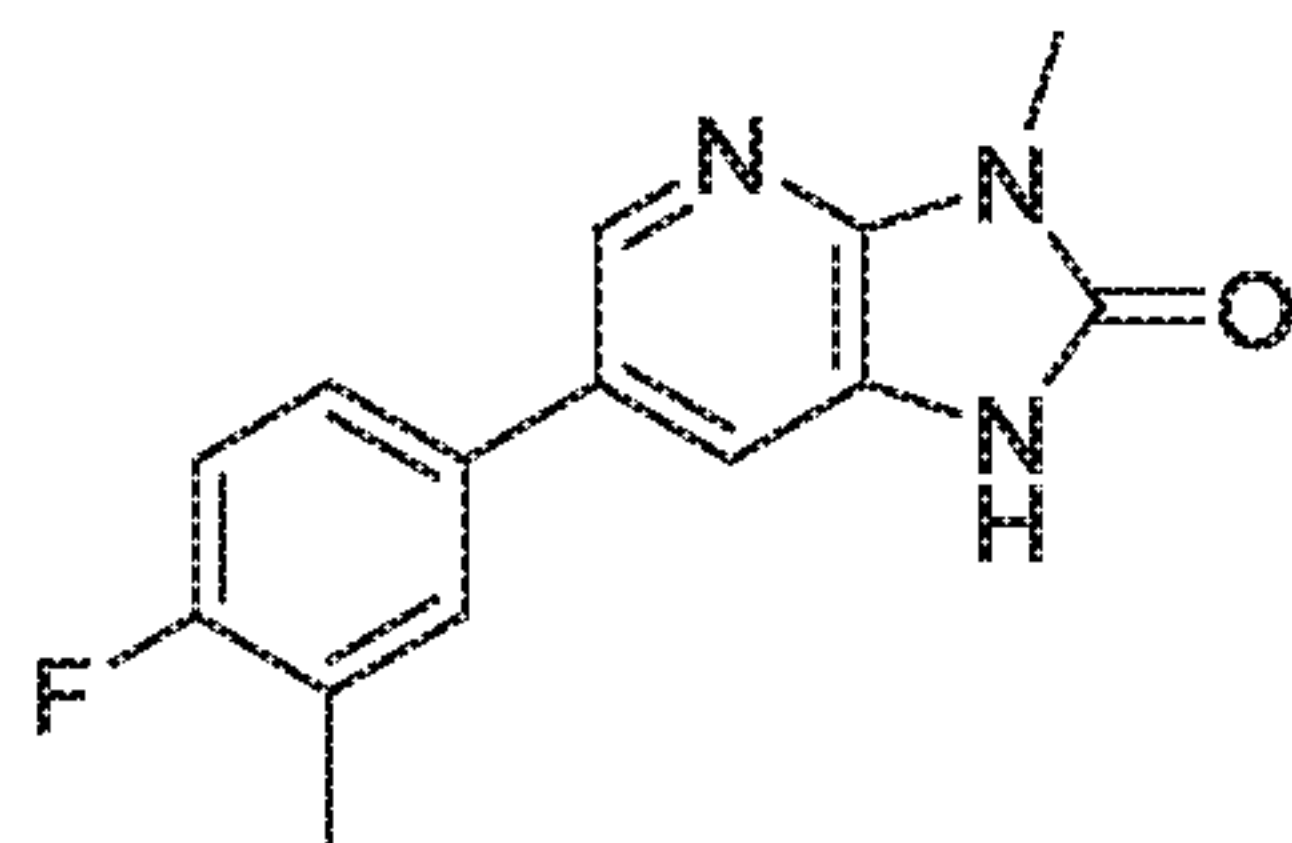
Step B: N<sup>2</sup>-Methyl-5-(3-(trifluoromethyl)phenyl)pyridine-2,3-diamine.

A mixture of N-methyl-3-nitro-5-(3-(trifluoromethyl)phenyl)pyridin-2-amine (2.6 g, 8.6 mmol) and 10% palladium on carbon (0.46 g, 0.43 mmol) in EtOH (80 mL) was allowed to stir at room temperature under a hydrogen atmosphere (1 atm, balloon). After 16 h, the reaction was filtered through a pad of Celite® and the filtrate was concentrated under vacuum. The material was dissolved in a minimum amount of MeOH and filtered through an acrodisc syringe filter and the filtrate was concentrated under vacuum to give the title compound (2.3 g, 99%), which was used in the next step without further purification. MS (ESI): mass calcd. for C<sub>13</sub>H<sub>12</sub>F<sub>3</sub>N<sub>3</sub>, 267.1; m/z found, 268.1 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 8.04 (d, J = 2.1 Hz, 1H), 7.74 – 7.71 (m, 1H), 7.70 – 7.66 (m, 1H), 7.56 – 7.48 (m, 2H), 7.09 (d, J = 2.1 Hz, 1H), 4.37 – 4.26 (m, 1H), 3.29 (s, 2H), 3.08 (d, J = 5.1 Hz, 3H).

Step C: 3-Methyl-6-(3-(trifluoromethyl)phenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. To a mixture of N<sup>2</sup>-methyl-5-(3-(trifluoromethyl)phenyl)pyridine-2,3-diamine (2.3 g,

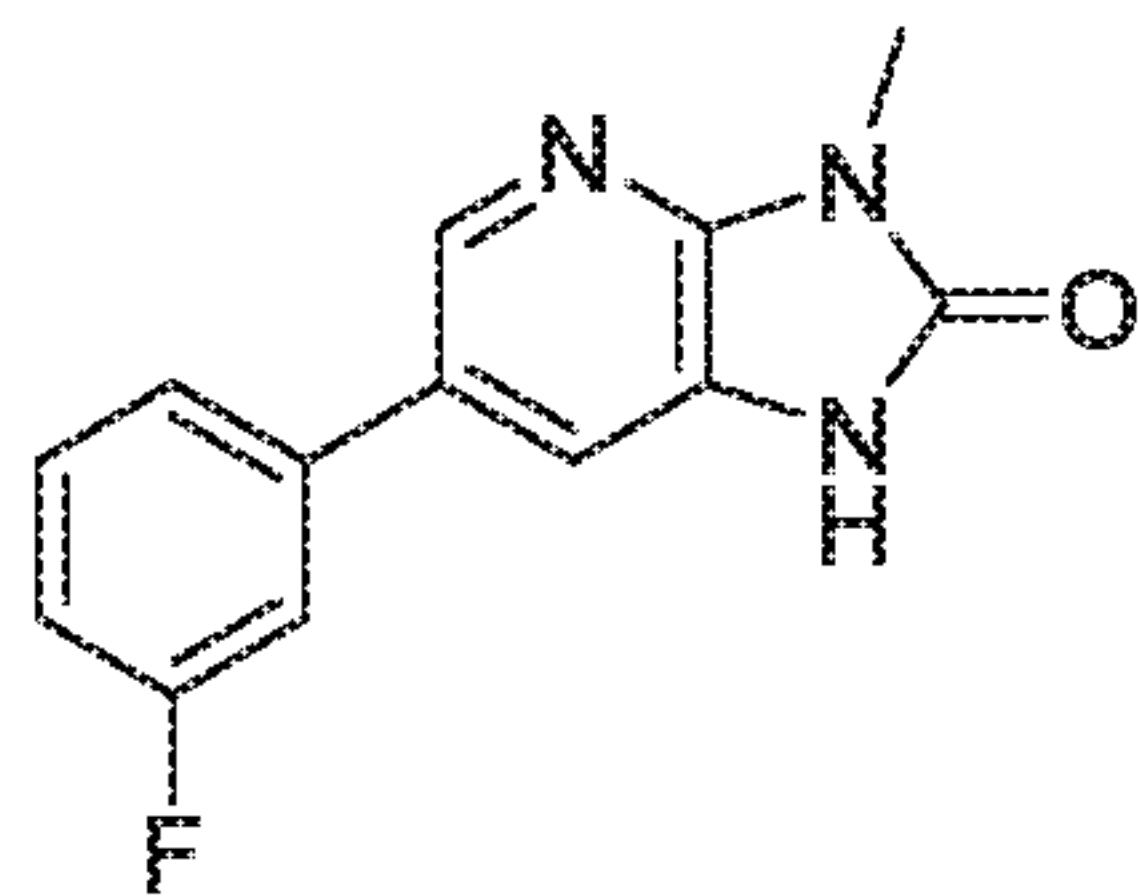
8.6 mmol) in DMF (87 mL), under a nitrogen atmosphere, at room temperature was added CDI (1.7 g, 10.3 mmol). After 16 h, conversion was not complete and additional CDI (2.1 g, 12.9 mmol) was added to the reaction mixture. After 3 h, complete conversion was observed and water (200 mL) was added. The precipitates were collected by filtration, washed with water and dried under vacuum to give the title compound (2.2 g, 87%). MS (ESI): mass calcd. for C<sub>14</sub>H<sub>10</sub>F<sub>3</sub>N<sub>3</sub>O, 293.1; m/z found, 294.1 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (400 MHz, DMSO) δ 11.29 (s, 1H), 8.33 (d, J = 2.0 Hz, 1H), 8.05 – 7.94 (m, 2H), 7.77 – 7.67 (m, 2H), 7.63 (d, J = 2.0 Hz, 1H), 3.34 (s, 3H).

10 Intermediate 27: 6-(4-Fluoro-3-methylphenyl)-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.



To a solution a 6-bromo-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 11, 75 mg, 0.29 mmol), (4-fluoro-3-methylphenyl)boronic acid (1.01 g, 6.58 mmol) and a saturated aqueous solution of NaHCO<sub>3</sub> (10 mL) in 1,4-dioxane (20 mL) was added Pd(Ph<sub>3</sub>)<sub>4</sub> (253 mg, 0.219 mmol). The reaction mixture was stirred at 120 °C for 20 min under microwave irradiation. Then, the crude reaction mixture cooled, diluted with EtOAc and washed with water. The organic layer was separated, dried Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated. The crude product was triturated with Et<sub>2</sub>O and filtered to yield the title compound as a black solid (1.1 g, 4.28 mmol), which was used in the next step without further purification. MS (ESI): mass calcd. for C<sub>14</sub>H<sub>12</sub>FN<sub>3</sub>O, 257.1; m/z found, 258.2 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 2.31 (d, J = 1.44 Hz, 3 H), 7.18 - 7.25 (m, 1 H), 7.49 (d, J = 2.02 Hz, 1 H), 7.49 - 7.52 (m, 1 H), 7.60 (dd, J = 7.37, 1.88 Hz, 1 H), 8.22 (d, J = 2.02 Hz, 1 H), 11.17 (s, 1 H).

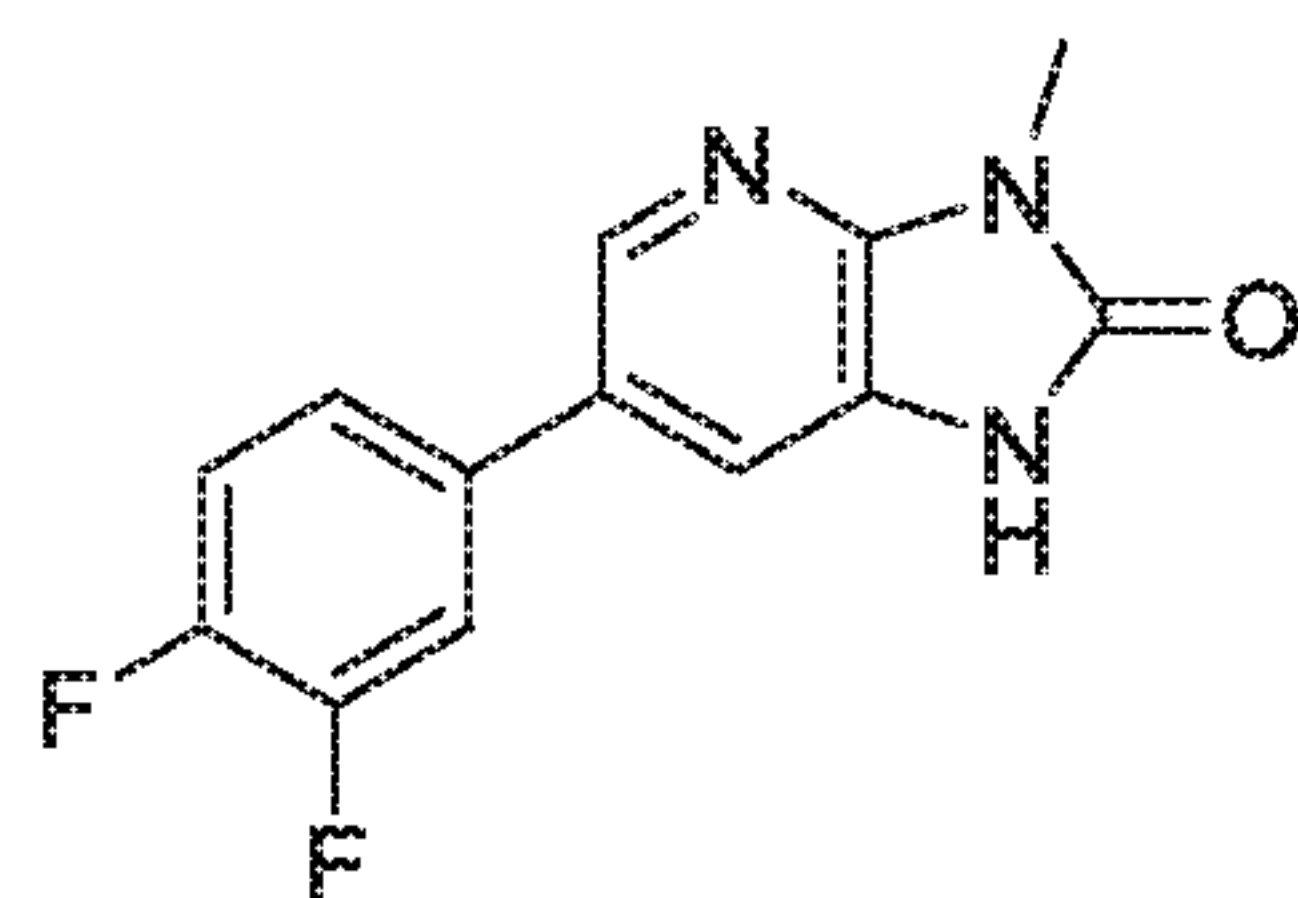
25 Intermediate 28: 6-(3-Fluorophenyl)-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.



To a solution a 6-bromo-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 11, 1 g, 4.4 mmol), (3-fluorophenyl)boronic acid (920 mg, 6.58 mmol) and Na<sub>2</sub>CO<sub>3</sub> (10 mL) in 1,4-dioxane (20 mL) was added PdCl<sub>2</sub>(dppf) (449 mg, 0.614 mmol).

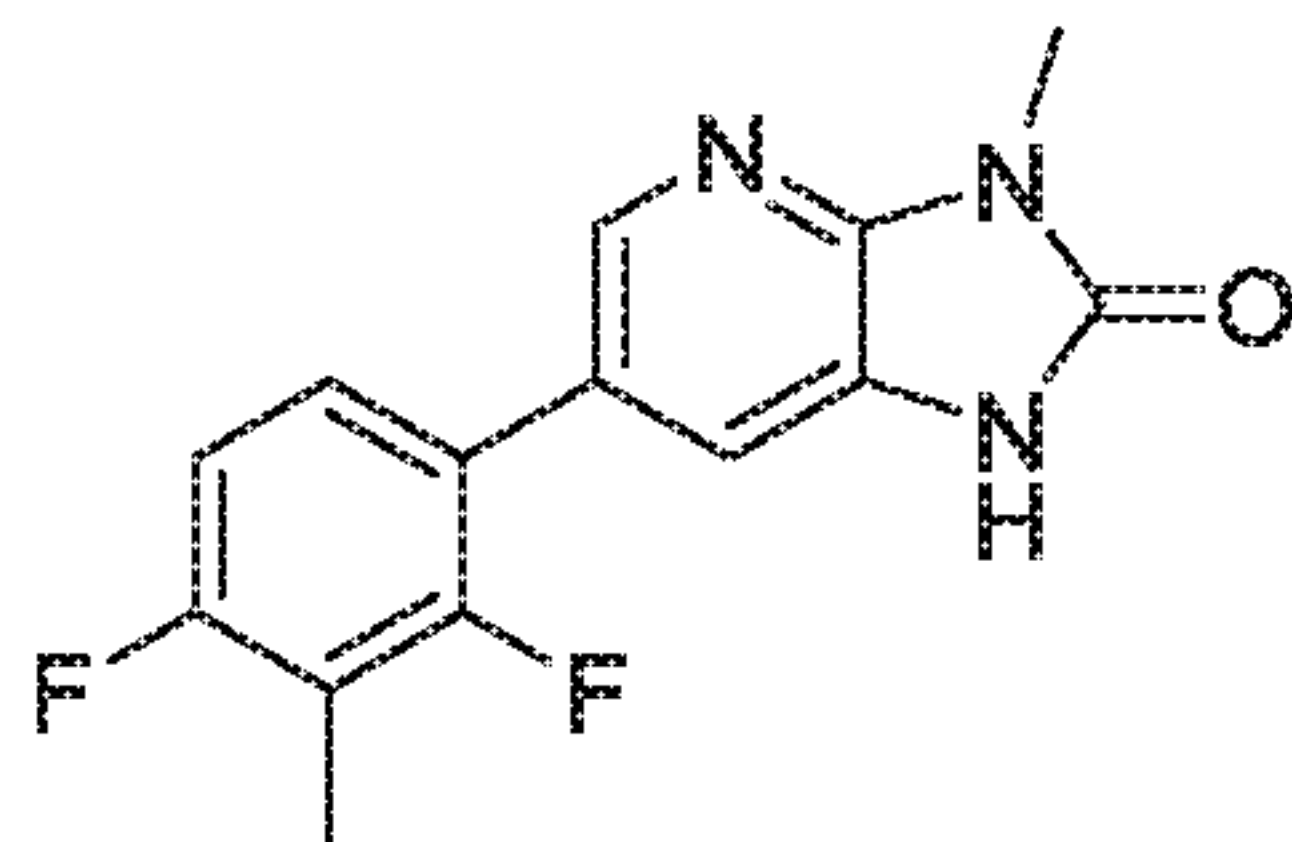
- 5 The reaction mixture was stirred at 170 °C for 15 min under microwave irradiation. Then, the crude reaction mixture was cooled, diluted with water and extracted with EtOAc. The organic layer was separated, dried Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated. The crude product was purified (FCC, SiO<sub>2</sub>, 0 -4% 7 M solution of NH<sub>3</sub>/MeOH in DCM) to yield the title compound as a brown solid (460 mg, 43%). MS (ESI): mass calcd. for
- 10 C<sub>13</sub>H<sub>10</sub>FN<sub>3</sub>O, 243.1 ; m/z found, 244.1 [M+H]<sup>+</sup>.

Intermediate 29: 6-(3,4-Difluorophenyl)-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.



- 15 The title compound was prepared in a manner analogous to Intermediate 28: 6-(3-fluorophenyl)-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one using (3,4-difluorophenyl)boronic acid. MS (ESI): mass calcd. for C<sub>13</sub>H<sub>9</sub>F<sub>2</sub>N<sub>3</sub>O, 261.1; m/z found, 262.1 [M+H]<sup>+</sup>.

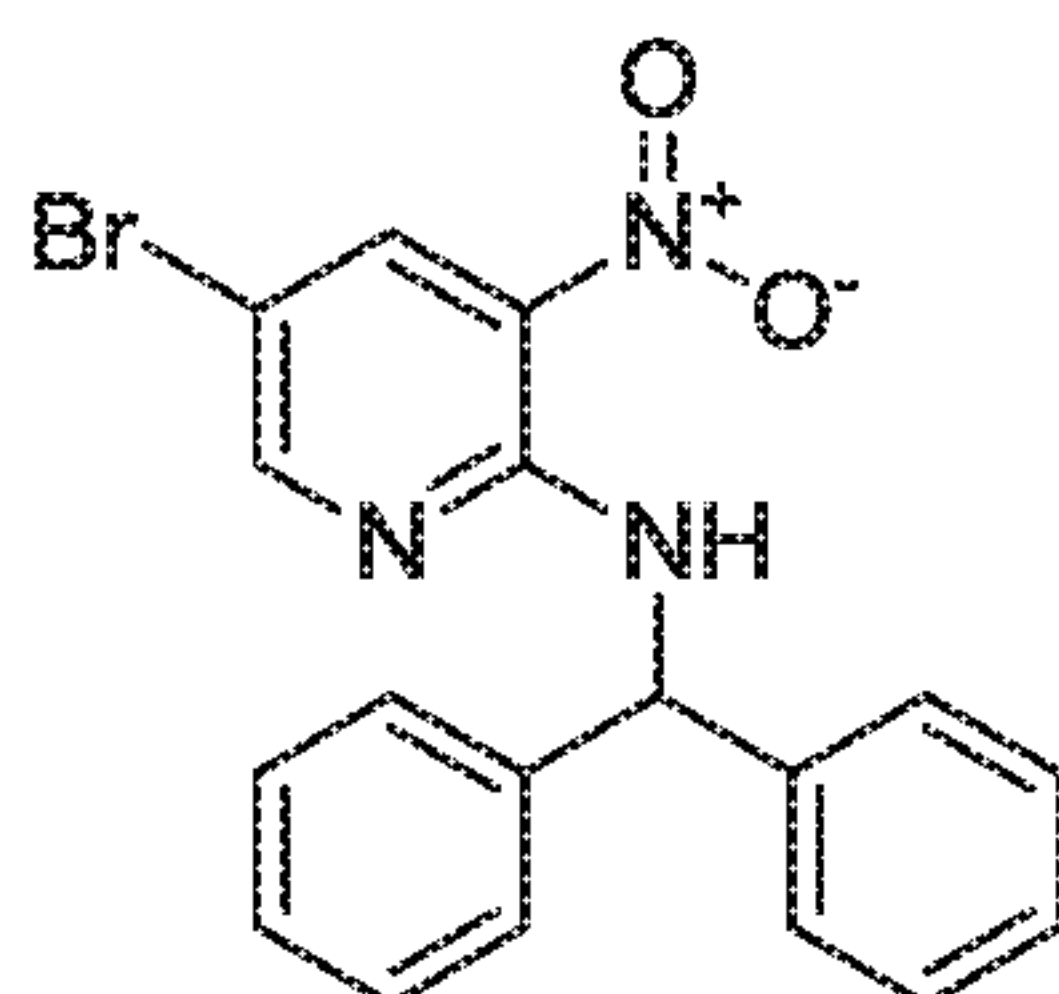
- 20 Intermediate 30: 6-(2,4-Difluoro-3-methylphenyl)-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.



The title compound was prepared in a manner analogous to Intermediate 27: 6-(4-fluoro-3-methylphenyl)-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one using Intermediate 8: 2-(2,4-difluoro-3-methylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.

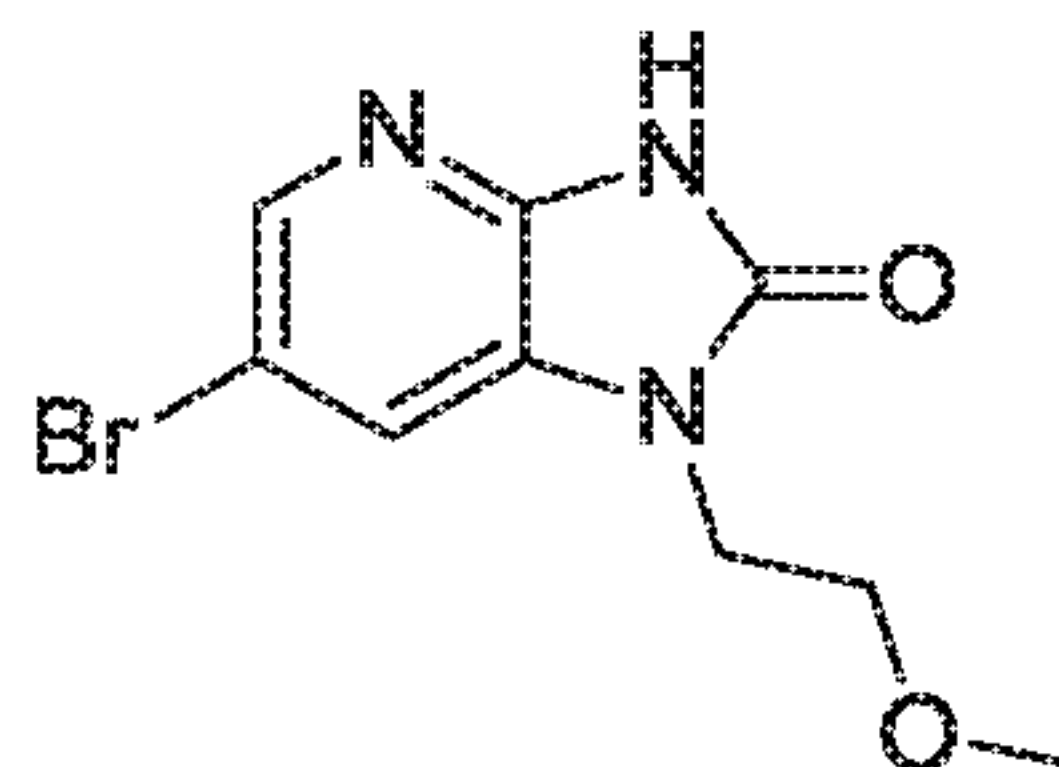
5 MS (ESI): mass calcd. for  $C_{14}H_{11}F_2N_3O$ , 275.1;  $m/z$  found, 276.1  $[M+H]^+$ .  $^1H$  NMR (400 MHz,  $DMSO-d_6$ )  $\delta$  2.22 (s, 3 H) 3.33 (s, 3 H) 7.17 (t,  $J = 8.67$  Hz, 1 H) 7.40 (s, 1 H) 7.36 - 7.46 (m, 1 H) 8.07 (s, 1 H) 11.20 (br s, 1 H).

Intermediate 31: N-Benzhydryl-5-bromo-3-nitropyridin-2-amine.



10 A solution of 5-bromo-2-chloro-3-nitropyridine (71.2 g, 300 mmol), benzhydrylamine (60 g, 330 mmol), and DIPEA (78 g, 600 mmol) in EtOH (600 mL) was heated to reflux overnight. Then solvent was removed in vacuo. Cold EtOH (1000 mL) was added to the crude residue and the mixture was stirred in an ice bath for 30 minutes upon which time  
15 a precipitate formed. The precipitate was filtered, collected and washed with cold EtOH to afford the title compound (93 g, 81%).

Intermediate 32: 6-Bromo-1-(2-methoxyethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.



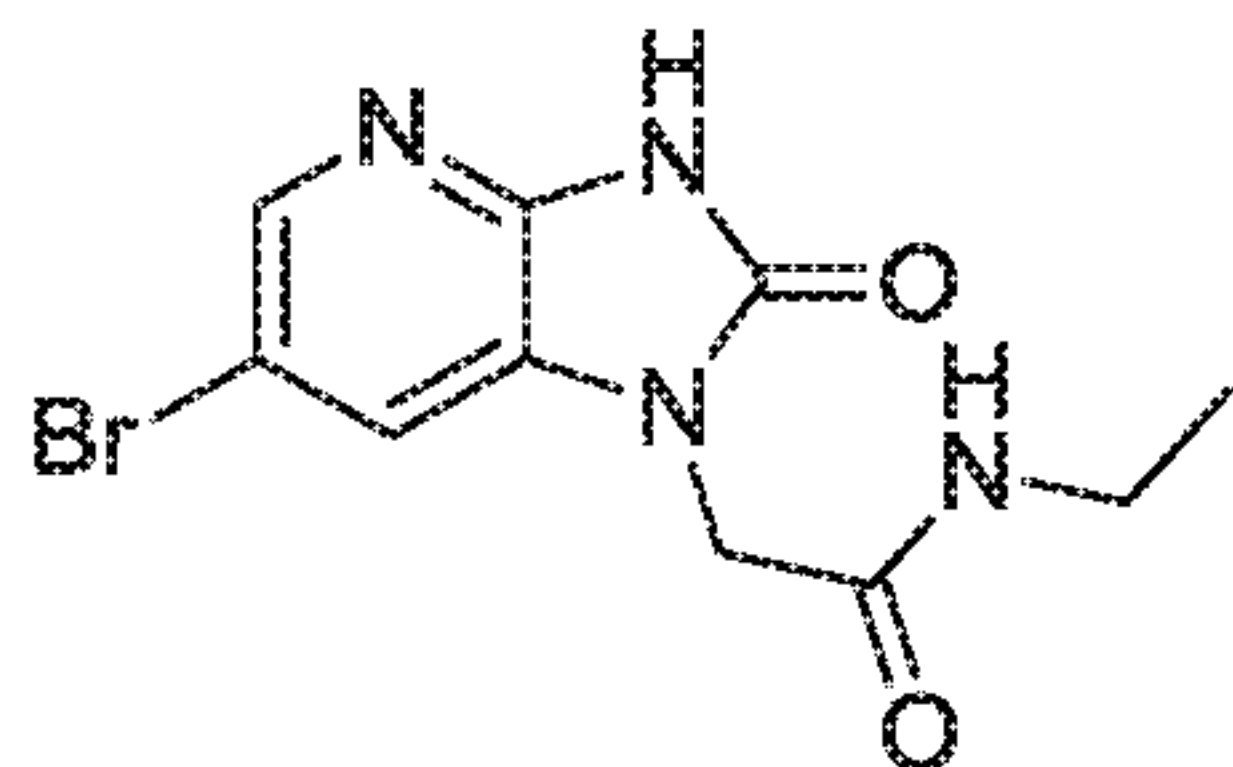
Step A: N<sup>2</sup>-benzhydryl-5-bromopyridine-2,3-diamine. To a solution of 28 % NH<sub>3</sub> in H<sub>2</sub>O (60 mL), THF (300 mL) and water (300 mL) was added N-benzhydryl-5-bromo-3-nitropyridin-2-amine (Intermediate 31, 60 g, 156 mmol). Then, Na<sub>2</sub>S<sub>2</sub>O<sub>4</sub> (81.5 g, 468 mmol) was added portion-wise to the reaction mixture, and the mixture was stirred at room temperature overnight. The crude reaction mixture was extracted with EtOAc (3 x 300 mL) and washed with water (300 mL). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated to yield the title compound (40 g, 73%), which was used in the next step without further purification.

Step B: 3-Benzhydryl-6-bromo-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. A solution of N<sup>2</sup>-benzhydryl-5-bromopyridine-2,3-diamine (50 g, 141 mmol) and CDI (45.7 g, 282 mmol) in 1,4-dioxane (500 mL) was refluxed for 5 h. Then, the solvent was evaporated and the resultant solid was washed with water and dried to yield the title compound (54 g, 99%), which was used in the next step without further purification.

Step C: 3-Benzhydryl-6-bromo-1-(2-methoxyethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. A solution of 3-benzhydryl-6-bromo-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (4 g, 11 mmol), 1-bromo-2-methoxyethane (3 g, 21 mmol) and K<sub>2</sub>CO<sub>3</sub> (4.3 g, 32 mmol) in MeCN (50 mL) was refluxed for 3 h. Then, the crude reaction mixture was filtered and the solvent was evaporated to yield the title compound (4.5 g, 97%), which was used in the next step without further purification.

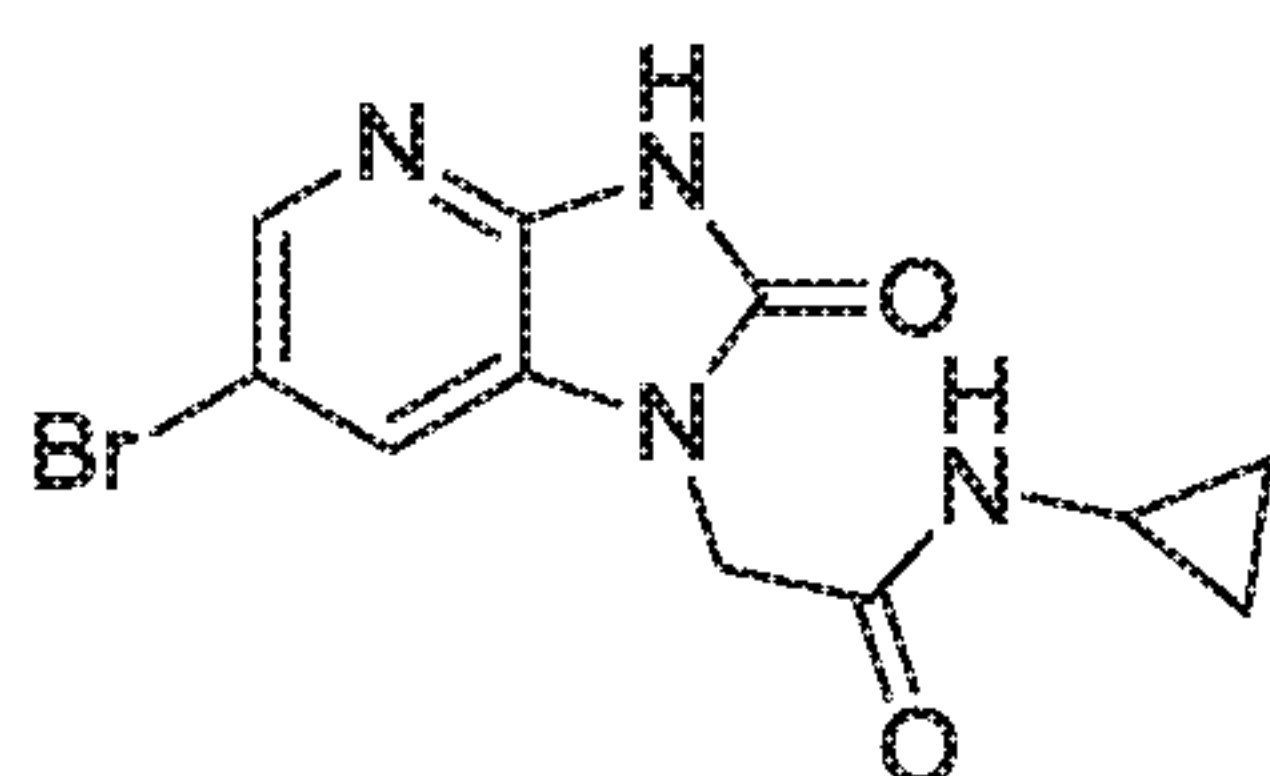
Step D: 6-Bromo-1-(2-methoxyethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. To a solution of 3-benzhydryl-6-bromo-1-(2-methoxyethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (4.5 g, 10.2 mmol) in TFA (40 mL) was added thioanisole (0.045 g), and the reaction mixture was stirred at 80 °C for 1 h. Then, the solvent was evaporated and the crude residue was purified (FCC, SiO<sub>2</sub>, 0-10% MeOH in DCM) to yield the title compound (1.4 g, 51%).

Intermediate 33: 2-(6-Bromo-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)-N-ethylacetamide.



The title compound was prepared in a manner analogous to Intermediate 32, using 2-chloro-N-ethylacetamide in Step C.

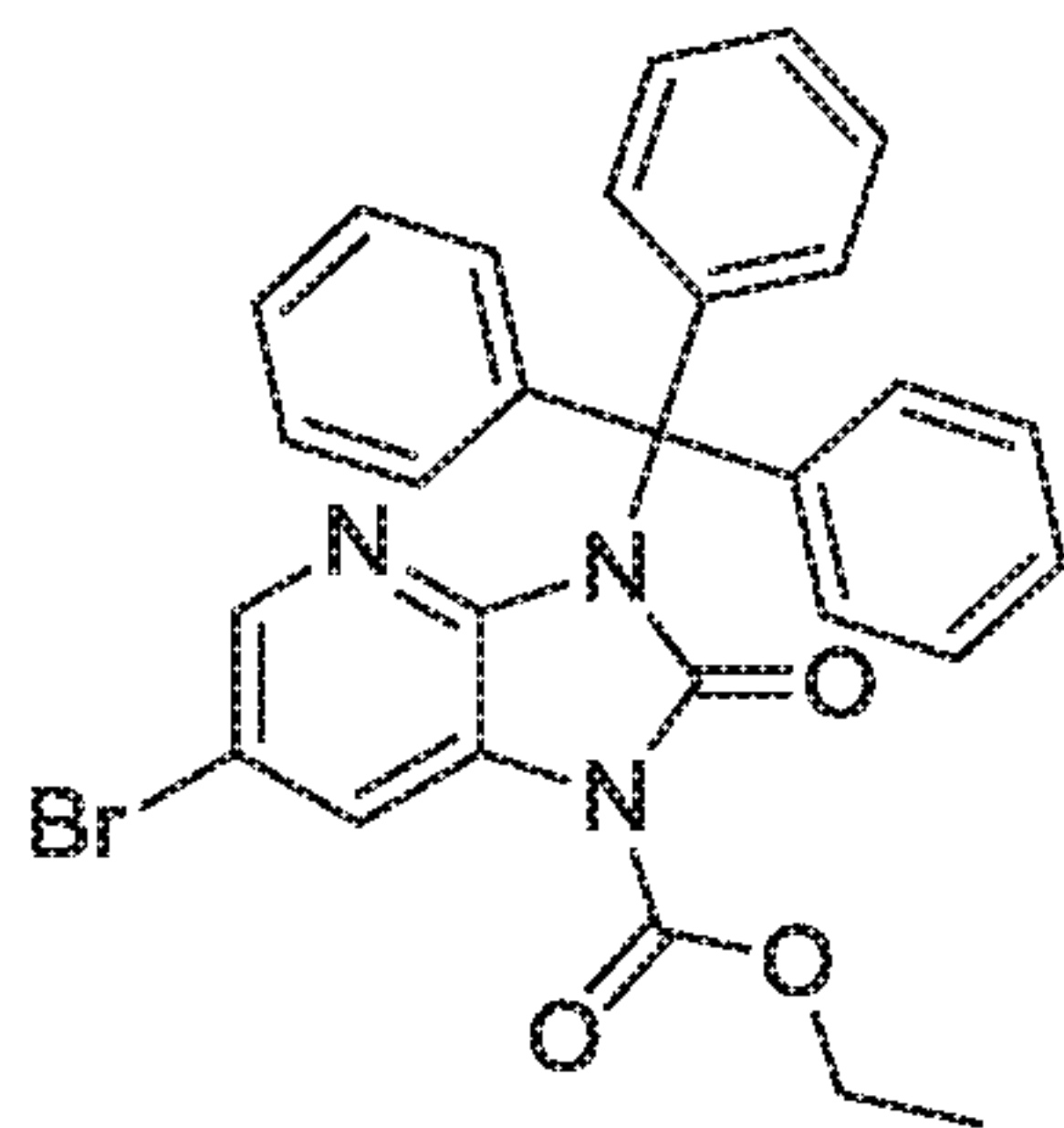
5 Intermediate 34: 2-(6-Bromo-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)-N-cyclopropylacetamide.



The title compound was prepared in a manner analogous to Intermediate 32, using 2-bromo-N-cyclopropylacetamide in Step C.

10

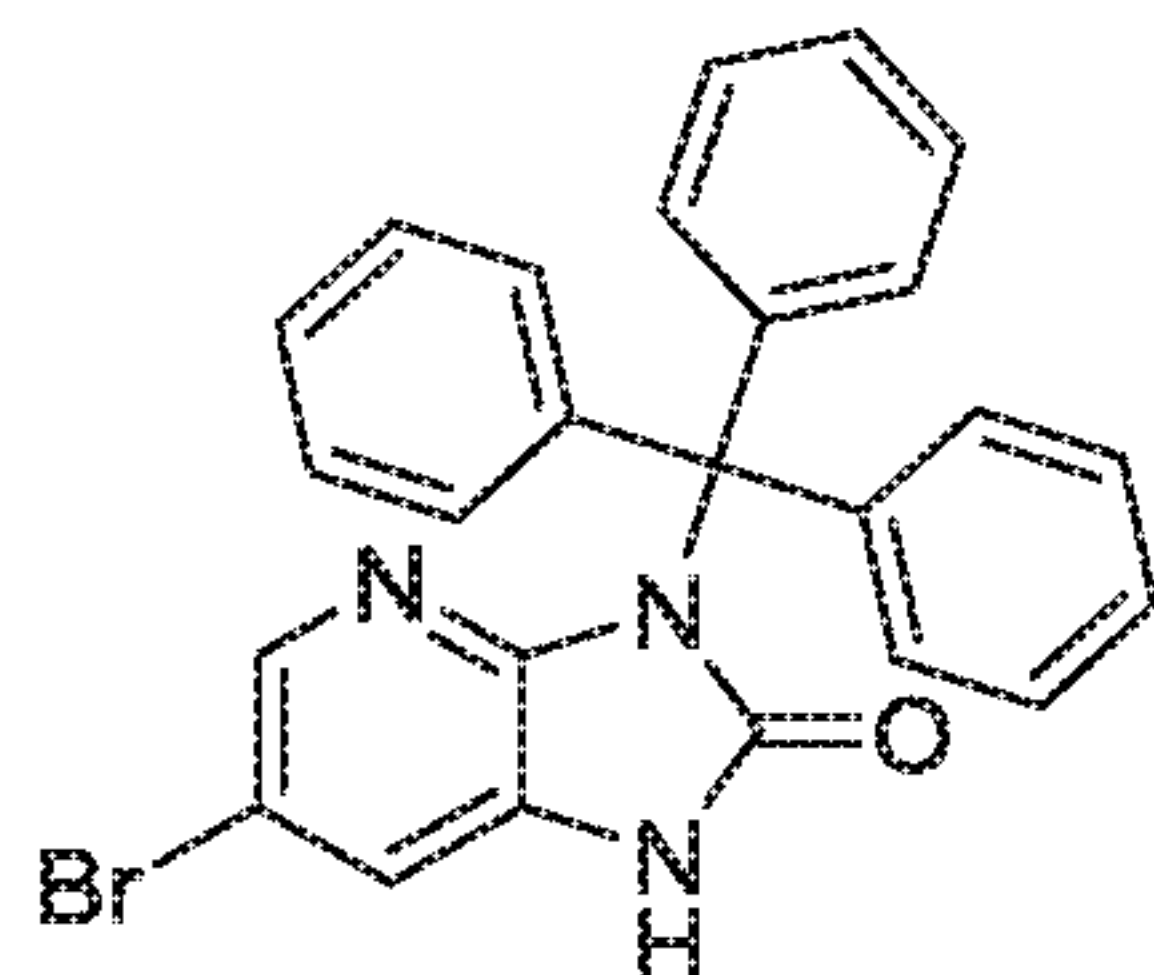
Intermediate 35: Ethyl 6-bromo-2-oxo-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridine-1-carboxylate.



To a solution of ethyl 6-bromo-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridine-1-  
 15 carboxylate (Intermediate 9, 703 mg, 2.46 mmol) in DCM (25 mL) was added trityl  
 chloride (788 mg, 2.82 mmol) followed by Et<sub>3</sub>N (615  $\mu$ L, 4.42 mmol). The mixture was  
 stirred at room temperature for 48 h then concentrated and the crude oil was purified by  
 SiO<sub>2</sub> (0 to 25% EtOAc in hexanes) to yield the title compound as an amorphous solid  
 (1.22 g, 94%). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): 8.15 (d, *J* = 2.1 Hz, 1H), 7.90 (d, *J* = 2.2 Hz,

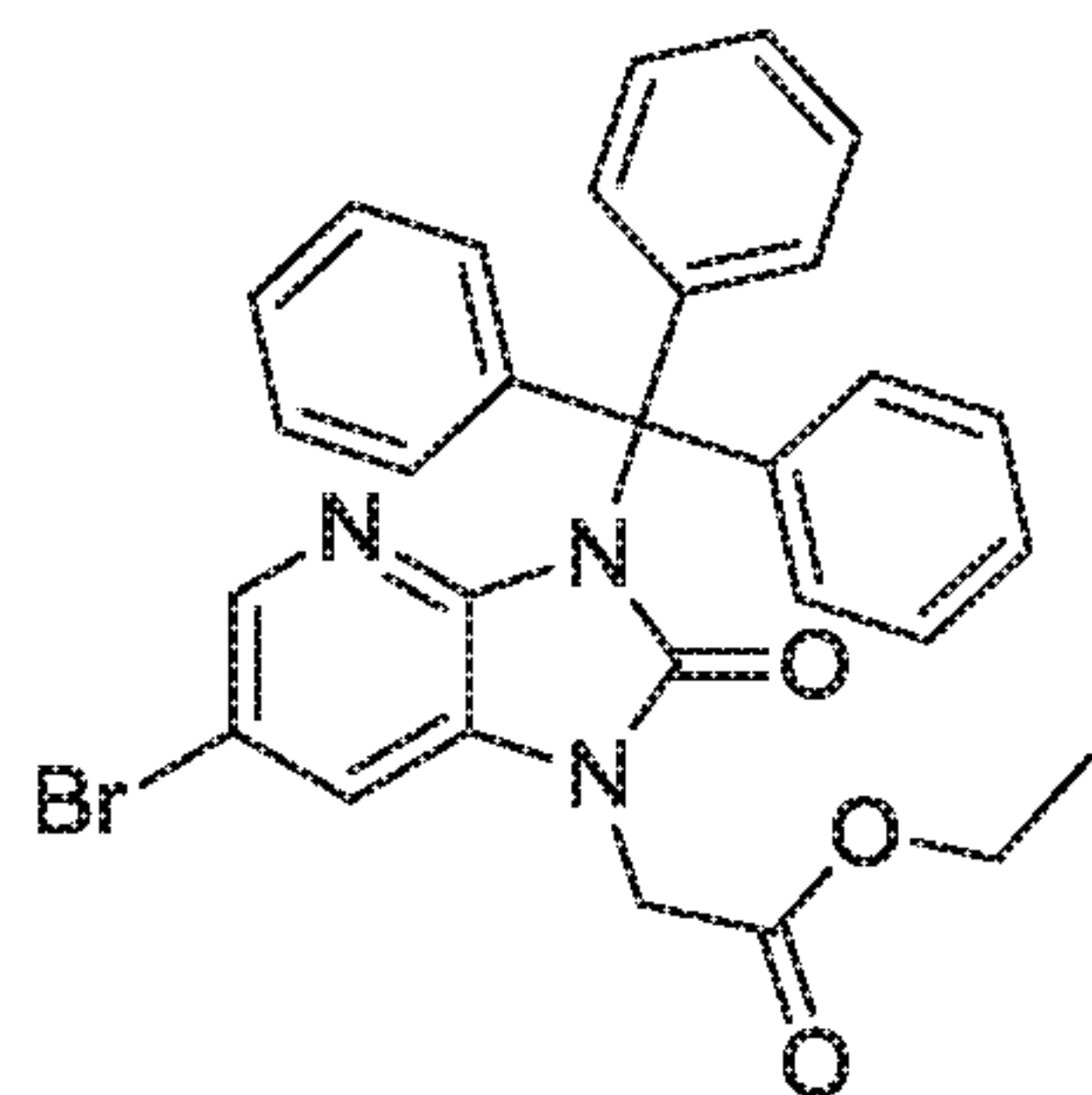
1H), 7.54 – 7.43 (m, 6H), 7.25 – 7.14 (m, 9H), 4.47 (q,  $J = 7.1$  Hz, 2H), 1.42 (t,  $J = 7.1$  Hz, 3H).

Intermediate 36: 6-Bromo-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.



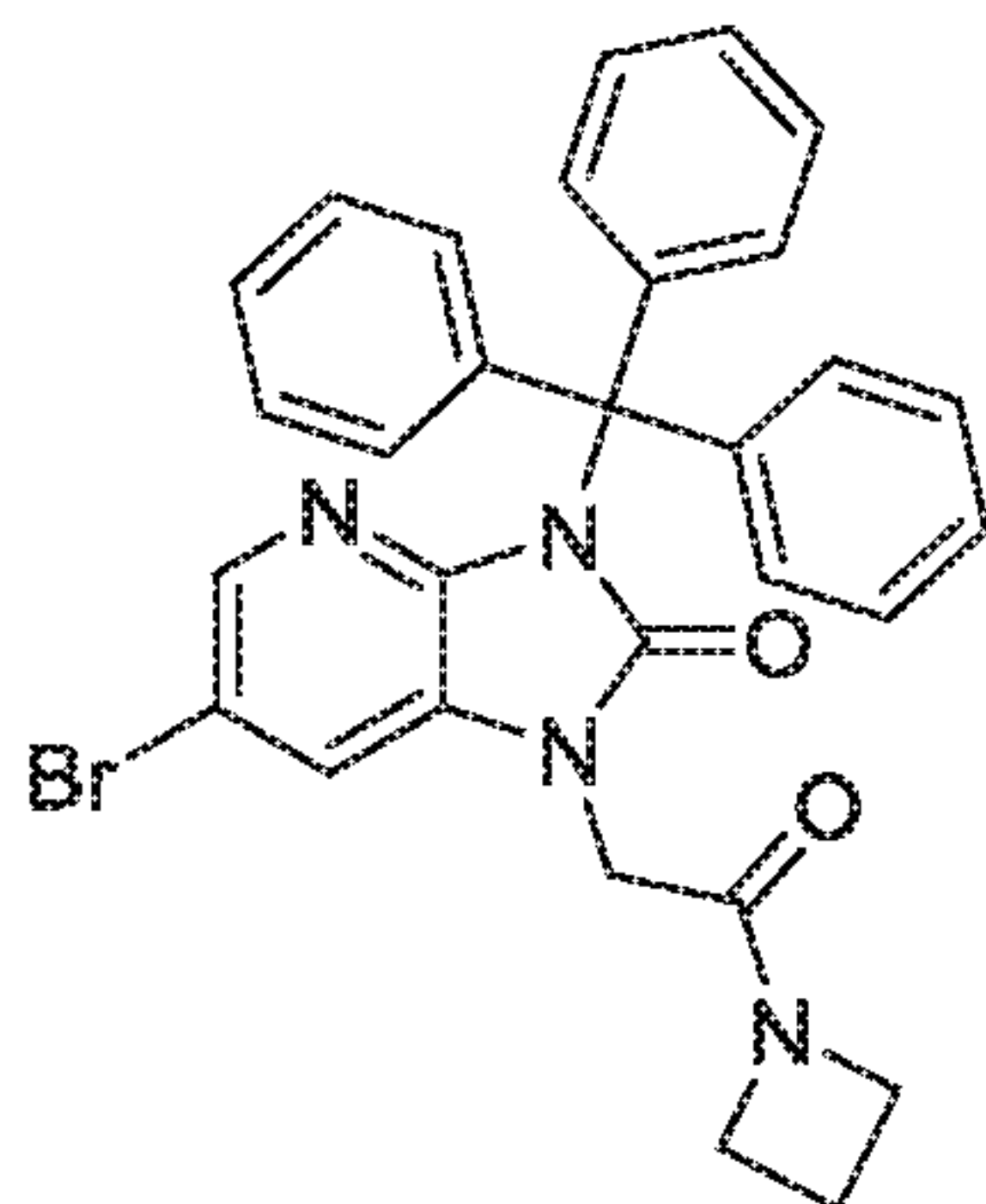
- 5 A mixture of ethyl 6-bromo-2-oxo-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridine-1-carboxylate (Intermediate 35, 3.7 g, 7.0 mmol) and isopropylamine (0.72 mL, 8.4 mmol) in THF (35 mL) was stirred at room temperature for 2 h. Then, the reaction mixture was concentrated under vacuum to yield the title compound as a yellow oil (3.2 g, 7.0 mmol, 100%), which was used without further purification. MS (ESI): mass calcd. for
- 10  $C_{25}H_{18}BrN_3O$ , 455.1;  $m/z$  found, 454  $[M+H]^+$ .

Intermediate 37: Ethyl 2-(6-bromo-2-oxo-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetate.



- 15 Under a nitrogen atmosphere was added 6-bromo-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 36, 2 g, 4.4 mmol) to a suspension of NaH (60% dispersion in mineral oil, 245 mg, 6.1 mmol) in DMF (20 mL). After 5 minutes, ethyl bromoacetate (0.68 mL, 6.1 mmol) was added to the reaction mixture. After 16 h, the reaction mixture was quenched with water (100 mL). The precipitates were filtered off,
- 20 washed with water and dried under vacuum to afford the title product. The crude material was moved forward to the next step as is.

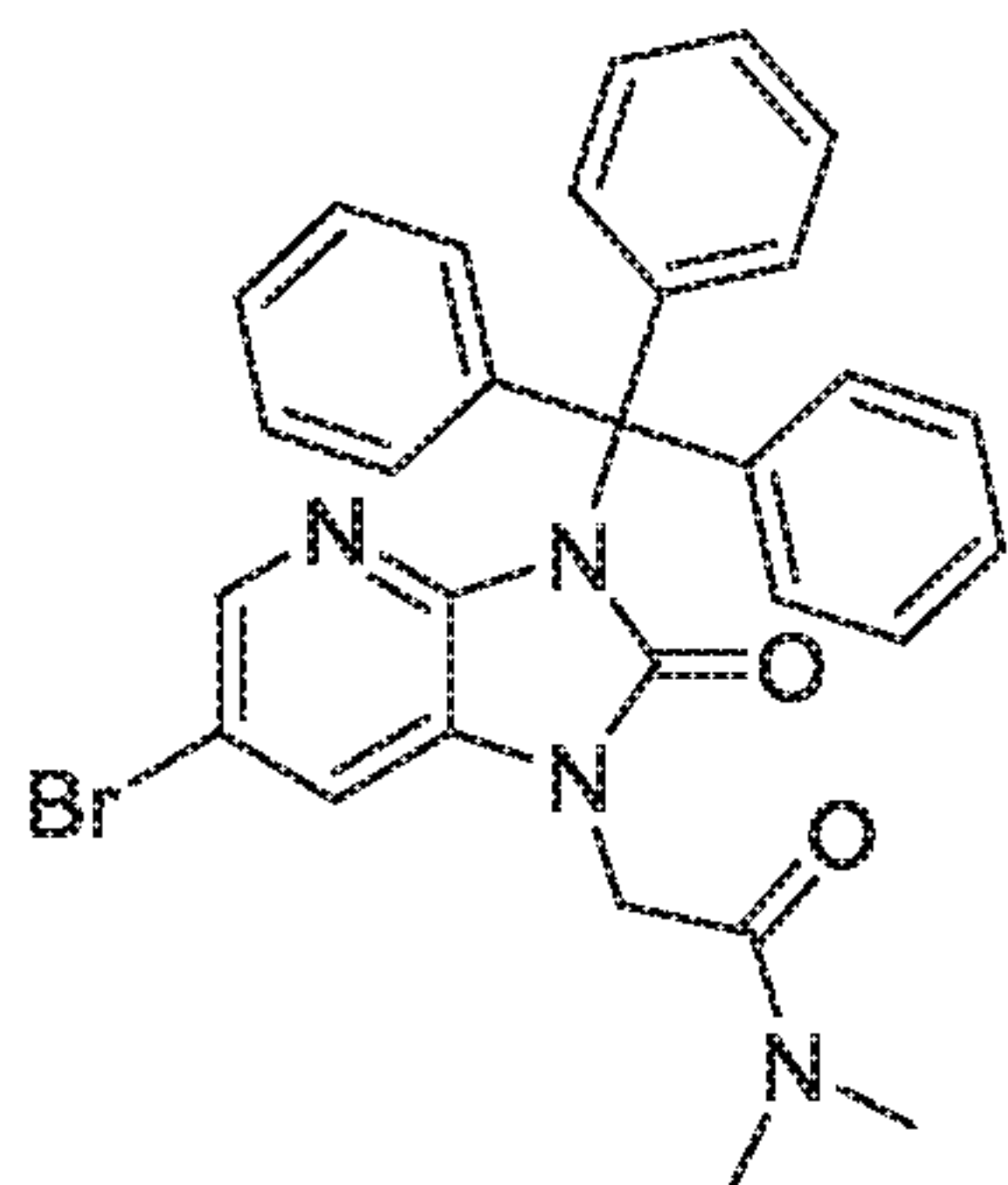
Intermediate 38: 1-(2-(Azetidin-1-yl)-2-oxoethyl)-6-bromo-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.



Step A: 2-(6-Bromo-2-oxo-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetic acid.

- 5 To a solution of ethyl 2-(6-bromo-2-oxo-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetate (Intermediate 37, 2.4 g, 4.4 mmol) in THF (60 mL) at room temperature was added LiOH (2 M, 3.1 mL, 6.1 mmol). After 16 h, the precipitates were collected by filtration, washed with water and dried under vacuum to afford the title compound (546 mg, 1.1 mmol, 24.3 %). A saturated aqueous solution of NH<sub>4</sub>Cl was added to the filtrate.
- 10 The mixture was extracted with EtOAc (3x) to remove organic impurities. The solids in the aqueous layer were collected by filtration, rinsed with water and dried under vacuum to afford the title compound (1.51 g, 67%). <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 7.70 (d, *J* = 2.1 Hz, 1H), 7.44 – 7.38 (m, 6H), 7.36 (d, *J* = 2.1 Hz, 1H), 7.25 – 7.11 (m, 10H), 3.93 (s, 2H).
- 15 Step B: 1-(2-(Azetidin-1-yl)-2-oxoethyl)-6-bromo-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. HATU (582 mg, 1.5 mmol) was added to a mixture of 2-(6-bromo-2-oxo-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetic acid (656 mg, 1.3 mmol), azetidine (0.103 mL, 1.5 mmol) and DIPEA (0.44 mL, 2.6 mmol) in DMF (15 mL) at room temperature. After completion, a saturated aqueous solution of NaHCO<sub>3</sub> (20 mL)
- 20 was added, and the mixture was extracted using EtOAc (3 x 30 mL). The combined organics were dried over MgSO<sub>4</sub>, filtered and concentrated under vacuum. The crude material was purified (FCC, SiO<sub>2</sub>, 0-90% EtOAc in hexanes) to afford the title compound (260 mg, 37 %). <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 7.79 (d, *J* = 2.1 Hz, 1H), 7.70 (d, *J* = 2.1 Hz, 1H), 7.42 – 7.38 (m, 6H), 7.26 – 7.12 (m, 9H), 4.47 (s, 2H), 4.09 (t, *J* = 7.6 Hz, 2H), 3.87 (t, *J* = 7.6 Hz, 2H), 2.22 (p, *J* = 7.8 Hz, 2H).
- 25

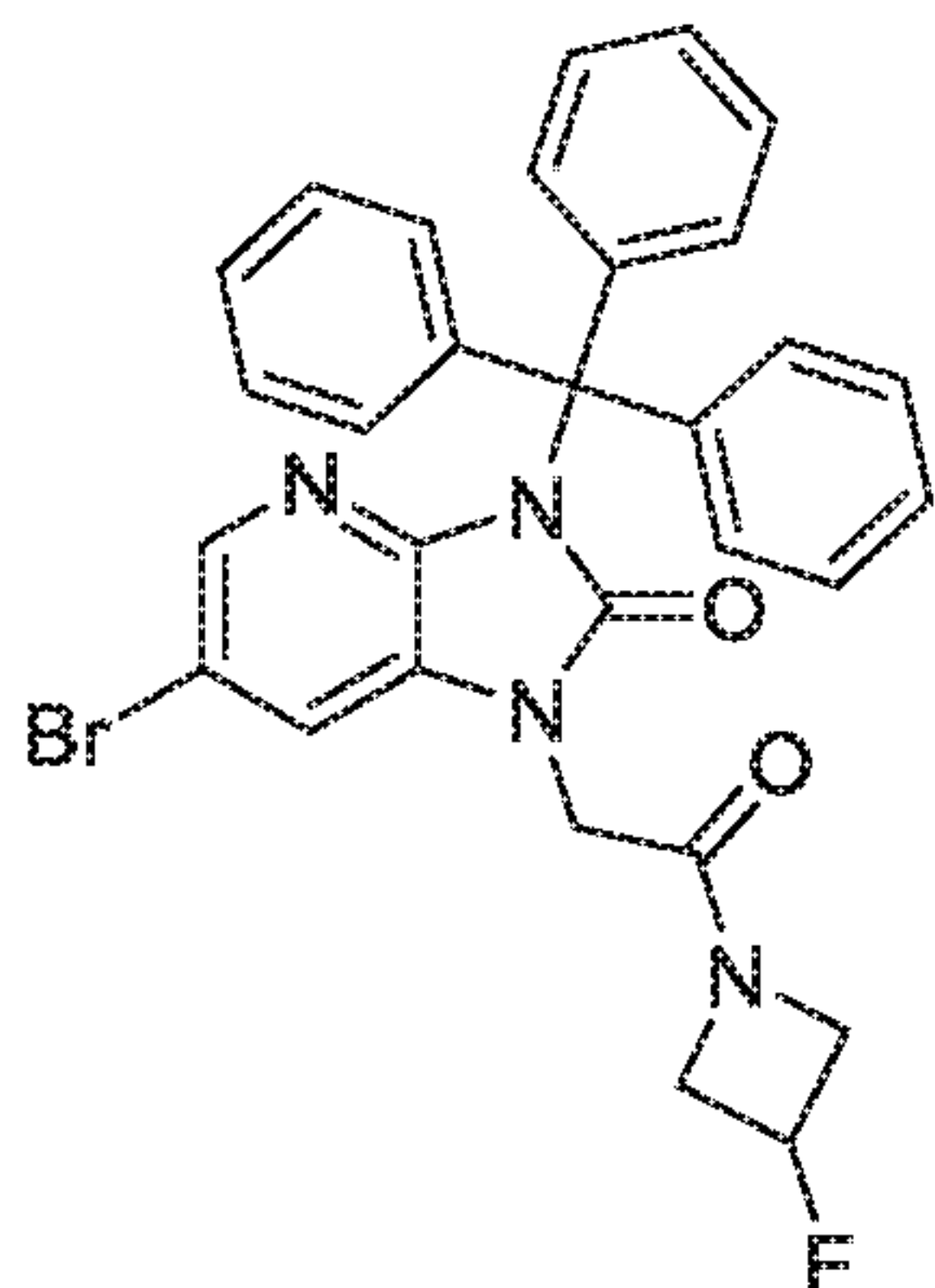
Intermediate 39: 2-(6-Bromo-2-oxo-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)-N,N-dimethylacetamide.



- 5 2,4,6-Tripropyl-1,3,5,2,4,6-trioxatriphosphorinane-2,4,6-trioxide solution (T3P<sup>®</sup>) (3.25 mL, 5.4 mmol) was added to a mixture of 2-(6-bromo-2-oxo-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetic acid (Intermediate 38, product from Step A, 941 mg, 1.8 mmol), dimethylamine hydrochloride (177 mg, 2.2 mmol) and DIPEA (0.94 mL, 5.4 mmol) in DCM (10 mL) at room temperature. After completion, a saturated aqueous
- 10 solution of NaHCO<sub>3</sub> (20 mL) was added, and the mixture was extracted using DCM (3 x 30 mL). The combined organics were dried over MgSO<sub>4</sub>, filtered and concentrated under vacuum. The crude material was purified (FCC, SiO<sub>2</sub>, 0-100% EtOAc in hexanes) to afford the title compound (927 mg, 1.7 mmol, 94 %). No NMR only LCMS of reaction. TFA used to deprotect trityl in LCMS sample; trityl group swamps out product signal.

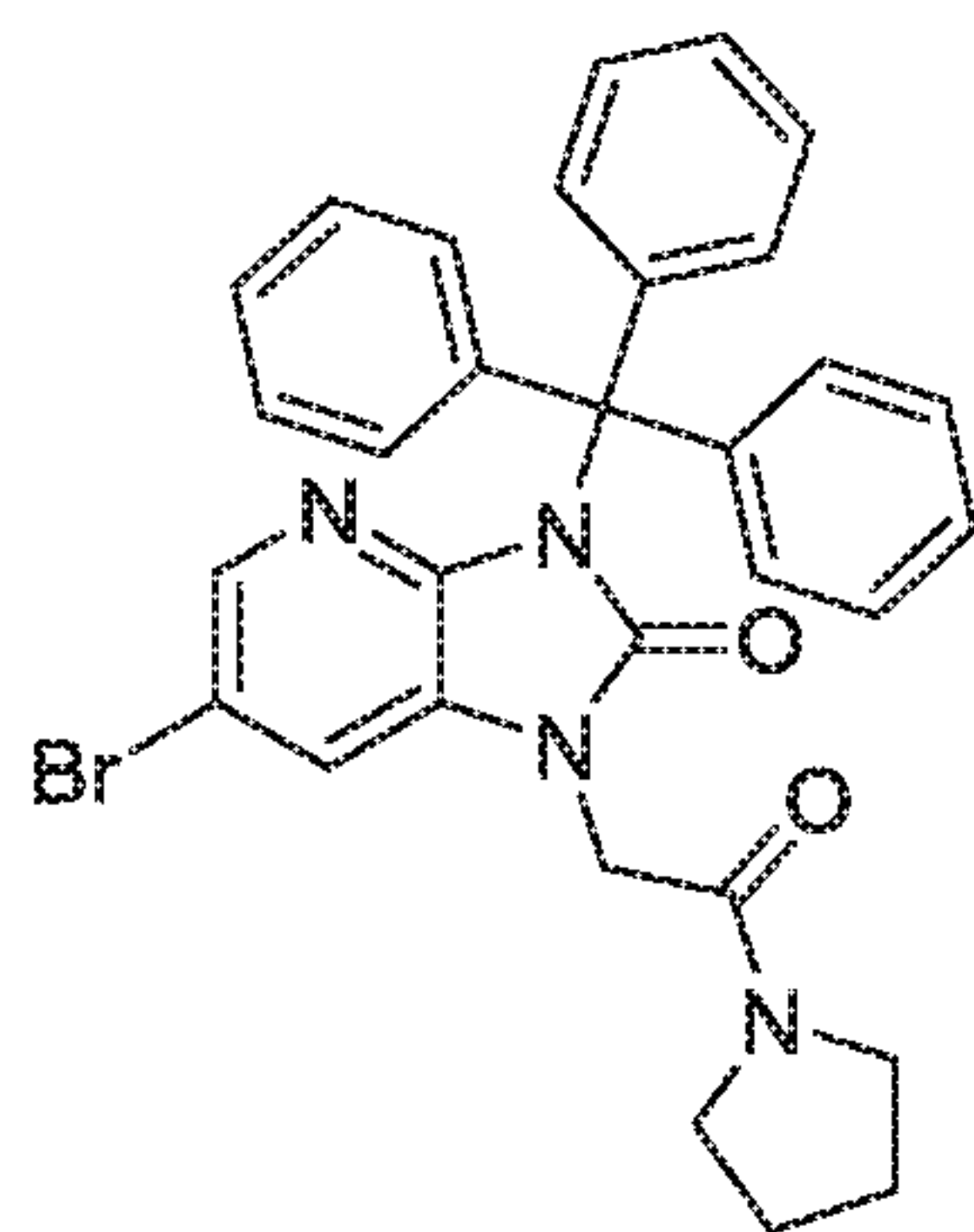
15

Intermediate 40: 1-(2-(3-Fluoroazetidin-1-yl)-2-oxoethyl)-6-bromo-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.



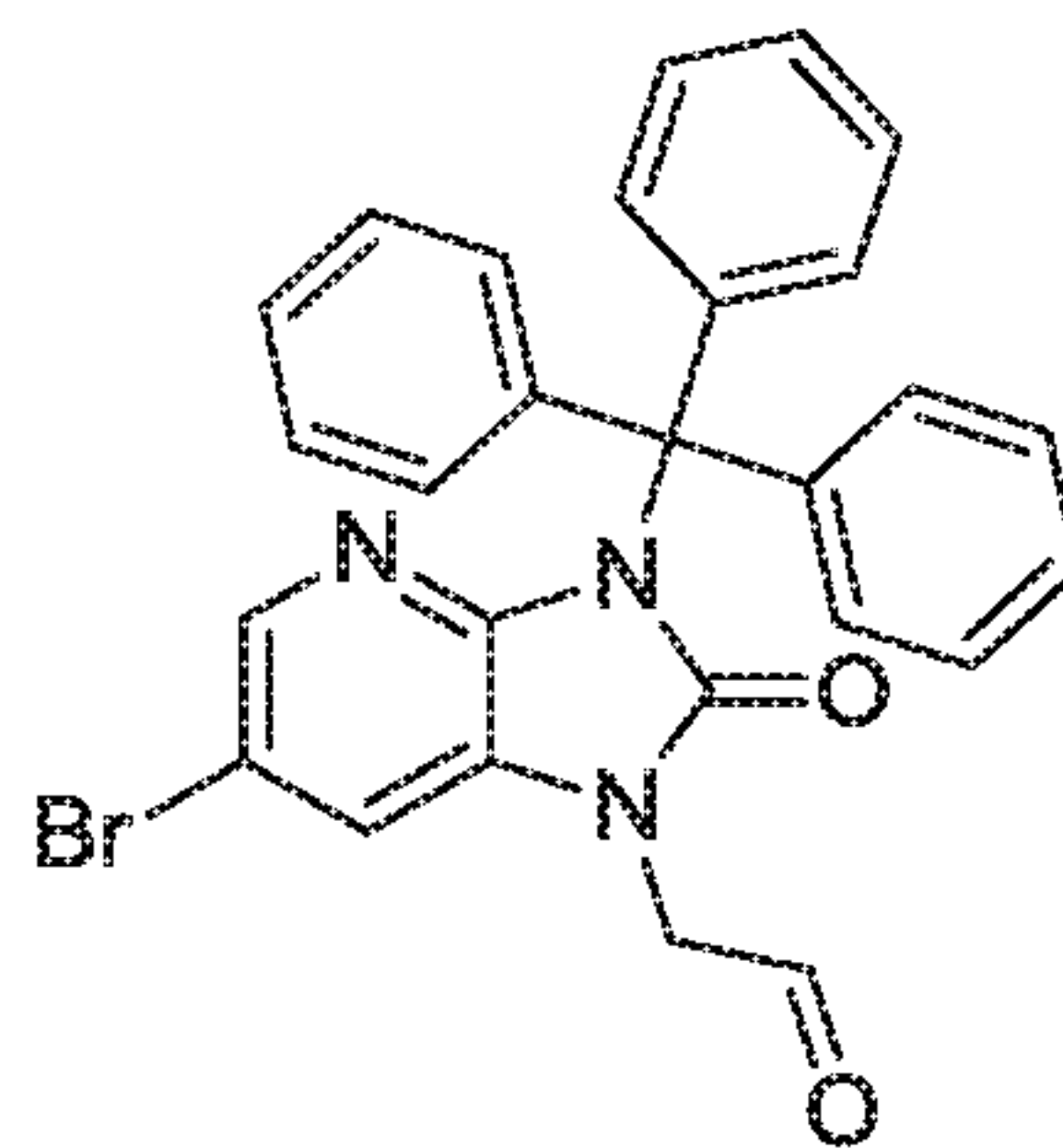
The title compounds was made in an analogous manner to 2-(6-bromo-2-oxo-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)-N,N-dimethylacetamide (Intermediate 39) using 3-fluoroazetidine hydrochloride in Step B. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.85 – 7.82 (m, 1H), 7.51 – 7.46 (m, 6H), 7.29 – 7.27 (m, 1H), 7.25 – 7.15 (m, 9H), 5.23 – 5.06 (m, 1H), 4.44 – 4.31 (m, 2H), 4.31 – 4.21 (m, 1H), 4.11 – 4.05 (m, 1H), 4.02 – 3.93 (m, 1H), 3.93 – 3.83 (m, 1H).

Intermediate 41: 1-(2-(Pyrrolidin-1-yl)-2-oxoethyl)-6-bromo-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.



The title compounds was made in an analogous manner to 2-(6-bromo-2-oxo-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)-N,N-dimethylacetamide (Intermediate 39) using pyrrolidine in Step B.

Intermediate 42: 2-(6-Bromo-2-oxo-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetaldehyde.



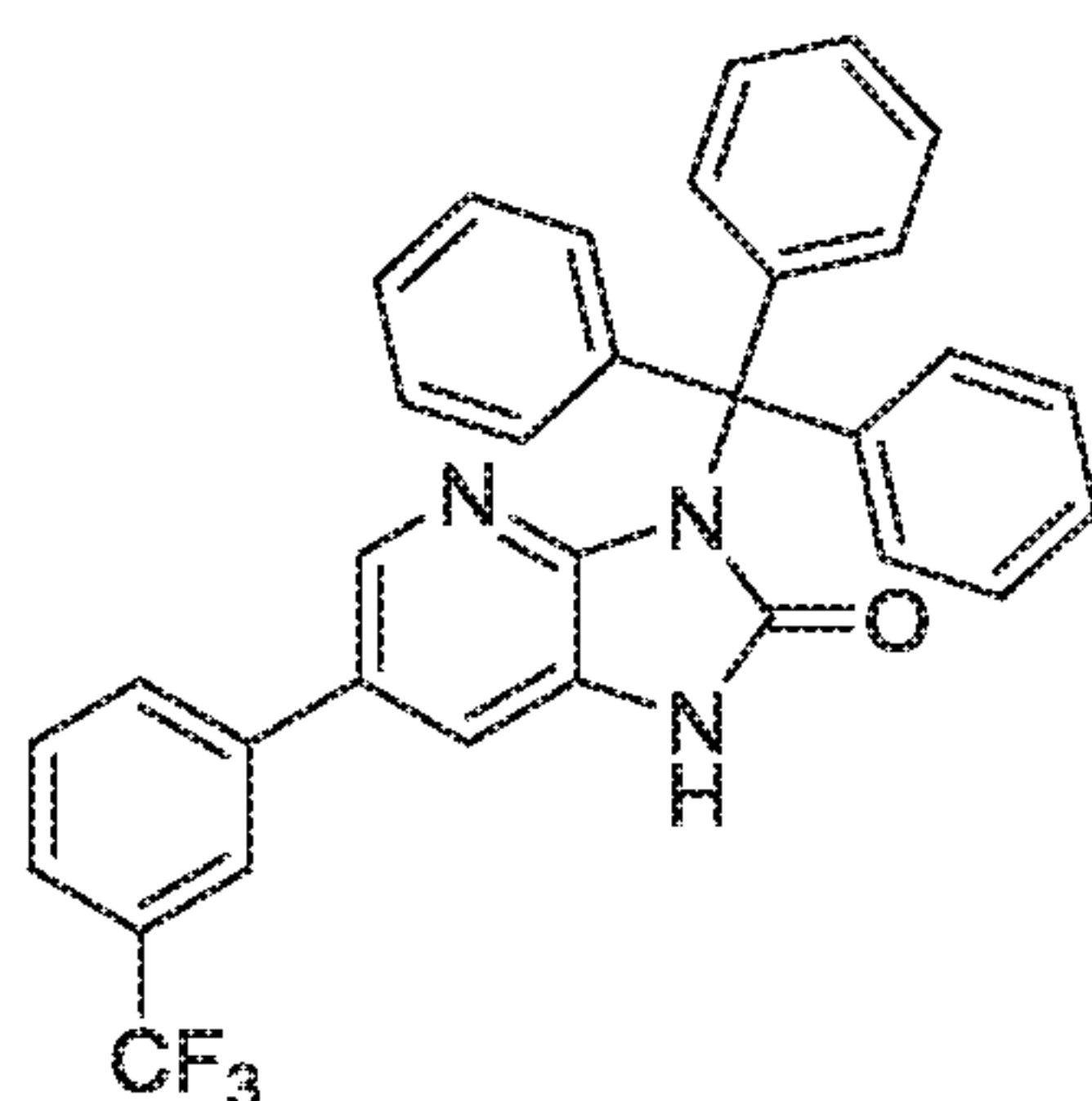
Step A: 6-Bromo-1-(2-hydroxyethyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.

A solution of ethyl 2-(6-bromo-2-oxo-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetate (Intermediate 37, 8.1 g, 15 mmol) in THF (406 mL) was cooled to 0°C in an

ice and acetone bath. To the reaction was added lithium borohydride (15 mL, 30 mmol) and the reaction was allowed to warm to room temperature for 10 minutes and then heated to 65°C for an additional hour. Then, the reaction mixture was cooled to room temperature, and the crude mixture was quenched with water (250 mL) and extracted with ethyl acetate (500 mL). The organics were dried over MgSO<sub>4</sub>, concentrated in vacuo, and purified (FCC, SiO<sub>2</sub>, 0-100% EtOAc in hexanes) to provide the title compound (6.6 g, 88%). <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 7.80 – 7.75 (m, 1H), 7.75 – 7.66 (m, 1H), 7.49 – 7.39 (m, 6H), 7.28 – 7.18 (m, 6H), 7.18 – 7.07 (m, 3H), 4.96 – 4.85 (m, 1H), 3.87 – 3.74 (m, 2H), 3.65 – 3.53 (d, *J* = 5.1 Hz, 2H).

Step B: 2-(6-Bromo-2-oxo-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetaldehyde. A solution of 6-bromo-1-(2-hydroxyethyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (5.5 g, 11 mmol) and sodium bicarbonate (2.8 g, 33 mmol) in DCM (48 mL) was cooled to 0°C in an ice and acetone bath, and Dess-Martin Periodinane (5.6 g, 13 mmol) was added. The reaction mixture was warmed to room temperature and stirred for 1 hour. Then, the reaction mixture was concentrated in vacuo and taken up in THF (50 mL). The crude reaction was filtered through a pad of Celite®, concentrated down in vacuo and purified (FCC, SiO<sub>2</sub>, 25-80% EtOAc in hexanes) to afford the title compound (4.2 g, 90%). <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 9.53 (s, 1H), 7.85 – 7.80 (d, *J* = 2.1 Hz, 1H), 7.75 – 7.69 (d, *J* = 2.1 Hz, 1H), 7.52 – 7.39 (m, 6H), 7.31 – 7.20 (m, 6H), 7.20 – 7.12 (m, 3H), 4.82 (s, 2H).

Intermediate 43: 6-(3-(trifluoromethyl)phenyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.



Step A: 5-(3-(Trifluoromethyl)phenyl)pyridine-2,3-diamine. A mixture of 2,3-diamino-5-bromopyridine (2 g, 10.6 mmol), 3-(trifluoromethyl)phenylboronic acid (4.04 g, 21.3

mmol), 1,1'-bis(diphenylphosphino)ferrocene palladium(II)dichloride dichloromethane complex (608 mg, 0.75 mmol), Cs<sub>2</sub>CO<sub>3</sub> (6.93 g, 21.3 mmol), dioxane (98 mL) and H<sub>2</sub>O (21 mL) was heated to 90 °C using an oil bath. After 16 h, starting material was completely consumed. The reaction mixture was cooled to room temperature and  
 5 volatiles were removed. A saturated aqueous solution of NaHCO<sub>3</sub> (30 mL) followed by solid NaCl was added to the reaction mixture, and the mixture was extracted with EtOAc (3 x 60 mL). The combined organic layers were dried over MgSO<sub>4</sub>, filtered and concentrated under vacuum. The crude material was purified (FCC, 0-100% EtOAc in hexanes), to give the title compound (2.6 g, 97%). MS (ESI): mass calcd. for  
 10 C<sub>12</sub>H<sub>10</sub>F<sub>3</sub>N<sub>3</sub>, 253.1; m/z found, 254.1 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 7.84 – 7.79 (m, 1H), 7.77 – 7.74 (m, 1H), 7.69 (d, *J* = 2.2 Hz, 1H), 7.64 – 7.56 (m, 2H), 7.06 (d, *J* = 2.3 Hz, 1H), 5.68 (s, 2H), 4.84 (s, 2H)

Step B: 6-(3-(Trifluoromethyl)phenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. Under a nitrogen atmosphere, CDI (8.2 g, 50.8 mmol) was added to a mixture of 5-(3-(trifluoromethyl)phenyl)pyridine-2,3-diamine (10.7 g, 42.3 mmol) in DMF (428 mL) at  
 15 room temperature. After 3 h, conversion was not complete and additional CDI (3.4 g, 21.4 mmol) was added to the reaction mixture. Once complete conversion was observed water was added, and the mixture was allowed to stir for an additional 30 min. The solids were collected by filtration, washed with water and dried under vacuum to  
 20 afford the title compound (11.3 g, 40.6 mmol, 96%), which was used in the next step without further purification. MS (ESI): mass calcd. for C<sub>13</sub>H<sub>8</sub>F<sub>3</sub>N<sub>3</sub>O, 279.1; m/z found, 280.1 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 11.47 (s, 1H), 11.02 (s, 1H), 8.25 (d, *J* = 2.0 Hz, 1H), 8.01 – 7.95 (m, 2H), 7.75 – 7.66 (m, 2H), 7.55 (d, *J* = 2.0 Hz, 1H).

Step C: Ethyl 2-oxo-6-(3-(trifluoromethyl)phenyl)-2,3-dihydro-1H-imidazo[4,5-b]pyridine-1-carboxylate. Under a nitrogen atmosphere, a mixture of 6-(3-(trifluoromethyl)phenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (2.86 g, 10.2 mmol), ethyl pyridin-2-yl carbonate (2.57 g, 15.4 mmol) and K<sub>2</sub>CO<sub>3</sub> (2.12 g, 15.4 mmol) in DMF (80 mL) was heated to 75 °C. After 16 h, water was added followed by 10% HCl until the mixture reached pH 1. The precipitates were filtered, washed with water and collected to afford  
 25 the title compound, which was used in the next step without further purification. MS (ESI): mass calcd. for C<sub>16</sub>H<sub>12</sub>F<sub>3</sub>N<sub>3</sub>O<sub>3</sub>, 351.1; m/z found, 352.1 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (400  
 30

MHz, DMSO)  $\delta$  12.15 (s, 1H), 8.46 (d,  $J$  = 2.1 Hz, 1H), 8.15 (d,  $J$  = 2.1 Hz, 1H), 8.01 – 7.94 (m, 2H), 7.80 – 7.70 (m, 2H), 4.44 (q,  $J$  = 7.1 Hz, 2H), 1.38 (t,  $J$  = 7.1 Hz, 3H).

Step D: Ethyl 2-oxo-6-(3-(trifluoromethyl)phenyl)-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridine-1-carboxylate. A mixture of TEA (1.42 mL, 10.2 mmol), ethyl 2-oxo-6-(3-

(trifluoromethyl)phenyl)-2,3-dihydro-1H-imidazo[4,5-b]pyridine-1-carboxylate (2.0 g, 5.7 mmol) and trityl chloride (1.9 g, 6.8 mmol) in DMF was stirred at room temperature.

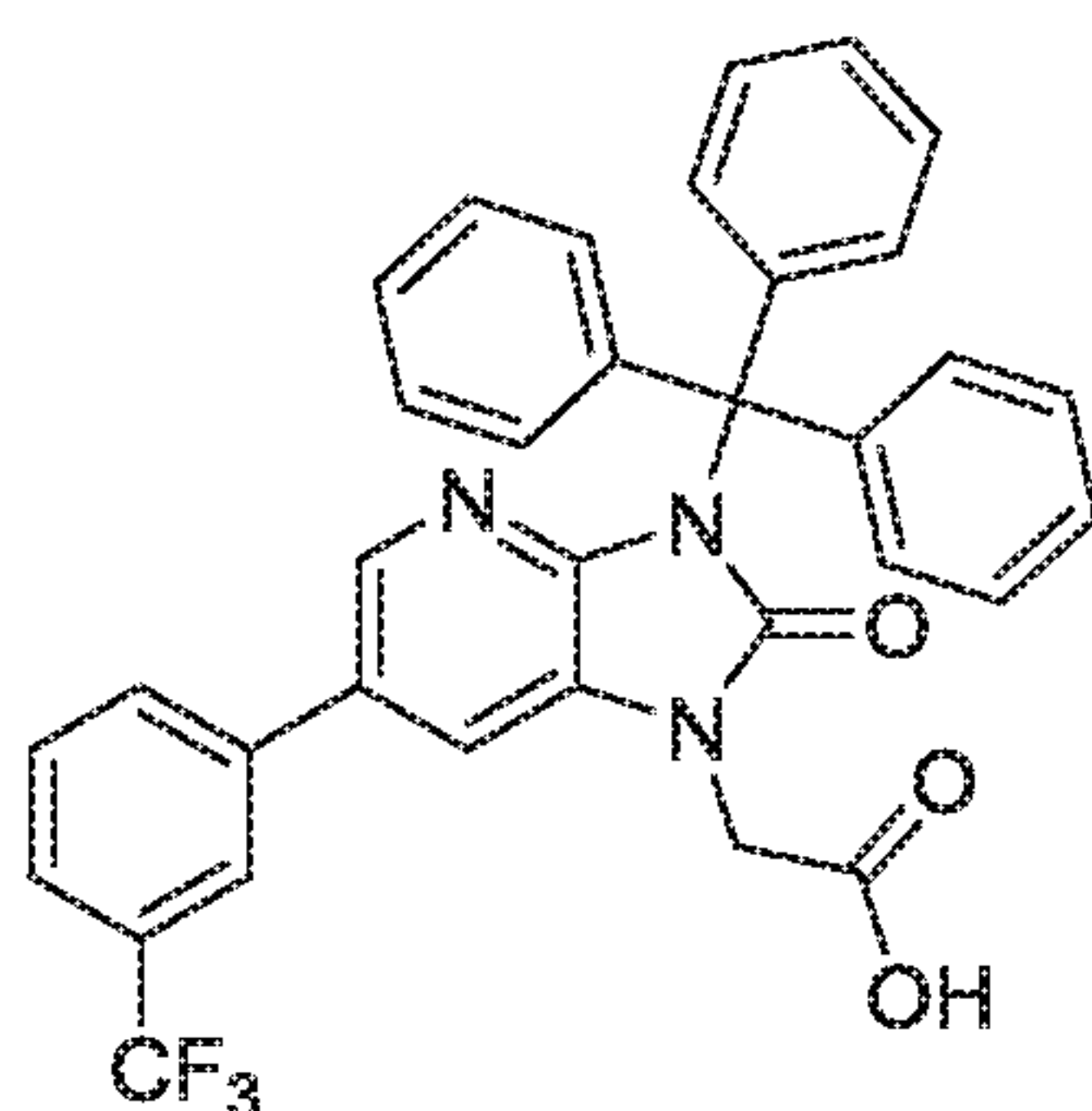
After 16 h, the reaction mixture was quenched with a saturated aqueous solution of  $\text{NH}_4\text{Cl}$  (40 mL). The precipitates were collected by filtration, washed with water and dried under vacuum to afford the title compound, which was contaminated with a small amount of impurities. The crude material was moved forward to the next step as is.

Step E: 6-(3-(Trifluoromethyl)phenyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.

A mixture of ethyl 2-oxo-6-(3-(trifluoromethyl)phenyl)-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridine-1-carboxylate (3.4 g, 5.7 mmol) and isopropylamine (0.59 mL, 6.8 mmol) in THF (30 mL) was stirred at room temperature. After 16 h, the reaction mixture was

concentrated under vacuum and the crude material was purified (FCC,  $\text{SiO}_2$ , 0-90% EtOAc in hexanes) to give the title compound (2.7 g, 92%).  $^1\text{H}$  NMR (500 MHz,  $\text{DMSO}-d_6$ )  $\delta$  11.21 (s, 1H), 8.08 (d,  $J$  = 2.1 Hz, 1H), 7.96 – 7.91 (m, 2H), 7.70 – 7.62 (m, 2H), 7.55 – 7.47 (m, 7H), 7.26 – 7.21 (m, 6H), 7.18 – 7.12 (m, 3H).

Intermediate 44: 2-(2-Oxo-6-(3-(trifluoromethyl)phenyl)-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetic acid.



Step A: Ethyl 2-(2-oxo-6-(3-(trifluoromethyl)phenyl)-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetate. Under a nitrogen atmosphere was added 6-(3-

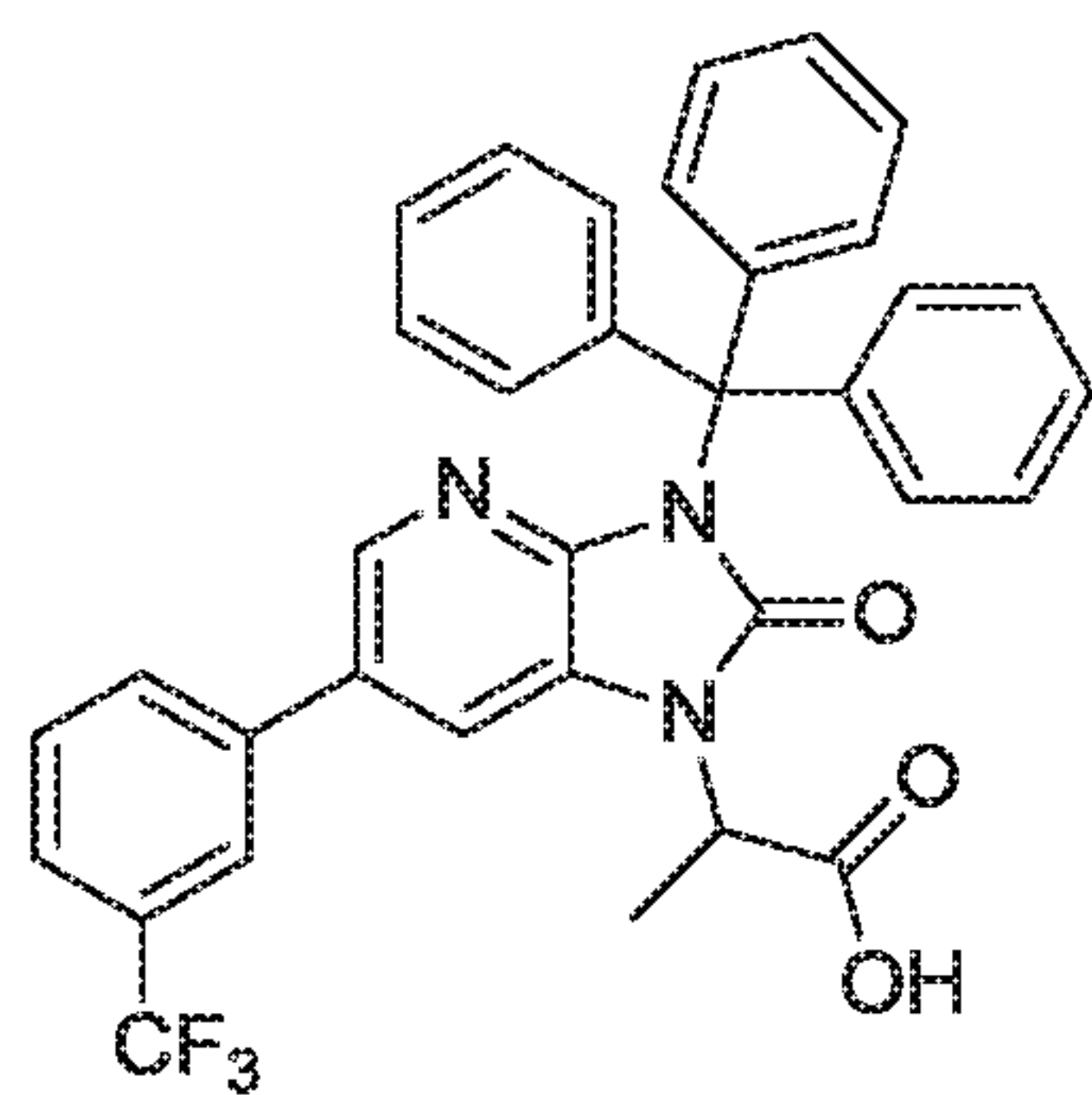
(trifluoromethyl)phenyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 43, 1 g, 1.9 mmol) to a suspension of NaH (60% dispersion in mineral oil, 107 mg, 2.7

mmol) in DMF (20 mL). After 5 minutes, ethyl bromoacetate (0.30 mL, 2.7 mmol) was added to the reaction mixture. After 16 h, the reaction mixture was quenched with water (100 mL). The precipitates were filtered off, washed with water and dried under vacuum. The crude material was purified (FCC, SiO<sub>2</sub>, 0-90% EtOAc in hexanes) to give the title compound (904 mg, 78%) as a foam. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 8.19 (d, *J* = 2.0 Hz, 1H), 8.02 (d, *J* = 2.1 Hz, 1H), 8.01 – 7.93 (m, 2H), 7.72 – 7.63 (m, 2H), 7.49 – 7.42 (m, 6H), 7.29 – 7.11 (m, 9H), 4.76 (s, 2H), 4.10 (q, *J* = 7.1 Hz, 2H), 1.14 (t, *J* = 7.1 Hz, 3H).

Step B: 2-(2-Oxo-6-(3-(trifluoromethyl)phenyl)-3-trityl-2,3-dihydro-1H-imidazo[4,5-

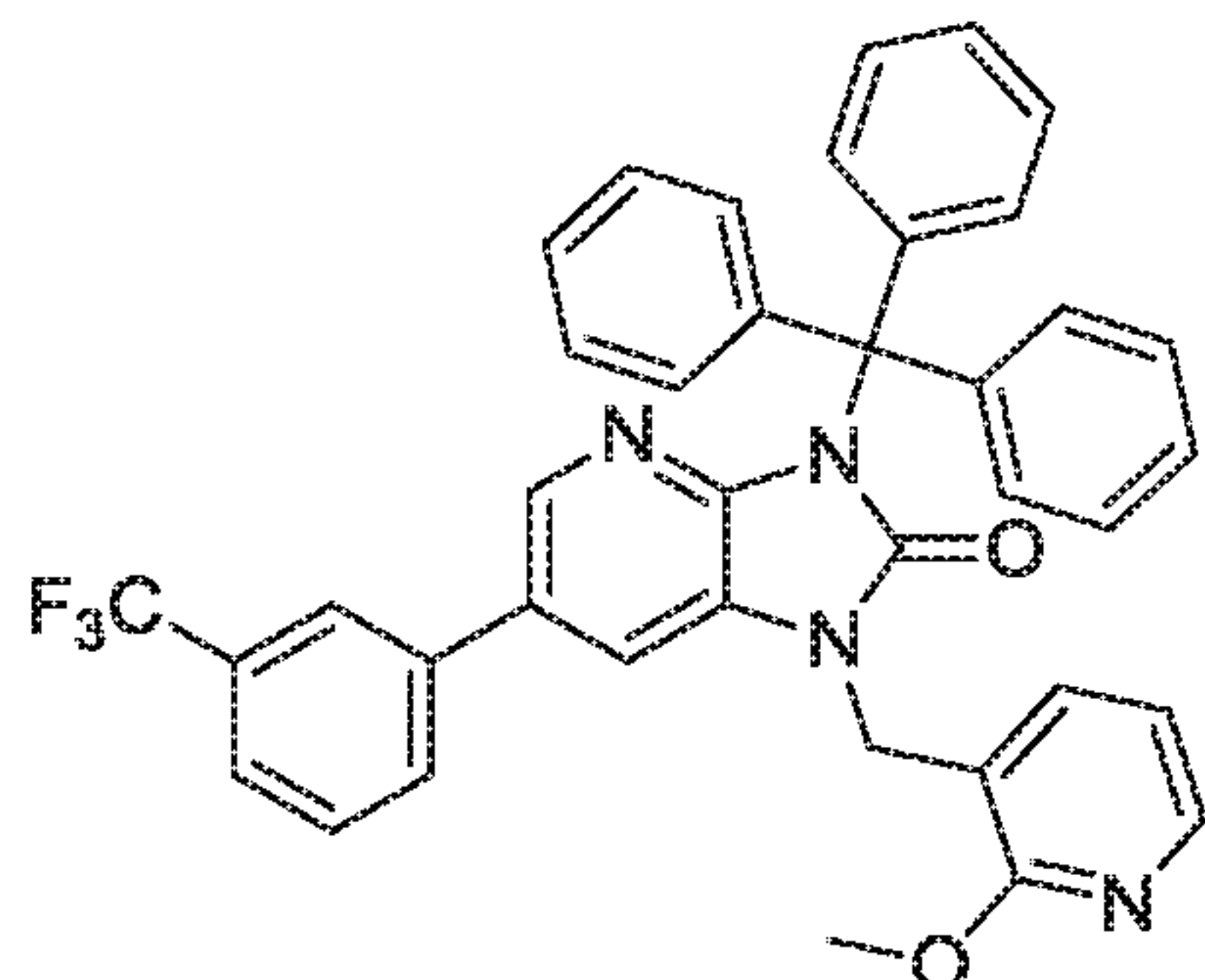
b]pyridin-1-yl)acetic acid. To a solution of ethyl 2-(2-oxo-6-(3-(trifluoromethyl)phenyl)-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetate (904 mg, 1.5 mmol) in THF at room temperature was added LiOH (2 M, 1.04 mL, 2.1 mmol). After 16 h, complete conversion was observed and a saturated aqueous solution of NH<sub>4</sub>Cl (20 mL) was added. The mixture was extracted using EtOAc (3 x 30 mL). The combined organics were dried over MgSO<sub>4</sub>, filtered and concentrated under vacuum to afford the title compound. The crude product was used in the next step without further purification.

Intermediate 45: 2-(2-Oxo-6-(3-(trifluoromethyl)phenyl)-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)propanoic acid.



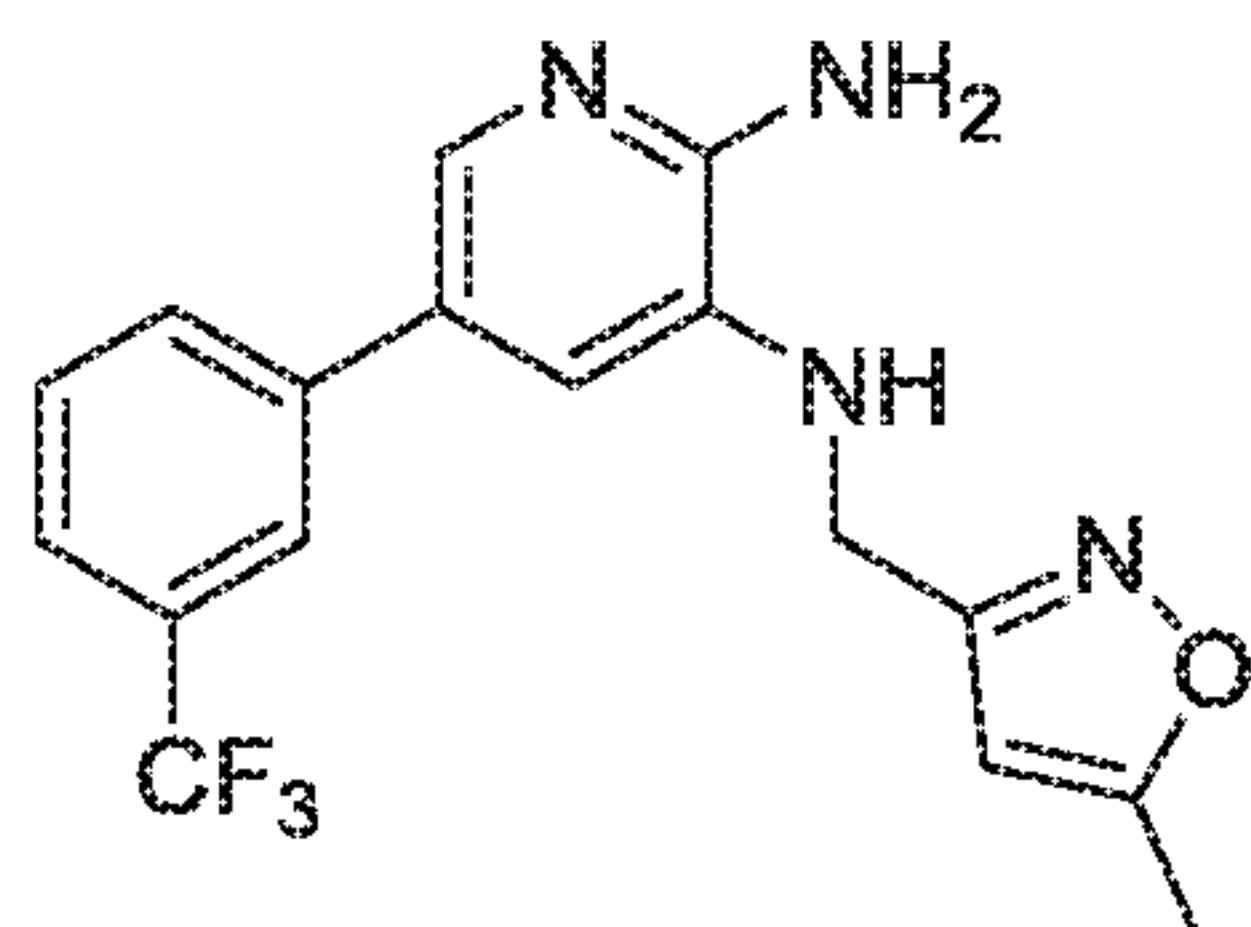
The title compound was prepared in a manner analogous to Intermediate 44, using ethyl 2-bromopropanoate in Step A. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 8.10 (d, *J* = 2.1 Hz, 1H), 7.98 – 7.89 (m, 2H), 7.82 – 7.60 (m, 3H), 7.51 – 7.40 (m, 6H), 7.29 – 7.10 (m, 9H), 5.04 – 4.88 (m, 1H), 1.53 (d, *J* = 7.2 Hz, 3H).

Intermediate 46: 1-((2-Methoxypyridin-3-yl)methyl)-6-(3-(trifluoromethyl)phenyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.



The title compound was prepared in a manner analogous to Intermediate 37 using 6-(3-(trifluoromethyl)phenyl)-3-trityl-1H-imidazo[4,5-b]pyridin-2(3H)-one (Intermediate 43) and 3-(chloromethyl)-2-methoxypyridine.

Intermediate 47: N<sup>3</sup>-((5-Methylisoxazol-3-yl)methyl)-5-(3-(trifluoromethyl)phenyl)pyridine-2,3-diamine.



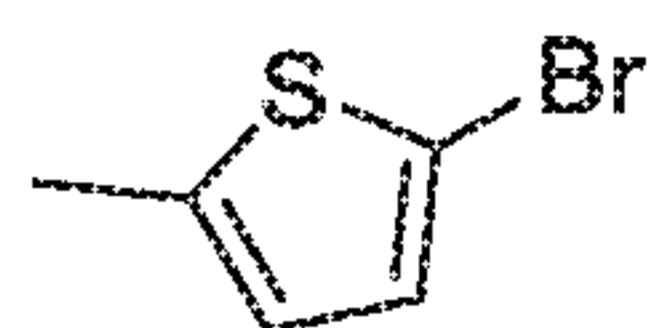
Step A: 5-Bromo-N<sup>3</sup>-((5-methylisoxazol-3-yl)methyl)pyridine-2,3-diamine. A 1 L round bottomed flask was charged with 5-bromopyridine-2,3-diamine (16 g), 5-methylisoxazole-3-carbaldehyde (11.3 g), activated 4Å molecular sieves (24 g) and THF (500 mL). The solution was heated to reflux at 70 °C overnight and then filtered to remove the molecular sieves. All volatiles were removed under vacuum to leave a crude yellow solid which consisted of a mixture of multiple products and excess aldehyde. This material was used directly in the next step without any further purification. The crude was dissolved in EtOH and NaBH<sub>4</sub> (1.40 g) was added and the solution was heated to reflux at 85 °C for 18 h. Then the reaction was quenched with water and the product was extracted with DCM, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated down to a red residue. The product was purified (FCC, SiO<sub>2</sub>, 0-10% MeOH in DCM) to afford the

title compound as solid.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.70 (d, 1H), 6.98 (d, 1H), 5.98 (s, 1H), 4.43 (d, 2H), 4.20 (br s, 2H), 3.81 (br s, 1H), 2.45 (s, 3H).

Step B:  $\text{N}^3$ -((5-Methylisoxazol-3-yl)methyl)-5-(3-(trifluoromethyl)phenyl)pyridine-2,3-

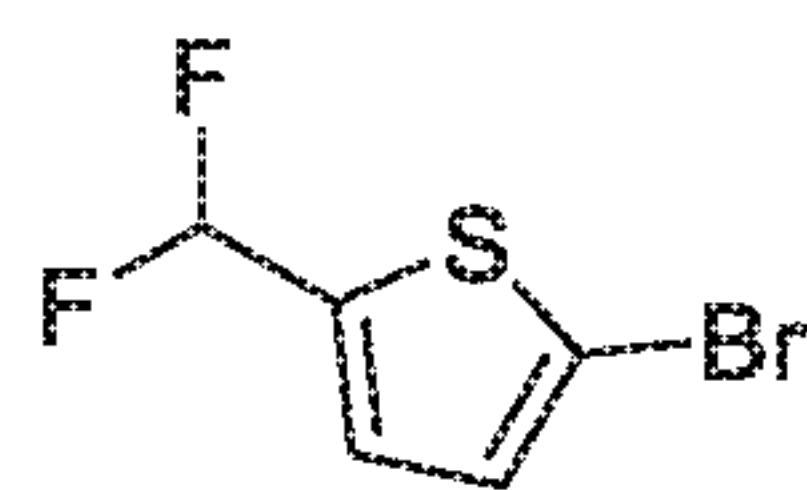
diamine. To a solution of 5-bromo- $\text{N}^3$ -((5-methylisoxazol-3-yl)methyl)pyridine-2,3-diamine (2.8 g, 9.8 mmol) in 1,4-dioxane (50 mL) was added 3-(trifluoromethyl)phenylboronic acid (2.8 g, 14.8 mmol). Then,  $\text{Na}_2\text{CO}_3$  (2.1 g, 19.7 mmol), deionized water (7 mL), and  $\text{Pd}(\text{PPh}_3)_4$  (569.4 mg, 0.49 mmol) was added, and the reaction was heated to  $100^\circ\text{C}$  overnight. The reaction was cooled to room temperature, diluted with ethyl acetate (100 mL) and washed with water (50 mL). The organic layer was collected, dried, filtered and concentrated in vacuo. The crude reaction was purified (FCC,  $\text{SiO}_2$ , 0-20% MeOH in DCM) to provide the title compound (1.0 g, 31%). MS (ESI): mass calcd. for  $\text{C}_{17}\text{H}_{15}\text{F}_3\text{N}_4\text{O}$ , 348.3;  $m/z$  found, 349.2  $[\text{M}+\text{H}]^+$ .

#### Intermediate 48: 2-Bromo-5-methylthiophene



NBS (1.1 eq, 4.0g, 22.7 mmol) was added to a solution of 2-methylthiophene (1.0 eq, 2 mL, 20.7 mmol) in a mixture of chloroform/AcOH (10:1, 20 mL) at  $0^\circ\text{C}$  in the absence of light. The mixture reaction was stirred at  $0^\circ\text{C}$  for 1h. Then the mixture was warmed to rt for 12 hours. The reaction was quenched with aqueous sat.  $\text{NaHCO}_3$  solution. The organic layer was dried ( $\text{MgSO}_4$ ), filtered and the solvents were evaporated in vacuo. The crude product was purified (FCC,  $\text{SiO}_2$ , 0-100 % EtOAc in heptane) to provide the title compound (2.5 g, 69%).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  6.83 (d,  $J = 3.6$  Hz, 1H), 6.52 (d,  $J = 2.5$  Hz, 1H), 2.43 (s, 3H).

#### Intermediate 49: 2-Bromo-5-(difluoromethyl)thiophene.

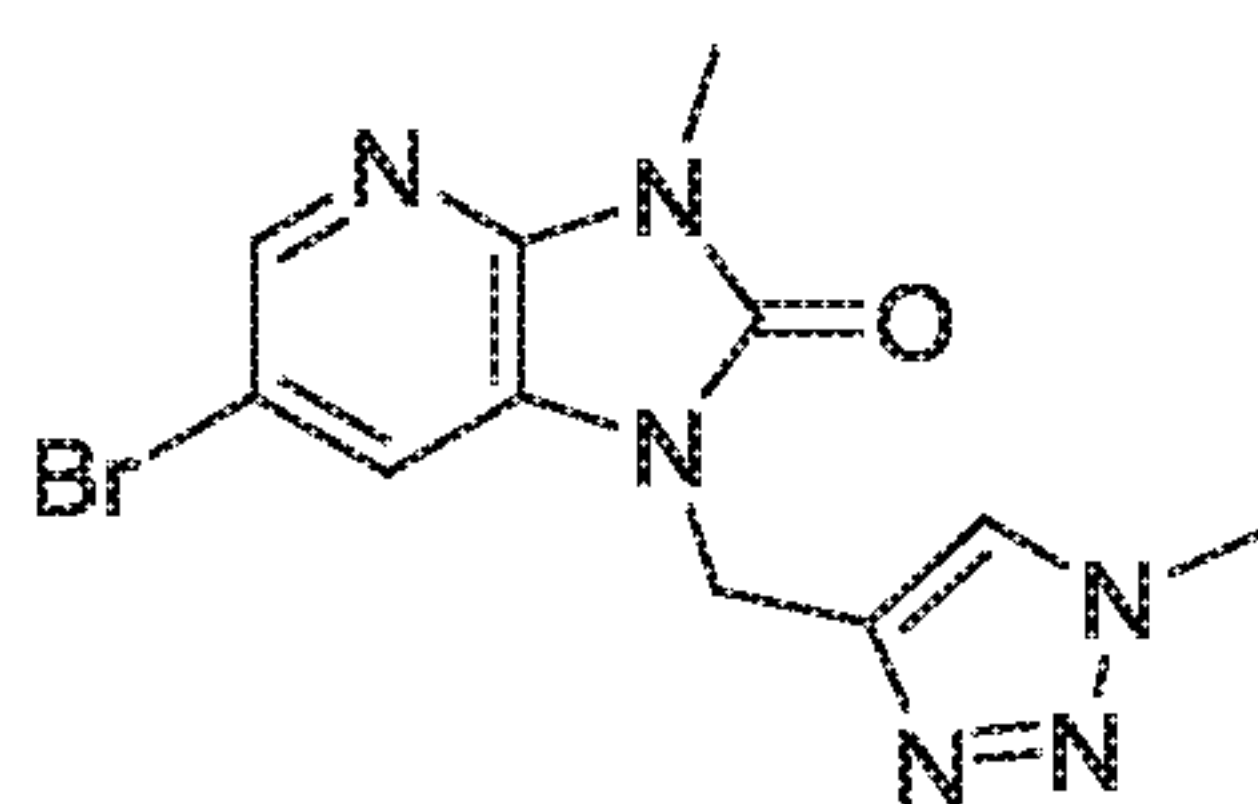


Step A: 5-bromothiophene-2-carbaldehyde. NBS (1.5 eq, 5.8g, 33 mmol) was added to a solution of thiophene-2-carbaldehyde (1.0 eq, 2 mL, 22 mmol) in a mixture of

chloroform/AcOH (10:1, 22 mL) at 0 °C in the absence of light. The reaction mixture was stirred at 0 °C for 1h. Then the mixture was allowed to warm to rt for 12 hours. The reaction was quenched with an aqueous sat. NaHCO<sub>3</sub> solution. The organic layer was washed with brine, dried (MgSO<sub>4</sub>), filtered, and the solvents were evaporated in vacuo. The crude product was purified (FCC, SiO<sub>2</sub>, 0-100 % EtOAc in heptane) to provide the title compound (1.4 g, 35%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 9.76 (s, 1H), 7.51 (d, *J* = 4.0 Hz, 1H), 7.18 (d, *J* = 4.0 Hz, 1H).

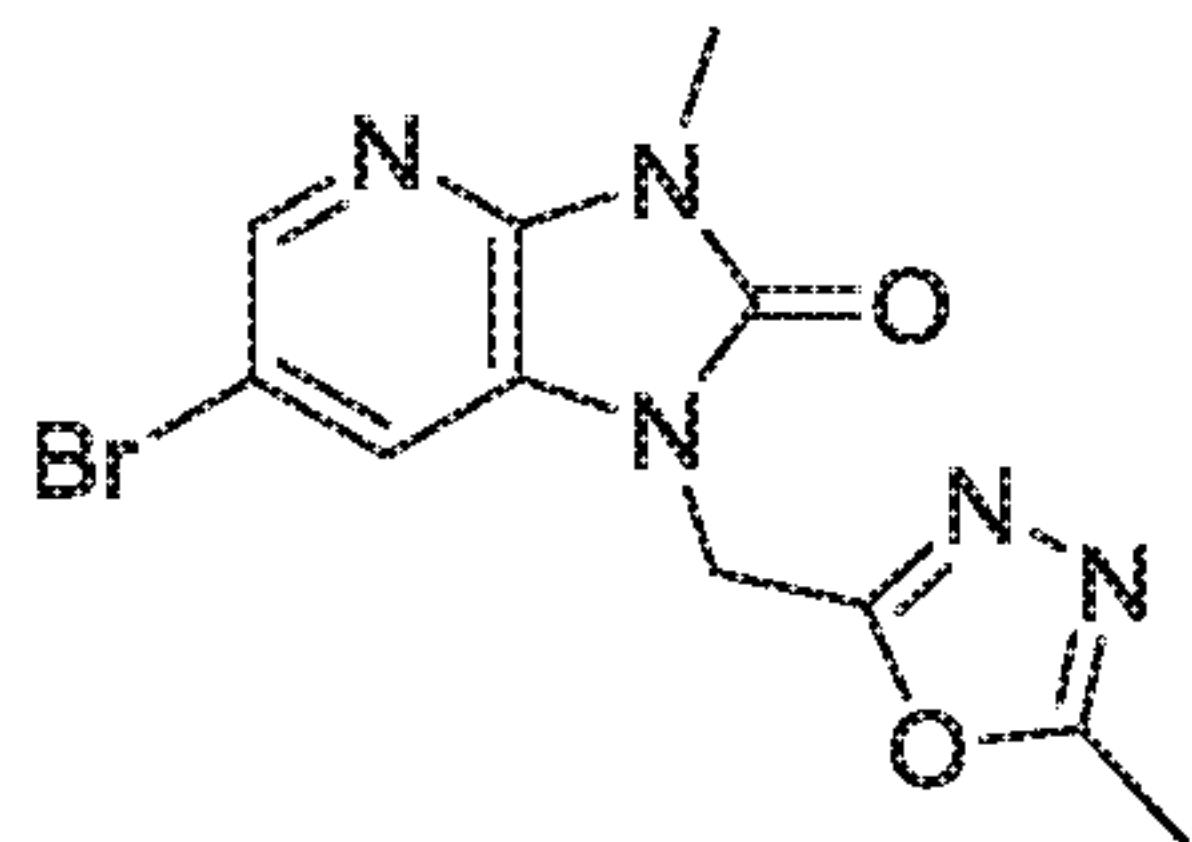
Step B: 2-Bromo-5-(difluoromethyl)thiophene. DAST (2.9 eq., 2.9 mL, 22 mmol) was added to a solution of 5-bromothiophene-2-carbaldehyde (1.0 eq., 1.44g, 7.5 mmol) in DCM at 0 °C under inert atmosphere. The mixture was stirred at rt for 16 hours. The mixture was quenched with ice-cold water and extracted with DCM. The combined organic extracts were washed with water and brine, the organic layer was separated, dried (MgSO<sub>4</sub>), filtered and the solvents were evaporated in vacuo. The crude product was purified (FCC, SiO<sub>2</sub>, 0-100 % EtOAc in heptane) to provide the title compound (511 mg, 32%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.03 (d, *J* = 3.9 Hz, 2H), 6.74 (t, *J* = 55.9 Hz, 1H).

Intermediate 50: 6-Bromo-3-methyl-1-((1-methyl-1H-1,2,3-triazol-4-yl)methyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.



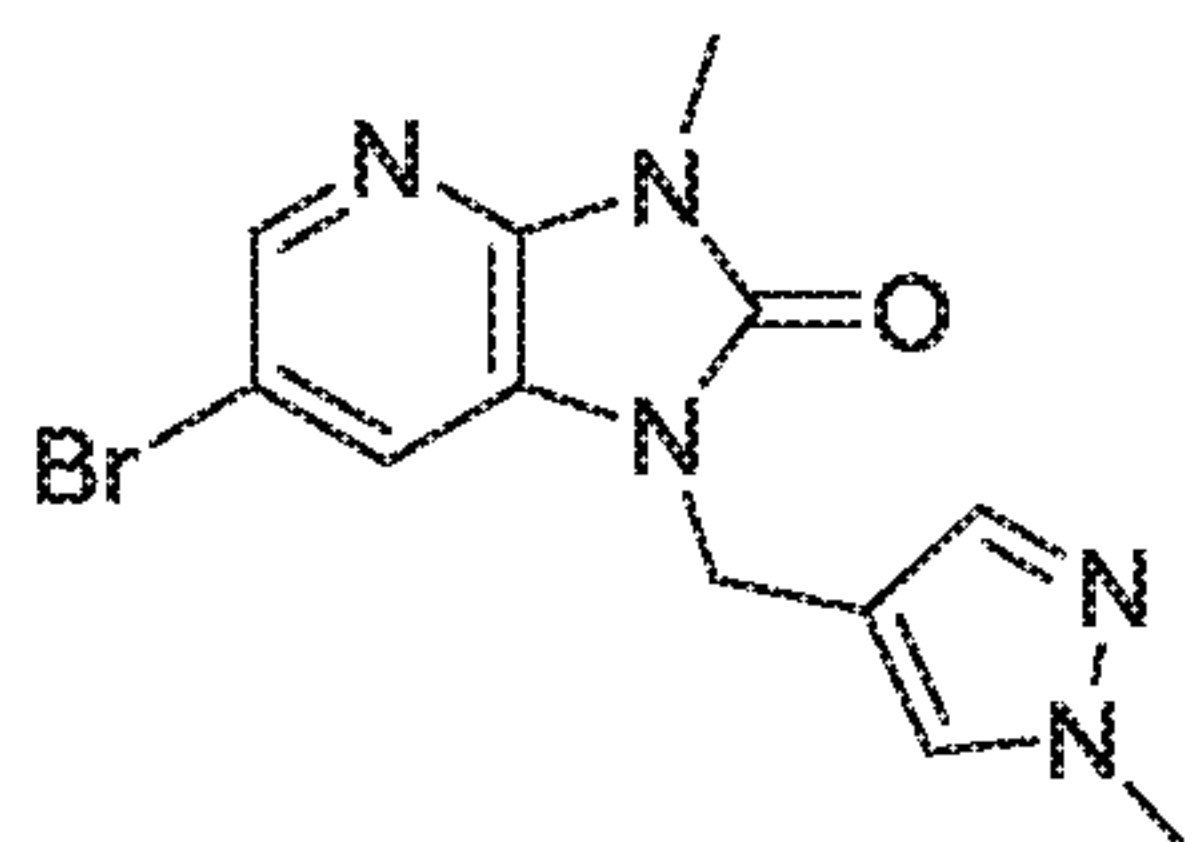
The title compound was prepared in a manner analogous to 6-bromo-3-methyl-1-((5-methylisoxazol-3-yl)methyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 22) using 4-(chloromethyl)-1-methyl-1H-1,2,3-triazole hydrochloride. MS (ESI): mass calcd. for C<sub>11</sub>H<sub>11</sub>BrN<sub>6</sub>O, 322.0; *m/z* found, 324 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (300 MHz, DMSO) δ 8.10 (d, *J* = 1.7 Hz, 1H), 8.05 (s, 1H), 7.83 (d, *J* = 1.6 Hz, 1H), 5.13 (s, 2H), 3.99 (s, 3H), 3.32 (s, 3H).

Intermediate 51: 6-Bromo-3-methyl-1-((5-methyl-1,3,4-oxadiazol-2-yl)methyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.



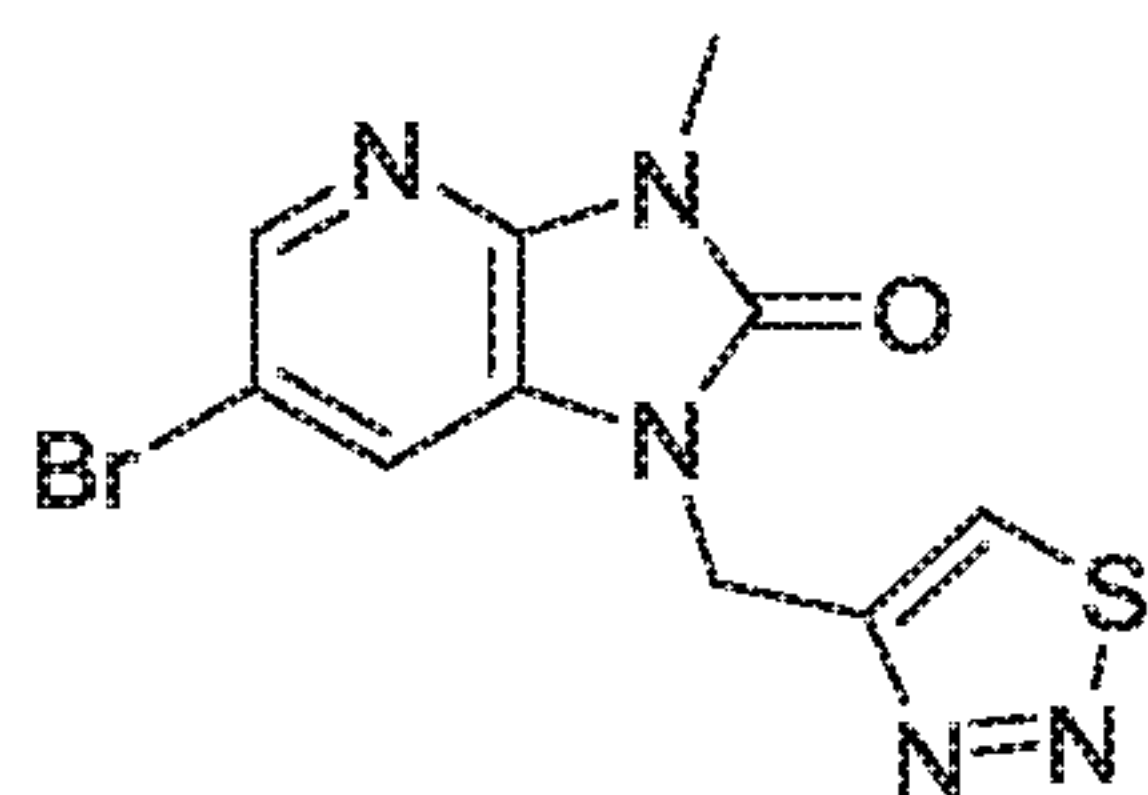
The title compound was prepared in a manner analogous to 6-bromo-3-methyl-1-((5-methylisoxazol-3-yl)methyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 22) using 2-(chloromethyl)-5-methyl-1,3,4-oxadiazole. MS (ESI): mass calcd. for  $C_{11}H_{10}BrN_5O_2$ , 323.0; m/z found, 325  $[M+H]^+$ .  $^1H$  NMR (300 MHz,  $CDCl_3$ )  $\delta$  8.14 (d,  $J$  = 1.6 Hz, 1H), 7.44 (d,  $J$  = 1.6 Hz, 1H), 5.25 (s, 2H), 3.50 (s, 3H), 2.52 (s, 3H).

Intermediate 52: 6-Bromo-3-methyl-1-((1-methyl-1H-pyrazol-4-yl)methyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.



The title compound was prepared in a manner analogous to 6-bromo-3-methyl-1-((5-methylisoxazol-3-yl)methyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 22) using 4-(chloromethyl)-1-methyl-1H-pyrazole. The halide was added as a solution of DMF (5 mL) and DIPEA (1 equivalent). MS (ESI): mass calcd. for  $C_{12}H_{12}BrN_5O$ , 321.0; m/z found, 322  $[M+H]^+$ .  $^1H$  NMR (300 MHz,  $DMSO-d_6$ )  $\delta$  8.07 (s, 1H), 7.87 (s, 1H), 7.70 (s, 1H), 7.43 (s, 1H), 4.89 (s, 2H), 3.75 (s, 3H), 3.27 (s, 3H).

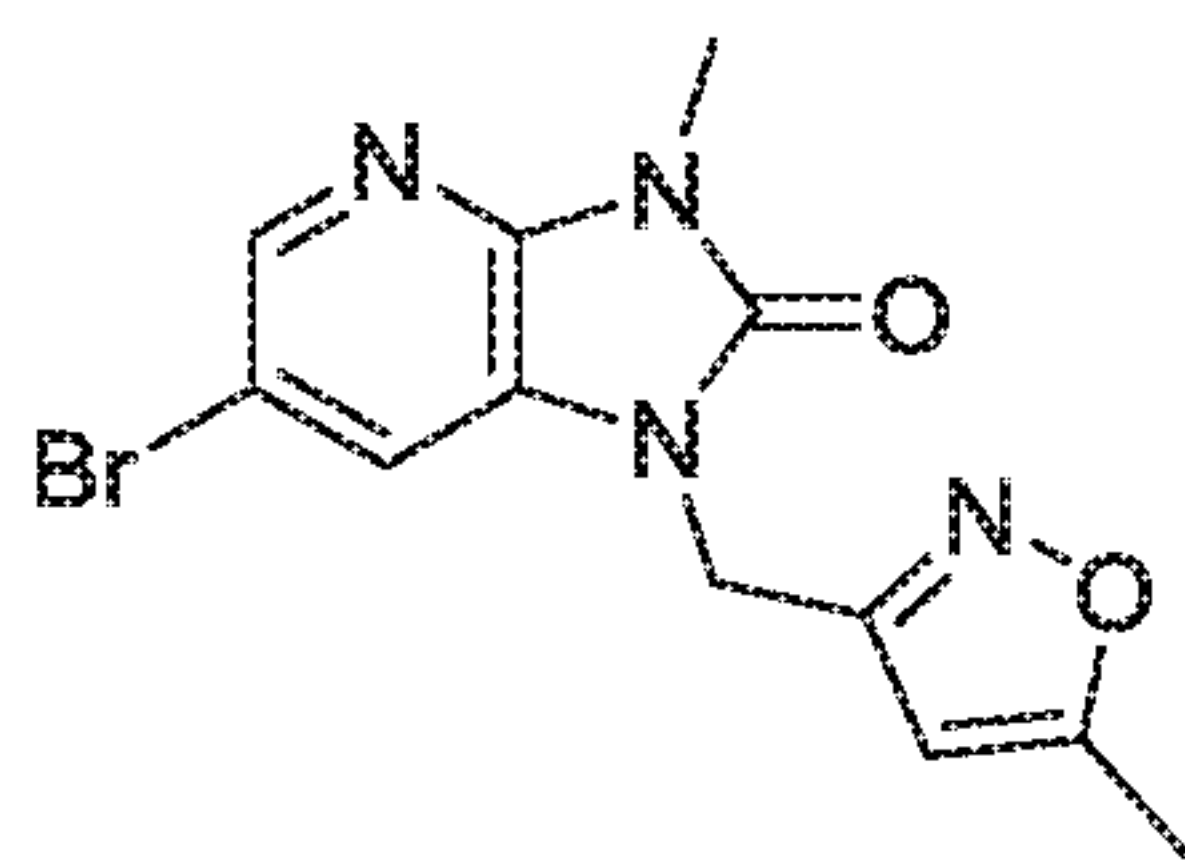
Intermediate 53: 1-((1,2,3-Thiadiazol-4-yl)methyl)-6-bromo-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.



The title compound was prepared in a manner analogous to 6-bromo-3-methyl-1-((5-methylisoxazol-3-yl)methyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 22) using 4-(chloromethyl)-1,2,3-thiadiazole (Intermediate 61). MS (ESI): mass calcd. for C<sub>10</sub>H<sub>8</sub>BrN<sub>5</sub>OS, 325.0 m/z found, 326 [M+H]<sup>+</sup>.

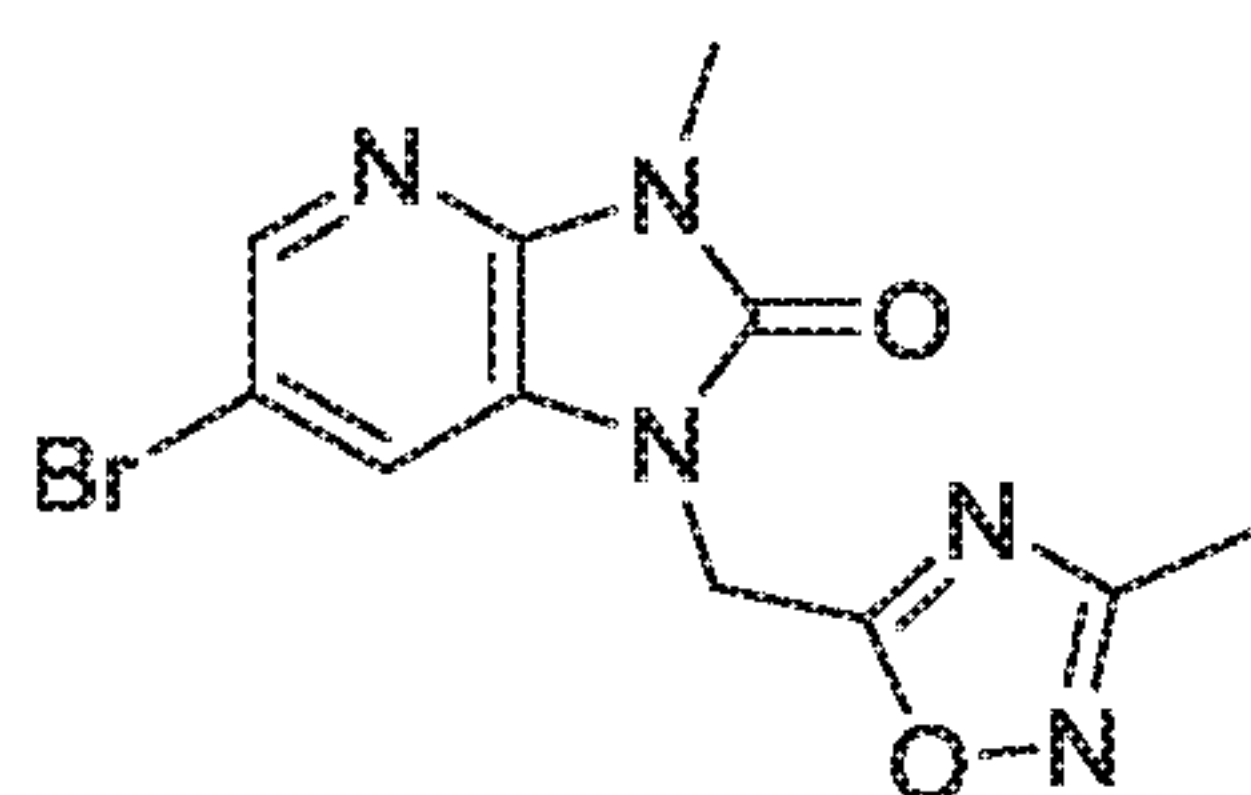
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Intermediate 54: 6-Bromo-3-methyl-1-((5-methylisoxazol-3-yl)methyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.



The title compound was prepared in a manner analogous to 6-bromo-3-methyl-1-((5-methylisoxazol-3-yl)methyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 22) using 3-chloromethyl-5-methylisoxazole. MS (ESI): mass calcd. for C<sub>11</sub>H<sub>11</sub>BrN<sub>6</sub>O, 322.0; m/z found, 324 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ 8.10 (d, *J* = 1.7 Hz, 1H), 8.05 (s, 1H), 7.83 (d, *J* = 1.6 Hz, 1H), 5.13 (s, 2H), 3.99 (s, 3H), 3.32 (s, 3H).

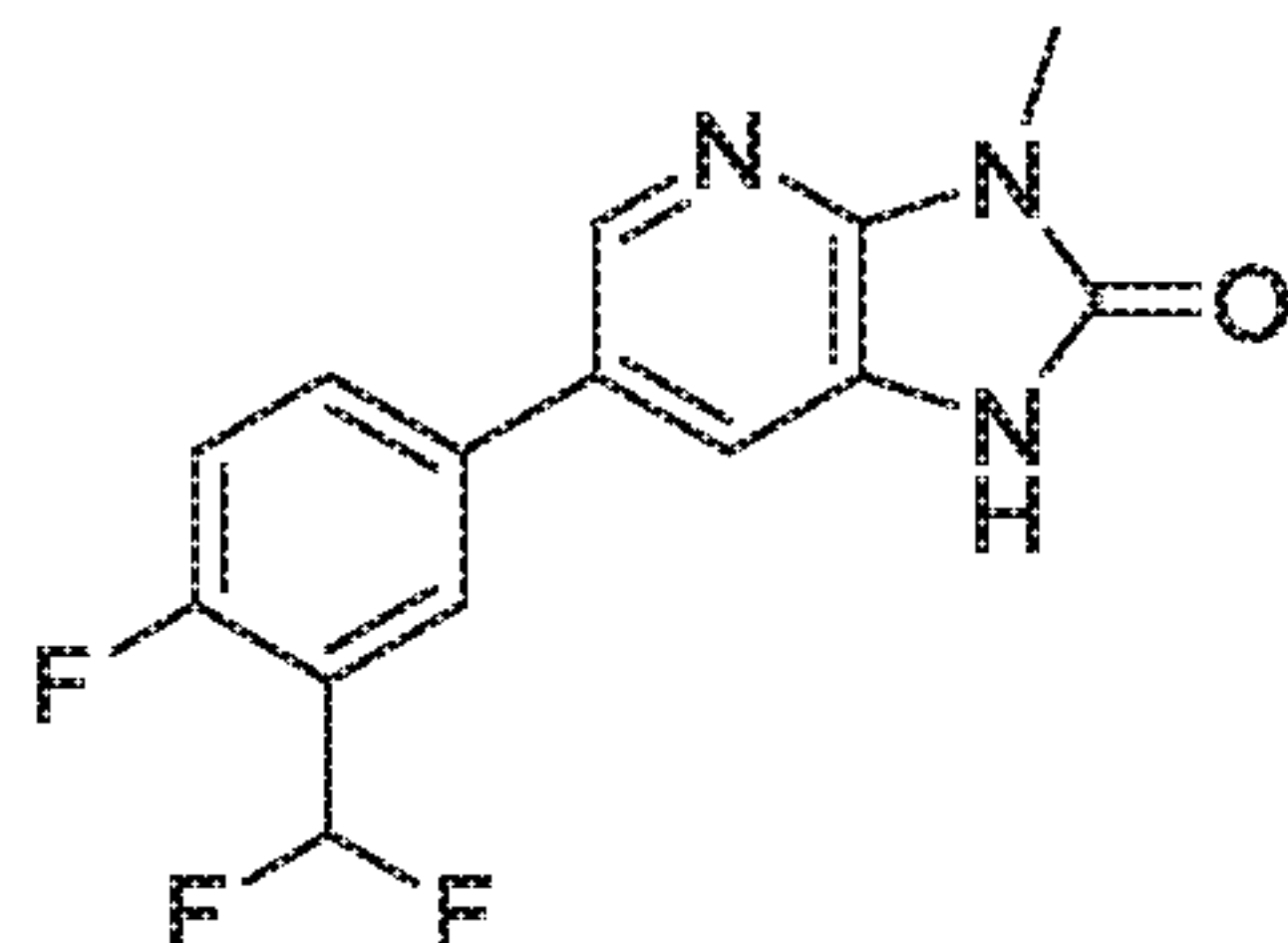
Intermediate 55: 6-Bromo-3-methyl-1-((3-methyl-1,2,4-oxadiazol-5-yl)methyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.



The title compound was prepared in a manner analogous to 6-bromo-3-methyl-1-((5-methylisoxazol-3-yl)methyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 22) using 5-(chloromethyl)-3-methyl-1,2,4-oxadiazole. <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ 8.17 (d, *J* = 1.7 Hz, 1H), 7.96 (d, *J* = 1.7 Hz, 1H), 5.48 (s, 2H), 3.36 (s, 3H), 2.29 (s, 3H).

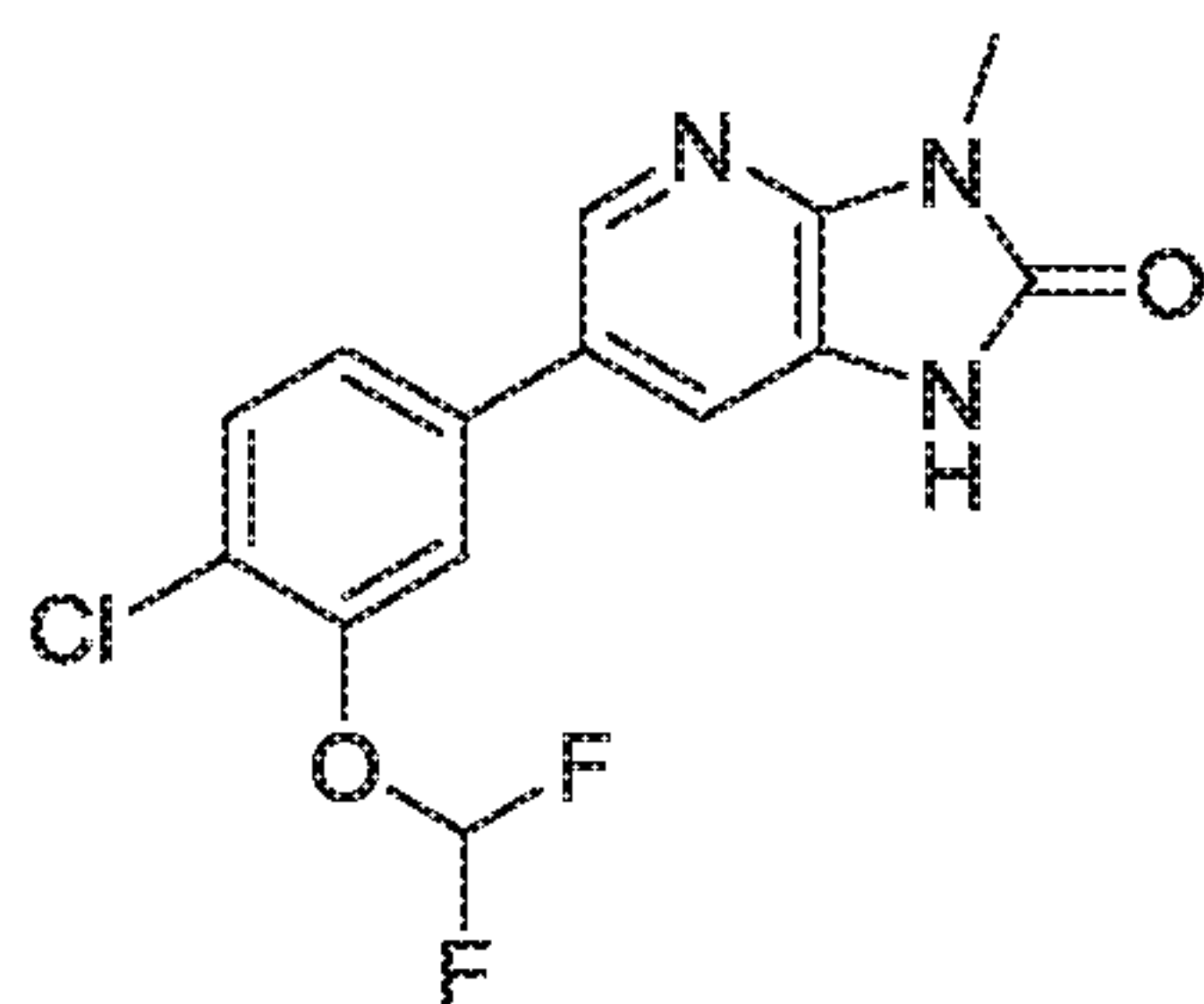
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Intermediate 56: 6-(3-(Difluoromethyl)-4-fluorophenyl)-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.



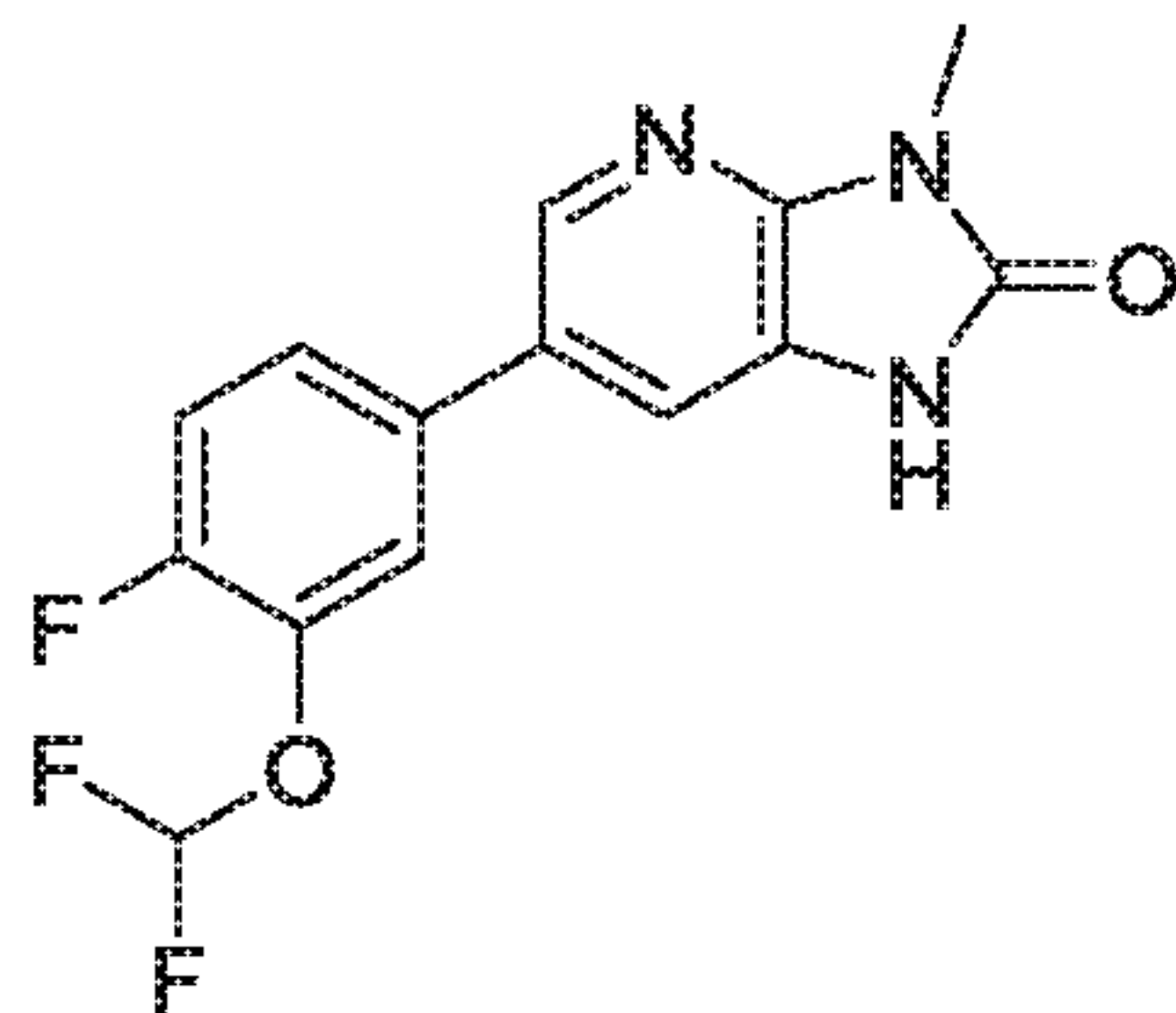
The title compound was prepared in a manner analogous to 6-(4-fluoro-3-methylphenyl)-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 27) using  $\text{PdCl}_2(\text{dppf})_2$  and (3-(difluoromethyl)-4-fluorophenyl)boronic acid (Intermediate 62). MS (ESI): mass calcd. for  $\text{C}_{14}\text{H}_{10}\text{F}_3\text{N}_3\text{O}$ , 293.1; m/z found, 294  $[\text{M}+\text{H}]^+$ .  $^1\text{H}$  NMR (300 MHz,  $\text{DMSO}-d_6$ )  $\delta$  11.28 (s, 1H), 8.25 (s, 1H), 7.89 (d,  $J = 6.1$  Hz, 2H), 7.54 (s, 1H), 7.47 (t,  $J = 9.7$  Hz, 1H), 7.23 (t,  $J = 54.2$  Hz, 1H), 3.33 – 3.31 (m, 3H).

Intermediate 57: 6-(4-Chloro-3-(difluoromethoxy)phenyl)-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.



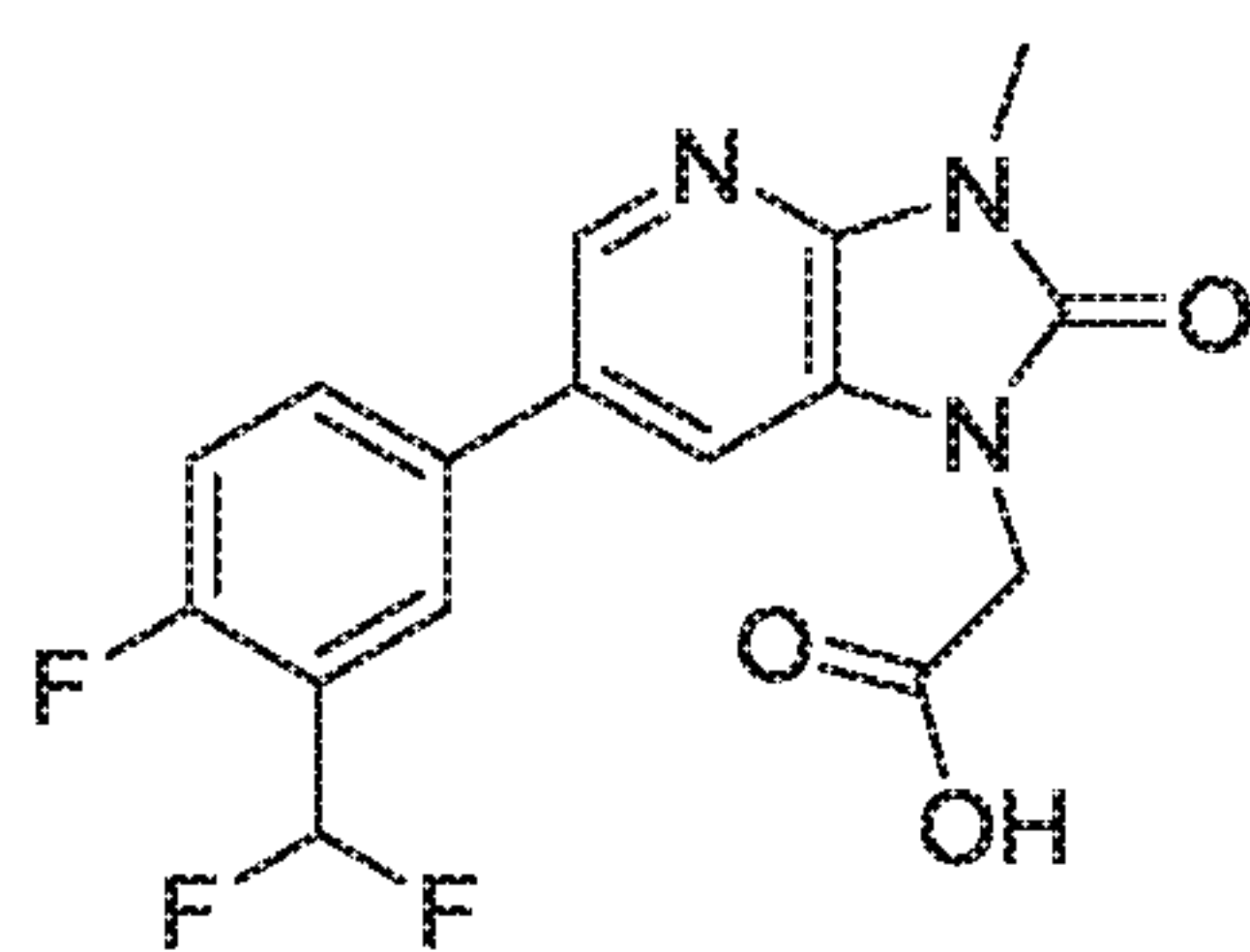
The title compound was prepared in a manner analogous to 6-(4-fluoro-3-methylphenyl)-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 27) using  $\text{PdCl}_2(\text{dppf})_2$  and 2-(4-chloro-3-(difluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Intermediate 63). MS (ESI): mass calcd. for  $\text{C}_{14}\text{H}_{10}\text{ClF}_2\text{N}_3\text{O}_2$ , 325.0 m/z found, 326  $[\text{M}+\text{H}]^+$ .

Intermediate 58: 6-(3-(Difluoromethoxy)-4-fluorophenyl)-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.



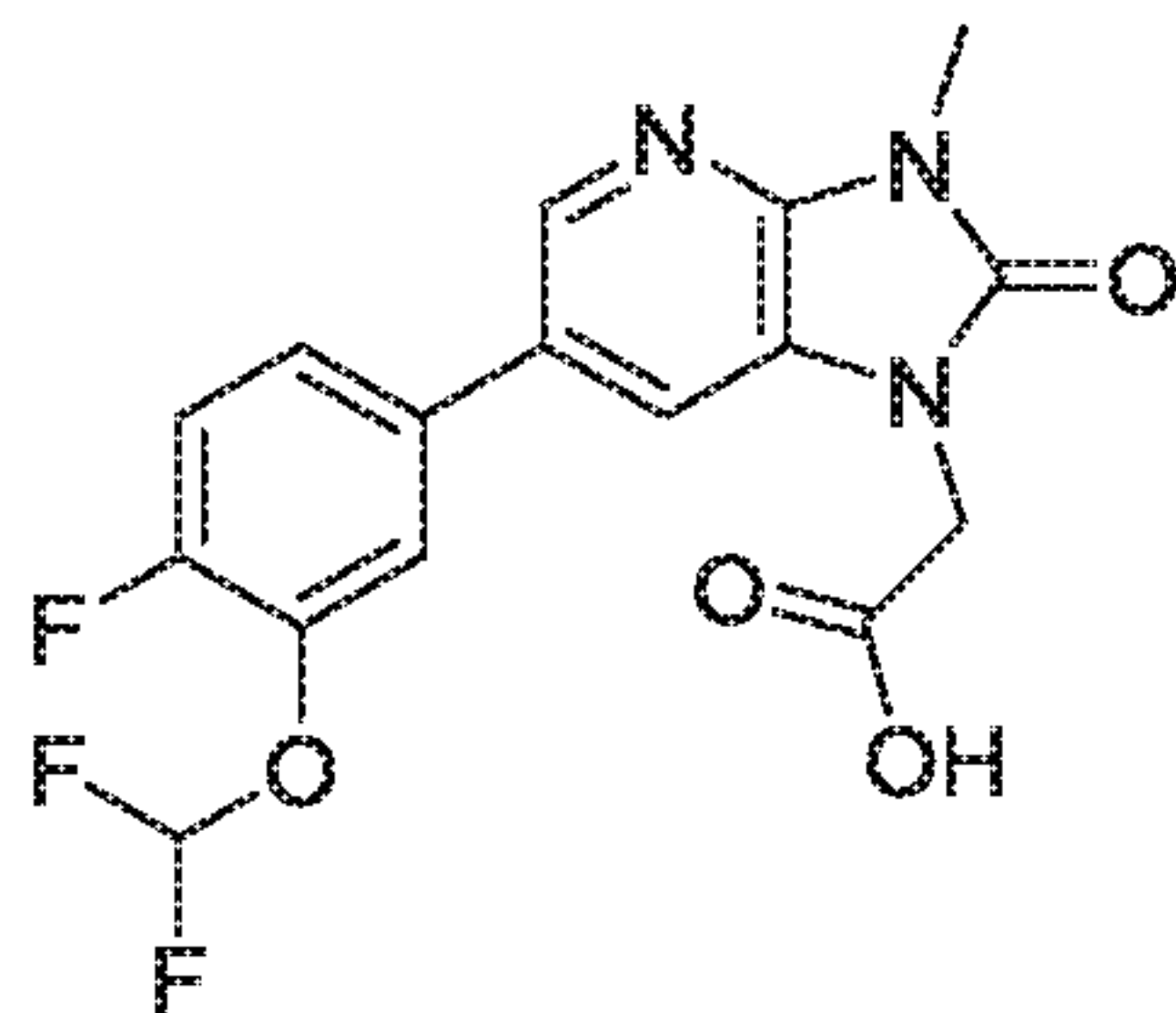
The title compound was prepared in a manner analogous to 6-(4-fluoro-3-methylphenyl)-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 27) , using PdCl<sub>2</sub>(dppf)<sub>2</sub> and (3-(difluoromethoxy)-4-fluorophenyl)boronic acid. MS (ESI):  
 5 mass calcd. for C<sub>14</sub>H<sub>10</sub>F<sub>3</sub>N<sub>3</sub>O<sub>2</sub>, 309.1; m/z found, 310 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ 11.28 (s, 1H), 8.26 (s, 1H), 7.69 – 7.10 (m, 5H), 3.34 (s, 3H).

Intermediate 59: 2-(6-(3-(Difluoromethyl)-4-fluorophenyl)-3-methyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetic acid.



The title compound was prepared in a manner analogous to 2-(6-bromo-3-methyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetic acid (Intermediate 13) using 6-(3-(difluoromethyl)-4-fluorophenyl)-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 56) in Step A and 3M sodium hydroxide in Step B. MS (ESI): mass calcd.  
 15 for C<sub>16</sub>H<sub>12</sub>F<sub>3</sub>N<sub>3</sub>O<sub>3</sub>, 351.1; m/z found, 352 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ 8.35 (s, 1H), 8.00 (s, 1H), 7.92 (d, *J* = 6.0 Hz, 2H), 7.50 (t, *J* = 9.7 Hz, 1H), 7.26 (t, *J* = 54.2 Hz, 1H), 4.70 (s, 2H), 3.39 (s, 3H).

Intermediate 60: 2-(6-(3-(Difluoromethoxy)-4-fluorophenyl)-3-methyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetic acid.



The title compound was prepared in a manner analogous to 2-(6-bromo-3-methyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetic acid (Intermediate 13) using 6-(3-(difluoromethoxy)-4-fluorophenyl)-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 58) in Step A and 3M sodium hydroxide in Step B. MS (ESI): mass calcd. for C<sub>16</sub>H<sub>12</sub>F<sub>3</sub>N<sub>3</sub>O<sub>4</sub>, 367.1; m/z found, 368 [M+H]<sup>+</sup>.

Intermediate 61: 4-(Chloromethyl)-1,2,3-thiadiazole.



Step A: Methyl 1,2,3-thiadiazole-4-carboxylate. 1,2,3-Thiadiazole-4-carboxylic acid (1.0, 1g, 7.7 mmol) was added to HCl (1.25 M in MeOH, 10 mL) and the reaction mixture was stirred at 65 °C for 16 h. The solvent was removed under reduced pressure and the resulting crude mixture was purified (FCC, SiO<sub>2</sub>, 0-100 % EtOAc in DCM) to provide the title compound (1.1g, 99.9%). MS (ESI): mass calcd. for C<sub>4</sub>H<sub>4</sub>N<sub>2</sub>O<sub>2</sub>S, 144.0; m/z found, 145 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 9.27 (s, 1H), 4.07 (s, 3H).

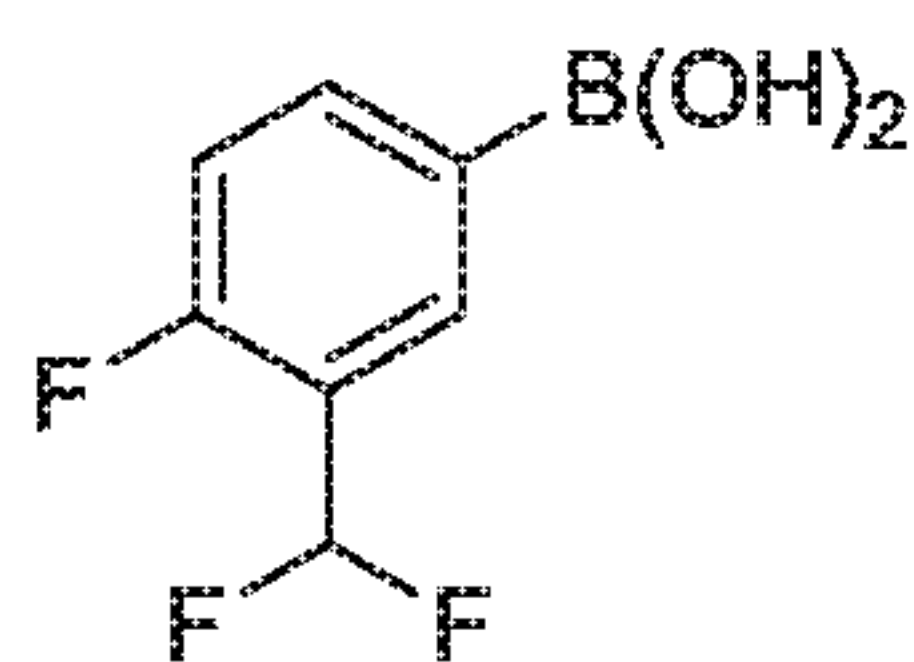
Step B: (1,2,3-Thiadiazol-4-yl)methanol. CaCl<sub>2</sub> (5 mg, 0.05 mmol) and NaBH<sub>4</sub> (945 mg, 25 mmol) were added to a mixture of methyl 1,2,3-thiadiazole-4-carboxylate (1.1 g, 7.8 mmol) in THF (9 mL) and EtOH (18 mL). The mixture was stirred at rt for 2 h. The mixture was diluted with water and extracted with DCM/MeOH (9:1). The organic layer was separated, dried (MgSO<sub>4</sub>), filtered, and concentrated under reduced pressure. Purification (FCC, SiO<sub>2</sub>, 0-10 % MeOH in DCM) provided the title compound (389 mg, 43%). MS (ESI): mass calcd. for C<sub>3</sub>H<sub>4</sub>N<sub>2</sub>OS, 116.0; m/z found, 117 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.51 (s, 1H), 6.45 (s, 1H), 5.22 (s, 2H).

Step C: 4-(Chloromethyl)-1,2,3-thiadiazole. A flask containing (1,2,3-thiadiazol-4-yl)methanol (380 mg, 3.3 mmol) and DCM (20 mL) was placed under N<sub>2</sub> atmosphere at

0 °C. To this solution was added SOCl<sub>2</sub> (1.5 eq., 357 µL, 4.9 mmol) portionwise and the reaction mixture was stirred at rt for 30 minutes. The solvent was removed under reduced pressure. Purification (FCC, SiO<sub>2</sub>, 0-100 % EtOAc in heptane) afforded the title compound (175 mg, 40%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.58 (s, 1H), 5.09 (s, 2H).

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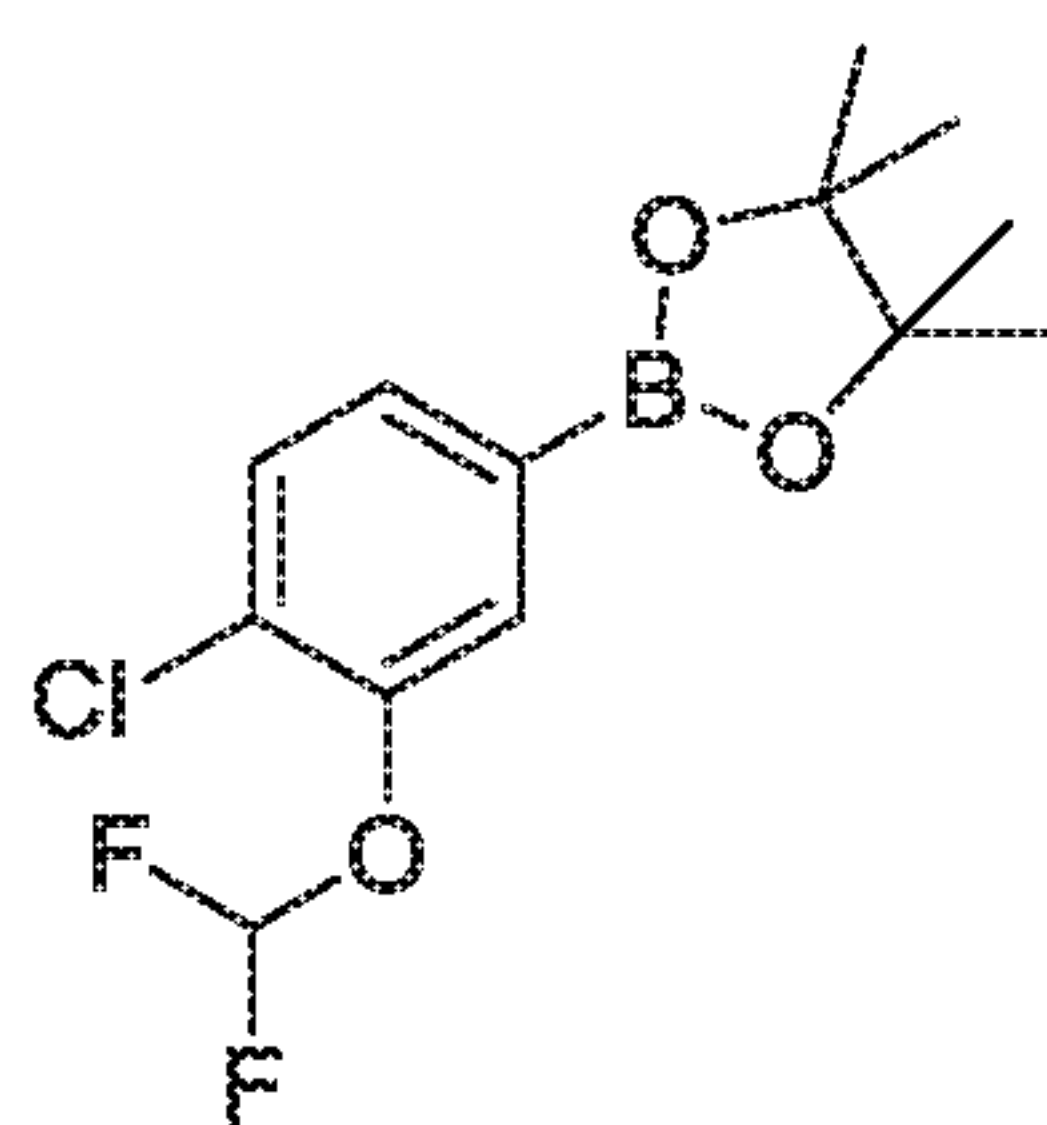
Intermediate 62: (3-(Difluoromethyl)-4-fluorophenyl)boronic acid.



To a cooled, -78 °C, solution of bromo-2-difluoromethyl-1-fluorobenzene (1.5 mL, 11.1 mmol) and triisopropyl borate (3.8 mL, 16.7 mmol) in THF (25 mL), under a nitrogen atmosphere, was added *n*BuLi (2.5 M in hexanes, 8.9 mL, 22.2 mmol). The reaction mixture was stirred at rt for 30 minutes. The reaction mixture was quenched using 2 N aq. HCl. The resulting mixture was extracted with EtOAc. The organic layers were separated and the aqueous was extracted with DCM. The combined organic layers were dried (MgSO<sub>4</sub>), filtered, and concentrated under reduced pressure to afford title compound (2.4g, 99%, 87% pure), which was used crude without further purification.

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Intermediate 63: 2-(4-Chloro-3-(difluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



Step A: 4-Bromo-1-chloro-2-(difluoromethoxy)benzene. To a mixture of 5-bromo-2-chlorophenol (7g, 34 mmol) and K<sub>2</sub>CO<sub>3</sub> (16g, 118 mmol) in DMF (200 mL) was added ethyl chlorodifluoroacetate (15 mL, 118 mmol). The reaction mixture was heated to 80 °C overnight. The residue was diluted with ice-water and was extracted with EtOAc. The combined organic layers were dried (MgSO<sub>4</sub>), filtered and concentrated under vacuo.

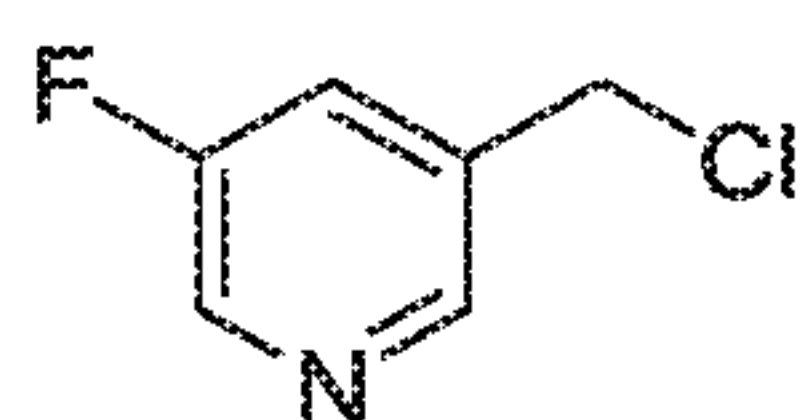
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Purification (FCC, SiO<sub>2</sub>, 0-100 % EtOAc in heptane) afforded the title compound (5.8g, 67%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.41 (s, 1H), 7.32 (s, 2H), 6.53 (t, *J* = 72.9 Hz, 1H).

Step B: 2-(4-Chloro-3-(difluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.

The title compound was prepared in a manner analogous to Intermediate 8, using 4-bromo-1-chloro-2-(difluoromethoxy)benzene.

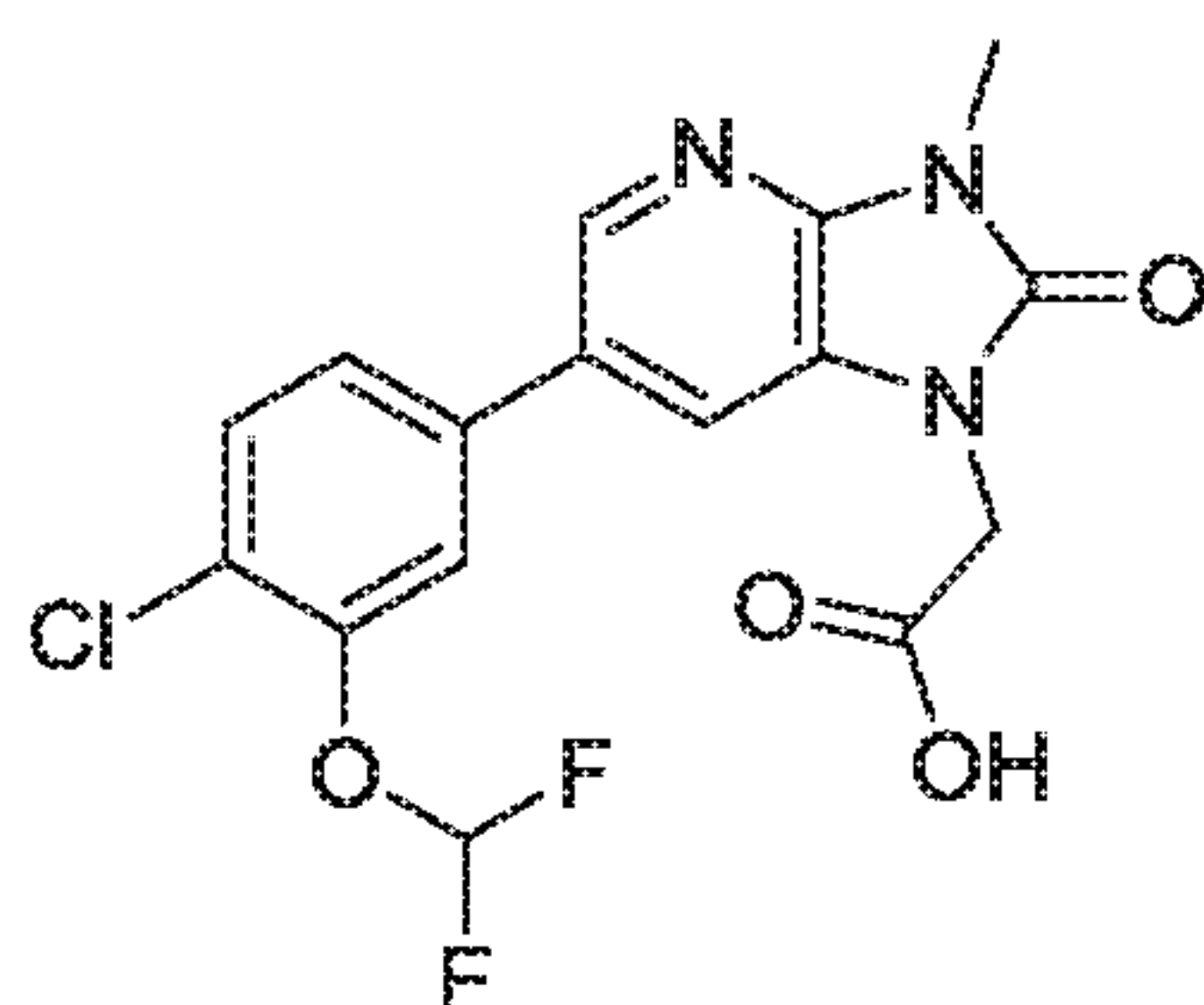
Intermediate 64: 3-(Chloromethyl)-5-fluoropyridine.



Step A: (5-Fluoropyridin-3-yl)methanol. To a cooled, 0 °C, solution of 5-fluoropyridine-3-carboxylic acid (1.0g, 7.1 mmol) in THF (30 mL) under a nitrogen atmosphere was added LAH (430 mg, 11 mmol). After 1h, the reaction mixture was quenched with water and extracted with DCM/MeOH (9:1). The organic layer was dried (MgSO<sub>4</sub>), filtered and concentrated under reduced pressure to provide title compound (480 mg, 53%) which was used crude without further purification. MS (ESI): mass calcd. for C<sub>6</sub>H<sub>6</sub>FN<sub>1</sub>O, 127.0; m/z found, 128 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.40 (s, 2H), 7.48 (d, *J* = 9.2 Hz, 1H), 4.78 (s, 2H).

Step B: 3-(Chloromethyl)-5-fluoropyridine. The title compound was prepared in a manner analogous to Intermediate 61, Step C, using (5-fluoropyridin-3-yl)methanol. MS (ESI): mass calcd. for C<sub>6</sub>H<sub>5</sub>ClFN, 145.0; m/z found, 146 [M+H]<sup>+</sup>.

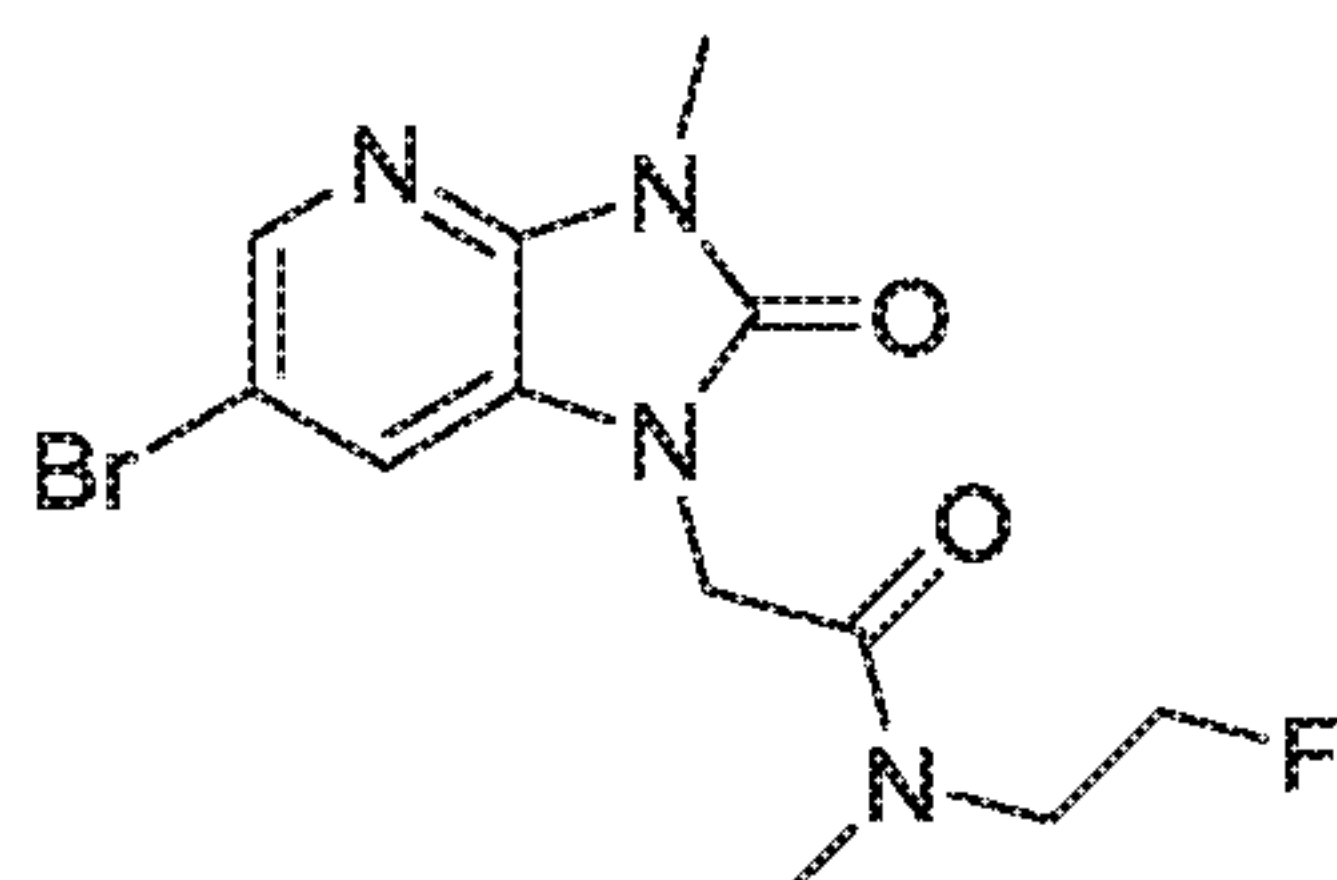
Intermediate 65: 2-(6-(4-Chloro-3-(difluoromethoxy)phenyl)-3-methyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetic acid.



The title compound was prepared in a manner analogous to 2-(6-bromo-3-methyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetic acid (Intermediate 13) using 6-(4-chloro-3-(difluoromethoxy)phenyl)-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 57). (ESI): mass calcd. for C<sub>16</sub>H<sub>12</sub>ClF<sub>2</sub>N<sub>3</sub>O<sub>4</sub>, 383.1; m/z found, 384 [M+H]<sup>+</sup>.

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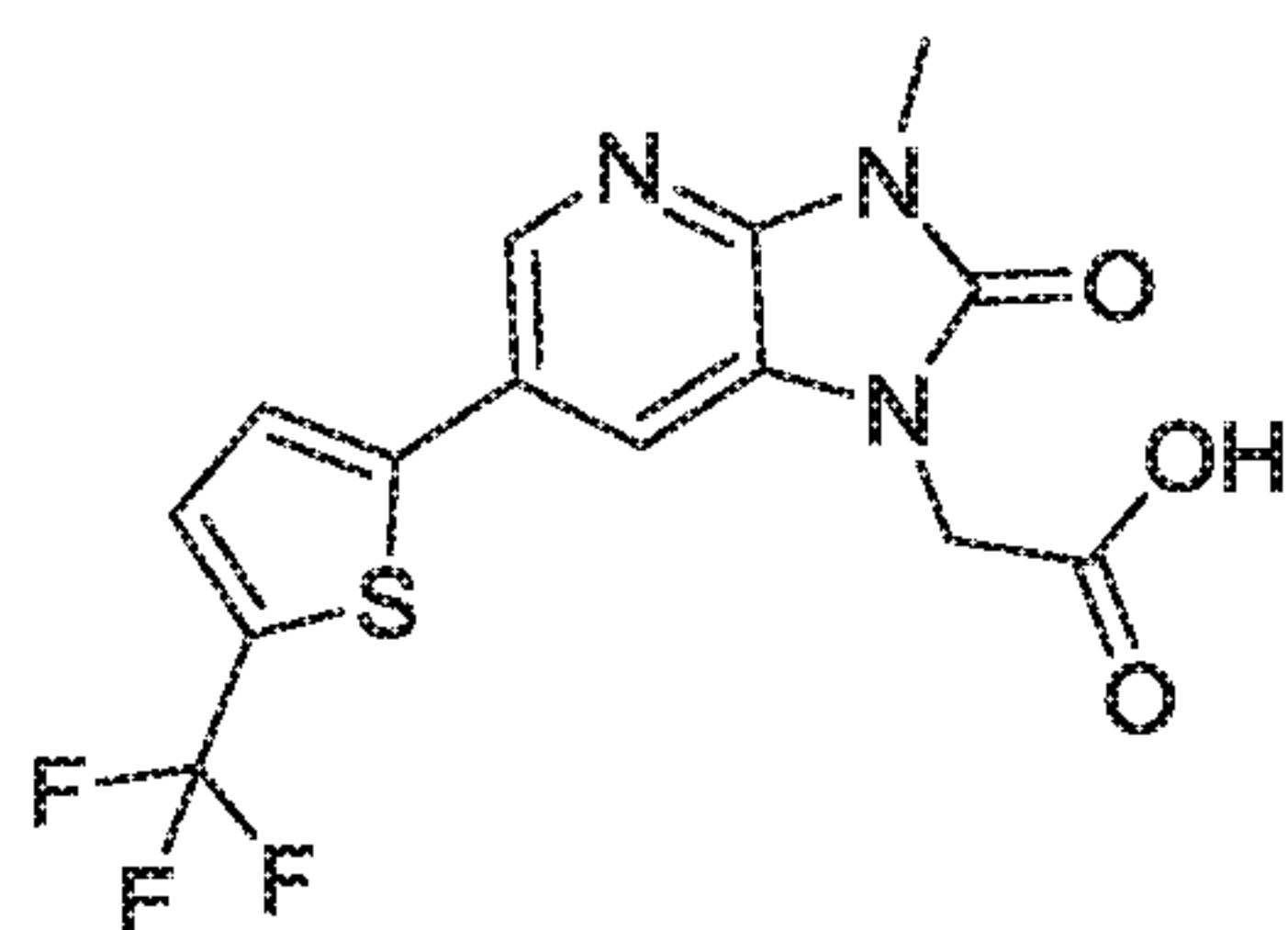
Intermediate 66: 2-(6-Bromo-3-methyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)-N-(2-fluoroethyl)-N-methylacetamide.



The title compound was prepared in a manner analogous to Intermediate 39, using 2-(6-bromo-3-methyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetic acid Lithium salt (Intermediate 13) and 2-fluoro-N-methylethan-1-amine HCl salt. MS (ESI): mass calcd. for C<sub>12</sub>H<sub>14</sub>BrFN<sub>4</sub>O<sub>2</sub>, 344.0 m/z found, 345.1 [M+H]<sup>+</sup>.

Intermediate 67: 2-(3-Methyl-2-oxo-6-(5-(trifluoromethyl)thiophen-2-yl)-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetic acid.

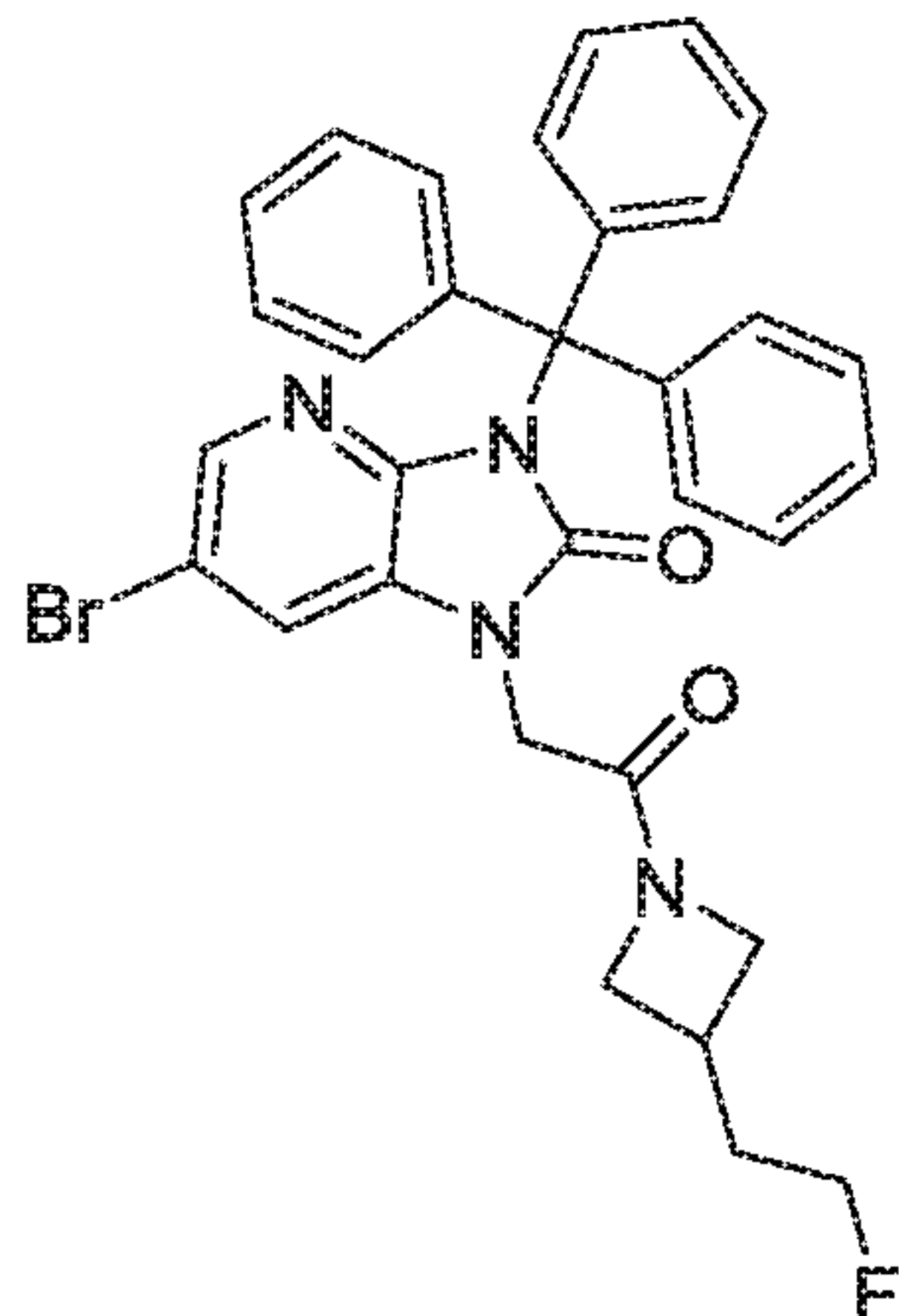
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The title compound was prepared in a manner analogous to Intermediate 26, Step A, using 2-(6-bromo-3-methyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetic acid (Intermediate 13) and (5-(trifluoromethyl)thiophen-2-yl)boronic acid. MS (ESI): mass calcd. for C<sub>14</sub>H<sub>10</sub>F<sub>3</sub>N<sub>3</sub>O<sub>3</sub>S, 357.3; m/z found, 358.1 [M+H]<sup>+</sup>.

20

Intermediate 68: 6-Bromo-1-(2-(3-(2-fluoroethyl)azetidin-1-yl)-2-oxoethyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.



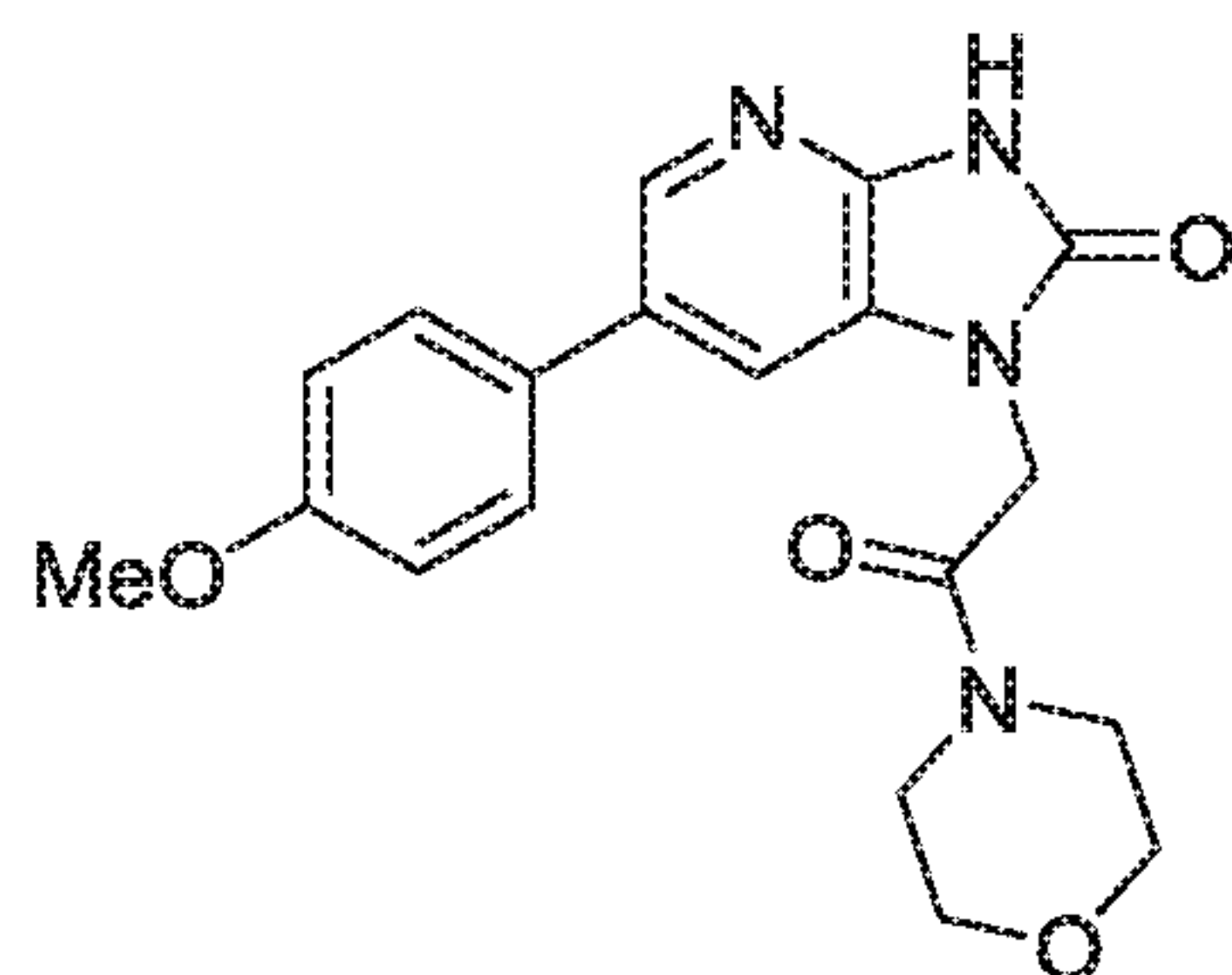
Step A: 6-Bromo-1-(2-(3-(2-hydroxyethyl)azetidin-1-yl)-2-oxoethyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. The title compound was prepared in a manner analogous to Intermediate 39 using 2-(6-bromo-2-oxo-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetic acid (Intermediate 38, product from Step A) and 2-(azetidin-3-yl)ethan-1-ol. MS (ESI): mass calcd. for C<sub>32</sub>H<sub>29</sub>BrFN<sub>4</sub>O<sub>3</sub>, 596.1 m/z found, 619.1 [M+Na]<sup>+</sup>.

Step B: 2-(1-(2-(6-Bromo-2-oxo-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetyl)azetidin-3-yl)ethyl 4-methanesulfonate. To a solution of 6-bromo-1-(2-(3-(2-hydroxyethyl)azetidin-1-yl)-2-oxoethyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (95 mg, 0.16 mmol) and 4-methylbenzenesulfonyl chloride (91 mg, 0.48 mmol) in DCM (0.5 mL), was added TEA (0.11 mL, 0.80 mmol). The reaction mixture was stirred at rt overnight. Purification (50 mg) (FCC, SiO<sub>2</sub>, Ethyl Acetate in hexanes (20-90%)) afforded the title compound. MS (ESI): mass calcd. for C<sub>39</sub>H<sub>35</sub>BrFN<sub>4</sub>O<sub>5</sub>S 750.2 m/z found, 783.2 [M+Na]<sup>+</sup>.

Step C: 6-Bromo-1-(2-(3-(2-fluoroethyl)azetidin-1-yl)-2-oxoethyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. 2-(1-(2-(6-Bromo-2-oxo-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetyl)azetidin-3-yl)ethyl 4-methanesulfonate (50 mg) was dissolved in THF (0.5 mL), and TBAF (1.0 M in THF, 200 μL, 0.2 mmol) was added. The reaction mixture was heated at 60 °C for an hour. The solvent was removed under vacuum. Purification (FCC, SiO<sub>2</sub>, Ethyl Acetate in hexanes (10% to 80%)) provided the title

compound as a colorless oil (26 mg, 26% over Steps B-C). MS (ESI): mass calcd. for  $C_{32}H_{28}BrFN_4O_2$ , 598.1 m/z found, 626.1  $[M+Na]^+$ .

5 Example 1: 6-(4-Methoxyphenyl)-1-(2-morpholino-2-oxo-ethyl)-3H-imidazo[4,5-b]pyridin-2-one and its trifluoroacetic acid salt.



10 Step A: N-Benzhydryl-5-(4-methoxyphenyl)-3-nitropyridin-2-amine. To a solution a N-benzhydryl-5-bromo-3-nitropyridin-2-amine (Intermediate 31, 7.58 g, 19.7 mmol) and 4-methoxyphenylboronic acid (3 g, 19.7 mmol) in EtOH (30 mL) and toluene (40 mL) was added an aqueous solution of 2 M  $Na_2CO_3$  (20 mL) and  $Pd(Ph_3)_4$  (2.27 g, 1.97 mmol). The reaction mixture was stirred at 80°C overnight. Then, the crude reaction mixture cooled, filtered, and the filtrate was evaporated. The crude residue was purified (FCC,  $SiO_2$ , 20:1 petroleum ether/EtOAc) to yield the title compound (2.8 g, 35%).

15 Step B: N<sup>2</sup>-Benzhydryl-5-(4-methoxyphenyl)pyridine-2,3-diamine. To a solution of N-benzhydryl-5-(4-methoxyphenyl)-3-nitropyridin-2-amine (2.7 g, 6.6 mmol) in EtOH (80 mL) was added  $Pd/C$  (0.27 g), and the reaction mixture was stirred at room temperature for 5 h under an atmosphere of  $H_2$ . After uptake of  $H_2$  (1 equivalent), the catalyst was filtered off and the filtrate as evaporated to yield the title compound (2.3 g, 92%), which  
20 was used in the next step without further purification.

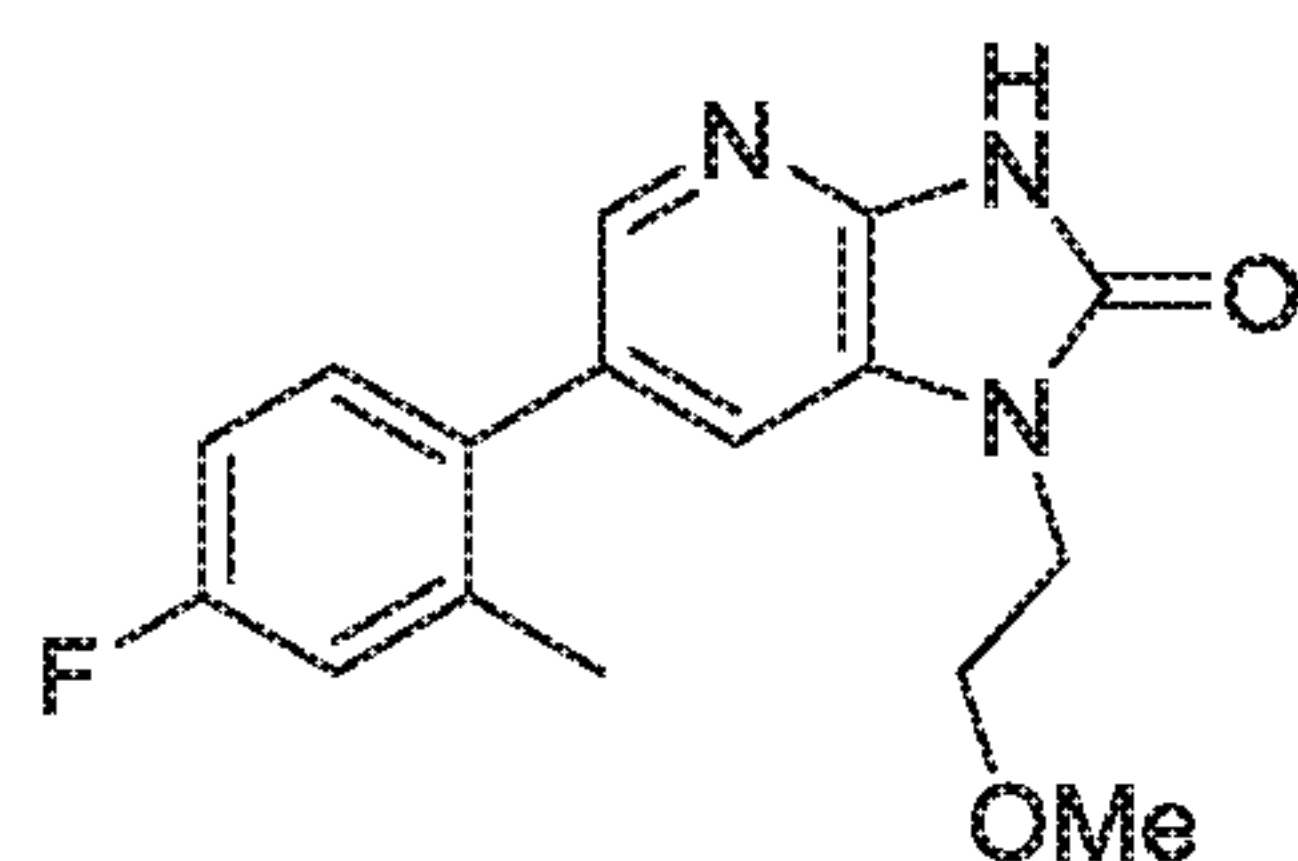
Step C: 3-Benzhydryl-6-(4-methoxyphenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. A solution of N<sup>2</sup>-benzhydryl-5-(4-methoxyphenyl)pyridine-2,3-diamine (2.2 g, 5.8 mmol) and CDI (1.9 g, 11.5 mmol) in 1,4-dioxane (100 mL) was refluxed for 5 h. Then, the solvent was evaporated and the resultant solid was washed with water and dried to  
25 yield the title compound (2.3 g, 100%), which was used in the next step without further purification.

Step D: tert-Butyl 2-(3-benzhydryl-6-(4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetate. A solution of 3-benzhydryl-6-(4-methoxyphenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (2.2 g, 5.4 mmol), tert-butyl bromoacetate (1.3 g, 6.5 mmol) and K<sub>2</sub>CO<sub>3</sub> (1.5 g, 10.8 mmol) in MeCN (80 mL) was heated to reflux for 5 h. Then, the reaction mixture was cooled, filtered, and the filtrate was evaporated to yield the title compound (2.8 g, 100%), which was used in the next step without further purification.

Step E: 2-(6-(4-Methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetic acid. To a solution of tert-butyl 2-(3-benzhydryl-6-(4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetate (2.8 g, 5.4 mmol) in TFA (50 mL) was added thioanisole (0.28 g), and the reaction mixture was stirred at 80 °C for 1 h. Then, the solvent was evaporated to yield the title compound as the TFA salt (2.2 g, 100%).

Step F: 6-(4-Methoxyphenyl)-1-(2-morpholino-2-oxo-ethyl)-3H-imidazo[4,5-b]pyridin-2-one. A solution of 2-(6-(4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetic acid TFA salt (0.4 g, 0.97 mmol), morpholine (0.25 g, 2.9 mmol), HBTU (0.38 g, 0.97 mmol), HOBT (0.13 g, 0.97 mmol), and NEt<sub>3</sub> (0.29 g, 2.9 mmol) in DMF (10 mL) was stirred at room temperature for 12 h. Then, water (20 mL) was added to the reaction mixture and the reaction was extracted with EtOAc (3x 30 mL). The combined organic layers were washed with water, brine, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated under reduced pressure to afford the free base of the title compound. The residue was purified by preparative HPLC (gradient elution: 0.1% TFA in CH<sub>3</sub>CN/ 0.1% TFA in H<sub>2</sub>O) and the desired fractions were collected and washed with a saturated aqueous solution of NaHCO<sub>3</sub>. The biphasic mixture was extracted with EtOAc (3x 30 mL). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated to yield the title compound as a white solid (0.11 g, 30%). MS (ESI): mass calcd. for C<sub>19</sub>H<sub>20</sub>N<sub>4</sub>O<sub>4</sub>, 368.1; m/z found, 369.0 [M+H]<sup>+</sup>. MP = 239.1 – 244.1 °C.

Example 2: 6-(4-Fluoro-2-methyl-phenyl)-1-(2-methoxyethyl)-3H-imidazo[4,5-b]pyridin-2-one.



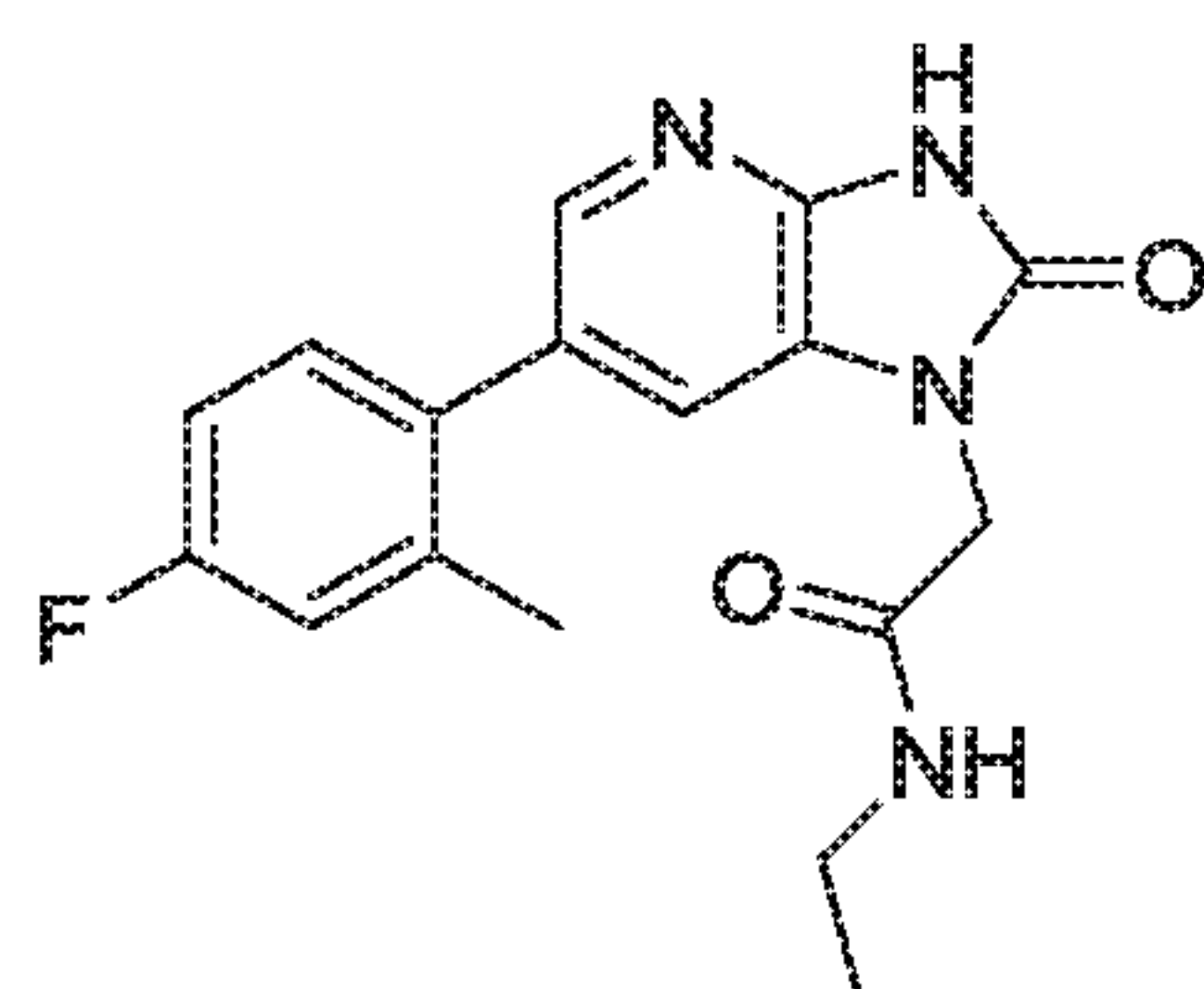
A solution of 6-bromo-1-(2-methoxyethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 32, 0.3 g, 1.1 mmol), (4-fluoro-2-methylphenyl)boronic acid (0.25 g, 1.7 mmol), Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (0.03 g, 0.04 mmol), and 2 M Na<sub>2</sub>CO<sub>3</sub> (2mL) in 1,2-

5 dimethoxyethane (6 mL) was heated to 140 °C via microwave irradiation for 10 min.

Then, water (30 mL) was added to the crude reaction mixture and the mixture was extracted with EtOAc (3 x 30 mL). The combined organic layers were washed with water, brine, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated under reduced pressure. The crude residue was purified by preparative HPLC (gradient elution: 0.1% TFA in CH<sub>3</sub>CN/ 0.1% TFA in H<sub>2</sub>O) and the desired fractions were collected and washed with a saturated aqueous solution of NaHCO<sub>3</sub>. The biphasic mixture was extracted with EtOAc (3x 30 mL). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated to yield the title compound as a white solid (0.23 g, 69%). MS (ESI): mass calcd. for C<sub>16</sub>H<sub>16</sub>FN<sub>3</sub>O<sub>2</sub>, 301.1; m/z found, 302.1 [M+H]<sup>+</sup>.

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Example 3: N-Ethyl-2-[6-(4-fluoro-2-methyl-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide.

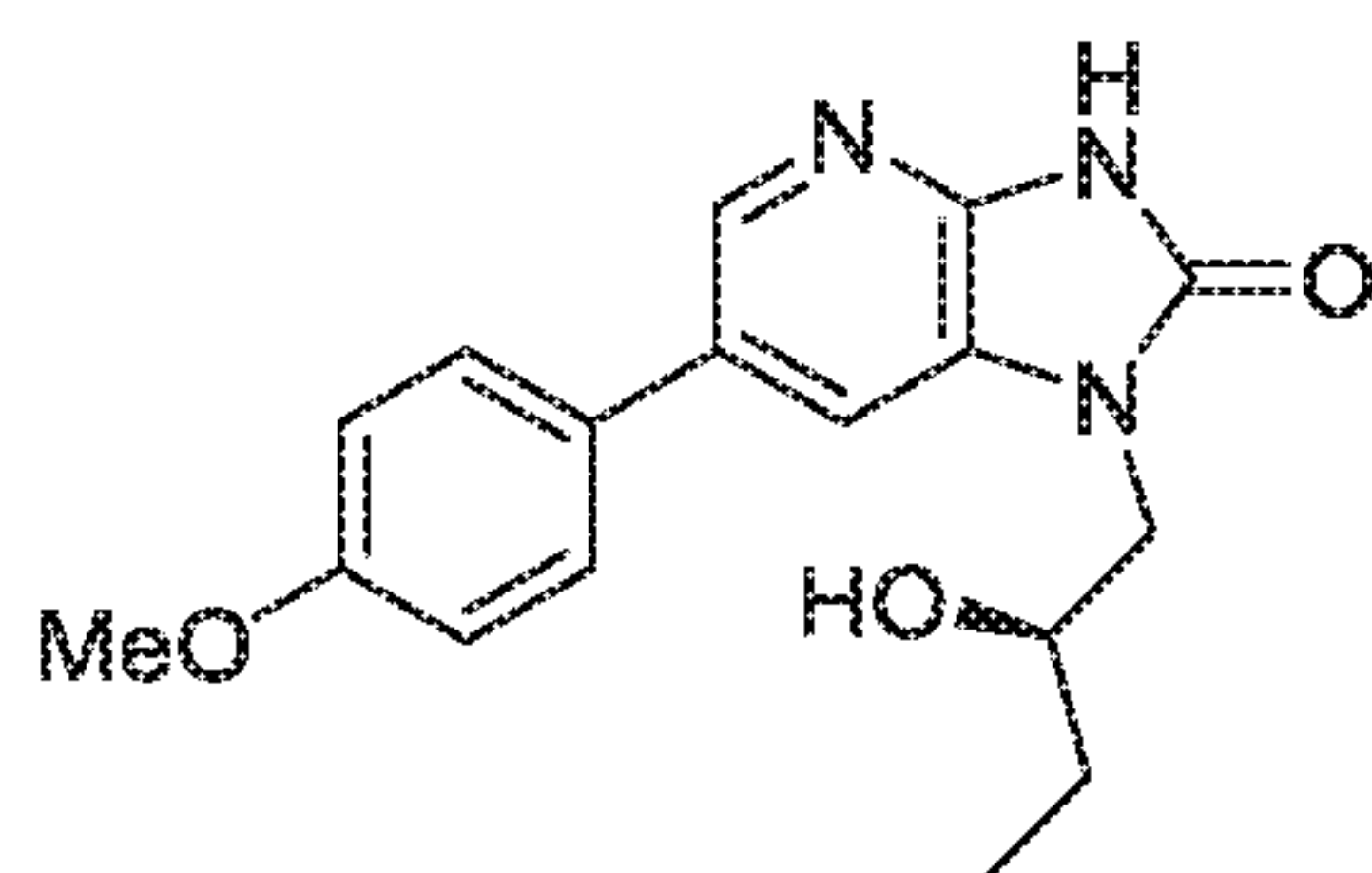


A solution of 2-(6-bromo-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)-N-ethylacetamide (Intermediate 33, 0.3 g, 1 mmol), (4-fluoro-2-methylphenyl)boronic acid (0.23 g, 1.5 mmol), Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (0.03 g, 0.04 mmol), and 2 M Na<sub>2</sub>CO<sub>3</sub> (2mL) in EtOH (6 mL) was heated to 180 °C via microwave irradiation for 1 h. Then, water (30 mL) was added to the crude reaction mixture and the mixture was extracted with EtOAc (3 x 30 mL). The combined organic layers were washed with water, brine, dried over Na<sub>2</sub>SO<sub>4</sub>,

20

filtered and concentrated under reduced pressure. The crude residue was purified by preparative HPLC (gradient elution: 0.1% TFA in CH<sub>3</sub>CN/ 0.1% TFA in H<sub>2</sub>O) and the desired fractions were collected and washed with a saturated aqueous solution of NaHCO<sub>3</sub>. The biphasic mixture was extracted with EtOAc (3x 30 mL). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated to yield the title compound as a white solid (0.061 g, 18%). MS (ESI): mass calcd. for C<sub>17</sub>H<sub>17</sub>FN<sub>4</sub>O<sub>2</sub>, 328.1; m/z found, 329.0 [M+H]<sup>+</sup>. MP = 225.1 – 232.3 °C.

Example 4: (S\*)-1-(2-Hydroxybutyl)-6-(4-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-one.



Step A: 3-Benzhydryl-6-bromo-1-(2-oxobutyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. 1-Bromobutan-2-one (1.6 g, 11 mmol) was added to a solution of 3-benzhydryl-6-bromo-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 32, Product from Step B, 2 g, 5.3 mmol), and Na<sub>2</sub>CO<sub>3</sub> (1.1 g, 11 mmol) in MeCN (30 mL), and the reaction mixture was refluxed for 2 h. Then, the crude reaction mixture was filtered and washed with MeOH. The solvent was evaporated to yield the title compound (2.3 g, 96%), which was used in the next step without further purification.

Step B: 3-Benzhydryl-6-bromo-1-(2-hydroxybutyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. To a solution of 3-benzhydryl-6-bromo-1-(2-oxobutyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (2.3 g, 5.1 mmol) in EtOH (50 mL) at 0 °C was added NaBH<sub>4</sub> (0.8 g, 21 mmol), and the mixture was warmed to room temperature and stirred for 2 h. Then water was added and the reaction mixture was filtered. The solids were collected and dried to yield the title compound (2 g, 87%), which was used in the next step without further purification.

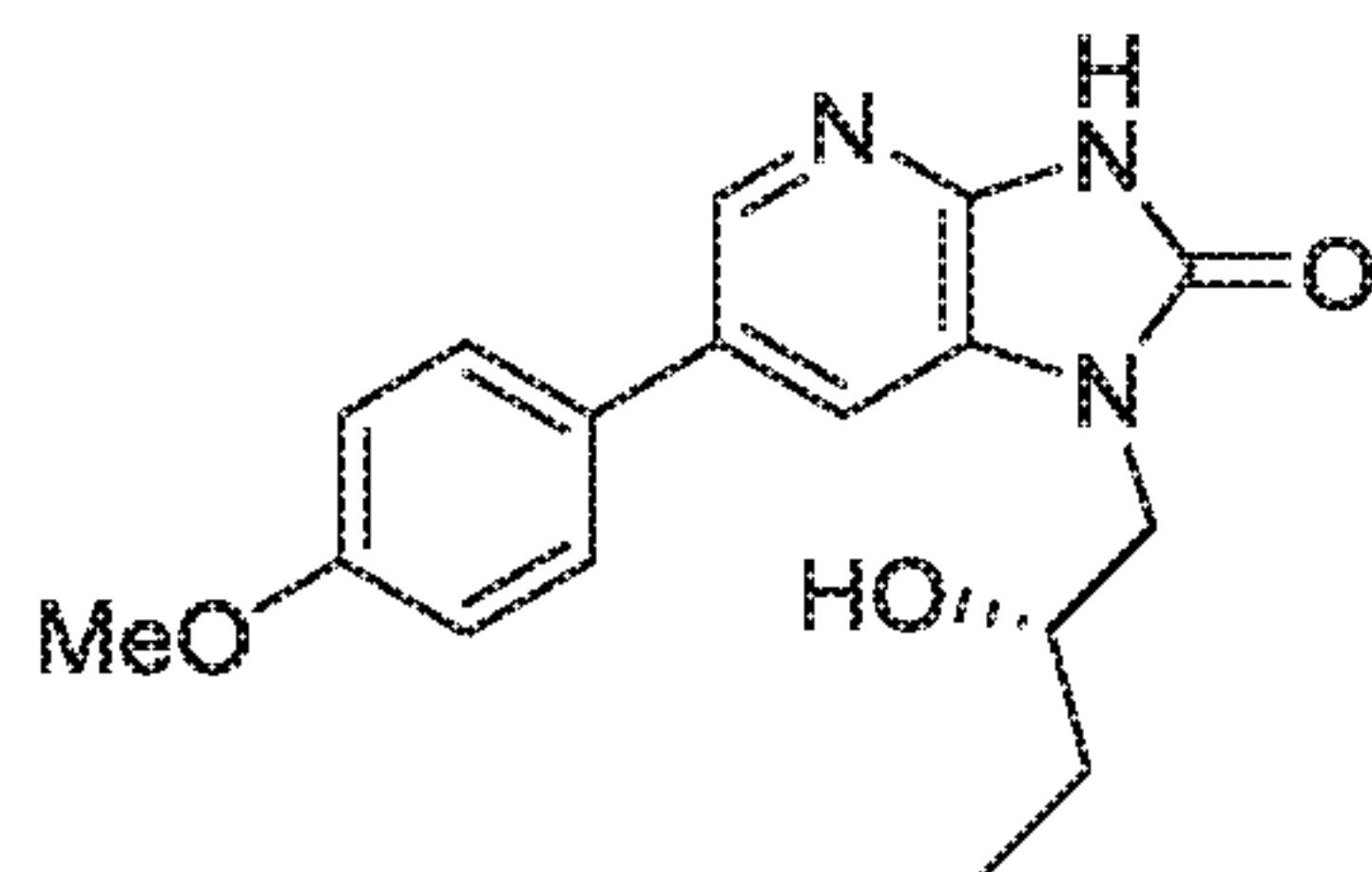
Step C: 6-Bromo-1-(2-hydroxybutyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one. A solution of 3-benzhydryl-6-bromo-1-(2-hydroxybutyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (2 g, 4.4 mmol) in TFA (20 mL) and thioanisole (0.05 mL) was heated to reflux for 4 h. The

reaction mixture was cooled, and concentrated under reduced pressure. Ammonia/water was added to adjust the pH to 8. The reaction mixture was concentrated under reduced pressure and purified (FCC, SiO<sub>2</sub>, DCM/MeOH 1:0 to 0:1) to afford the title compound the desired (1.2 g, 96%).

5 Step D: (S\*)-1-(2-Hydroxybutyl)-6-(4-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-one.

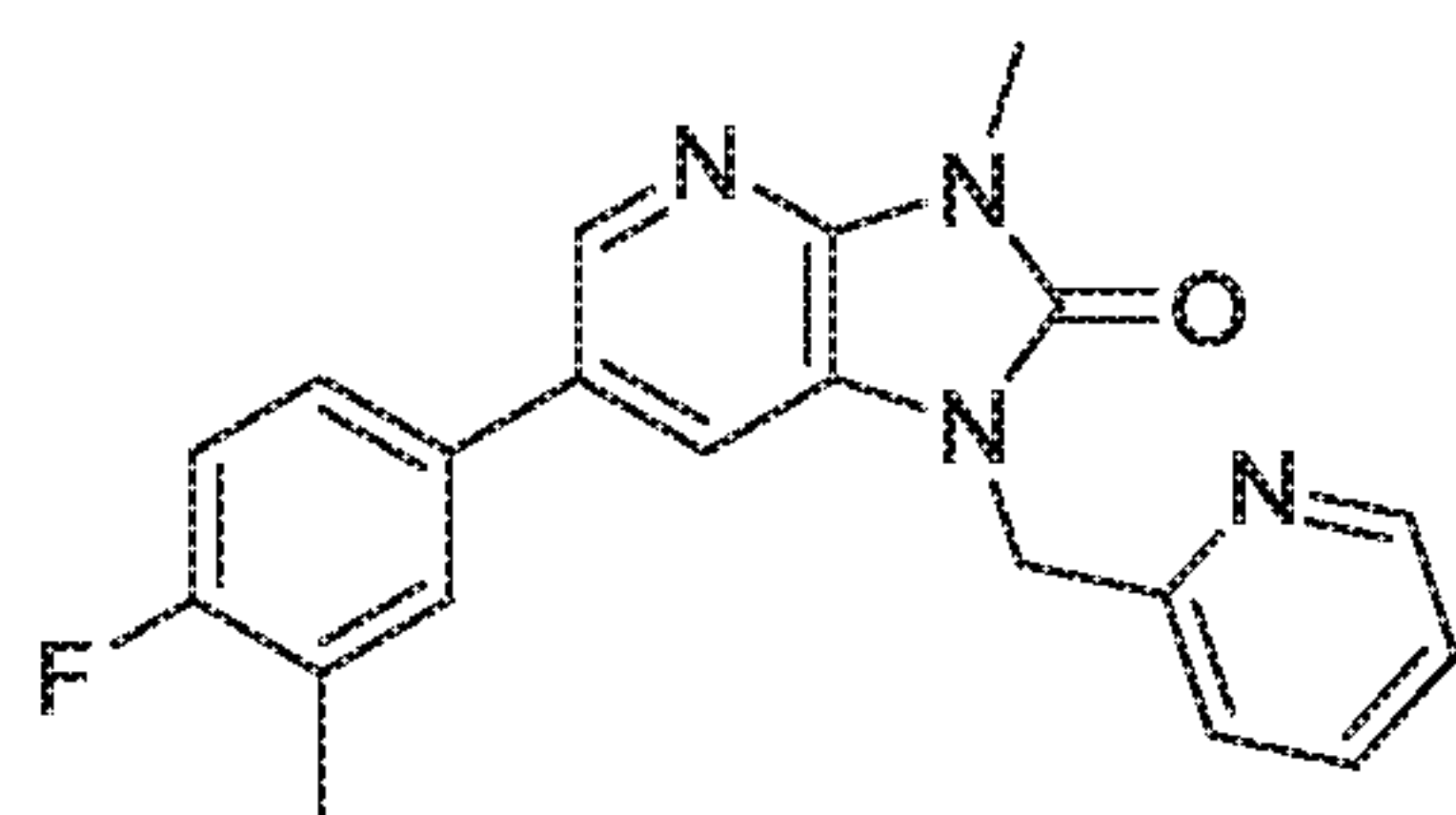
The title compound was prepared in a manner analogous to Example 2, using (4-methoxyphenyl)boronic acid in and 6-bromo-1-(2-hydroxybutyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one. Purification (SFC separation, Chiralcel AD-H, 20μm; Supercritical CO<sub>2</sub>: MeOH, v/v, 200mL/min) afforded the title compound and (R\*)-1-(2-Hydroxybutyl)-  
10 6-(4-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-one (Example 5). MS (ESI): mass calcd. for C<sub>17</sub>H<sub>19</sub>N<sub>3</sub>O<sub>3</sub>, 313.1; m/z found, 314.0 [M+H]<sup>+</sup>.

Example 5: (R\*)-1-(2-Hydroxybutyl)-6-(4-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-one.



15 The title compound was separated as a product from Example 4. MS (ESI): mass calcd. for C<sub>17</sub>H<sub>19</sub>N<sub>3</sub>O<sub>3</sub>, 313.1; m/z found, 314.1 [M+H]<sup>+</sup>.

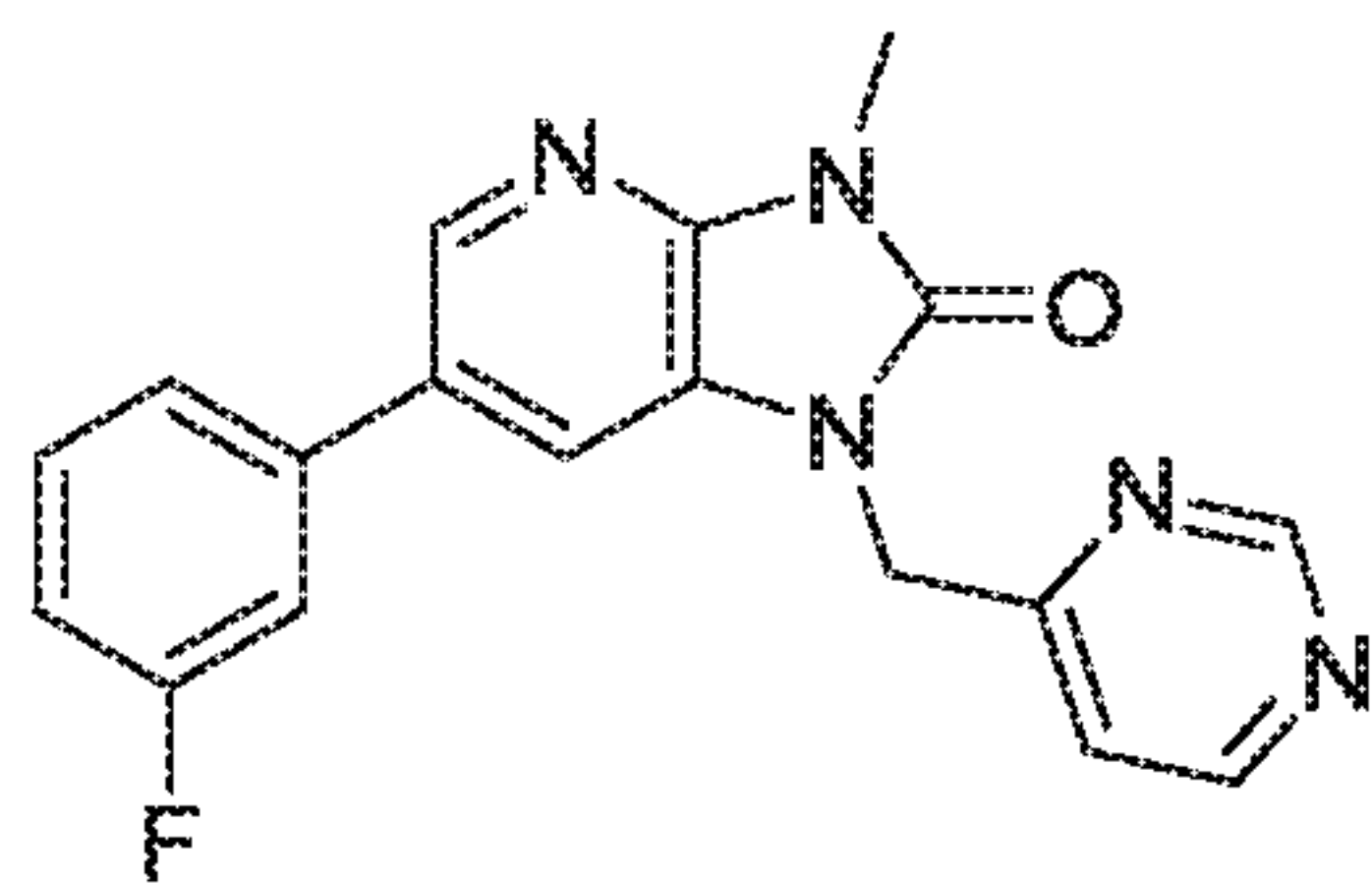
20 Example 6: 6-(4-Fluoro-3-methyl-phenyl)-3-methyl-1-(2-pyridylmethyl)imidazo[4,5-b]pyridin-2-one.



To a solution a 6-(4-fluoro-3-methylphenyl)-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 27, 75 mg, 0.29 mmol) and 2-(chloromethyl)pyridine hydrochloride (74 mg, 0.45 mmol) in DMF (7.5 mL) at 0 °C was added portion-wise NaH

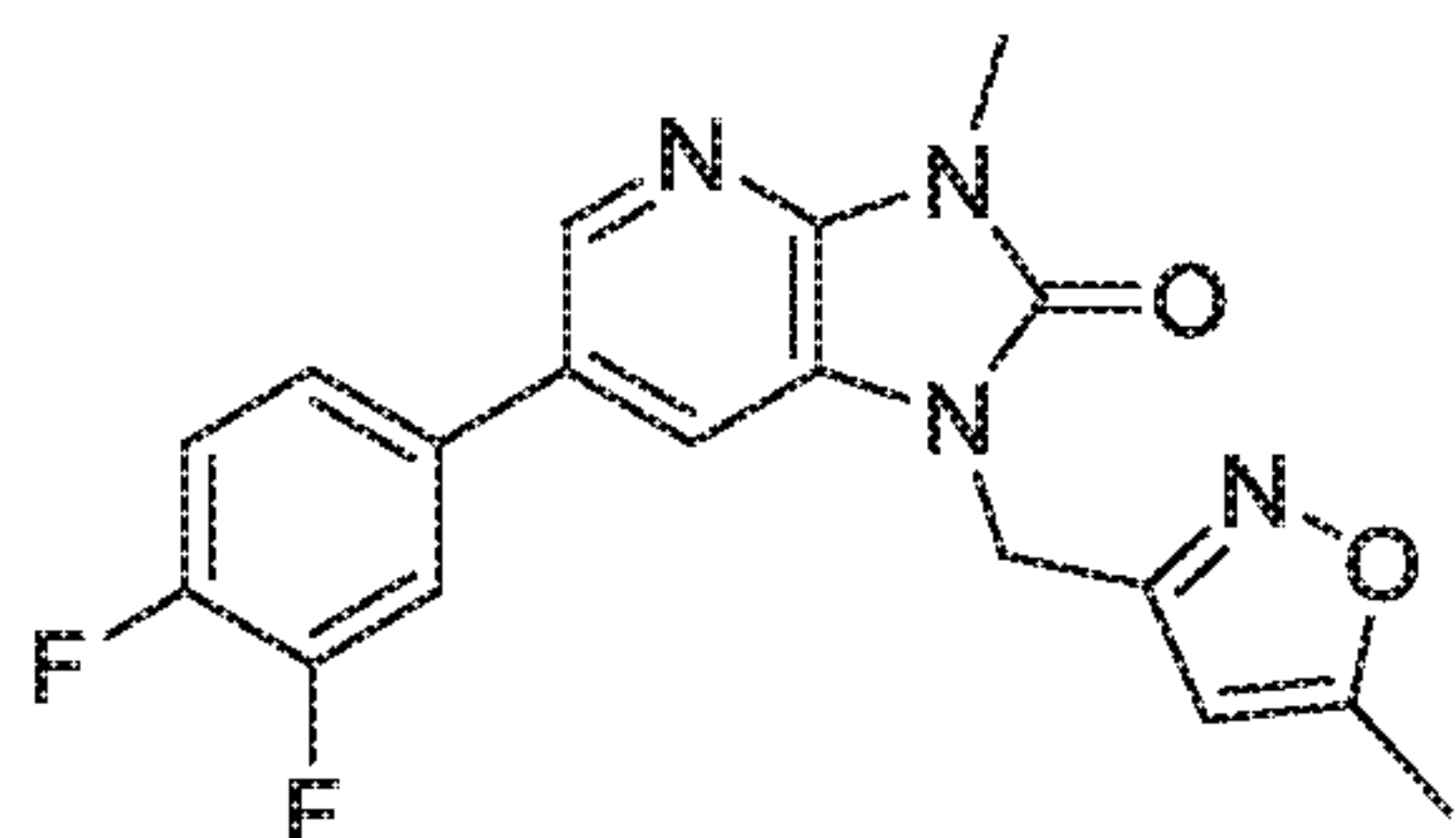
(60% dispersion in mineral oil, 27 mg, 0.67 mmol), and the reaction mixture was stirred at 0 °C for 20 min. Then, the mixture was heated to 75 °C and stirred for 2 h. Upon completion, water was added followed by EtOAc. The resulting biphasic mixture was separated and the aqueous layer further extracted with DCM. The combined organic layers were dried (MgSO<sub>4</sub>), filtered and concentrated under reduced pressure. The residue was purified (FCC, SiO<sub>2</sub>, 0 -10% 7 M solution of NH<sub>3</sub>/MeOH in EtOAc) to yield the title compound as a pink solid (25 g, 25%). MS (ESI): mass calcd. for C<sub>20</sub>H<sub>17</sub>FN<sub>4</sub>O, 348.1; m/z found, 349.1 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 2.22 (d, *J* = 1.62 Hz, 3 H), 3.34 (s, 3 H), 5.19 (s, 2 H), 7.15 (t, *J* = 9.13 Hz, 1 H), 7.21 (dd, *J* = 7.40, 4.85 Hz, 1 H), 7.25 (d, *J* = 7.86 Hz, 1 H), 7.36 - 7.44 (m, 1 H), 7.50 (dd, *J* = 7.40, 1.85 Hz, 1 H), 7.65 - 7.74 (m, 2 H), 8.21 (d, *J* = 1.85 Hz, 1 H), 8.41 (d, *J* = 3.93 Hz, 1 H).

Example 7: 6-(3-Fluorophenyl)-3-methyl-1-(pyrimidin-4-ylmethyl)imidazo[4,5-b]pyridin-2-one.



To a solution of 6-(3-fluorophenyl)-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 28, 60 mg, 0.25 mmol), pyrimidin-4-ylmethanol (27 mg, 0.25 mmol) and triphenylphosphine (129 mg, 0.493 mmol) in CH<sub>3</sub>CN (7.5 mL) at 0 °C was added di-*tert*-butyl azodicarboxylate (85 mg, 0.37 mmol), and the reaction mixture was stirred at 110 °C for 15 min under microwave irradiation. Then, the mixture was concentrated to dryness and the crude product was purified by HPLC purification (Stationary phase: C18 XBridge 30 x 100 mm 5 μm), Mobile phase: Gradient from 74% 10mM NH<sub>4</sub>CO<sub>3</sub>H pH 9 solution in Water, 26% CH<sub>3</sub>CN to 58% 10mM NH<sub>4</sub>CO<sub>3</sub>H pH 9 solution in Water, 42% CH<sub>3</sub>CN) to yield the title compound as a white solid (36 mg, 44%). MS (ESI): mass calcd. for C<sub>18</sub>H<sub>14</sub>FN<sub>5</sub>O, 335.1; m/z found, 336.1 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 3.42 (s, 3 H), 5.31 (s, 2 H), 7.09 - 7.30 (m, 1 H), 7.41 - 7.58 (m, 4 H), 7.91 (d, *J* = 2.08 Hz, 1 H), 8.41 (d, *J* = 2.08 Hz, 1 H), 8.75 (d, *J* = 5.32 Hz, 1 H), 9.08 (d, *J* = 1.39 Hz, 1 H).

Example 8: 6-(3,4-Difluorophenyl)-3-methyl-1-[(5-methylisoxazol-3-yl)methyl]imidazo[4,5-b]pyridin-2-one.

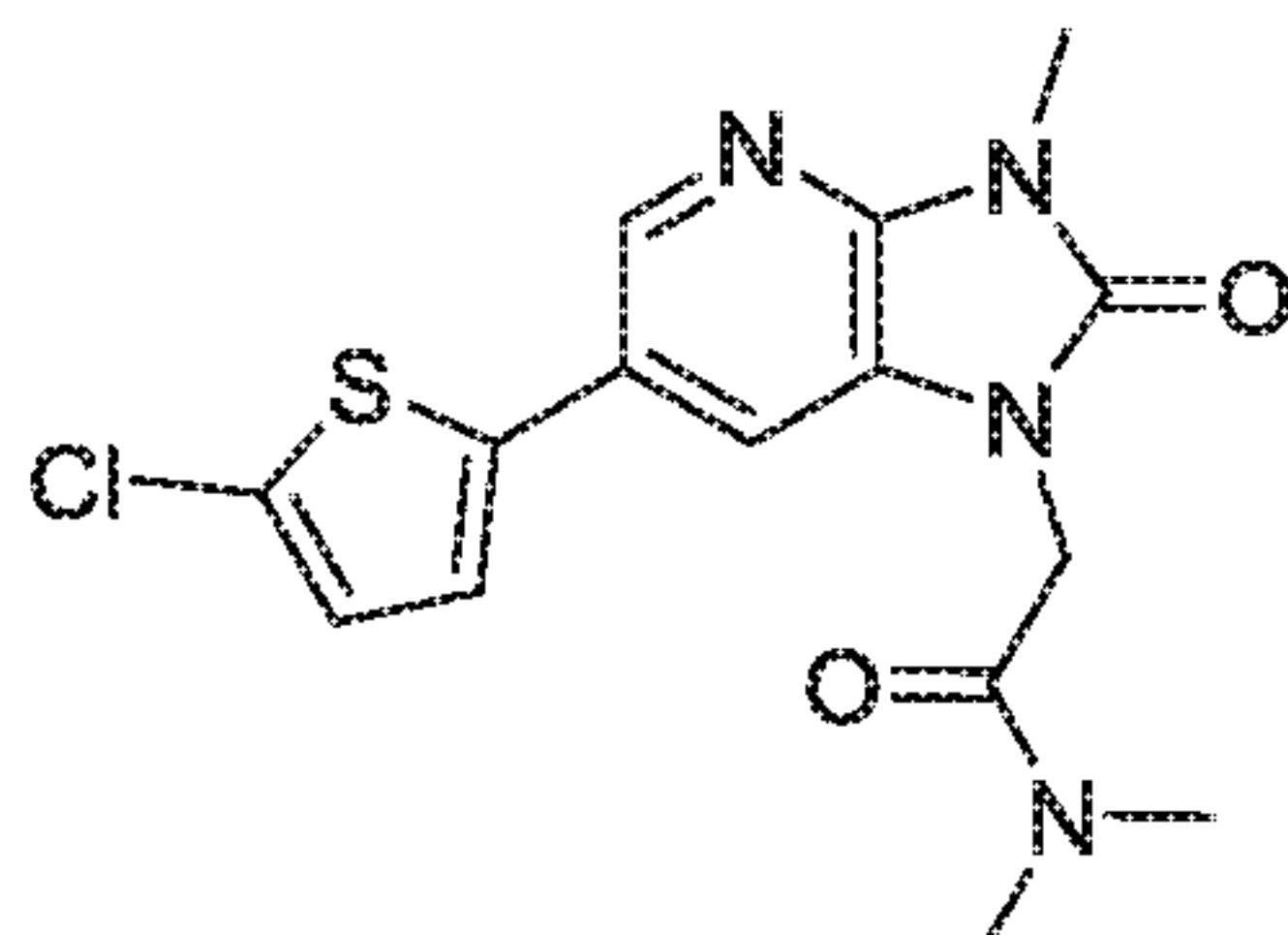


5 Step A: 3-Methyl-1-[(5-methylisoxazol-3-yl)methyl]-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. To a solution of 6-bromo-3-methyl-1-[(5-methylisoxazol-3-yl)methyl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 22, 150 mg, 0.46) in 1,4-dioxane (3 mL) was added bis(pinacolato)diboron (140 mg, 0.551 mmol), KOAc (135 mg, 1.38 mmol) and  
10 PdCl<sub>2</sub>(dppf) (11 mg, 0.014 mmol). The reaction mixture was stirred at 130 °C for 2 h. Then, the crude reaction mixture was cooled and filtered through Celite®. The filtrate was diluted with water and extracted with EtOAc. The combined organic layers were dried (MgSO<sub>4</sub>), filtered and concentrated under reduced pressure. The residue was purified (FCC, SiO<sub>2</sub>, 0-40% EtOAc in heptanes) to yield the title compound (130 mg,  
15 76%). MS (ESI): mass calcd. for C<sub>18</sub>H<sub>23</sub>BN<sub>4</sub>O<sub>4</sub>, 370.2; m/z found, 371 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.44 (s, 1H), 7.60 (s, 1H), 5.99 (s, 1H), 5.08 (s, 2H), 3.53 (s, 3H), 2.37 (s, 3H), 1.34 (s, 12H).

Step B: 6-(3,4-Difluorophenyl)-3-methyl-1-[(5-methylisoxazol-3-yl)methyl]imidazo[4,5-b]pyridin-2-one. To a solution of 3-methyl-1-[(5-methylisoxazol-3-yl)methyl]-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (210  
20 mg, 0.567 mmol), 1-bromo-3,4-difluorobenzene (84 µL, 0.732 mmol) and NaHCO<sub>3</sub> (164 mg, 1.95 mmol) in 1,4-dioxane (4 mL) and water (0.9 mL) was added [1,1'-bis(di-tert-butylphosphino)ferrocene]dichloropalladium(II) (32 mg, 0.049 mmol). The reaction mixture was stirred at 70 °C for 3 h. Then, the crude reaction mixture was cooled,  
25 diluted with water and extracted with EtOAc. The organic layer was separated, dried Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated. The crude product was purified (FCC, SiO<sub>2</sub>, 0-80% EtOAc in heptanes) and the fractions containing desired product were concentrated. The product was then triturated with DIPE to yield the title compound (204 mg, 36%).

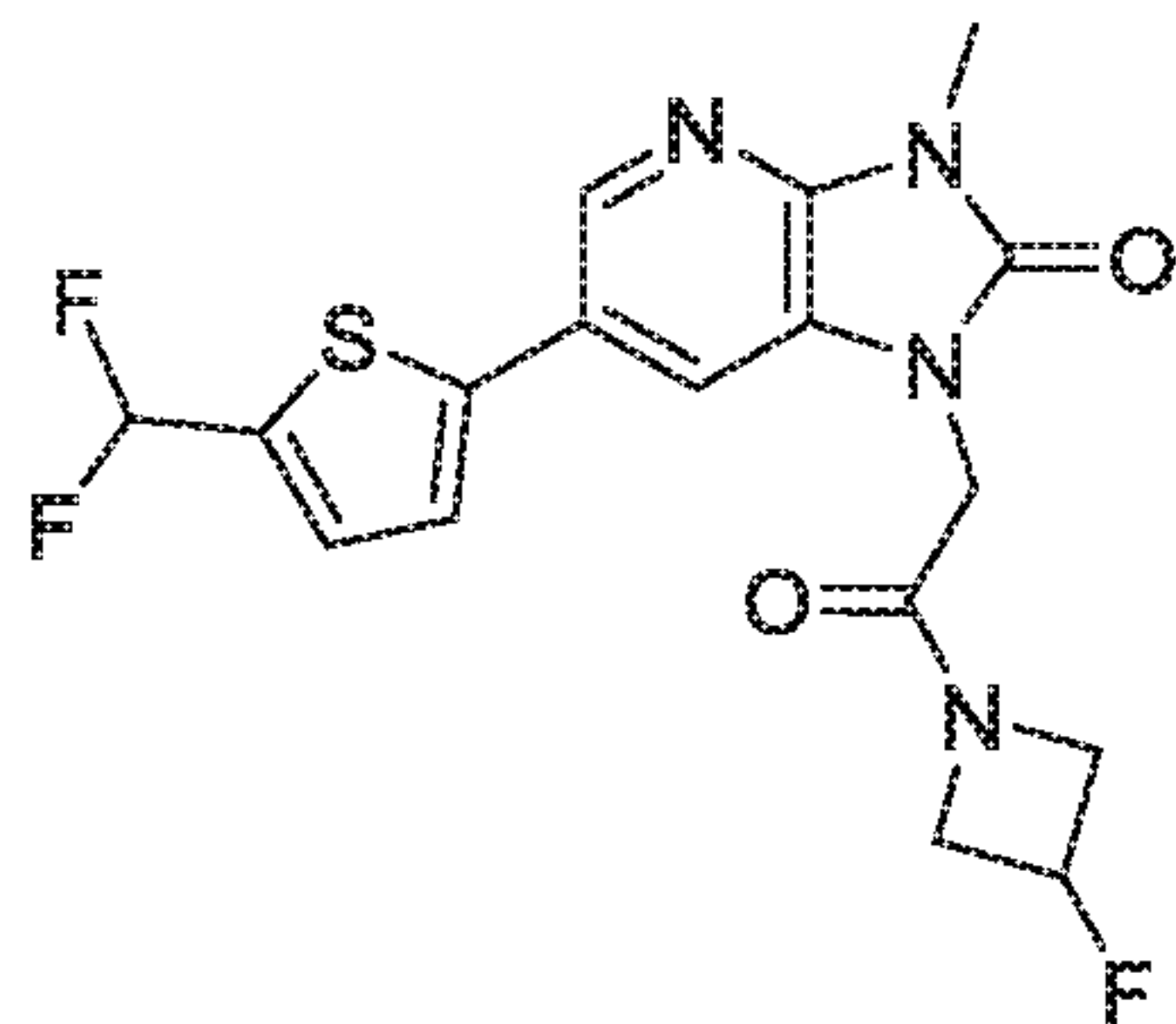
MS (ESI): mass calcd. for C<sub>18</sub>H<sub>14</sub>F<sub>2</sub>N<sub>4</sub>O<sub>2</sub>, 356.1; m/z found, 357 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.19 (s, 1H), 7.40 (s, 1H), 7.36 – 7.26 (m, 2H), 7.25 – 7.21 (m, 1H), 6.03 (s, 1H), 5.13 (s, 2H), 3.54 (s, 3H), 2.38 (s, 3H).

5 Example 9: 2-[6-(5-Chloro-2-thienyl)-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide.



A mixture of 2-(6-bromo-3-methyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)-N,N-dimethylacetamide (Intermediate 15, 180 mg, 0.58 mmol), 5-chlorothiophene-2-boronic acid (140 mg, 0.86 mmol), Cs<sub>2</sub>CO<sub>3</sub> (375 mg, 1.15 mmol), and Pd(dppf)Cl<sub>2</sub>.DCM (29.4 mg, 0.04 mmol) in dioxane (5 mL) and water (1 mL) was sealed in a microwave vial and heated to 90°C. The reaction mixture was stirred at 90°C for 3 hours then cooled down to room temperature and quenched with a saturated aqueous solution of NaHCO<sub>3</sub>. The resulting reaction mixture was extracted with EtOAc (3 x 60 mL) and the combined organic layers were dried using MgSO<sub>4</sub>, filtered and concentrated under vacuum. The crude material was purified via basic HPLC (Agilent prep system, Waters XBridge C18 5 μm 50x100 mm column, 5-95% MeCN/20 mM NH<sub>4</sub>OH over 22 min at 80 mL/min) to provide the title compound (42 mg, 21%). MS (ESI): mass calcd. for C<sub>15</sub>H<sub>15</sub>ClN<sub>4</sub>O<sub>2</sub>S, 350.1; m/z found, 351.1 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.23 – 8.17 (d, J = 1.9 Hz, 1H), 7.26 – 7.25 (m, 1H), 7.02 – 6.97 (d, J = 3.9 Hz, 1H), 6.92 – 6.86 (d, J = 3.8 Hz, 1H), 4.73 – 4.69 (s, 2H), 3.54 – 3.49 (s, 3H), 3.19 – 3.14 (s, 3H), 3.02 – 2.97 (s, 3H).

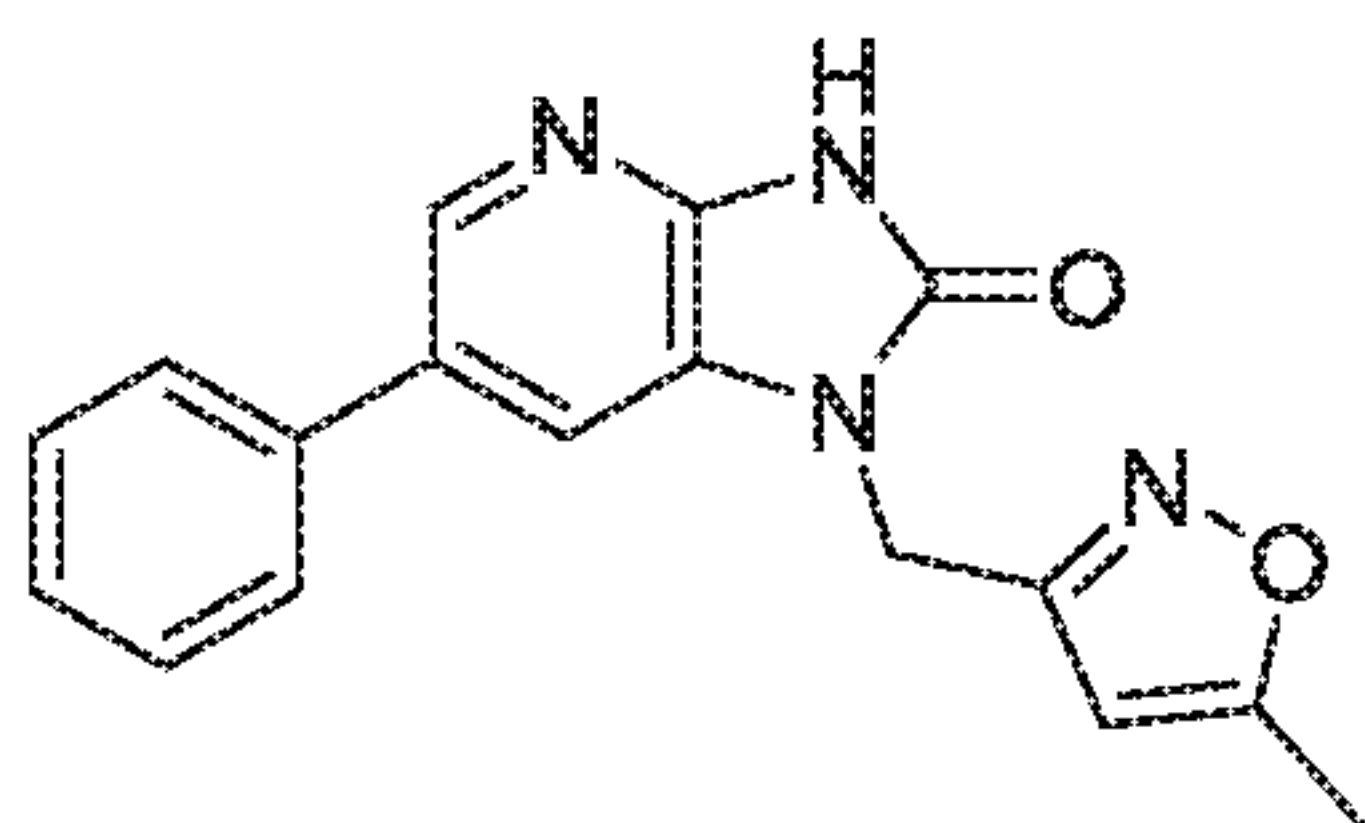
Example 10: 6-[5-(Difluoromethyl)-2-thienyl]-1-[2-(3-fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-imidazo[4,5-b]pyridin-2-one.



To a solution of 2-bromo-5-(difluoromethyl)thiophene (100 mg, 0.47 mmol) in dioxane (3 mL) was added bis(pinacolato)diboron (143 mg, 0.56 mmol), KOAc (138 mg, 1.4 mmol), and PdCl<sub>2</sub>(dppf).DCM (34mg, 0.5 mmol). The resulting reaction mixture was stirred at 5 90°C for 2 hours under a nitrogen atmosphere. The reaction mixture was then cooled down to room temperature and 6-bromo-1-(2-(3-fluoroazetidin-1-yl)-2-oxoethyl)-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 18) (32 mg, 0.09 mmol) was subsequently added to the reaction mixture along with Cs<sub>2</sub>CO<sub>3</sub> (114 mg, 0.35 mmol), dioxane (2 mL) and an additional amount of PdCl<sub>2</sub>(dppf).DCM (34 mg, 0.5 10 mmol). The resulting reaction mixture was stirred at 90°C for an additional 2 hours under a nitrogen atmosphere. The reaction was cooled to room temperature and washed with water. The organic layer was dried with MgSO<sub>4</sub> and concentrated into a brown residue which was purified (FCC, SiO<sub>2</sub>, 0-7% 2M NH<sub>3</sub>/MeOH in DCM). Further purification via basic HPLC (Agilent prep system, Waters XBridge C18 5 μm 50x100 15 mm column, 5-95% MeCN/20 nM NH<sub>4</sub>OH over 22 min at 80 mL/min) to provide the title compound (6 mg, 16%). MS (ESI): mass calcd. for C<sub>17</sub>H<sub>15</sub>F<sub>3</sub>N<sub>4</sub>O<sub>2</sub>S, 396.1; m/z found, 396.9 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.34 – 8.30 (d, *J* = 1.9 Hz, 1H), 7.45 – 7.42 (d, *J* = 1.9 Hz, 1H), 7.28 – 7.26 (m, 1H), 7.20 – 7.17 (m, 1H), 6.98 – 6.68 (m, 1H), 5.48 – 5.25 (m, 1H), 4.68 – 4.11 (m, 6H), 3.56 – 3.50 (s, 3H).

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Example 11: 1-[(5-Methylisoxazol-3-yl)methyl]-6-phenyl-3H-imidazo[4,5-b]pyridin-2-one.



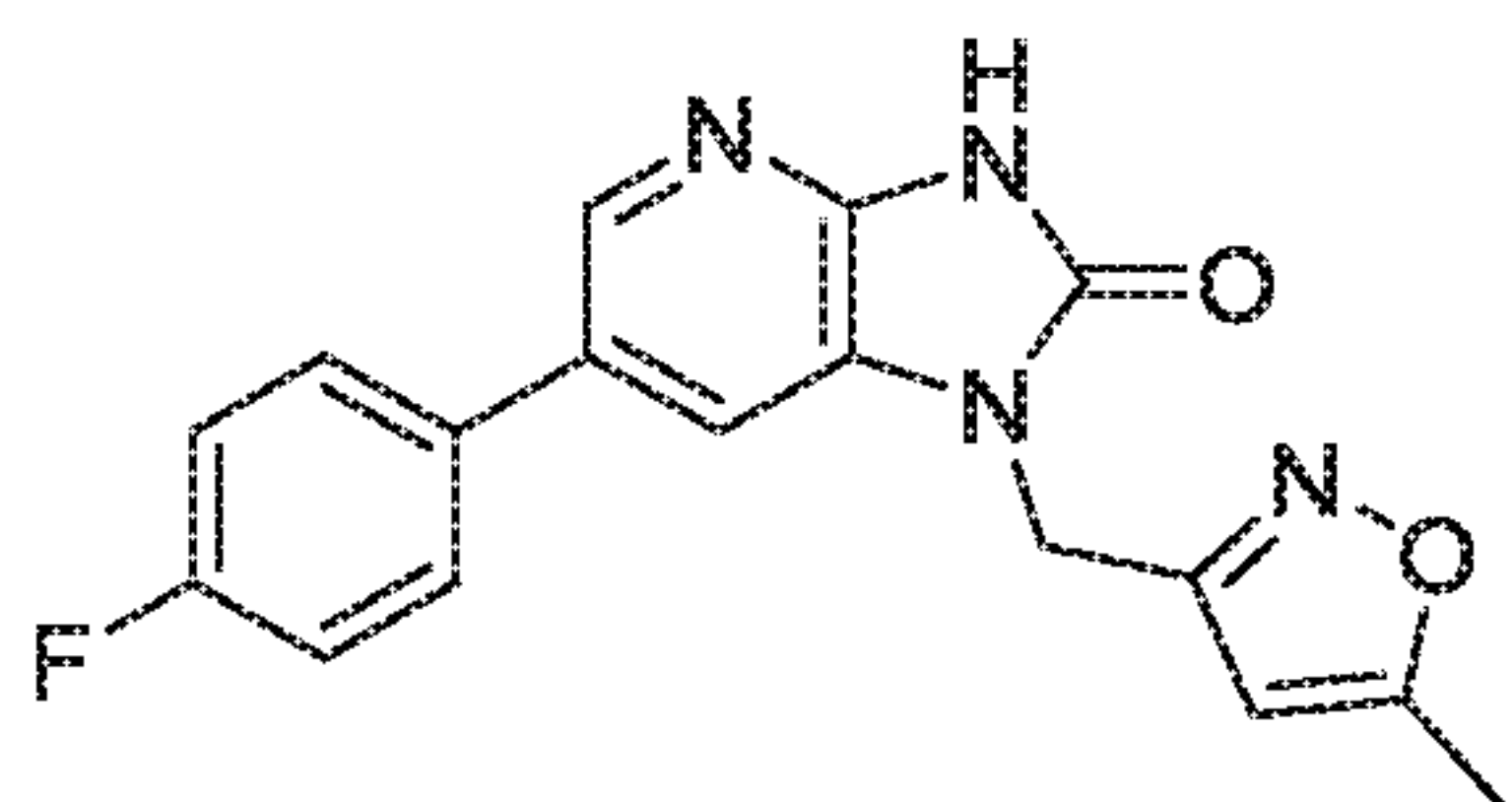
Step A: 6-Bromo-1-((5-methylisoxazol-3-yl)methyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. To a solution of 6-bromo-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 36, 303 mg, 0.66 mmol) in DMF (3 mL) was added NaH (60% dispersion in mineral oil, 35 mg, 0.87 mmol) in one portion at room temperature. The reaction was stirred until gas evolution had ceased, then 3-(chloromethyl)-5-methylisoxazole (87  $\mu$ L, 0.79 mmol) was added. The mixture was stirred at room temperature overnight then diluted with water. The aqueous layer was extracted with EtOAc. The combined organic layers were washed with water (2X), then dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated under reduced pressure. The crude solid was purified (FCC, SiO<sub>2</sub>, 0 to 25% EtOAc in hexanes) to yield the title compound as a solid (356 mg, 97%). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.79 (d, *J* = 2.0 Hz, 1H), 7.53 – 7.45 (m, 6H), 7.29 (d, *J* = 2.0 Hz, 1H), 7.25 – 7.16 (m, 9H), 5.67 (d, *J* = 0.9 Hz, 1H), 4.94 (s, 2H), 2.34 (d, *J* = 0.9 Hz, 3H).

Step B: 1-((5-Methylisoxazol-3-yl)methyl)-6-phenyl-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. To a microwave tube was added solid 6-bromo-1-((5-methylisoxazol-3-yl)methyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (184 mg, 0.33 mmol) followed by phenylboronic acid (60 mg, 0.49 mmol) and Pd(PPh<sub>3</sub>)<sub>4</sub> (25 mg, 0.02 mmol). To these solids were added dioxane (1.6 mL) followed by 2M Na<sub>2</sub>CO<sub>3</sub> (332  $\mu$ L, 0.67 mmol). The vial was capped and heated at 100 °C for 5 h. Then dioxane was removed via pipette and the remaining solids were triturated with EtOAc (3X). The combined organic layers were concentrated to yield the title compound (287 mg, 81%) as a solid, which was used in the next step without further purification.

Step C: 1-[(5-Methylisoxazol-3-yl)methyl]-6-phenyl-3H-imidazo[4,5-b]pyridin-2-one. To a solution of 1-((5-methylisoxazol-3-yl)methyl)-6-phenyl-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (183 mg, 0.33 mmol) in DCM (3 mL) was added TFA (666  $\mu$ L). The mixture was stirred at room temperature overnight and then concentrated. The residue was dissolved in DCM and washed with a saturated aqueous solution of NaHCO<sub>3</sub>. The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated under reduced pressure. The crude oil was purified (FCC, SiO<sub>2</sub>, 0 to 50% EtOAc in hexanes) to yield the title compound as a solid (62 mg, 60%). MS (ESI): mass calcd. for C<sub>17</sub>H<sub>14</sub>N<sub>4</sub>O<sub>2</sub>, 306.1; *m/z* found, 307.1 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  10.44 (s,

1H), 8.31 (d,  $J = 1.9$  Hz, 1H), 7.57 – 7.52 (m, 2H), 7.51 (d,  $J = 1.9$  Hz, 1H), 7.50 – 7.43 (m, 2H), 7.41 – 7.36 (m, 1H), 6.05 (d,  $J = 1.0$  Hz, 1H), 5.14 (s, 2H), 2.38 (d,  $J = 0.9$  Hz, 3H).

5 Example 12: 6-(4-Fluorophenyl)-1-[(5-methylisoxazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one.



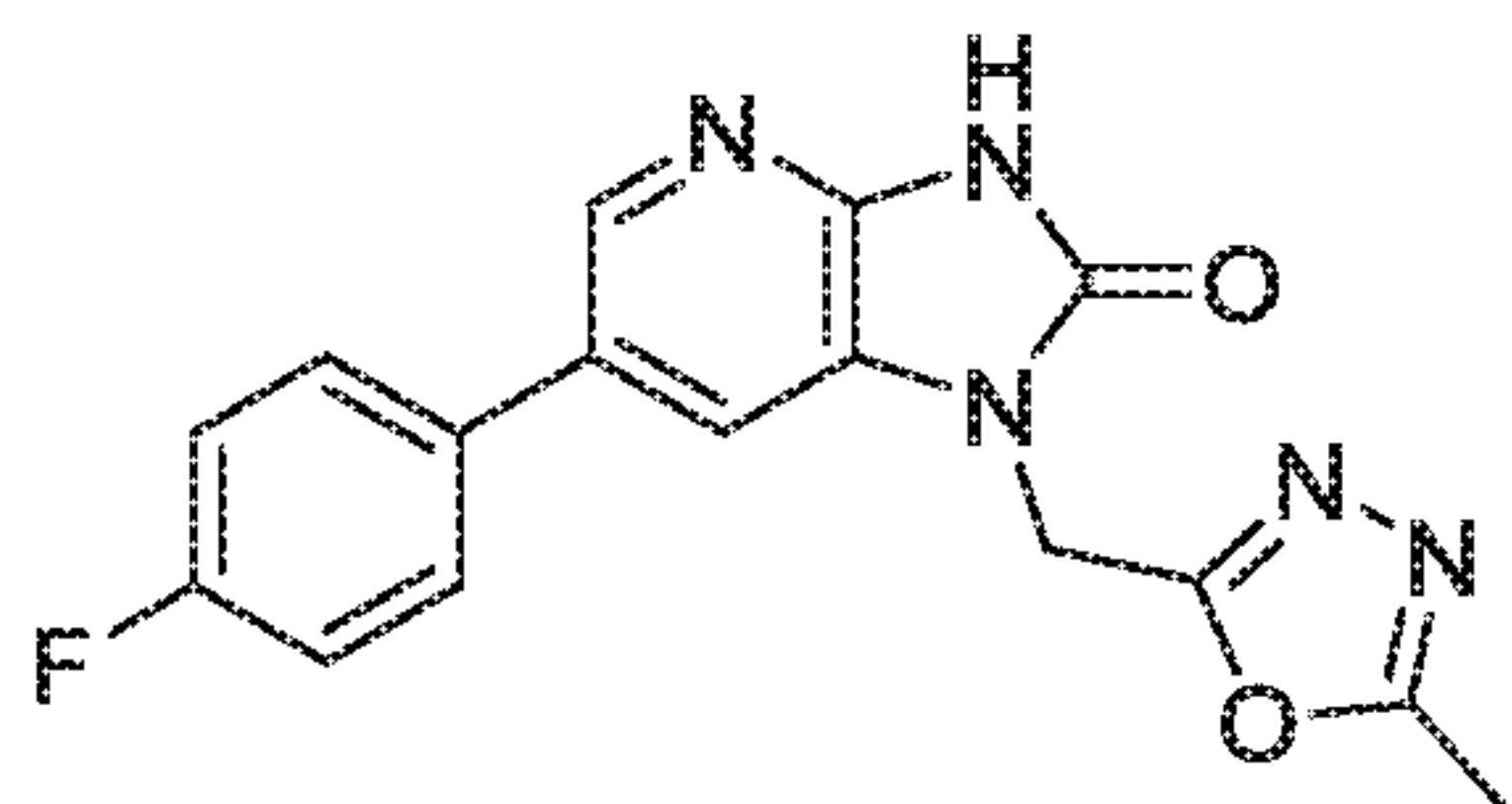
Step A: 6-(4-Fluorophenyl)-3-(4-methoxybenzyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. To a microwave tube was added 6-bromo-3-(4-methoxybenzyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 10, 287 mg, 0.86 mmol) followed by 4-fluorophenylboronic acid (159 mg, 1.14 mmol) and Pd(PPh<sub>3</sub>)<sub>4</sub> (51 mg, 0.04 mmol). To these solids were added dioxane (4 mL) followed by 2 M Na<sub>2</sub>CO<sub>3</sub> (859  $\mu$ L, 1.72 mmol). The vial was capped and heated in the microwave at 150 °C for 1 h. Then dioxane was removed via pipette and the remaining solids were triturated with EtOAc (3X). The combined organic layers were concentrated and the crude solid was purified (FCC, SiO<sub>2</sub>, 0 to 55% 1% IPA in EtOAc in hexanes) to yield the title compound (52 mg, 17%) as a solid. MS (ESI): mass calcd. for C<sub>20</sub>H<sub>16</sub>FN<sub>3</sub>O<sub>2</sub>, 349.1;  $m/z$  found, 350.1 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  9.34 (s, 1H), 8.24 (d,  $J = 2.0$  Hz, 1H), 7.52 – 7.45 (m, 4H), 7.43 (d,  $J = 1.9$  Hz, 1H), 7.19 – 7.11 (m, 2H), 6.88 – 6.81 (m, 2H), 5.14 (s, 2H), 3.76 (s, 3H).

Step B: 6-(4-Fluorophenyl)-3-(4-methoxybenzyl)-1-[(5-methylisoxazol-3-yl)methyl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. To a solution of 6-(4-fluorophenyl)-3-(4-methoxybenzyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (43 mg, 0.12 mmol) in DMF (2 mL) was added NaH (60% dispersion in mineral oil, 6 mg, 0.16 mmol) in one portion at room temperature. The reaction was stirred until gas evolution ceased, and then 3-(chloromethyl)-5-methylisoxazole (16  $\mu$ L, 0.15 mmol) was added. The mixture was stirred at room temperature overnight but was incomplete. To the reaction mixture was added additional NaH (60% dispersion in mineral oil, 6 mg, 0.16 mmol) in one portion at

room temperature. The reaction was stirred until gas evolution ceased, and then additional 3-(chloromethyl)-5-methylisoxazole (16  $\mu$ L, 0.15 mmol) was added. The mixture was again stirred at room temperature overnight. Then, the reaction was diluted with water and the aqueous layer was extracted with EtOAc. The combined organic  
 5 layers were dried over  $\text{Na}_2\text{SO}_4$ , filtered and concentrated to yield the title compound (66 mg) as a solid, which was used in the next step without further purification. MS (ESI): mass calcd. for  $\text{C}_{25}\text{H}_{21}\text{FN}_4\text{O}_3$ , 444.2;  $m/z$  found, 445.2  $[\text{M}+\text{H}]^+$ .  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.21 (d,  $J = 1.9$  Hz, 1H), 7.51 – 7.42 (m, 4H), 7.40 (d,  $J = 1.9$  Hz, 1H), 7.17 – 7.10 (m, 2H), 6.88 – 6.82 (m, 2H), 6.03 – 5.96 (m, 1H), 5.18 – 5.07 (m, 4H), 3.77 (s,  
 10 3H), 2.37 (d,  $J = 0.9$  Hz, 3H).

Step C: 6-(4-Fluorophenyl)-1-[(5-methylisoxazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one. A solution of 48% aqueous HBr (3 mL) was added to 6-(4-fluorophenyl)-3-(4-methoxybenzyl)-1-((5-methylisoxazol-3-yl)methyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (55 mg, 0.12 mmol) and the mixture was heated at 115  $^\circ\text{C}$  for 7 h. The mixture  
 15 was concentrated and the residue was partitioned between DCM and a saturated aqueous solution of  $\text{NaHCO}_3$ . The layers were separated and the aqueous layer was extracted with DCM. The combined organic layers were dried over  $\text{Na}_2\text{SO}_4$ , filtered and concentrated under reduced pressure. The crude material was purified (FCC,  $\text{SiO}_2$ , 0 to 50% 1.5% IPA in EtOAc in hexanes) to yield the title compound (33 mg, 82%) as a  
 20 solid. MS (ESI): mass calcd. for  $\text{C}_{17}\text{H}_{13}\text{FN}_4\text{O}_2$ , 324.1;  $m/z$  found, 325.1  $[\text{M}+\text{H}]^+$ .  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  10.08 (s, 1H), 8.24 (d,  $J = 1.9$  Hz, 1H), 7.52 – 7.45 (m, 3H), 7.18 – 7.11 (m, 2H), 6.06 (d,  $J = 1.0$  Hz, 1H), 5.13 (s, 2H), 2.38 (d,  $J = 1.0$  Hz, 3H).

Example 13: 6-(4-Fluorophenyl)-1-[(5-methyl-1,3,4-oxadiazol-2-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one.  
 25



Step A: 6-(4-Fluorophenyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. To a round bottom flask was added 6-bromo-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-

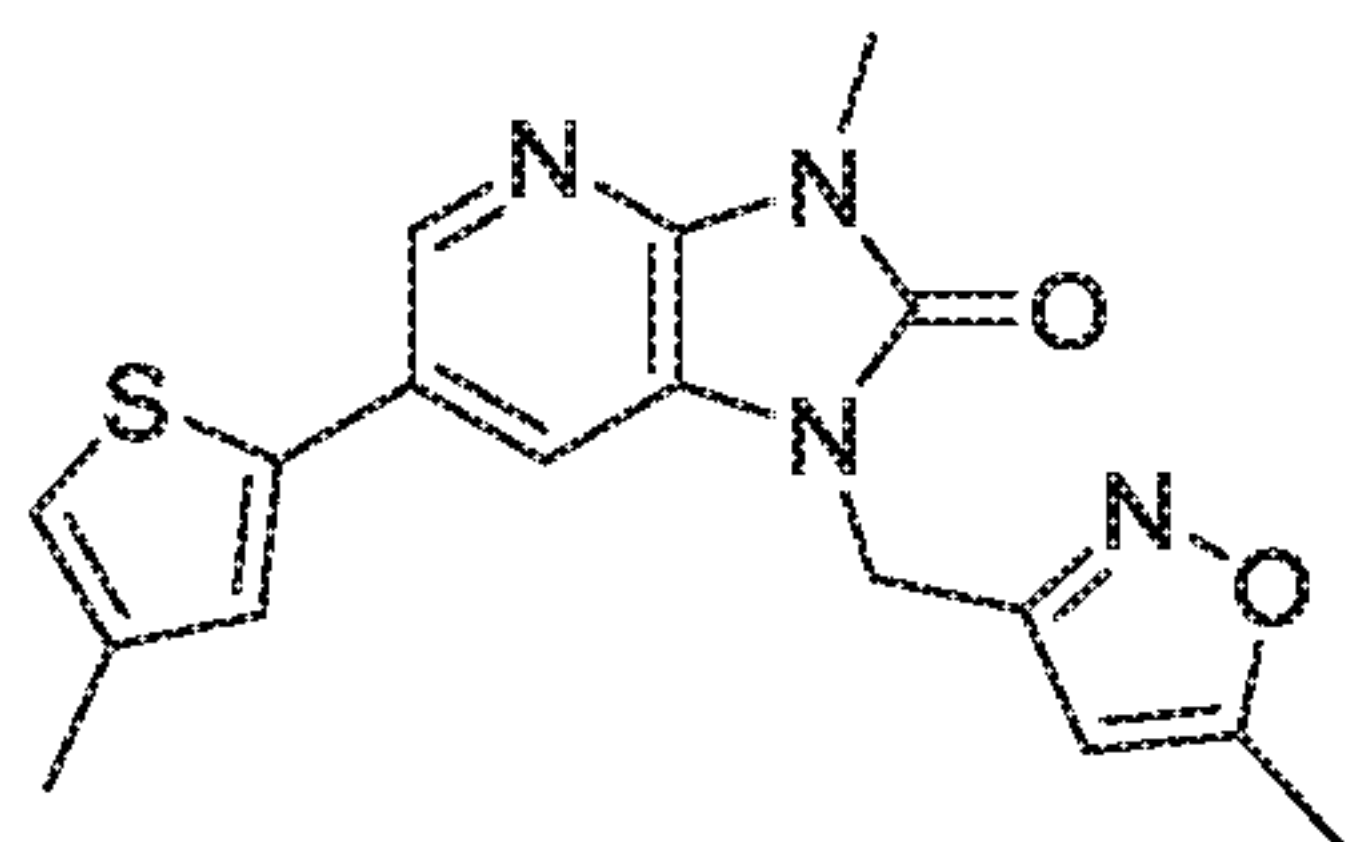
one (Intermediate 36, 706 mg, 1.55 mmol) followed by 4-fluorophenylboronic acid (294 mg, 2.10 mmol) and Pd(PPh<sub>3</sub>)<sub>4</sub> (357 mg, 0.31 mmol). To these solids were added dioxane (8 mL) followed by 2M Na<sub>2</sub>CO<sub>3</sub> (2.3 mL, 4.64 mmol). The mixture was heated at 90 °C for 15 h. Then, the crude reaction mixture was concentrated to remove dioxane, and the resultant residue was partitioned between EtOAc and water. The layers were separated and the aqueous layer was extracted with EtOAc. The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated under reduced pressure. The crude material was purified (FCC, SiO<sub>2</sub>, 0 to 50% 1.5% IPA in EtOAc in hexanes) to yield the title compound (400 mg, 55%) as a solid. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 8.26 – 8.18 (m, 1H), 7.95 (d, *J* = 2.0 Hz, 1H), 7.78 – 7.72 (m, 1H), 7.59 – 7.52 (m, 6H), 7.44 – 7.38 (m, 2H), 7.31 – 7.08 (m, 10H).

Step B: 6-(4-Fluorophenyl)-1-((5-methyl-1,3,4-oxadiazol-2-yl)methyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. To a solution of 6-(4-fluorophenyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (205 mg, 0.44 mmol) in DMF (4 mL) was added NaH (60% dispersion in mineral oil, 23 mg, 0.57 mmol) in one portion at room temperature. The reaction was stirred until gas evolution had ceased, then 2-(chloromethyl)-5-methyl-1,3,4-oxadiazole (58 µL, 0.57 mmol) was added. The mixture was stirred at room temperature overnight. Then the reaction mixture was diluted with water and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with water (2X), dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated. The crude solid was purified (FCC, SiO<sub>2</sub>, 0 to 60% EtOAc in hexanes) to yield the title compound (129 mg, 52%) as a foam. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.97 (d, *J* = 2.0 Hz, 1H), 7.57 – 7.50 (m, 6H), 7.44 – 7.36 (m, 2H), 7.34 (d, *J* = 2.0 Hz, 1H), 7.28 – 7.26 (m, 1H), 7.26 – 7.17 (m, 7H), 7.12 – 7.05 (m, 2H), 5.21 (s, 2H), 2.49 (s, 3H).

Step C: 6-(4-Fluorophenyl)-1-[(5-methyl-1,3,4-oxadiazol-2-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one. To a solution of 6-(4-fluorophenyl)-1-((5-methyl-1,3,4-oxadiazol-2-yl)methyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (129 mg, 0.23 mmol) in DCM (2 mL) was added TFA (455 µL). The mixture was stirred at room temperature overnight and then concentrated. The crude residue was purified (FCC, SiO<sub>2</sub>, 0 to 10% IPA in EtOAc) to yield the title compound (61 mg, 83%) as a solid. MS (ESI): mass calcd. for C<sub>18</sub>H<sub>12</sub>FN<sub>5</sub>O<sub>2</sub>, 325.1; *m/z* found, 326.1 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (500 MHz, DMF-d<sub>7</sub>) δ

11.86 (br s, 1H), 8.30 (d,  $J = 2.0$  Hz, 1H), 7.91 (d,  $J = 2.0$  Hz, 1H), 7.79 – 7.70 (m, 2H), 7.38 – 7.29 (m, 2H), 5.50 (s, 2H), 2.50 (s, 3H).

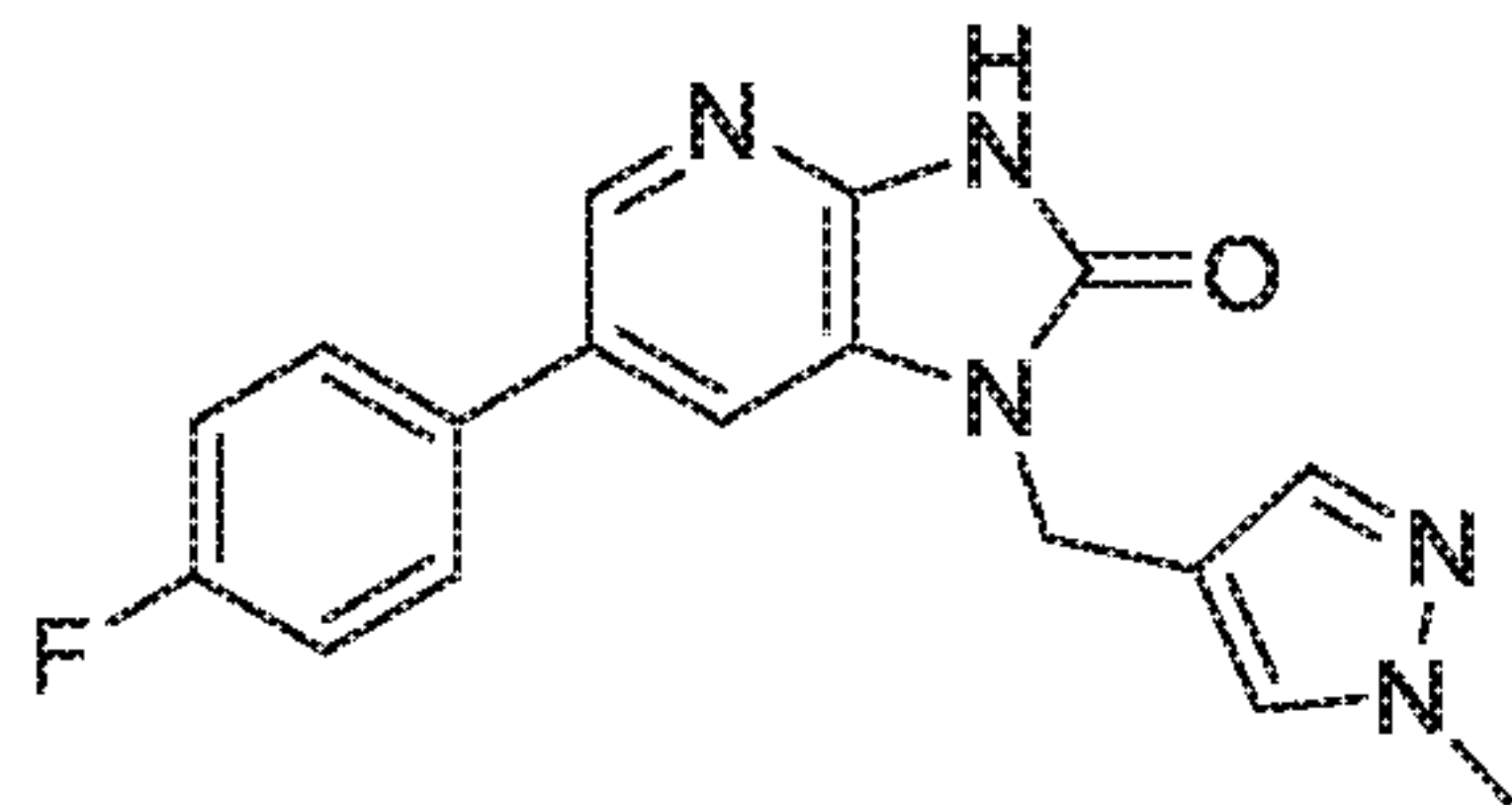
Example 14: 3-Methyl-1-[(5-methylisoxazol-3-yl)methyl]-6-(4-methyl-2-thienyl)imidazo[4,5-b]pyridin-2-one.



Step A: 1-((5-Methylisoxazol-3-yl)methyl)-6-(4-methylthiophen-2-yl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. The title compound was prepared in a manner analogous to Example 11 using (4-methylthiophen-2-yl)boronic acid in Step B. MS (ESI): mass calcd. for  $C_{16}H_{14}N_4O_2S$ , 326.1;  $m/z$  found, 327.1  $[M+H]^+$ .  $^1H$  NMR (500 MHz, DMF- $d_7$ )  $\delta$  11.79 (s, 1H), 8.25 (d,  $J = 2.0$  Hz, 1H), 7.77 (d,  $J = 1.9$  Hz, 1H), 7.36 – 7.31 (m, 1H), 7.16 – 7.11 (m, 1H), 6.25 (t,  $J = 0.9$  Hz, 1H), 5.24 (s, 2H), 2.40 (d,  $J = 0.9$  Hz, 3H), 2.26 (d,  $J = 1.0$  Hz, 3H).

Step B: 3-Methyl-1-[(5-methylisoxazol-3-yl)methyl]-6-(4-methyl-2-thienyl)imidazo[4,5-b]pyridin-2-one. To a solution of 1-((5-methylisoxazol-3-yl)methyl)-6-(4-methylthiophen-2-yl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (43 mg, 0.13 mmol) in DMF (2 mL) was added NaH (60% dispersion in mineral oil, 13 mg, 0.87 mmol) in one portion at room temperature. The reaction was stirred until gas evolution had ceased, then iodomethane (11  $\mu$ L, 0.17 mmol) was added. The mixture was stirred at room temperature overnight then diluted with water. The aqueous layer was extracted with EtOAc. The combined organic layers were dried over  $Na_2SO_4$ , filtered and concentrated under reduced pressure. The crude solid was purified (FCC,  $SiO_2$ , 0 to 50% 1% IPA in EtOAc in DCM) to yield the title compound as a solid (37 mg, 82%). MS (ESI): mass calcd. for  $C_{17}H_{16}N_4O_2S$ , 340.1;  $m/z$  found, 341.1  $[M+H]^+$ .  $^1H$  NMR (500 MHz,  $CDCl_3$ )  $\delta$  8.28 (d,  $J = 1.9$  Hz, 1H), 7.42 (d,  $J = 1.9$  Hz, 1H), 7.06 (d,  $J = 1.4$  Hz, 1H), 6.87 (p,  $J = 1.2$  Hz, 1H), 6.01 (d,  $J = 1.0$  Hz, 1H), 5.11 (s, 2H), 3.53 (s, 3H), 2.38 (d,  $J = 0.8$  Hz, 3H), 2.29 (d,  $J = 1.0$  Hz, 3H).

Example 15: 6-(4-Fluorophenyl)-1-[(1-methylpyrazol-4-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one.



Step A: 5-(4-Fluorophenyl)-3-nitropyridin-2-amine. A solution of 2-amino-5-bromo-3-nitropyridine (623 mg, 2.86 mmol), 4-fluorophenylboronic acid (525 mg, 3.75 mmol), Cs<sub>2</sub>CO<sub>3</sub> (1.87 g, 5.74 mmol), and PdCl<sub>2</sub>(dppf) (209 mg, 0.29 mmol) in 1,4-dioxane (14 mL) and water (3 mL) was heated to 80 °C for 4 h and then concentrated. The residue was partitioned between DCM and water, upon which time the product crashed out. The heterogeneous mixture was redissolved with a solution of EtOAc containing 1.5% IPA.

10 The aqueous layer was further extracted with EtOAc containing 1.5% IPA. The combined organic layers were dried, filtered and concentrated to yield the title compound (400 mg, 60%) as a solid, which was used in the next step without further purification.

Step B: Bis-*tert*-Butyl (5-(4-fluorophenyl)-3-nitropyridin-2-yl)carbamate. To a heterogeneous mixture of 5-(4-fluorophenyl)-3-nitropyridin-2-amine (400 mg, 1.72 mmol) in THF (9 mL) was added boc-anhydride (1.14 g, 5.2 mmol) followed by DMAP (316 mg, 2.59 mmol). The mixture became homogeneous and was complete after 30 min. The reaction was concentrated and the crude residue was purified (0 to 25% EtOAc in hexanes) to yield the title compound (663 mg, 89%) as a solid. <sup>1</sup>H NMR (400

20 MHz, CDCl<sub>3</sub>) δ 8.92 (d, *J* = 2.3 Hz, 1H), 8.57 (d, *J* = 2.3 Hz, 1H), 7.68 – 7.59 (m, 2H), 7.29 – 7.19 (m, 3H), 1.45 (s, 18H).

Step C: Bis-*tert*-Butyl (3-amino-5-(4-fluorophenyl)pyridin-2-yl)carbamate. To a round bottom flask containing bis-*tert*-butyl (5-(4-fluorophenyl)-3-nitropyridin-2-yl)carbamate (649 mg, 1.50 mmol) dissolved in EtOH (15) was added 10% Pd/C (301 mg), and the

25 reaction mixture was stirred under an atmosphere of H<sub>2</sub> (balloon). After 3 h the reaction was complete and the Pd/C was removed by filtration and washed with EtOH. The filtrate was concentrated and the crude residue was purified (FCC, SiO<sub>2</sub>, 0 to 50% EtOAc in hexanes) to yield the title compound (459 mg, 76%) as a solid. MS (ESI):

mass calcd. for  $C_{21}H_{28}FN_3O_4$ , 403.2;  $m/z$  found, 404.2  $[M+H]^+$ .  $^1H$  NMR (500 MHz,  $CDCl_3$ )  $\delta$  8.11 (d,  $J = 2.2$  Hz, 1H), 7.56 – 7.50 (m, 2H), 7.20 (d,  $J = 2.1$  Hz, 1H), 7.18 – 7.11 (m, 2H), 3.84 (s, 2H), 1.45 (s, 19H).

Step D: Bis-tert-Butyl (5-(4-fluorophenyl)-3-(((1-methyl-1H-pyrazol-4-

5 yl)methyl)amino)pyridin-2-yl)carbamate. To a heterogeneous mixture of bis-tert-butyl (3-amino-5-(4-fluorophenyl)pyridin-2-yl)carbamate (101 mg, 0.25 mmol) in DCE (3.5 mL) was added HOAc (14  $\mu$ L, 0.25 mmol) followed by 1-methyl-1h-pyrazole-4-carbaldehyde (43 mg, 0.39 mmol). After 10 min  $NaBH(OAc)_3$  (162 mg, 0.76 mmol) was added and the mixture stirred at room temperature overnight. LCMS analysis showed that the reaction  
10 was not complete, and additional 1-methyl-1h-pyrazole-4-carbaldehyde (43 mg, 0.39 mmol) was added. After 5 h the reaction had progressed further and no sign of over alkylated product was seen. Additional 1-methyl-1h-pyrazole-4-carbaldehyde (43 mg, 0.39 mmol) was added and the mixture was stirred overnight during which time it went to completion. The reaction was quenched by the addition of a saturated aqueous  
15 solution of  $NaHCO_3$  and the layers separated. The aqueous layer was extracted with DCM and the combined organic extracts were dried over  $Na_2SO_4$ , filtered and concentrated under reduced pressure. The crude residue was purified by (FCC,  $SiO_2$ , 0 to 55% EtOAc in hexanes) to yield the title compound (107 mg, 85%) as a foam. MS (ESI): mass calcd. for  $C_{26}H_{32}FN_5O_4$ , 497.2;  $m/z$  found, 498.3  $[M+H]^+$ .  $^1H$  NMR (400  
20 MHz,  $CDCl_3$ )  $\delta$  8.04 (d,  $J = 2.1$  Hz, 1H), 7.56 – 7.49 (m, 2H), 7.43 (s, 1H), 7.30 (s, 1H), 7.18 – 7.10 (m, 3H), 4.29 (d,  $J = 5.4$  Hz, 2H), 4.18 – 4.10 (m, 1H), 3.87 (s, 3H), 1.43 (s, 18H).

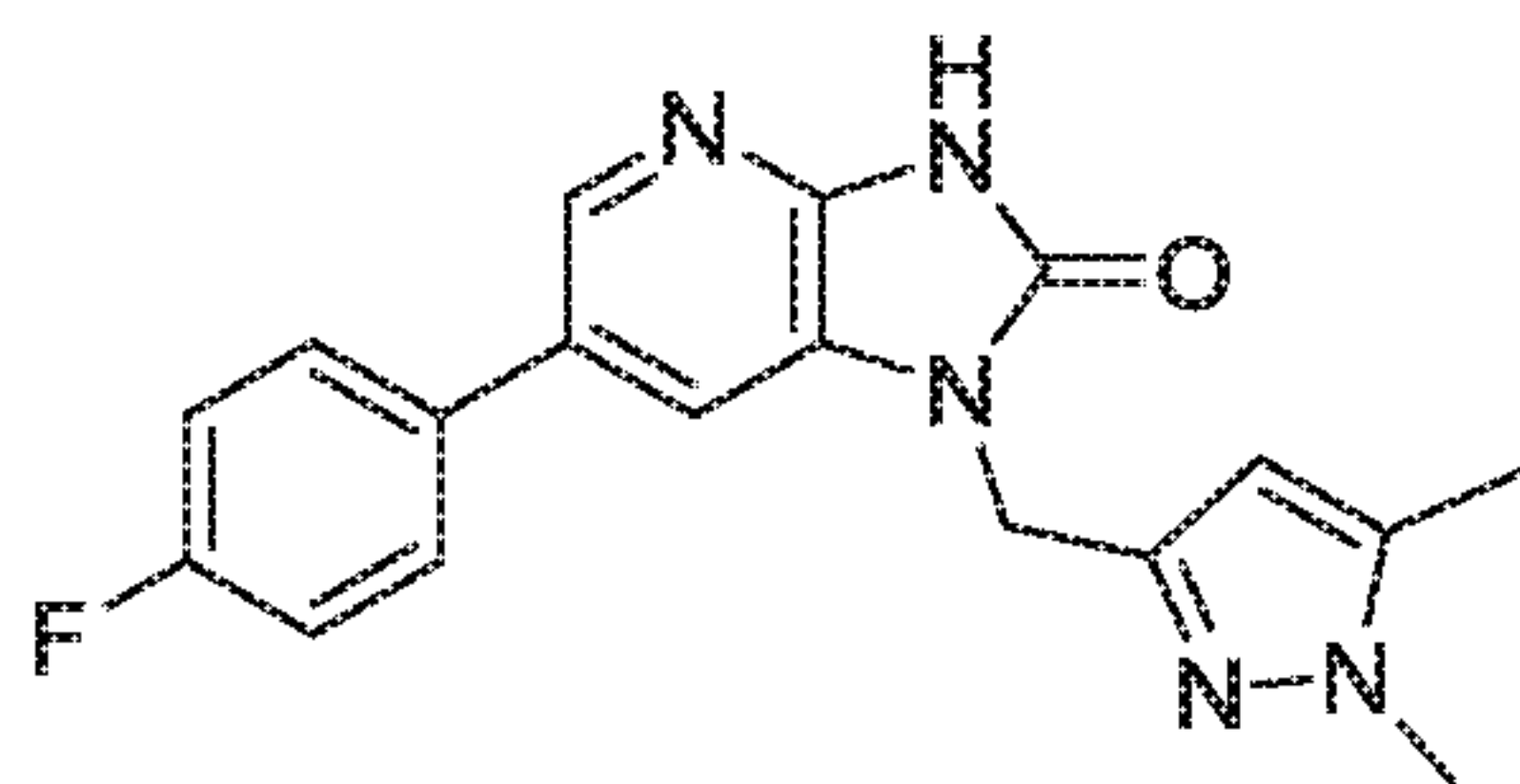
Step E: 5-(4-Fluorophenyl)-N3-((1-methyl-1H-pyrazol-4-yl)methyl)pyridine-2,3-diamine.

To a solution of bis-tert-butyl (5-(4-fluorophenyl)-3-(((1-methyl-1H-pyrazol-4-  
25 yl)methyl)amino)pyridin-2-yl)carbamate. (107 mg, 0.22 mmol) in DCM (2 mL) was added TFA (430  $\mu$ L). After 3 h at room temperature the reaction was concentrated and the crude residue was purified (FCC,  $SiO_2$ , 0 to 9% 2M  $NH_3$  in MeOH in DCM) to yield the title compound (59 mg, 93%) as an oil. MS (ESI): mass calcd. for  $C_{16}H_{16}FN_5$ , 297.2;  $m/z$  found, 298.2  $[M+H]^+$ .

30 Step F: 6-(4-Fluorophenyl)-1-[(1-methylpyrazol-4-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one. To a solution of 5-(4-fluorophenyl)-N3-((1-methyl-1H-pyrazol-4-yl)methyl)pyridine-

2,3-diamine (28 mg, 0.09 mmol) in THF (2 mL) was added CDI (22 mg, 0.14 mmol), and the reaction was stirred at room temperature overnight. The reaction did not go to completion and additional CDI (34 mg, 0.21 mmol) was added, and the reaction was stirred at room temperature for 5 h. Analysis showed that the reaction was still not complete and additional CDI (22 mg, 0.14 mmol) was added and the mixture stirred at room temperature overnight and then concentrated. The residue was purified (FCC, SiO<sub>2</sub>, 0 to 100% 2% IPA in EtOAc in hexanes), but the material was contaminated with imidazole. The compound was dissolved in DCM and washed with a 2 M citric acid solution. The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated to yield the title compound (29 mg, 94%) as a foam. MS (ESI): mass calcd. for C<sub>17</sub>H<sub>14</sub>FN<sub>5</sub>O, 323.1; m/z found, 324.1 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (500 MHz, DMF-d<sub>7</sub>) δ 11.62 (s, 1H), 8.22 (d, *J* = 2.0 Hz, 1H), 7.91 (d, *J* = 2.0 Hz, 1H), 7.83 (s, 1H), 7.81 – 7.74 (m, 2H), 7.56 (s, 1H), 7.38 – 7.28 (m, 2H), 5.03 (s, 2H), 3.83 (s, 3H).

Example 16: 1-[(1,5-Dimethylpyrazol-3-yl)methyl]-6-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-one.



Step A: Bis-tert-Butyl (5-bromo-3-nitropyridin-2-yl)carbamate. To a heterogeneous mixture of 2-amino-5-bromo-3-nitropyridine (2.28 g, 10.45 mmol) in THF (52 mL) was added boc-anhydride (6.84 g, 31.34 mmol) followed by DMAP (1.91 g, 15.67 mmol). The mixture was stirred at room temperature overnight during which time it became homogeneous. The mixture was concentrated and purified (FCC, SiO<sub>2</sub>, 0 to 30% EtOAc in hexanes) to yield the title compound (3.09 g, 71%) as a foam. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.80 (d, *J* = 2.3 Hz, 1H), 8.56 (d, *J* = 2.3 Hz, 1H), 1.43 (s, 18H).

Step B: tert-Butyl (5-bromo-3-nitropyridin-2-yl)carbamate. To a solution of bis-tert-butyl (5-bromo-3-nitropyridin-2-yl)carbamate (269 mg, 0.64 mmol) dissolved in EtOAc (3 mL) was added N,N-dimethylethylenediamine (351 μL, 3.22 mmol). The mixture was stirred at room temperature overnight and then concentrated. The residue was purified (FCC,

SiO<sub>2</sub>, 0 to 30% EtOAc in hexanes) to afford the title compound (200 mg, 98 %) as a yellow solid. MS (ESI): mass calcd. for C<sub>10</sub>H<sub>12</sub>BrN<sub>3</sub>O<sub>4</sub>, 317.0; m/z found, 262.0 [M+H-tBu]<sup>+</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 9.45 (s, 1H), 8.74 (d, *J* = 2.3 Hz, 1H), 8.62 (d, *J* = 2.3 Hz, 1H), 1.54 (s, 9H).

5 Step C: tert-Butyl (5-(4-fluorophenyl)-3-nitropyridin-2-yl)carbamate. To a microwave vial was added tert-butyl (5-bromo-3-nitropyridin-2-yl)carbamate (198 mg, 0.62 mmol), 4-fluorophenylboronic acid (124 mg, 0.88 mmol) and Pd(PPh<sub>3</sub>)<sub>4</sub> (41 mg, 0.035 mmol). Then, dioxane (4 mL) followed by 2M Na<sub>2</sub>CO<sub>3</sub> (653 μL, 1.31 mmol) was added and the reaction was heated conventionally at 90 °C for 2 h. Then, the reaction mixture was  
10 cooled to room temperature, concentrated and the solids were washed with EtOAc (3X). The combined organic layers were concentrated and purified (FCC, SiO<sub>2</sub>, 0 to 20% 1.5% IPA in EtOAc in hexanes) to afford the title compound (197 mg, 95%) as a solid. MS (ESI): mass calcd. for C<sub>16</sub>H<sub>16</sub>FN<sub>3</sub>O<sub>4</sub>, 333.1; m/z found, 278.1 [M+H-tBu]<sup>+</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 9.57 (s, 1H), 8.94 – 8.89 (m, 1H), 8.67 – 8.61 (m, 1H), 7.59 – 7.52  
15 (m, 2H), 7.25 – 7.18 (m, 2H), 1.58 (s, 9H).

Step D: tert-Butyl (3-amino-5-(4-fluorophenyl)pyridin-2-yl)carbamate. To a heterogeneous mixture of tert-butyl (5-(4-fluorophenyl)-3-nitropyridin-2-yl)carbamate (191 mg, 0.57 mmol) in EtOH (8 mL) was added 10% Pd/C (154 mg) followed by a H<sub>2</sub> balloon. The mixture slowly turned homogeneous and after 1 h the reaction was filtered.  
20 The filter cake and Pd/C was washed with EtOH. The filtrate was concentrated to afford the title compound (152 mg, 87%) as an oil, which was used in the next step without further purification.

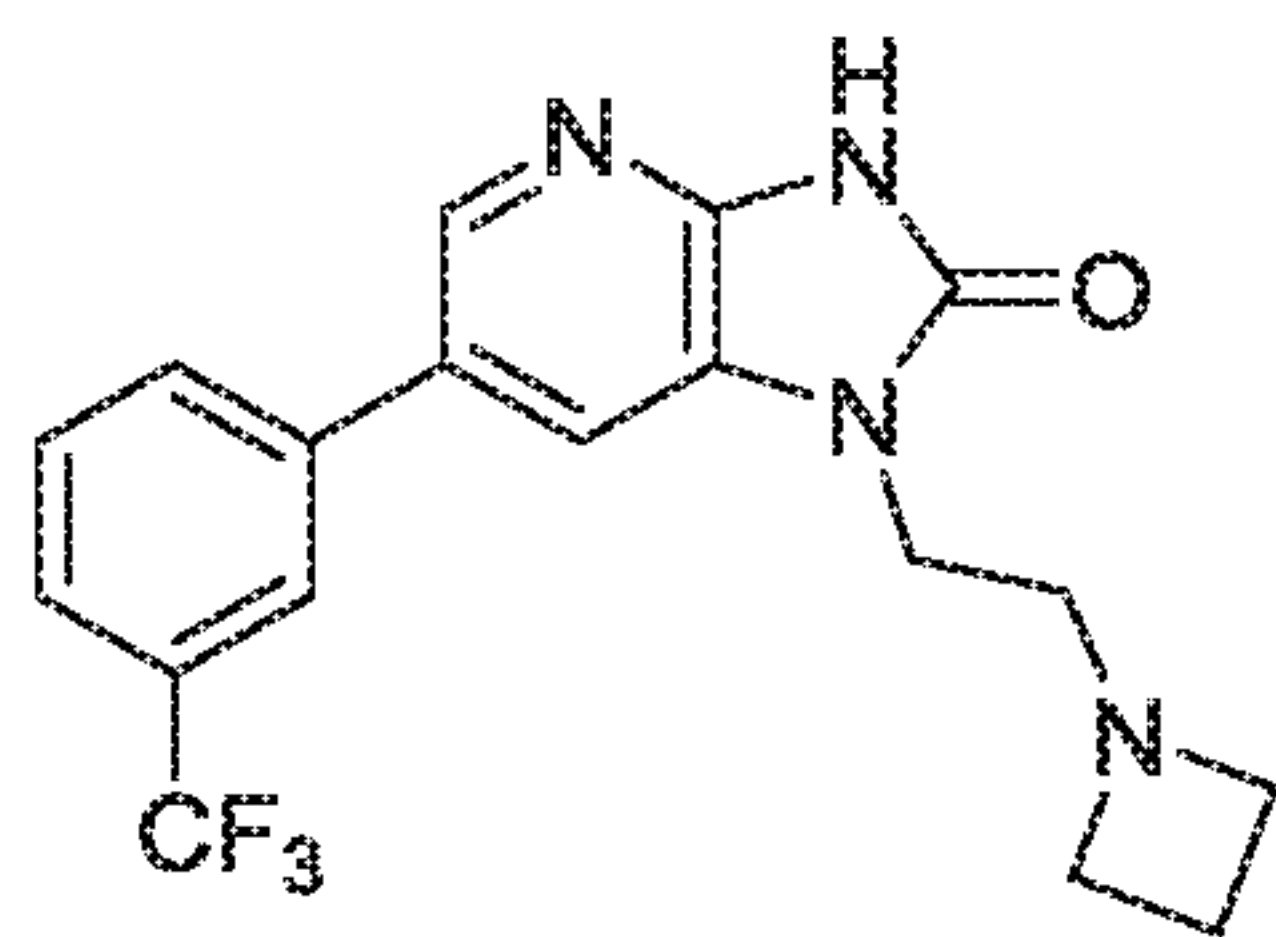
Step E: tert-Butyl (3-(((1,5-dimethyl-1H-pyrazol-3-yl)methyl)amino)-5-(4-fluorophenyl)pyridin-2-yl)carbamate. To a heterogeneous mixture of tert-butyl (3-amino-5-(4-fluorophenyl)pyridin-2-yl)carbamate (152 mg, 0.50 mmol) dissolved in DCE (9 mL) was added HOAc (28 μL, 0.50 mmol) followed by 1,5-dimethyl-1h-pyrazole-3-carbaldehyde (158 mg, 1.28 mmol). After 10 min NaBH(OAc)<sub>3</sub> (321 mg, 1.51 mmol) was added and the mixture stirred at room temperature overnight. The reaction was quenched by the addition of a saturated aqueous solution of NaHCO<sub>3</sub> and the layers  
25 separated. The aqueous layer was extracted with DCM and the combined organic  
30 extracts were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated under reduced pressure.

The crude material was taken on to the next step without further purification. MS (ESI): mass calcd. for  $C_{22}H_{26}FN_5O_2$ , 411.2; m/z found, 412.2  $[M+H]^+$ .

Step F: 1-[(1,5-Dimethylpyrazol-3-yl)methyl]-6-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-one.

To a solution of tert-butyl (3-(((1,5-dimethyl-1H-pyrazol-3-yl)methyl)amino)-5-(4-fluorophenyl)pyridin-2-yl)carbamate (206 mg, 0.50 mmol) in DCM (9 mL) was added TFA (2 mL). The mixture was stirred at room temperature for 3 h, concentrated and purified (FCC,  $SiO_2$ , 0 to 9% 2M  $NH_3$  in MeOH in DCM) to afford impure material. This material was then stirred in  $Et_2O$  overnight and then filtered to afford the title compound (46 mg, 27%) as a foam. MS (ESI): mass calcd. for  $C_{18}H_{16}FN_5O$ , 337.1; m/z found, 338.2  $[M+H]^+$ .  $^1H$  NMR (500 MHz,  $DMF-d_7$ )  $\delta$  11.64 (s, 1H), 8.22 (d,  $J = 2.1$  Hz, 1H), 7.78 – 7.68 (m, 3H), 7.38 – 7.27 (m, 2H), 5.99 (s, 1H), 5.03 (s, 2H), 3.69 (s, 3H), 2.20 (s, 3H).

Example 17: 1-[2-(Azetidin-1-yl)ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one and its trifluoroacetic acid salt.



Step A: 1-(2-(Azetidin-1-yl)ethyl)-6-bromo-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one.

To a solution of 2-(6-bromo-2-oxo-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetaldehyde (Intermediate 42, 400 mg, 0.80 mmol) in DCM (1 mL) was added azetidine (0.11 mL, 1.61 mmol) followed by sodium triacetoxyborohydride (336 mg, 1.6 mmol). The reaction was stirred at room temperature overnight and then diluted with a saturated aqueous solution of  $NaHCO_3$  (25 mL) and stirred for 30 minutes. The organics were then extracted with DCM, combined, dried, and purified (FCC,  $SiO_2$ , 0-20% MeOH in DCM) to provide the title compound (195 mg, 45%).  $^1H$  NMR (500 MHz,  $DMSO-d_6$ )  $\delta$  7.84 – 7.70 (m, 2H), 7.55 – 7.38 (m, 6H), 7.32 – 7.19 (m, 6H), 7.19 – 7.10 (m, 3H), 3.81 – 3.55 (m, 2H), 3.02 – 2.77 (m, 4H), 1.88 – 1.79 (m, 2H).

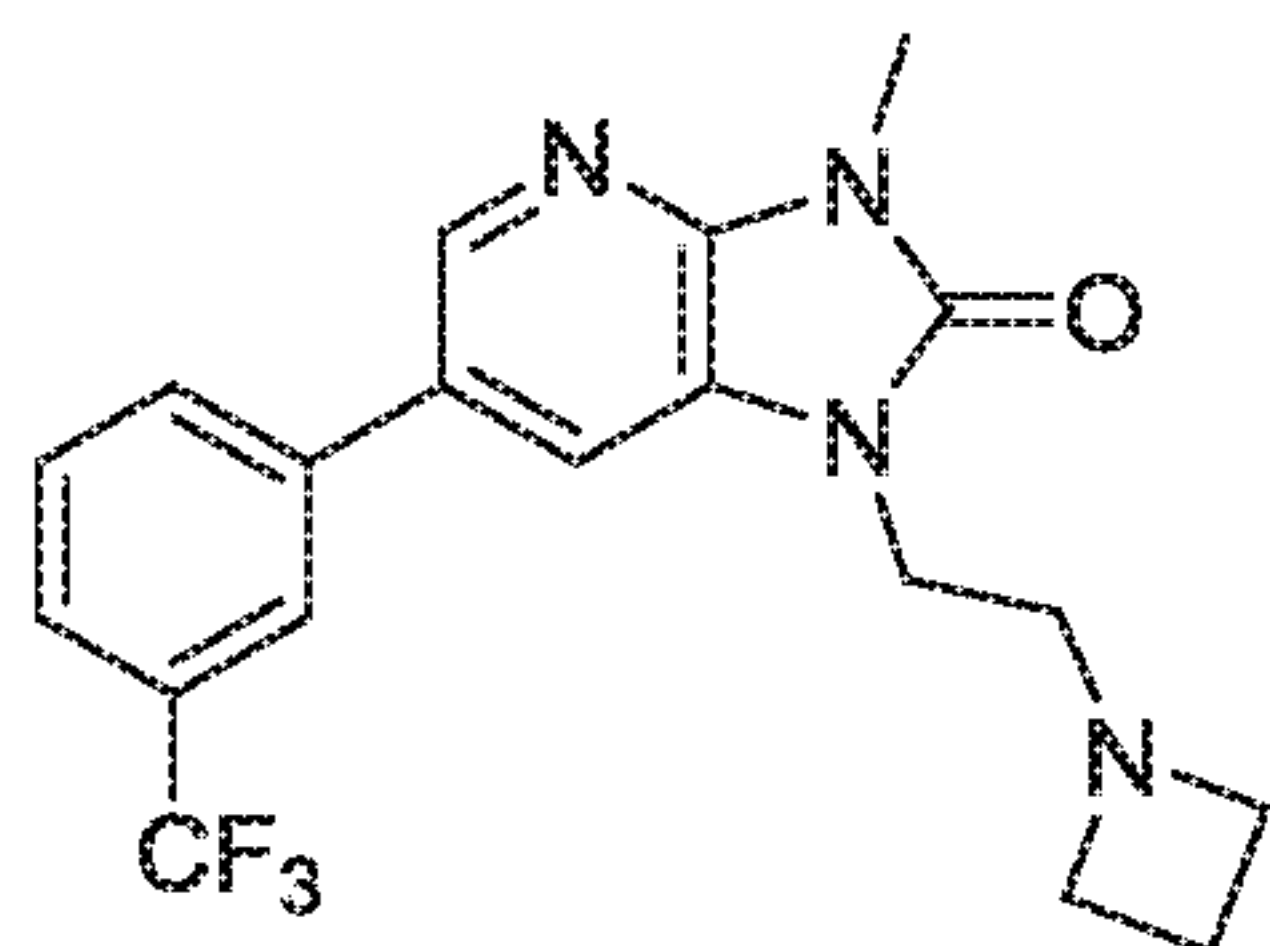
Step B: 1-(2-(Azetidin-1-yl)ethyl)-6-(3-(trifluoromethyl)phenyl)-3-trityl-1H-imidazo[4,5-b]pyridin-2(3H)-one. To a solution of 1-(2-(azetidin-1-yl)ethyl)-6-bromo-3-trityl-1,3-

dihydro-2H-imidazo[4,5-b]pyridin-2-one (22.7 mg, 0.042 mmol) and 3-trifluoromethyl phenyl boronic acid (12 mg, 0.063 mmol) in 1,4-dioxane (0.5 mL) was added sodium bicarbonate (8.9 mg, 0.084 mmol), distilled water (0.03 mL, 1.7 mmol), and tetrakis(triphenylphosphine)palladium (2.4 mg, 0.002 mmol). The reaction was heated to 100°C overnight. The reaction was then cooled to room temperature and diluted with ethyl acetate (10 mL) and water (10 mL). The organic layer was extracted, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo. The title compound was used crude in the next step without further purification.

Step C: 1-[2-(Azetidin-1-yl)ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one and its trifluoroacetic acid salt. Crude 1-(2-(azetidin-1-yl)ethyl)-6-(3-

(trifluoromethyl)phenyl)-3-trityl-1H-imidazo[4,5-b]pyridin-2(3H)-one was taken up in DCM (2 mL) and TFA (2 mL) and stirred at room temperature for 30 minutes. The reaction was concentrated down, taken up in 2 mL of methanol and loaded onto the acidic HPLC (Method C) to provide the title compound. MS (ESI): mass calcd. for C<sub>18</sub>H<sub>17</sub>F<sub>3</sub>N<sub>4</sub>O, 362.1; m/z found, 363.2 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 11.85 (s, 1H), 9.77 – 9.64 (s, 1H), 8.43 – 8.31 (m, 1H), 8.10 – 8.01 (m, 2H), 8.00 – 7.93 (d, *J* = 2.0 Hz, 1H), 7.79 – 7.66 (m, 2H), 4.17 – 4.04 (d, *J* = 11.4 Hz, 6H), 3.63 – 3.56 (d, *J* = 5.3 Hz, 2H), 2.46 – 2.35 (m, 1H), 2.26 (s, 1H).

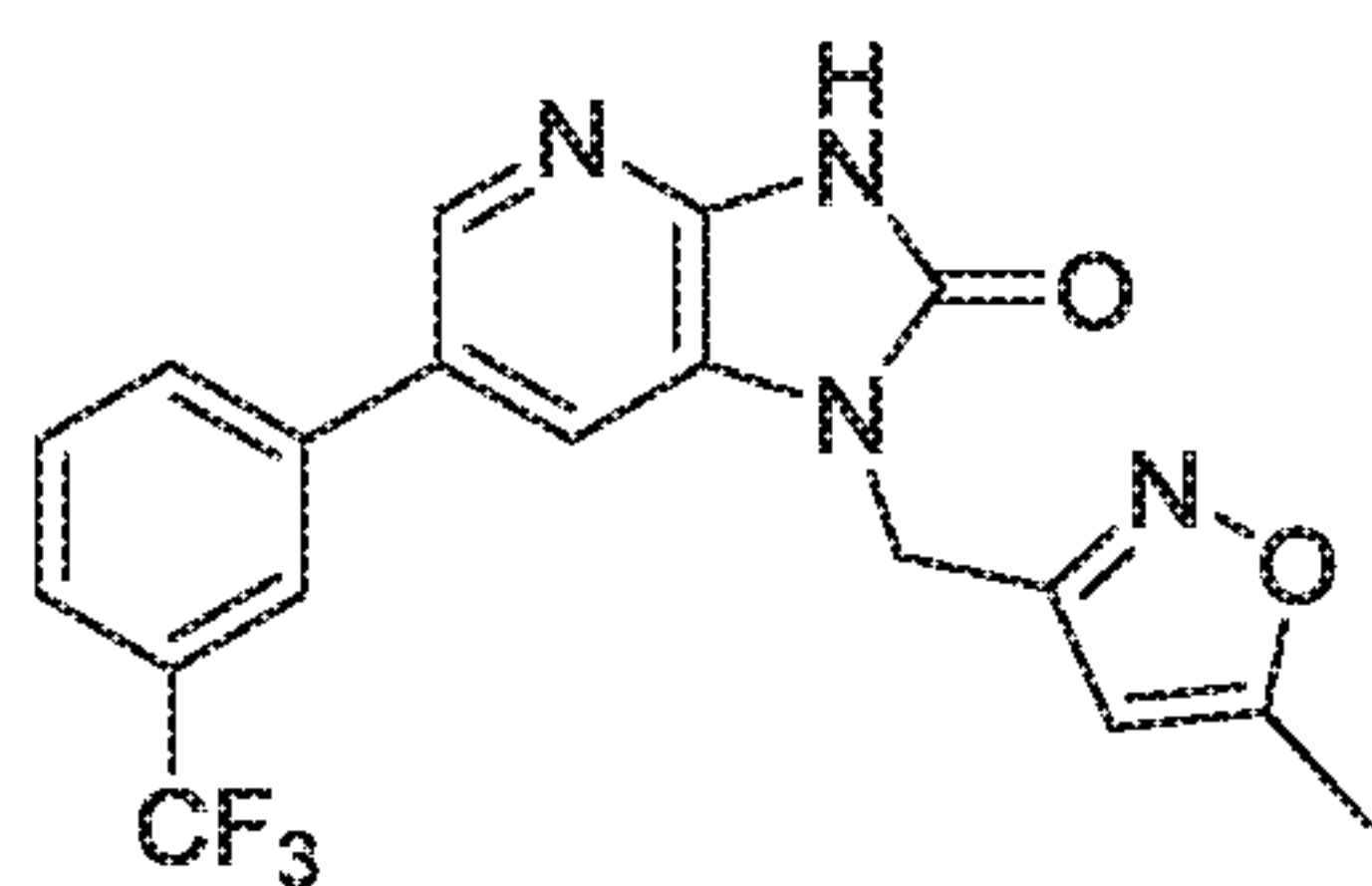
Example 18: 1-[2-(Azetidin-1-yl)ethyl]-3-methyl-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one.



To a solution of 1-[2-(azetidin-1-yl)ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one (Example 17, 49.6 mg, 0.10 mmol) in DMF (2 mL) was added sodium hydride (60% dispersion in oil, 8.3 mg, 0.21 mmol), and the reaction mixture was stirred

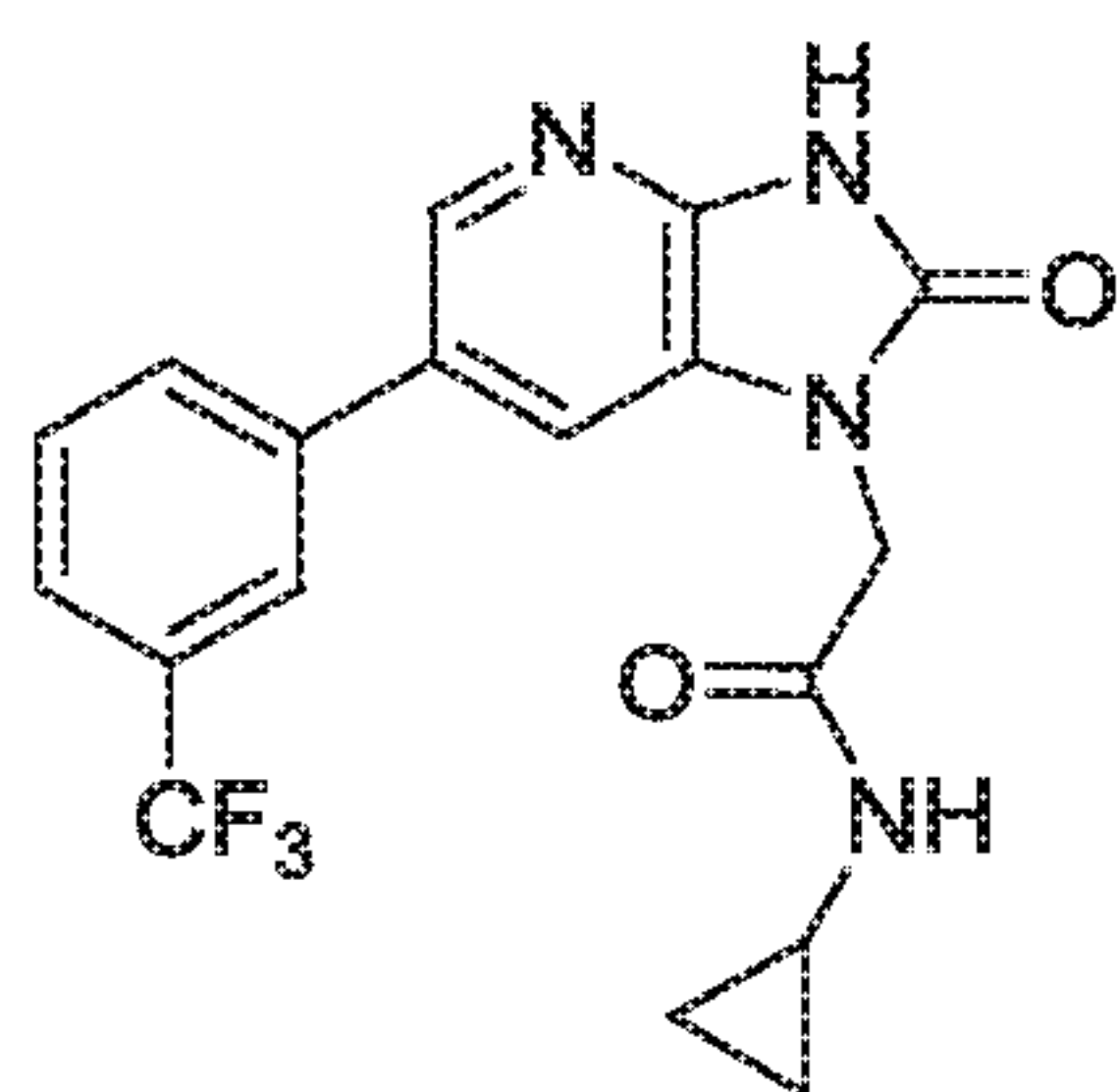
at room temperature for 10 minutes. Then, iodomethane (0.0078 mL, 0.13 mmol) was added, and the reaction mixture was stirred at room temperature for an additional 3 hours. The crude reaction mixture was quenched with distilled water (1 mL) and concentrated in vacuo. The reaction was taken up in MeOH, filtered, and loaded onto the basic HPLC for purification (Method A) to provide the title compound (11.8 mg, 30%). MS (ESI): mass calcd. for  $C_{19}H_{19}F_3N_4O$ , 376.2;  $m/z$  found, 377.2  $[M+H]^+$ .  $^1H$  NMR (500 MHz, DMSO- $d_6$ )  $\delta$  8.43 – 8.29 (d,  $J$  = 1.9 Hz, 1H), 8.10 – 8.01 (d,  $J$  = 2.8 Hz, 2H), 8.01 – 7.91 (m, 1H), 7.78 – 7.59 (m, 2H), 3.91 – 3.79 (t,  $J$  = 6.1 Hz, 2H), 3.38 (s, 3H), 3.15 – 3.06 (t,  $J$  = 7.0 Hz, 4H), 2.71 – 2.64 (m, 2H), 1.97 – 1.83 (m, 2H).

Example 19: 1-[(5-Methylisoxazol-3-yl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one.



To a solution of  $N^3$ -((5-methylisoxazol-3-yl)methyl)-5-(3-(trifluoromethyl)phenyl)pyridine-2,3-diamine (Intermediate 47, 1.0 g, 3.0 mmol) in DMF (19.5 mL) was added 1,1'-carbonyldiimidazole (1.5 g, 9.0 mmol). The reaction was heated to 85°C for one hour. The crude mixture was cooled to room temperature and a saturated aqueous solution of  $NH_4Cl$  (10 mL) was added. The resulting solid was collected via filtration, triturated with  $Et_2O$  and filtered to provide the title compound (761 mg, 68%). MS (ESI): mass calcd. for  $C_{18}H_{13}F_3N_4O_2$ , 374.1;  $m/z$  found, 375.1  $[M+H]^+$ .  $^1H$  NMR (400 MHz, DMSO- $d_6$ )  $\delta$  11.97 – 11.79 (s, 1H), 8.42 – 8.25 (d,  $J$  = 2.0 Hz, 1H), 8.06 – 7.96 (m, 2H), 7.93 – 7.87 (d,  $J$  = 2.0 Hz, 1H), 7.78 – 7.64 (m, 2H), 6.25 – 6.13 (s, 1H), 5.24 – 4.92 (s, 2H), 2.39 – 2.26 (s, 3H).

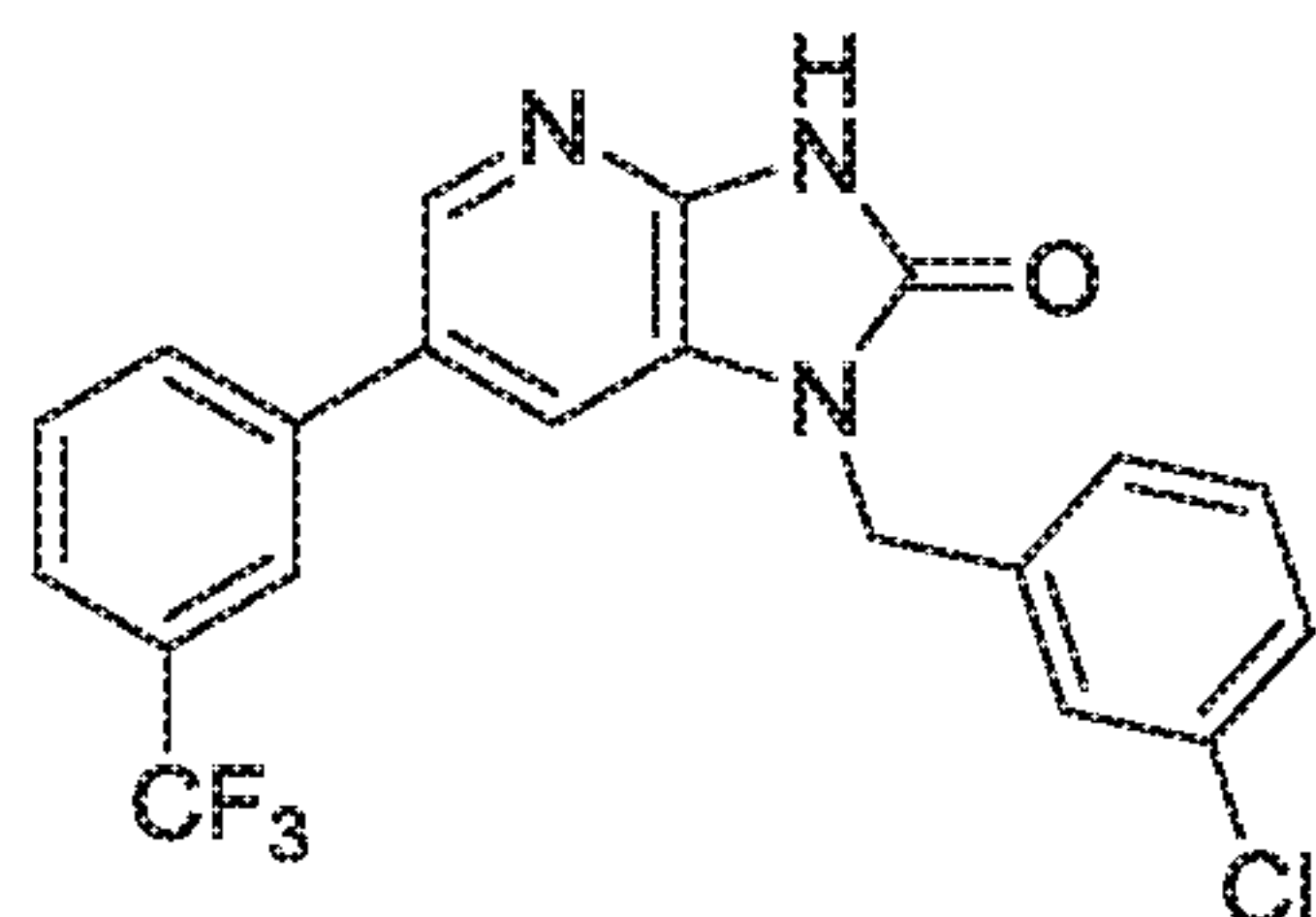
Example 20: N-Cyclopropyl-2-[2-oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-yl]acetamide and its trifluoroacetic acid salt.



Step A: N-cyclopropyl-2-(2-oxo-6-(3-(trifluoromethyl)phenyl)-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetamide. HATU (59 mg, 0.16 mmol) was added to a mixture of 2-(2-oxo-6-(3-(trifluoromethyl)phenyl)-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetic acid (Intermediate 44, 75 mg, 0.13 mmol), cyclopropylamine (0.011 mL, 0.16 mmol) and DIPEA (0.045 mL, 0.26 mmol) in DMF at room temperature. After completion, a saturated aqueous solution of NaHCO<sub>3</sub> (10 mL) was added and the mixture was extracted using EtOAc (3 x 15 mL). The combined organics were dried over MgSO<sub>4</sub>, filtered and concentrated under vacuum. The crude material was purified (FCC, SiO<sub>2</sub>, 0-90% EtOAc in hexanes) to afford the title compound (61 mg, 76 %). <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 8.28 (d, *J* = 4.2 Hz, 1H), 8.19 – 8.13 (m, 1H), 8.00 – 7.94 (m, 2H), 7.87 (d, *J* = 2.1 Hz, 1H), 7.72 – 7.63 (m, 2H), 7.51 – 7.44 (m, 6H), 7.29 – 7.13 (m, 9H), 4.44 (s, 2H), 2.71 – 2.61 (m, 1H), 0.64 (td, *J* = 7.0, 4.8 Hz, 2H), 0.47 – 0.41 (m, 2H).

Step B: N-cyclopropyl-2-[2-oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-yl]acetamide and its trifluoroacetic acid salt. To a solution of N-cyclopropyl-2-(2-oxo-6-(3-(trifluoromethyl)phenyl)-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetamide (90 mg, 0.15 mmol) in DCM at room temperature was added TFA (0.34 mL, 4.4 mmol). After completion the reaction mixture was concentrated under vacuum. MeOH was added and a precipitate appeared. The solids were filtered off and rinsed with MeOH to afford the title compound (11 mg, 15%). MS (ESI): mass calcd. for C<sub>18</sub>H<sub>15</sub>F<sub>3</sub>N<sub>4</sub>O<sub>2</sub>, 376.1; *m/z* found, 377.1 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 11.73 (s, 1H), 8.33 (d, *J* = 2.0 Hz, 1H), 8.29 (d, *J* = 4.2 Hz, 1H), 8.04 – 7.97 (m, 2H), 7.84 (d, *J* = 1.9 Hz, 1H), 7.76 – 7.68 (m, 2H), 4.48 (s, 2H), 2.65 (tq, *J* = 7.7, 4.0 Hz, 1H), 0.62 (td, *J* = 7.0, 4.8 Hz, 2H), 0.43 (dt, *J* = 7.1, 4.6 Hz, 2H).

Example 21: 1-[(3-Chlorophenyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one and its trifluoroacetic acid salt.



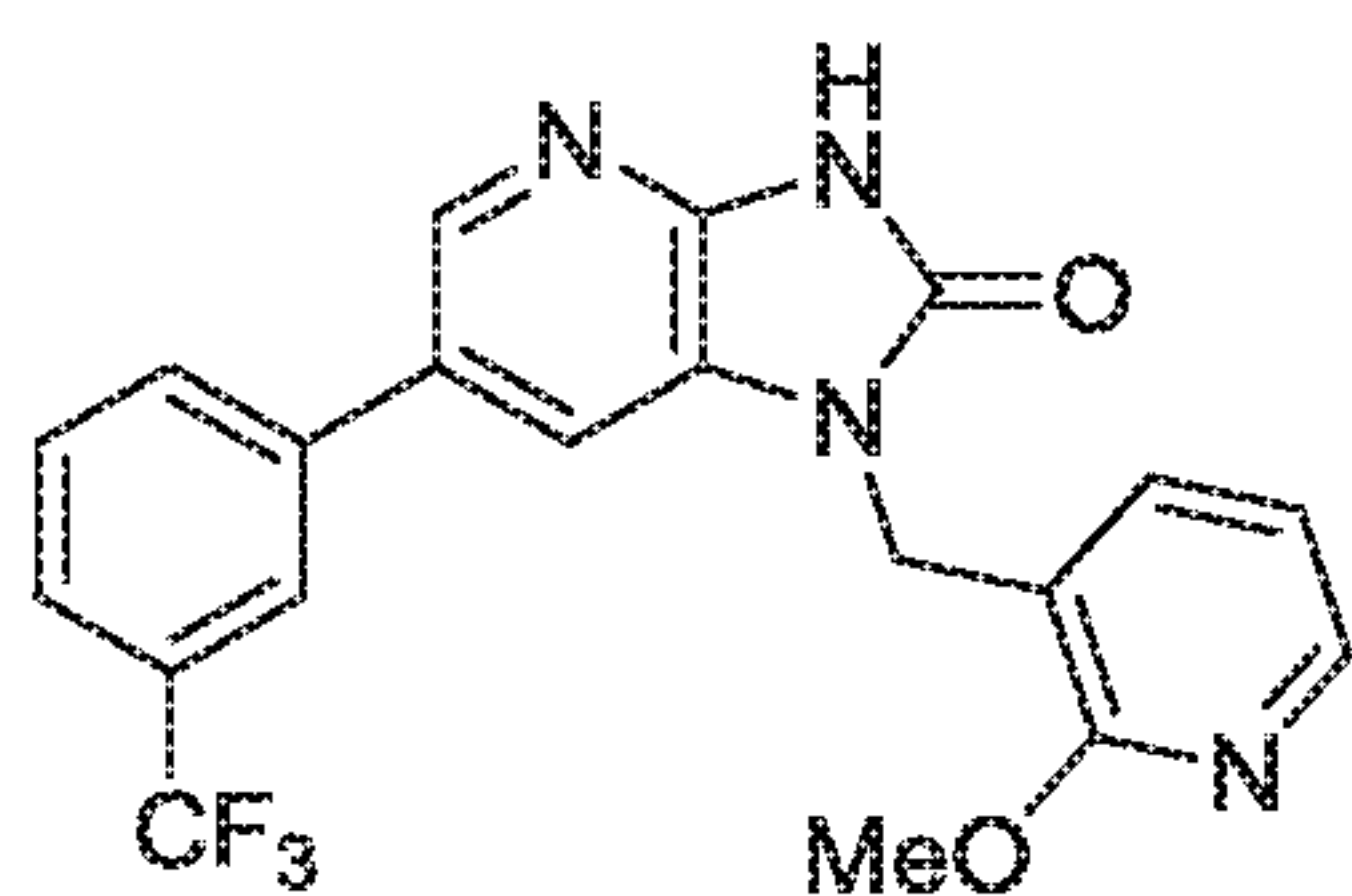
Step A: 1-(3-Chlorobenzyl)-6-(3-(trifluoromethyl)phenyl)-3-trityl-1,3-dihydro-2H-

5 imidazo[4,5-b]pyridin-2-one. Under a nitrogen atmosphere was added 6-(3-(trifluoromethyl)phenyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 43, 100 mg, 0.19 mmol) to a suspension of NaH (60% dispersion in mineral oil, 10.7 mg, 0.3 mmol) in THF (2.1 mL). After 10 minutes 1-(bromomethyl)-3-chlorobenzene (0.035 mL, 0.3 mmol) was added to the reaction mixture, and the reaction mixture was  
10 heated to 75 °C. After 6 h, complete conversion was observed. The reaction mixture was cooled down to room temperature and quenched with water (10 mL). The mixture was extracted using EtOAc (3 x 20 mL). The combined organics were dried over MgSO<sub>4</sub>, filtered and concentrated under vacuum to give the title compound. The crude material was moved forward to the next step as is.

15 Step B: 1-[(3-chlorophenyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one and its trifluoroacetic acid salt. To a solution of 1-(3-chlorobenzyl)-6-(3-(trifluoromethyl)phenyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (153 mg, 0.24 mmol) in DCM at room temperature was added TFA (0.55 mL, 7.1 mmol). After completion, the reaction mixture was concentrated under vacuum. The crude material  
20 was purified using reversed phase HPLC (Method C) to afford the title compound (29 mg, 23%). MS (ESI): mass calcd. for C<sub>20</sub>H<sub>13</sub>ClF<sub>3</sub>N<sub>3</sub>O, 403.1; m/z found, 404.1 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 11.87 (s, 1H), 8.34 (d, *J* = 2.0 Hz, 1H), 8.01 – 7.96 (m, 2H), 7.94 (d, *J* = 2.0 Hz, 1H), 7.75 – 7.68 (m, 2H), 7.49 – 7.45 (m, 1H), 7.40 – 7.29 (m, 3H), 5.13 (s, 2H).

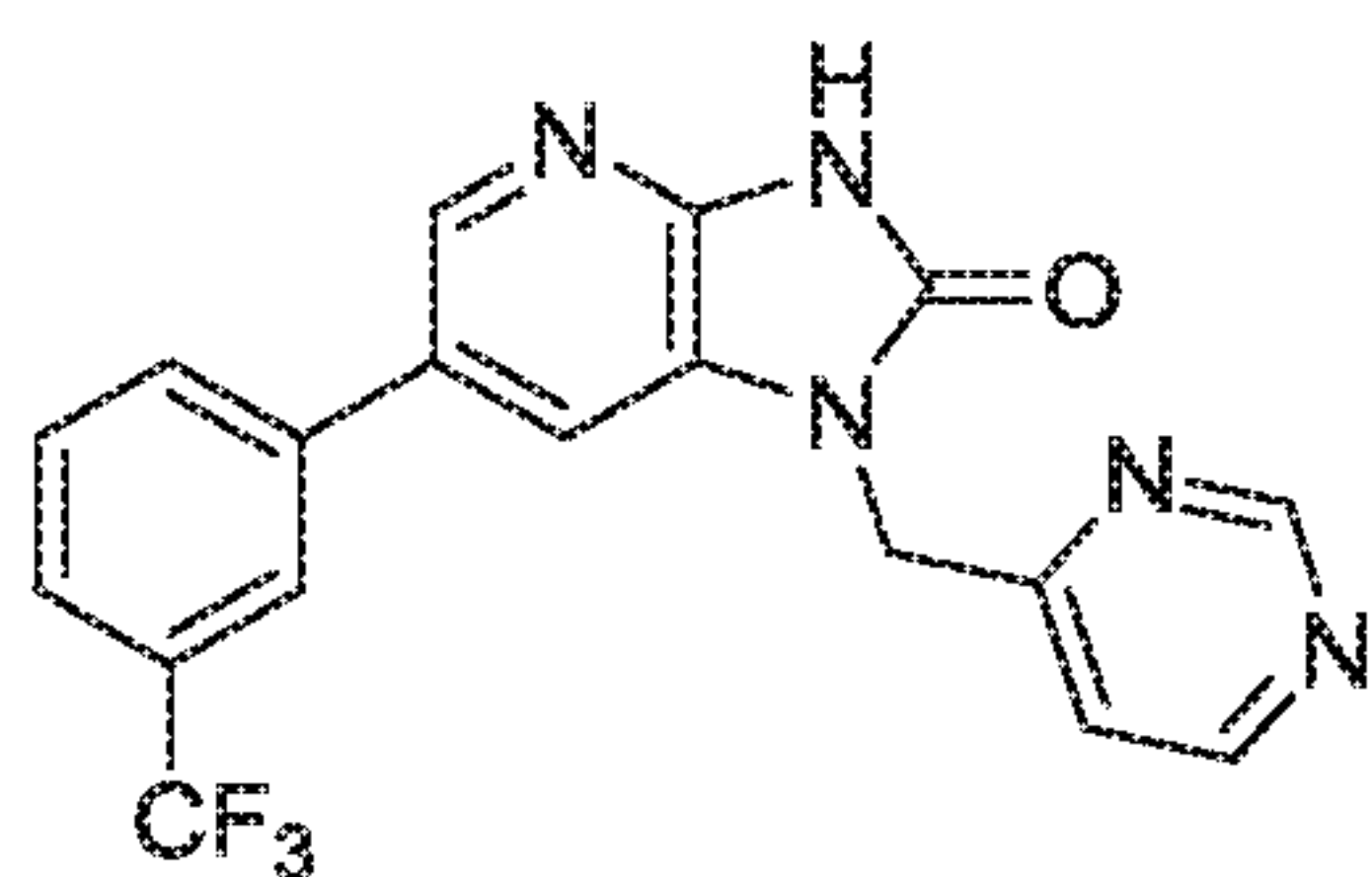
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Example 22: 1-[(2-Methoxy-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one and its trifluoroacetic acid salt.



The title compound was prepared in a manner analogous to Example 21 using 3-(chloromethyl)-2-methoxypyridine. MS (ESI): mass calcd. for  $C_{20}H_{15}F_3N_4O_2$ , 400.1; m/z found,  $[M+H]^+$ .  $^1H$  NMR (500 MHz, DMSO)  $\delta$  11.84 (s, 1H), 8.34 (d,  $J = 2.0$  Hz, 1H), 8.09 (dd,  $J = 5.0, 1.8$  Hz, 1H), 8.01 – 7.96 (m, 2H), 7.85 (d,  $J = 2.0$  Hz, 1H), 7.74 – 7.66 (m, 2H), 7.33 (dd,  $J = 7.3, 1.8$  Hz, 1H), 6.93 (dd,  $J = 7.3, 5.0$  Hz, 1H), 5.04 (s, 2H), 3.93 (s, 3H).

Example 23: 1-(Pyrimidin-4-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one and its trifluoroacetic acid salt.

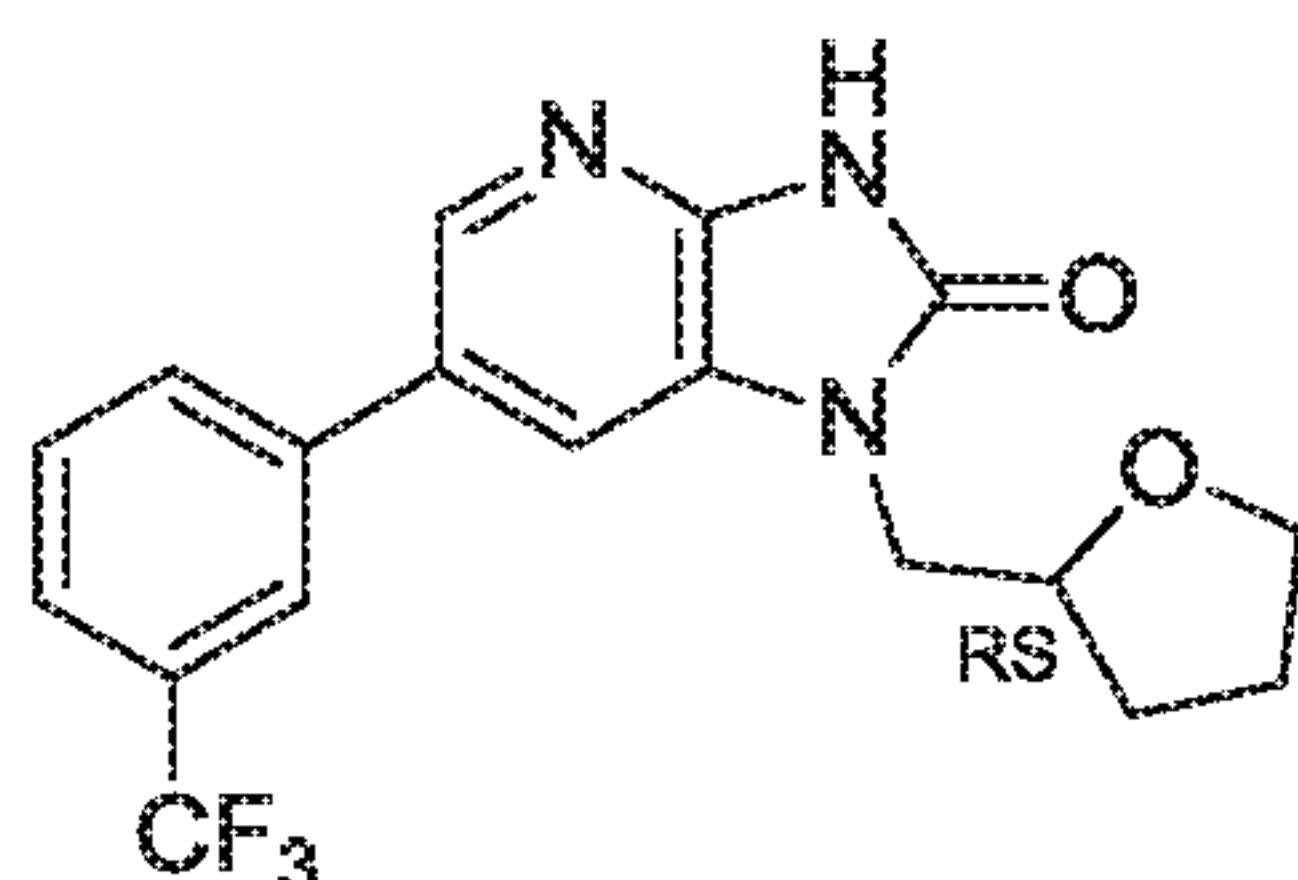


Step A: Pyrimidin-4-ylmethyl methanesulfonate. To a mixture of pyrimidin-4-ylmethanol (100 mg, 0.9 mmol) and triethylamine (0.2 mL, 1.4 mmol) in DCM (3.5 mL) at 0°C was added methanesulfonyl chloride (0.9 mL, 1.2 mmol). After 30 minutes, water (10 mL) and a saturated aqueous solution of  $NaHCO_3$  (10 mL) were added to the reaction mixture, respectively. The mixture was extracted with DCM (2 x 30 mL). The combined organics were dried ( $MgSO_4$ ), filtered and concentrated under vacuum to give the title compound (170 mg, 99%).  $^1H$  NMR (400 MHz,  $DMSO-d_6$ )  $\delta$  9.20 (d,  $J = 1.4$  Hz, 1H), 8.89 (d,  $J = 5.1$  Hz, 1H), 7.63 – 7.60 (m, 1H), 5.35 (s, 2H), 3.34 (s, 3H).

Step B: 1-(Pyrimidin-4-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one and its trifluoroacetic acid salt. The title compound was prepared in a manner analogous to Example 21 using pyrimidin-4-ylmethyl methanesulfonate and 6-(3-(trifluoromethyl)phenyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 43) in Step A. MS (ESI): mass calcd. for  $C_{18}H_{12}F_3N_5O$ , 371.1; m/z found, 372.1  $[M+H]^+$ .

$^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ )  $\delta$  11.87 (s, 1H), 9.09 (d,  $J$  = 1.4 Hz, 1H), 8.75 (d,  $J$  = 5.2 Hz, 1H), 8.36 (d,  $J$  = 2.0 Hz, 1H), 8.01 – 7.96 (m, 2H), 7.91 (d,  $J$  = 2.0 Hz, 1H), 7.73 – 7.65 (m, 2H), 7.44 (dd,  $J$  = 5.2, 1.4 Hz, 1H), 5.27 (s, 2H).

5 Example 24: (R/S)-1-(Tetrahydrofuran-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one and its trifluoroacetic acid salt.

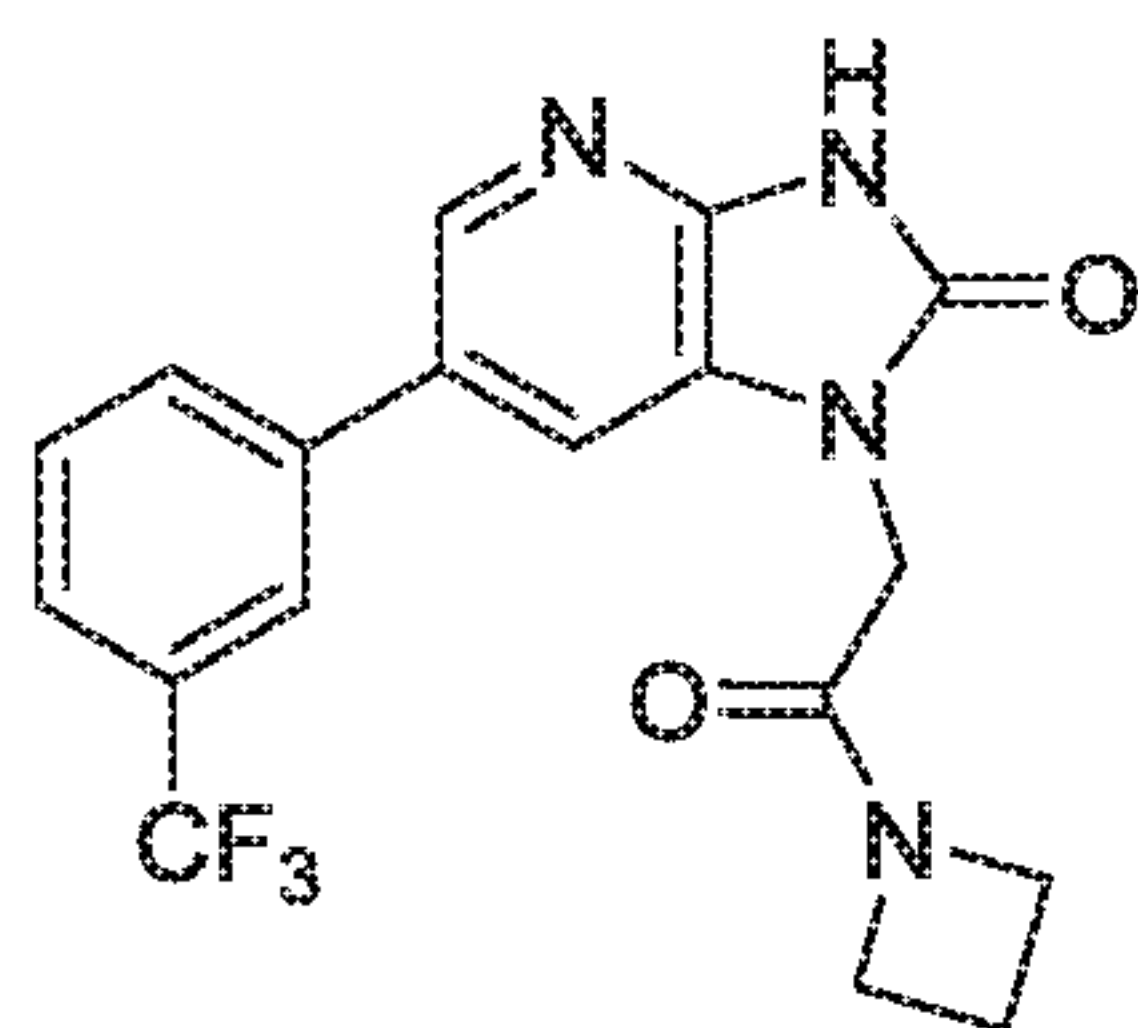


Step A: 6-Bromo-1-((tetrahydrofuran-2-yl)methyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. To a solution of 6-bromo-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 36, 500 mg, 1.10 mmol) and NaH (60% dispersion in mineral oil, 61 mg, 1.5 mmol) in DMF (11 mL), was added tetrahydrofurfuryl bromide (0.18 mL, 1.5 mmol). After 16 h, low conversion to the desired product was observed and additional NaH (60% dispersion in mineral oil, 131 mg, 3.29 mmol) and tetrahydrofurfuryl bromide (0.37 mL, 3.29 mmol) was added and the reaction mixture was heated to 80 °C. After completion, the reaction mixture was quenched with a saturated aqueous solution of  $\text{NH}_4\text{Cl}$  (50 mL). The precipitates were filtered off, washed with water and dried under vacuum to afford the title product, contaminated with some impurities. The crude material was moved forward to the next step as is.

Step B: 1-((tetrahydrofuran-2-yl)methyl)-6-(3-(trifluoromethyl)phenyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. A mixture of 6-bromo-1-((tetrahydrofuran-2-yl)methyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (150 mg, 0.3 mmol), 3-(trifluoromethyl)phenylboronic acid (105 mg, 0.6 mmol), 1,1'-bis(diphenylphosphino)ferrocene palladium(II)dichloride dichloromethane complex ( $\text{Pd}(\text{dppf})\text{Cl}_2 \cdot \text{CH}_2\text{Cl}_2$ ) (16 mg, 0.02 mmol),  $\text{Cs}_2\text{CO}_3$  (181 mg, 0.6 mmol), dioxane (2.6 mL) and  $\text{H}_2\text{O}$  (0.5 mL) was heated to 90 °C using an oil bath. After 16 h, the reaction mixture was concentrated under vacuum. The crude material was purified (FCC,  $\text{SiO}_2$ , 0-100% EtOAc in hexanes), to give the title compound (51 mg, 30%).

Step C: (R/S)-1-(tetrahydrofuran-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one and its trifluoroacetic acid salt. To a solution of 1-((tetrahydrofuran-2-yl)methyl)-6-(3-(trifluoromethyl)phenyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (51 mg, 0.08 mmol) in DCM at room temperature was added TFA (0.59 mL, 9.2 mmol). After completion, the reaction mixture was concentrated under vacuum. The crude material was purified using reversed phase HPLC (Method C) to give the title compound (32 mg, 23%). MS (ESI): mass calcd. for  $C_{18}H_{16}F_3N_3O_2$ , 363.1;  $m/z$  found, 364.1  $M+H^+$ .  $^1H$  NMR (400 MHz, DMSO- $d_6$ )  $\delta$  11.71 (s, 1H), 8.30 (d,  $J = 2.0$  Hz, 1H), 8.04 – 7.98 (m, 2H), 7.89 (d,  $J = 2.0$  Hz, 1H), 7.76 – 7.69 (m, 2H), 4.27 – 4.18 (m, 1H), 3.99 – 3.87 (m, 2H), 3.77 – 3.69 (m, 1H), 3.65 – 3.56 (m, 1H), 2.00 – 1.73 (m, 3H), 1.70 – 1.60 (m, 1H).

Example 25: 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one and its trifluoroacetic acid salt.

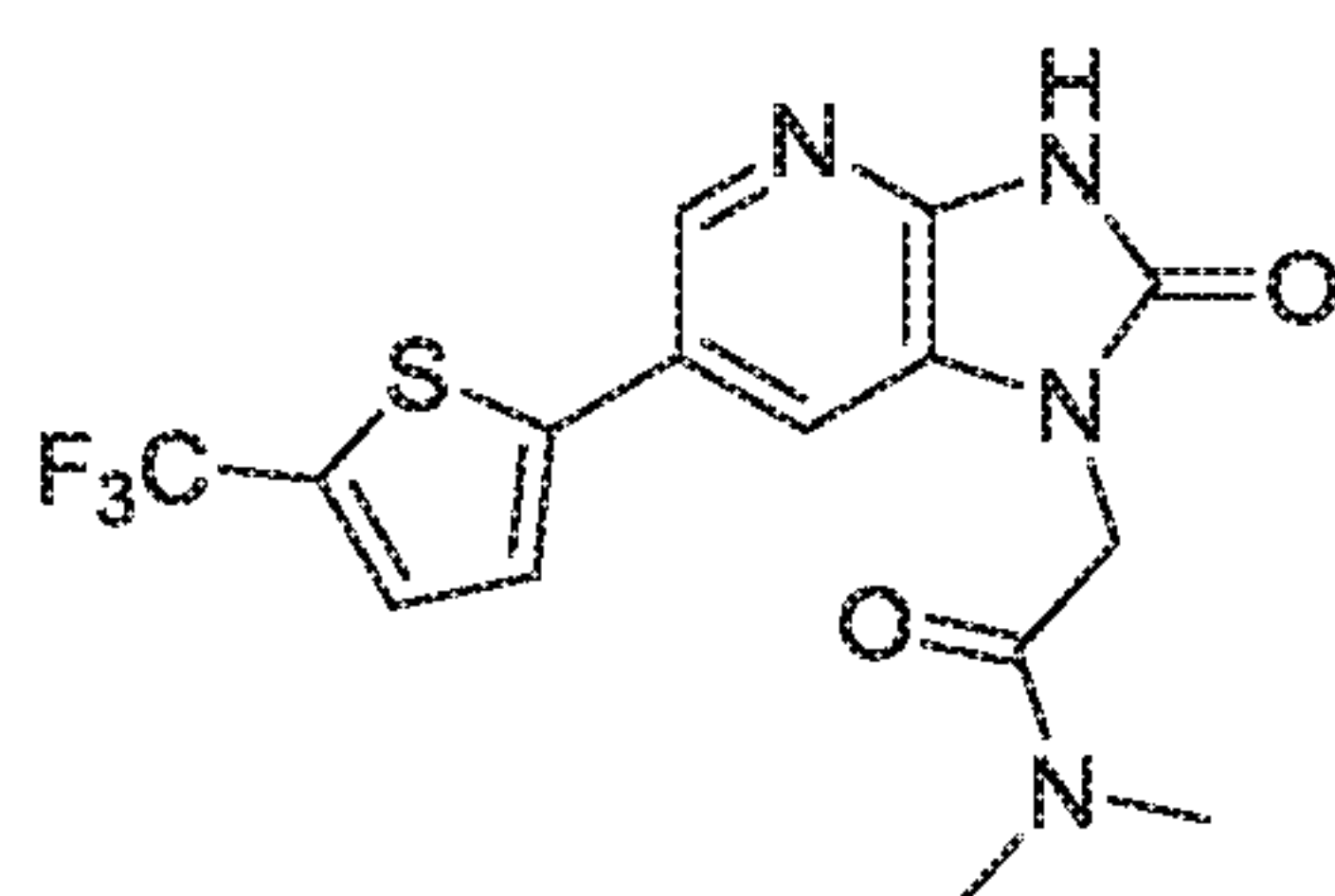


Step A: 1-(2-(Azetidin-1-yl)-2-oxoethyl)-6-(3-(trifluoromethyl)phenyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. A mixture of 1-(2-(azetidin-1-yl)-2-oxoethyl)-6-bromo-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 38, 260 mg, 0.47 mmol), 1,1'-bis(diphenylphosphino) ferrocene palladium(II)dichloride dichloromethane complex (24 mg, 0.033 mmol),  $Cs_2CO_3$  (306 mg, 0.94 mmol), (3-(trifluoromethyl)phenyl)boronic acid (178 mg, 0.94 mmol), dioxane (5 mL) and  $H_2O$  (0.9 mL) was heated to 90 °C using an oil bath. After 16 h, the reaction mixture was cooled to room temperature and volatiles were removed. The crude material was purified (FCC  $SiO_2$ , 0-100% EtOAc in hexanes), to give the title compound (90 mg, 31%).

Step B: 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one and its trifluoroacetic acid salt. To a solution of 1-(2-(azetidin-1-yl)-2-oxoethyl)-6-(3-(trifluoromethyl)phenyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-

one (80 mg, 0.13 mmol) in DCM at room temperature was added TFA (0.30 mL, 3.9 mmol). After completion the reaction mixture was concentrated under vacuum. The crude material was purified (Method C) to afford the title compound (13 mg, 21%). MS (ESI): mass calcd. for  $C_{18}H_{15}F_3N_4O_2$ , 376.1;  $m/z$  found, 377.1[M+H]<sup>+</sup>. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  11.76 (s, 1H), 8.32 (d,  $J$  = 2.0 Hz, 1H), 8.03 – 7.97 (m, 2H), 7.82 (d,  $J$  = 2.0 Hz, 1H), 7.76 – 7.70 (m, 2H), 4.86 (s, 2H), 4.28 (t,  $J$  = 7.6 Hz, 2H), 3.91 (t,  $J$  = 7.7 Hz, 2H), 2.33 – 2.23 (m, 2H).

Example 26: N,N-Dimethyl-2-[2-oxo-6-[5-(trifluoromethyl)-2-thienyl]-3H-imidazo[4,5-b]pyridin-1-yl]acetamide.



Method A:

Step A: Ethyl 2-(2-oxo-6-(5-(trifluoromethyl)thiophen-2-yl)-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetate.

A mixture of ethyl 2-(6-bromo-2-oxo-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetate (Intermediate 37, 230 mg, 0.4 mmol), 4,4,5,5-tetramethyl-2-(5-(trifluoromethyl)thiophen-2-yl)-1,3,2-dioxaborolane (153 mg, 0.6 mmol), Cs<sub>2</sub>CO<sub>3</sub> (240 mg, 0.7 mmol) and PdCl<sub>2</sub>(dppf).DCM (21 mg, 0.06 mmol) in dioxane (3.5 mL) was combined in a microwave vial and heated to 75°C. The reaction mixture was stirred at 75°C for 16 hours then cooled down to room temperature and quenched with a saturated aqueous solution of NaHCO<sub>3</sub>. The resulting reaction mixture was extracted with EtOAc (3 x 60 mL) and the combined organic layers were dried using MgSO<sub>4</sub>, filtered and concentrated under vacuum. The crude material was purified (FCC, SiO<sub>2</sub>, 0-40% EtOAc in hexanes) to afford the title compound (215 mg, 0.4 mmol, 82%). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.97 – 7.95 (d,  $J$  = 2.1 Hz, 1H), 7.45 – 7.40 (m, 6H), 7.30 – 7.27 (m, 1H), 7.19 – 7.14 (m, 6H), 7.14 – 7.09 (m, 3H), 7.04 – 7.03 (d,  $J$  = 2.0 Hz, 1H), 7.03 – 7.00 (m, 1H), 4.49 – 4.45 (s, 2H), 4.17 – 4.10 (m, 2H), 1.19 – 1.15 (m, 3H).

Step B: 2-(2-Oxo-6-(5-(trifluoromethyl)thiophen-2-yl)-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetic acid. To a solution ethyl 2-(2-oxo-6-(5-(trifluoromethyl)thiophen-2-yl)-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetate (210 mg, 0.34 mmol) in THF (4.5 mL) at room temperature was added LiOH (2 M, 0.24 mL, 0.47 mmol). After stirring  
 5 over the weekend, 2 M HCl was added (~0.1 mL). The mixture was rotovaped, then placed on high vac overnight. The solids were used as is in the next step (450 mg, contains water).

Step C: N,N-Dimethyl-2-(2-oxo-6-(5-(trifluoromethyl)thiophen-2-yl)-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetamide. T<sub>3</sub>P (w/w 50% in DCM)) (0.365 mL, 0.61

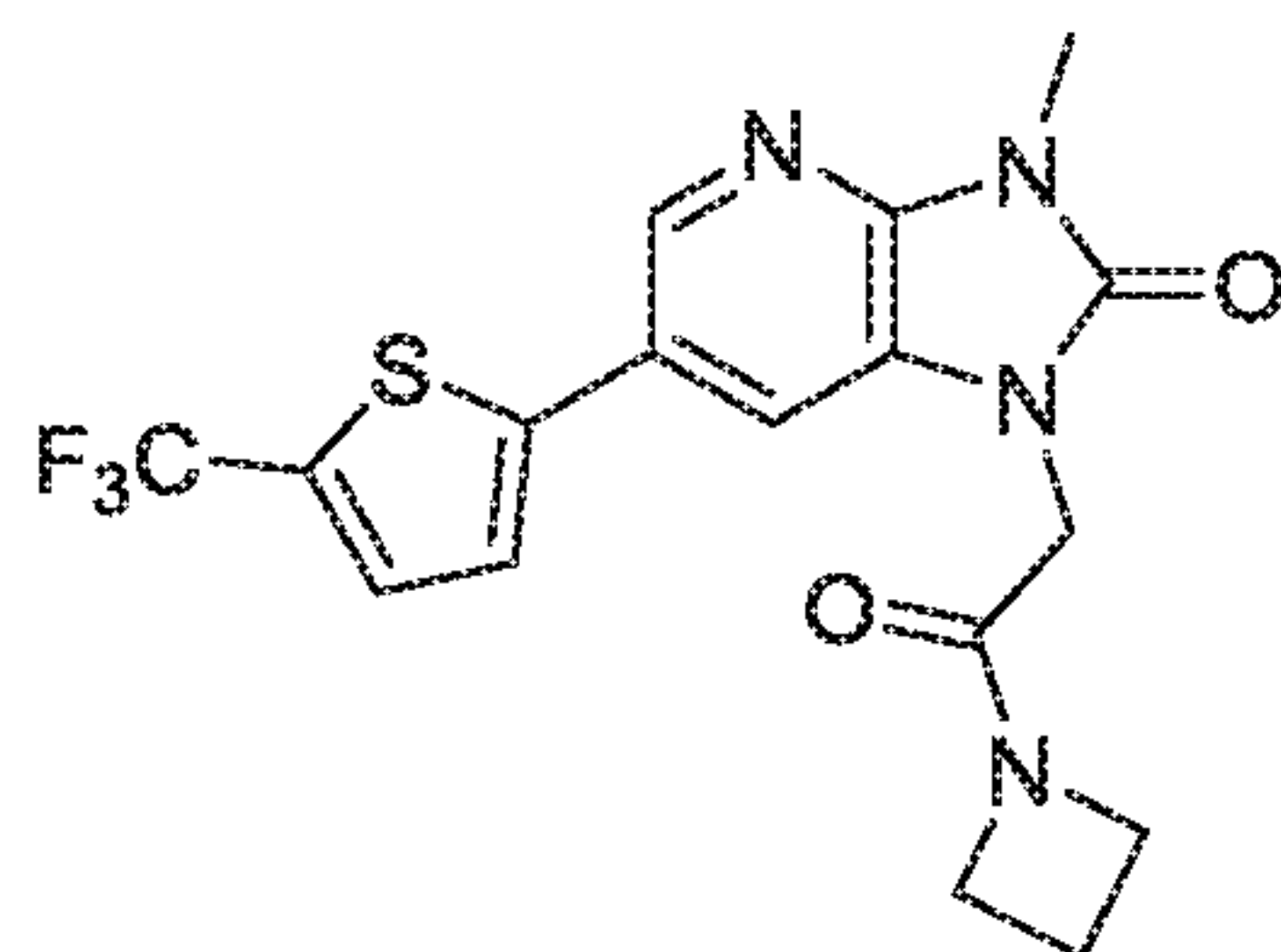
10 mmol) was added to a mixture of 2-(2-oxo-6-(5-(trifluoromethyl)thiophen-2-yl)-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetic acid (246 mg, 0.20 mmol), dimethylamine hydrochloride (20 mg, 0.24 mmol) and DIPEA (0.11 mL, 0.61 mmol) in DCM (1 mL) at room temperature for 16 hours. After completion, the reaction mixture was concentrated under reduced pressure and the crude material was purified (FCC, SiO<sub>2</sub>, 0-100% EtOAc in hexanes). To the EA/hexanes solution containing the product  
 15 was added 1 mL TFA. The resulting reaction mixture was allowed to stir at room temperature for 16 hours. The excess TFA was evaporated under reduced pressure and the crude material was purified (FCC, SiO<sub>2</sub>, 0-15% 2M NH<sub>3</sub>/MeOH in DCM) to afford the title compound (25 mg, 33%). MS (ESI): mass calcd. for C<sub>15</sub>H<sub>13</sub>F<sub>3</sub>N<sub>4</sub>O<sub>2</sub>S, 370.1; m/z found, 371.0 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 11.8 – 11.7 (s, 1H), 8.34 – 8.32 (d, *J* = 2.0 Hz, 1H), 7.79 – 7.76 (s, 1H), 7.76 – 7.74 (d, *J* = 3.7 Hz, 1H), 7.57 – 7.55 (s, 1H), 4.80 – 4.75 (s, 2H), 3.12 – 3.07 (s, 3H), 2.87 – 2.83 (s, 3H).  
 20

#### Method B:

The title compound was prepared in a manner analogous to Example 25, Steps A-B,  
 25 using 2-(6-bromo-2-oxo-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)-N,N-dimethylacetamide (Intermediate 39) and (5-(trifluoromethyl)thiophen-2-yl)boronic acid in step A.

Example 27: 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one.

30



#### Method A:

The title compound was prepared in a manner analogous to Example 15, Step B, using 1-[2-(azetidin-1-yl)-2-oxo-ethyl]-6-[5-(trifluoromethyl)-2-thienyl]-3H-imidazo[4,5-b]pyridin-2-one (Example 323).

#### Method B:

Step A: Ethyl 2-(3-methyl-2-oxo-6-(5-(trifluoromethyl)thiophen-2-yl)-2,3-dihydroimidazo[4,5-b]pyridin-1-yl)acetate. Into a 10 L four-necked flask was charged

with ethyl 2-(6-bromo-3-methyl-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetate (Intermediate 12, 410.0 g, 1.31 mol), K<sub>2</sub>CO<sub>3</sub> (360.8 g, 2.62 mol), PdCl<sub>2</sub>(dppf)·CH<sub>2</sub>Cl<sub>2</sub> (32.0 g, 0.04 mol), a solution of 4,4,5,5-tetramethyl-2-(5-(trifluoromethyl)thiophen-2-yl)-1,3,2-dioxaborolane in toluene (5100 g, 10% w/w, assay by Q-NMR, 1.83 mol), toluene (291 mL) and H<sub>2</sub>O (559 mL) successively under N<sub>2</sub> atmosphere. The resulting mixture was stirred at 80 to 85 °C for 2.5 h and then cooled to 60 to 65 °C followed by filtration through a pad of Celite®. The cake was washed with toluene (500 mL) and the filtrate was concentrated at 40 to 45 °C under vacuum until the total volume was less than 2 V. *n*-heptane (1500 mL) was added into the residue and the resulting mixture was stirred at 25 to 30 °C for 3 min followed by filtration. The cake was washed with *n*-heptane (500 mL) and dried in vacuum oven at 50 °C for 8 h to give the title compound (530 g).

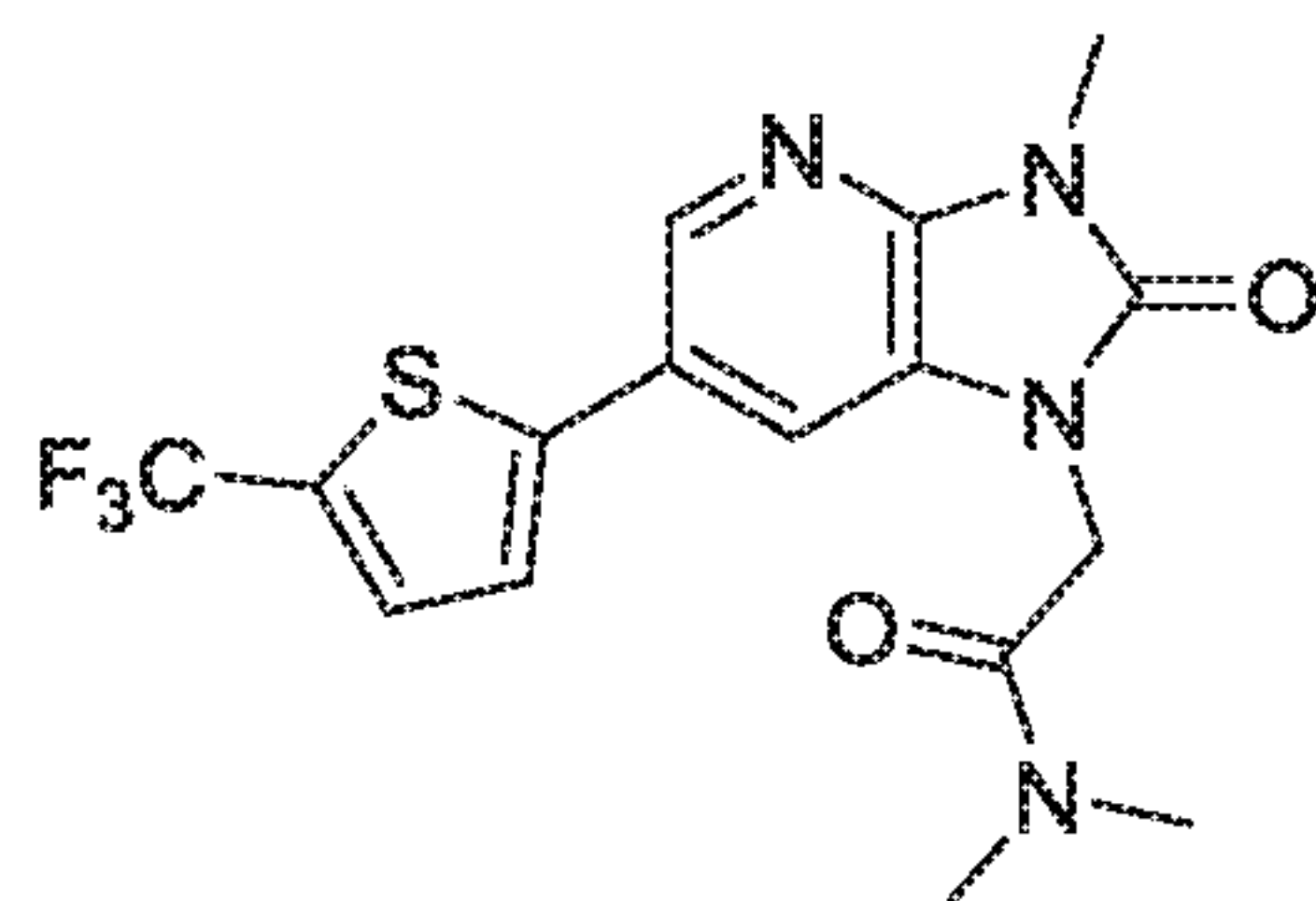
The title compound (530 g) and THF (11 L, 20 V) was charged into a 50 L reactor followed by stirring at 25 to 30 °C for 5 min. Then Darco®-G60 (60 g, 11 % w/w) was charged into the THF solution and the resulting mixture was stirred at 25 to 30 °C for 2 h followed by filtration through a pad of Celite®. After washing the cake with THF (500 mL), the combined filtrate and Darco®-G60 (60 g, 11 % w/w) was charged into the reactor again. The mixture was stirred at 25 to 30 °C for another 2 h followed by filtration through a pad of Celite®. The cake was washed with THF (500 mL) then the combined filtrate and SiliaMetS (50 g, 10 % w/w) was charged into the reactor. After

stirring at 25 to 30 °C overnight, the mixture was filtered through a pad of Celite® and the cake was washed with THF (500 mL). The filtrate was concentrated at 40 to 45 °C under vacuum until 3 ~ 4 volume of THF was left. *n*-Heptane (3500 mL) was added into the residue and the resulting mixture was stirred at 25 to 30 °C for 5 min followed by

filtration. The cake was washed with *n*-heptane (500 mL) and dried at 50°C vacuum oven to give the title compound (402 g, 80%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.33 (d, *J* = 1.9 Hz, 1H), 7.42 (dq, *J* = 4.0, 1.3 Hz, 1H), 7.23 (d, *J* = 3.0 Hz, 1H), 7.18 (dq, *J* = 4.0, 1.3 Hz, 1H), 4.68 (s, 2H), 4.27 (q, *J* = 7.1 Hz, 2H), 3.55 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H).  
Step B: 2-(3-Methyl-2-oxo-6-(5-(trifluoromethyl)thiophen-2-yl)-2,3-dihydroimidazo[4,5-  
b]pyridin-1-yl)acetic acid. The title compound was prepared in a manner analogous to Intermediate 38, Step A, using ethyl 2-(3-methyl-2-oxo-6-(5-(trifluoromethyl)thiophen-2-yl)-2,3-dihydroimidazo[4,5-b]pyridin-1-yl)acetate. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 8.42 (d, *J* = 1.9 Hz, 1H), 8.03 (d, *J* = 2.0 Hz, 1H), 7.76 (dq, *J* = 3.9, 1.3 Hz, 1H), 7.60 (dq, *J* = 3.9, 1.3 Hz, 1H), 4.69 (s, 2H).

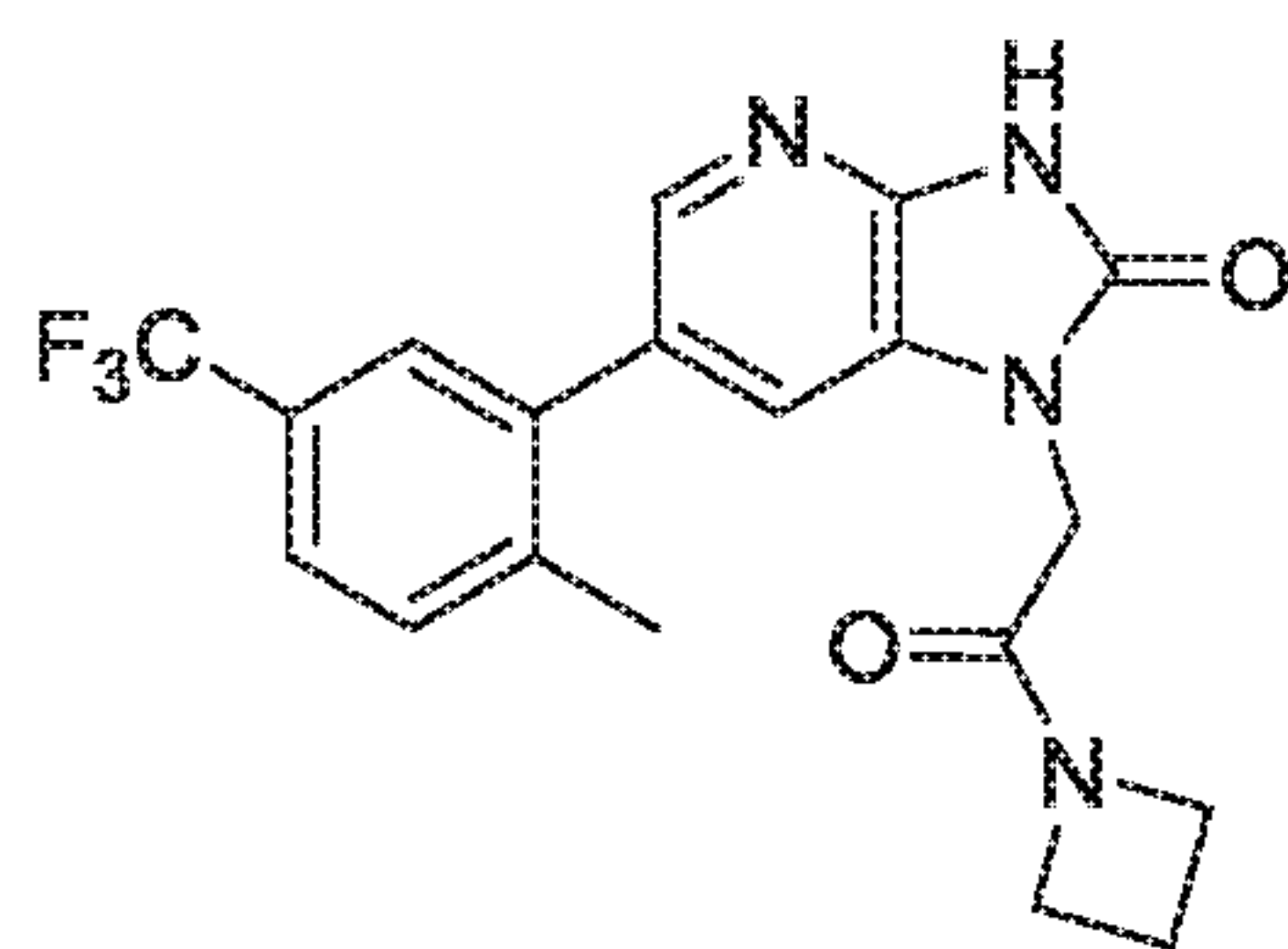
Step C: 1-(2-(Azetidin-1-yl)-2-oxoethyl)-3-methyl-6-(5-(trifluoromethyl)thiophen-2-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one. Into a suspension of 2-(3-methyl-2-oxo-6-(5-(trifluoromethyl)thiophen-2-yl)-2,3-dihydroimidazo[4,5-b]pyridin-1-yl)acetic acid (357.4 g, 1.0 mol, 1.0 eq.) and ACN (7.2 L) was added DIEA (530.02 g, 4.1 mol, 4.1 eq.). Then T<sub>3</sub>P (w/w 50 % in EA, 1368.52 g, 2.15 mol, 2.15 eq.) was added dropwise into the mixture at 10 to 20 °C followed by the addition of azetidine (74.24 g, 1.3 mol, 1.3 eq.) at the same temperature. After stirring at 10 to 15 °C for 2 h, the mixture was poured into water (14.4 L) and stirred for 10 min followed by filtration. The cake was washed with water (500 mL) and dried at 50 °C vacuum oven for 24 h to give 340 g of crude solid as a light purple solid of the title compound. Purification (FCC, SiO<sub>2</sub>, eluent: EA/*n*-heptane = 50/1 to 100/1 then DCM/MeOH= 10/1) afforded the title compound (260 g). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.32 (d, *J* = 1.9 Hz, 1H), 7.46 (d, *J* = 1.9 Hz, 1H), 7.43 (dq, *J* = 3.7, 1.1 Hz, 1H), 7.21 (dq, *J* = 3.7, 1.1 Hz, 1H), 4.51 (s, 2H), 4.36 (t, *J* = 7.8 Hz, 2H), 4.11 (t, *J* = 7.8 Hz, 2H), 3.55 (s, 3H), 2.43–2.35 (m, 2H). <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ -55.34. <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 165.56, 153.75, 145.16, 143.99, 138.72, 129.46, 129.42, 124.42, 123.64, 123.19, 112.78, 77.35, 77.23, 77.03, 76.71, 50.47, 48.62, 40.70, 26.39, 15.73. LC/MS (ES<sup>+</sup>) *m/z* 397.1 (M + H).

Example 28: N,N-Dimethyl-2-[3-methyl-2-oxo-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-1-yl]acetamide.



- 5 The title compound was prepared in a manner analogous to Example 14, Step B, using N,N-dimethyl-2-(2-oxo-6-(5-(trifluoromethyl)thiophen-2-yl)-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetamide (Example 26). MS (ESI): mass calcd. for C<sub>18</sub>H<sub>15</sub>F<sub>3</sub>N<sub>4</sub>O<sub>2</sub>S, 384.1; m/z found, 385.2 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.31 – 8.29 (d, J = 1.9 Hz, 1H), 7.42 – 7.39 (m, 1H), 7.34 – 7.32 (d, J = 1.9 Hz, 1H), 7.19 – 7.16 (m, 1H), 4.75 – 4.70 (s, 2H), 3.56 – 3.50 (s, 3H), 3.20 – 3.17 (s, 3H), 3.02 – 2.97 (s, 3H).
- 10

Example 29: 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[2-methyl-5-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one.



- 15 Step A: 2-(6-(2-Methyl-5-(trifluoromethyl)phenyl)-2-oxo-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetic acid. A solution of 2-(6-bromo-2-oxo-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetic acid (Intermediate 38, product from Step A, 200 mg, 0.39 mmol), 1,1'-bis(diphenylphosphino) ferrocene palladium(II)dichloride dichloromethane complex (22 mg, 0.027 mmol), Cs<sub>2</sub>CO<sub>3</sub> (253 mg, 0.78 mmol), (2-methyl-5-(trifluoromethyl)phenyl)boronic acid (135 mg, 0.66 mmol), dioxane (3.6 mL) and H<sub>2</sub>O (0.8 mL) was heated to 90 °C using an oil bath. After 16 h, the reaction mixture was cooled to room temperature and quenched with a saturated aqueous solution of NH<sub>4</sub>Cl (15 mL). The mixture was extracted with EtOAc (3 x 20 mL). The combined
- 20

organics were dried over  $\text{MgSO}_4$ , filtered and concentrated under vacuum to afford the title compound, contaminated with some impurities. The crude material was moved forward to the next step as is.

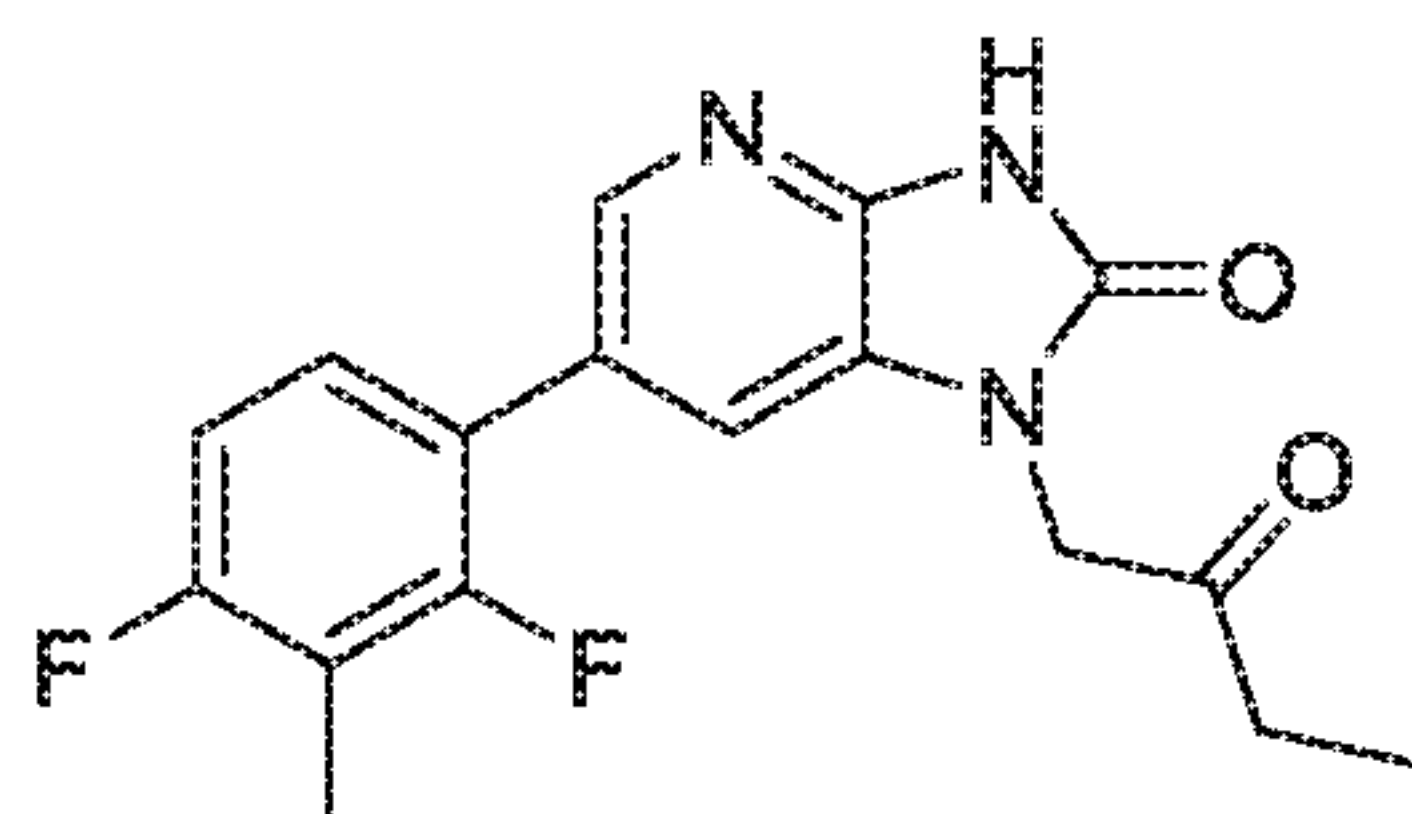
Step B: 1-(2-(Azetidin-1-yl)-2-oxoethyl)-6-(2-methyl-5-(trifluoromethyl)phenyl)-3-trityl-

5 1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. HATU (177 mg, 0.5 mmol) was added to a mixture of 2-(6-(2-methyl-5-(trifluoromethyl)phenyl)-2-oxo-3-trityl-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetic acid (230 mg, 0.4 mmol), azetidine (0.031 mL, 0.47 mmol) and DIPEA (0.13 mL, 0.78 mmol) in DMF (3 mL) at room temperature. After completion, a saturated aqueous solution of  $\text{NaHCO}_3$  (10 mL) was added, and the  
10 mixture was extracted using EtOAc (3 x 15 mL). The combined organics were dried over  $\text{MgSO}_4$ , filtered and concentrated under vacuum to afford the title compound. The crude material was moved forward to the next step as is.

Step C: 1-[2-(azetidin-1-yl)-2-oxo-ethyl]-6-[2-methyl-5-(trifluoromethyl)phenyl]-3H-  
imidazo[4,5-b]pyridin-2-one. TFA (0.89 mL, 12 mmol) was added to a mixture of 1-(2-

15 (azetidin-1-yl)-2-oxoethyl)-6-(2-methyl-5-(trifluoromethyl)phenyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (245 mg, 0.39 mmol) in DCM at room temperature. After 1 h, complete conversion was observed and the mixture was purified using reversed phase HPLC (Method C) to afford the title compound contaminated with impurities. The material was triturated between EtOAc (10 mL) and a saturated aqueous solution of  
20  $\text{NaHCO}_3$  (10 mL). The organic layer was collected and the aqueous layer was washed with EtOAc (3 x 15 mL). The combined organics were dried over  $\text{MgSO}_4$ , filtered and concentrated under vacuum. The material was further purified (FCC,  $\text{SiO}_2$ , 0-90% EtOAc in hexanes) to afford the title compound (17 mg, 11% over 3 steps). MS (ESI): mass calcd. for  $\text{C}_{19}\text{H}_{17}\text{F}_3\text{N}_4\text{O}_2$ , 390.1; m/z found, 391.1  $[\text{M}+\text{H}]^+$ .  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta$  11.73 (br s, 1H), 7.92 (d,  $J = 1.9$  Hz, 1H), 7.68 – 7.64 (m, 1H), 7.60 – 7.55 (m, 1H), 7.54 – 7.50 (m, 1H), 7.46 (d,  $J = 1.9$  Hz, 1H), 4.51 (s, 2H), 4.24 (t,  $J = 7.6$  Hz, 2H), 3.88 (t,  $J = 7.7$  Hz, 2H), 2.33 (s, 3H), 2.34 – 2.20 (m, 2H).

Example 30: 6-(2,4-Difluoro-3-methyl-phenyl)-1-(2-oxobutyl)-3H-imidazo[4,5-b]pyridin-2-  
30 one.



Step A: 6-Bromo-3-(4-methoxybenzyl)-1-(2-oxobutyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. Under a nitrogen atmosphere was added 6-bromo-3-(4-

methoxybenzyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 10, 2 g, 6.0  
5 mmol) to a suspension of NaH (527 mg, 13 mmol) in DMF (30 mL). After 10 minutes, 1-bromo-2-butanone (1.3 mL, 13.2 mmol) was added to the reaction mixture, and the reaction was heated to 65 °C. After 3 h, the reaction mixture was cooled to room temperature and quenched with water (150 mL) and a solid precipitate appeared. The precipitates were collected by filtration, washed with water and dried under vacuum to  
10 give the title compound (1.7 g, 68 %). MS (ESI): mass calcd. for C<sub>18</sub>H<sub>18</sub>BrN<sub>3</sub>O<sub>3</sub>, 403.1; m/z found, 404.0 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 8.10 (d, *J* = 2.0 Hz, 1H), 7.80 (d, *J* = 2.0 Hz, 1H), 7.28 – 7.24 (m, 2H), 6.91 – 6.84 (m, 2H), 4.98 (s, 2H), 4.88 (s, 2H), 3.71 (s, 3H), 2.61 (q, *J* = 7.3 Hz, 2H), 0.98 (t, *J* = 7.3 Hz, 3H).

Step B: 6-(2,4-difluoro-3-methylphenyl)-3-(4-methoxybenzyl)-1-(2-oxobutyl)-1,3-dihydro-

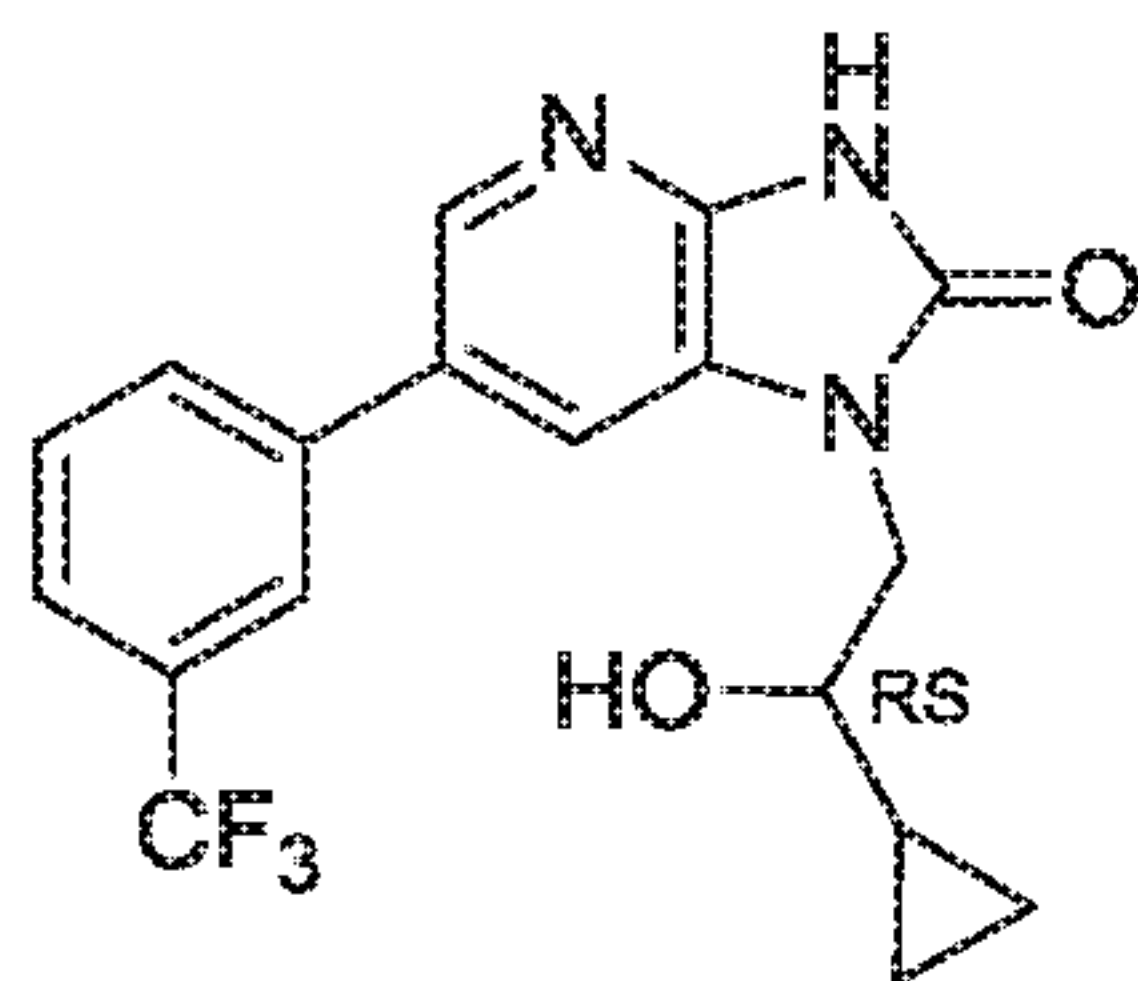
2H-imidazo[4,5-b]pyridin-2-one. A mixture of 6-bromo-3-(4-methoxybenzyl)-1-(2-  
15 oxobutyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (200 mg, 0.5 mmol), (2,4-difluoro-3-methylphenyl)boronic acid (128 mg, 0.7 mmol), 1,1'-bis(diphenylphosphino)ferrocene palladium(II)dichloride dichloromethane complex (25 mg, 0.03 mmol), Cs<sub>2</sub>CO<sub>3</sub> (322 mg, 1.0 mmol), dioxane (4.6 mL) and H<sub>2</sub>O (0.4 mL) was heated to 110 °C using an oil bath.  
20 After 16 h, the reaction mixture was cooled to room temperature and volatiles were removed. The crude material was purified (FCC, SiO<sub>2</sub>, 0-100% EtOAc in hexanes) to give the title compound (148 mg, 66%). MS (ESI): mass calcd. for C<sub>25</sub>H<sub>23</sub>F<sub>2</sub>N<sub>3</sub>O<sub>3</sub>, 451.2; m/z found, 452.1 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 8.11 (t, *J* = 1.6 Hz, 1H), 7.65 (t, *J* = 1.6 Hz, 1H), 7.42 – 7.35 (m, 1H), 7.34 – 7.28 (m, 2H), 7.21 – 7.14 (m, 1H), 6.92 –  
25 6.87 (m, 2H), 5.04 (s, 2H), 4.92 (s, 2H), 3.71 (s, 3H), 2.61 (q, *J* = 7.4 Hz, 2H), 2.22 (t, *J* = 1.9 Hz, 3H), 0.98 (t, *J* = 7.3 Hz, 3H).

Step C: 6-(2,4-difluoro-3-methylphenyl)-1-(2-oxobutyl)-3H-imidazo[4,5-b]pyridin-2-one.

A mixture of 6-(2,4-difluoro-3-methylphenyl)-3-(4-methoxybenzyl)-1-(2-oxobutyl)-1,3-

dihydro-2H-imidazo[4,5-b]pyridin-2-one (140 mg, 0.31 mmol) and hydrobromic acid (48% in H<sub>2</sub>O, 6 mL) was heated to 115 °C. After completion, the reaction was cooled to 0 °C and sodium hydroxide pellets were added until basic pH was reached. The mixture was extracted with EtOAc (3X). The combined organics were dried over MgSO<sub>4</sub>, filtered and concentrated under vacuum. The crude material was triturated in MeOH and the solids were filtered off and rinsed with MeOH to afford the title compound (16 mg, 16%). MS (ESI): mass calcd. for C<sub>17</sub>H<sub>15</sub>F<sub>2</sub>N<sub>3</sub>O<sub>2</sub>, 331.1; m/z found, 332.1 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 11.76 (s, 1H), 8.04 (t, *J* = 1.6 Hz, 1H), 7.55 (t, *J* = 1.6 Hz, 1H), 7.42 – 7.35 (m, 1H), 7.21 – 7.14 (m, 1H), 4.82 (s, 2H), 2.59 (q, *J* = 7.2 Hz, 2H), 2.22 (t, *J* = 1.8 Hz, 3H), 0.97 (t, *J* = 7.3 Hz, 3H).

Example 31: (R/S)-1-(2-Cyclopropyl-2-hydroxy-ethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one and its trifluoroacetic acid salt.



Step A: 1-(2-Cyclopropyl-2-oxoethyl)-6-(3-(trifluoromethyl)phenyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. Under a nitrogen atmosphere was added 6-(3-(trifluoromethyl)phenyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 43, 200 mg, 0.38 mmol) to a suspension of NaH (60% dispersion in mineral oil, 30.7 mg, 0.8 mmol) in DMF (4 mL). After 10 minutes 2-bromo-1-cyclopropylethanone (93.8 mg, 0.6 mmol) was added to the reaction mixture, and the reaction mixture was heated to 75 °C. After completion, the reaction mixture was cooled down to room temperature and quenched with water (20 mL). The mixture was extracted using EtOAc (3 x 20 mL). The precipitates were collected by filtration, washed with water and dried under vacuum to give the title compound which was used crude without further purification.

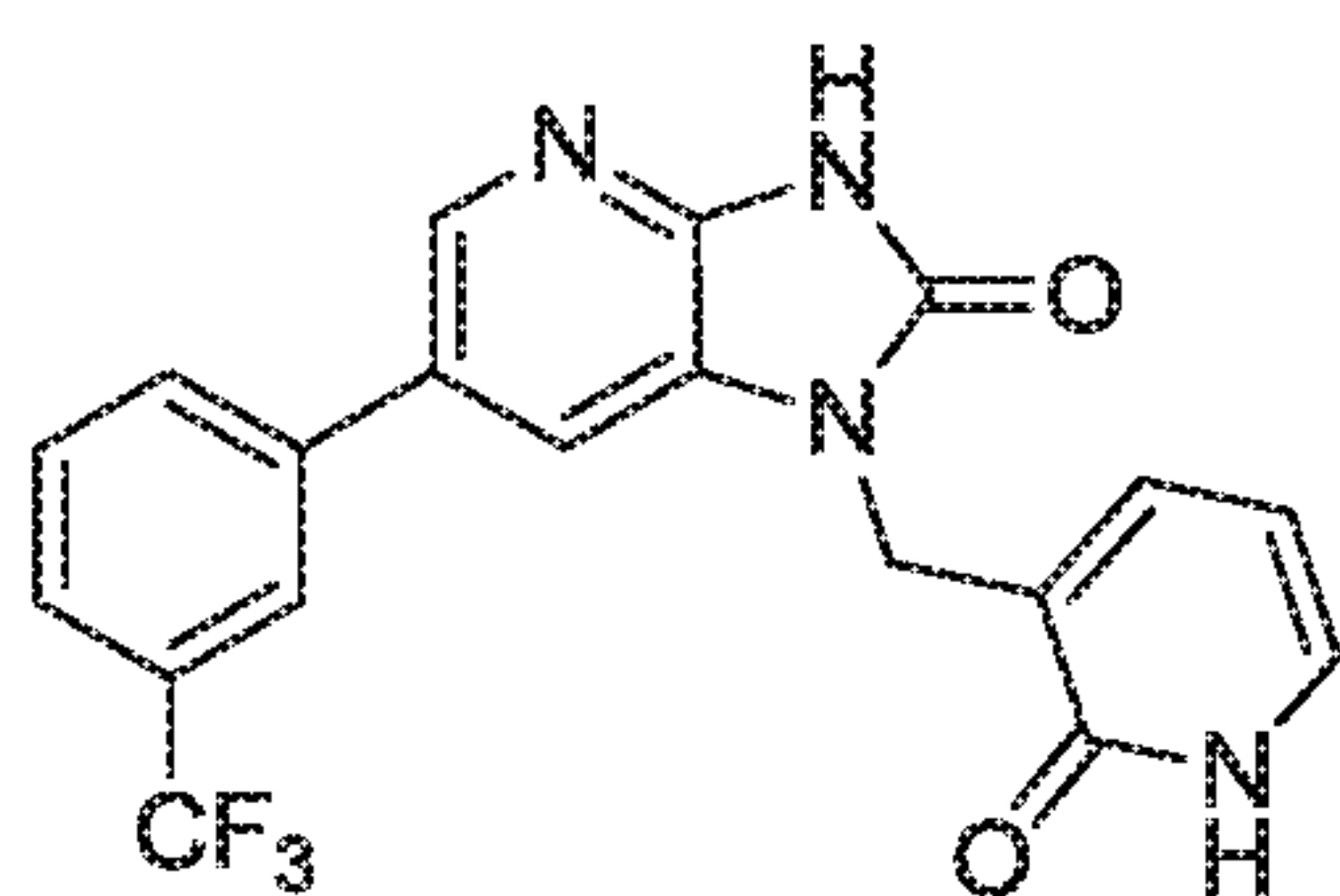
Step B: 1-(2-Cyclopropyl-2-hydroxyethyl)-6-(3-(trifluoromethyl)phenyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. Under a nitrogen atmosphere was added sodium borohydride (18 mg, 0.5 mmol) to a mixture of 1-(2-cyclopropyl-2-oxoethyl)-6-(3-

(trifluoromethyl)phenyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (140 mg, 0.2 mmol) in MeOH at 0 °C, and then the reaction mixture was allowed to warm to room temperature. After completion, the reaction mixture was concentrated under vacuum. The crude material was partitioned between EtOAc (20 mL) and water (20 mL). The organic layer was isolated and the aqueous layer was washed with EtOAc (2 x 30 mL). The combined organics were dried over MgSO<sub>4</sub>, filtered and concentrated under vacuum to afford the title compound, which was used in the next step without further purification.

Step C: (R/S)-1-(2-Cyclopropyl-2-hydroxy-ethyl)-6-[3-(trifluoromethyl)phenyl]-3H-

imidazo[4,5-b]pyridin-2-one and its trifluoroacetic acid salt. To a solution of 1-(2-cyclopropyl-2-hydroxyethyl)-6-(3-(trifluoromethyl)phenyl)-3-trityl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (140 mg, 0.2 mmol) in DCM at room temperature was added TFA (0.26 mL, 3.5 mmol). After completion the reaction mixture was concentrated under vacuum and the crude material was purified using reversed phase HPLC (Method C) to afford the title compound (30 mg, 27%). MS (ESI): mass calcd. for C<sub>18</sub>H<sub>16</sub>F<sub>3</sub>N<sub>3</sub>O<sub>2</sub>, 363.1; m/z found, 364.1 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) δ 11.65 (s, 1H), 8.28 (d, J = 2.0 Hz, 1H), 8.03 – 7.97 (m, 2H), 7.86 (d, J = 2.0 Hz, 1H), 7.75 – 7.69 (m, 2H), 3.31 – 3.24 (m, 1H), 0.94 – 0.84 (m, 1H), 0.41 – 0.23 (m, 3H), 0.15 – 0.07 (m, 1H).

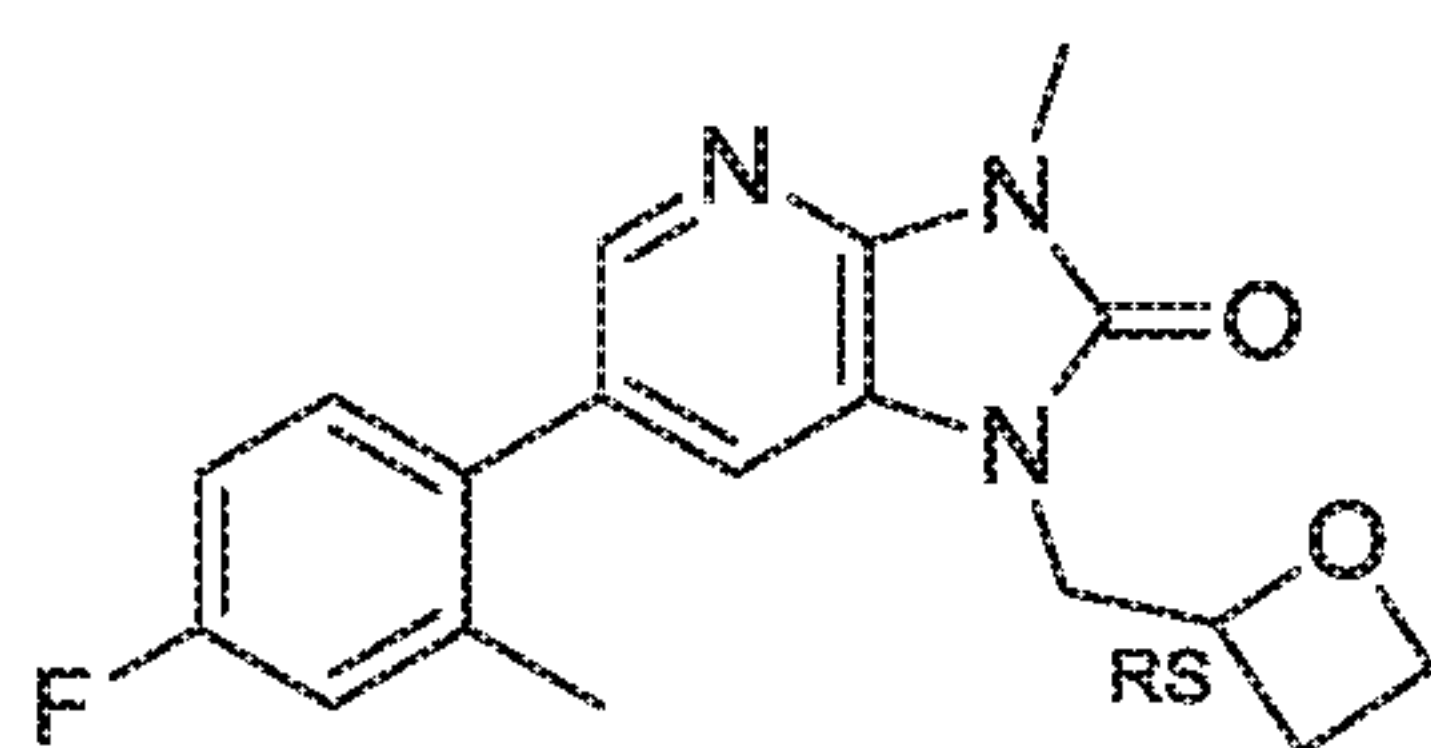
Example 32: 1-[(2-Oxo-1H-pyridin-3-yl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-  
imidazo[4,5-b]pyridin-2-one and its trifluoroacetic acid salt.



Under a nitrogen atmosphere was added chlorotrimethylsilane (0.06 mL, 0.5 mmol) to a mixture of 1-[(2-methoxy-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one (Example 22, 100 mg, 0.2 mmol) and sodium iodide (73 mg, 0.5 mmol) in MeCN (0.7 mL) at room temperature. After 16 hours, almost complete conversion was observed, and the reaction mixture was concentrated under vacuum to

afford the title compound as a free base. The crude material was purified using reversed phase HPLC (Method C) to afford title compound (36 mg, 37%). MS (ESI): mass calcd. for  $C_{19}H_{13}F_3N_4O_2$ , 386.1;  $m/z$  found, 387.0  $[M+H]^+$ .  $^1H$  NMR (500 MHz, DMSO- $d_6$ )  $\delta$  11.82 – 11.72 (m, 2H), 8.32 (d,  $J = 2.0$  Hz, 1H), 8.01 – 7.96 (m, 2H), 7.93 (d,  $J = 2.0$  Hz, 1H), 7.73 – 7.67 (m, 2H), 7.32 (dd,  $J = 6.5, 2.0$  Hz, 1H), 7.15 – 7.11 (m, 1H), 6.13 (t,  $J = 6.6$  Hz, 1H), 4.85 (s, 2H).

Example 33: (R/S)-6-(4-Fluoro-2-methyl-phenyl)-3-methyl-1-(oxetan-2-ylmethyl)imidazo[4,5-b]pyridin-2-one.



Step A: 6-Bromo-3-methyl-1-(oxetan-2-ylmethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one. The title compound was prepared in a manner analogous to Intermediate 22, using 6-bromo-3-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 11) and 2-(bromomethyl)oxetane.

Step B: (R/S)-6-(4-Fluoro-2-methyl-phenyl)-3-methyl-1-(oxetan-2-ylmethyl)imidazo[4,5-b]pyridin-2-one. A mixture of 6-bromo-3-methyl-1-(oxetan-2-ylmethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (Intermediate 25, 85 mg, 0.3 mmol), (4-fluoro-2-methylphenyl)boronic acid (57 mg, 0.4 mmol), 1,1'-bis(diphenylphosphino)ferrocene palladium(II)dichloride dichloromethane complex (15 mg, 0.02 mmol),  $Cs_2CO_3$  (186 mg, 0.6 mmol) and dioxane (2.6 mL) was heated to 110 °C. After completion, the reaction mixture was filtered and was (Method C). The collected fractions were combined and diluted with a saturated aqueous solution of  $NaHCO_3$ . The mixture was extracted using DCM (3X). The combined organics were dried over  $MgSO_4$ , filtered and concentrated under vacuum to give title compound (9.9 mg, 11%). MS (ESI): mass calcd. for  $C_{18}H_{18}FN_3O_2$ , 327.1;  $m/z$  found, 328.2  $[M+H]^+$ .  $^1H$  NMR (400 MHz, DMSO- $d_6$ )  $\delta$  7.93 (d,  $J = 1.8$  Hz, 1H), 7.60 (d,  $J = 1.9$  Hz, 1H), 7.29 – 7.24 (m, 1H), 7.22 – 7.17 (m, 1H), 7.15 – 7.09 (m, 1H), 5.05 – 4.95 (m, 1H), 4.48 – 4.40 (m, 1H), 4.35 – 4.27 (m, 1H), 4.23 – 4.03 (m, 2H), 3.40 (s, 3H), 2.71 – 2.57 (m, 1H), 2.51 – 2.37 (m, 1H), 2.24 (s, 3H).

## DEMANDE OU BREVET VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVET COMPREND PLUS D'UN TOME.

CECI EST LE TOME           1    DE    3  
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## JUMBO APPLICATIONS/PATENTS

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CONTAINING PAGES    1    TO    180

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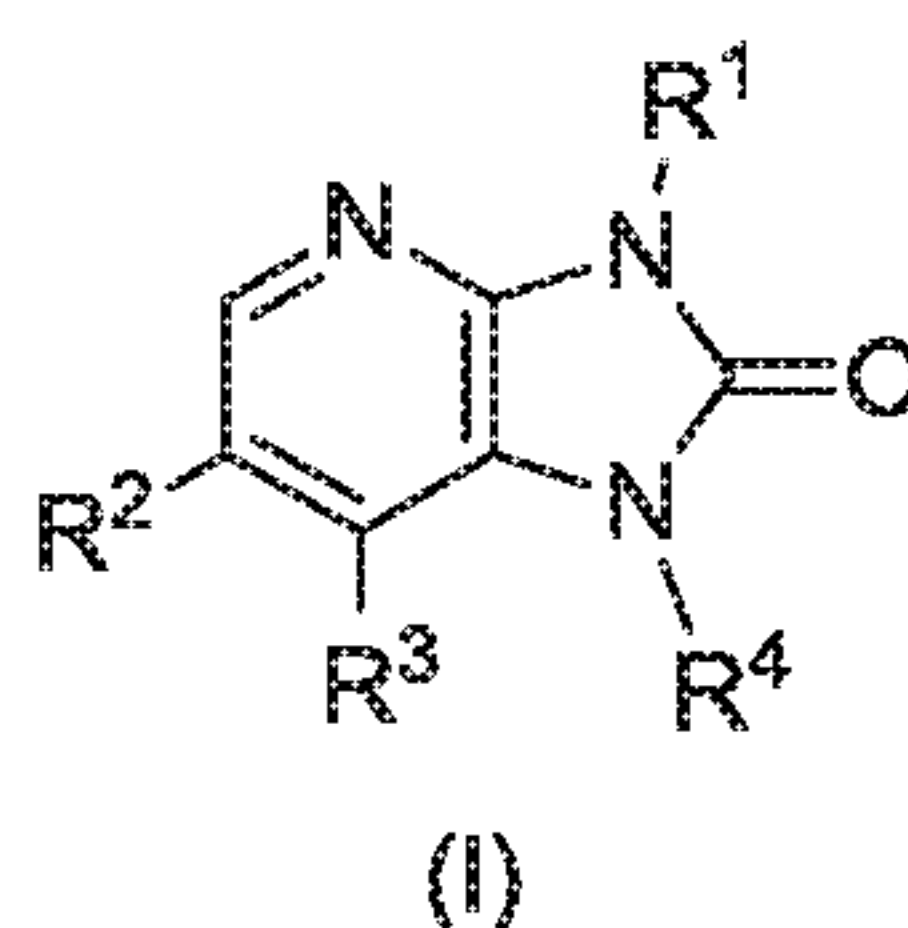
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## CLAIMS

What is claimed:

1. A compound, and pharmaceutically acceptable salts, solvates, stereoisomers, isotopic variants, or N-oxides thereof, having the structure of Formula (I):



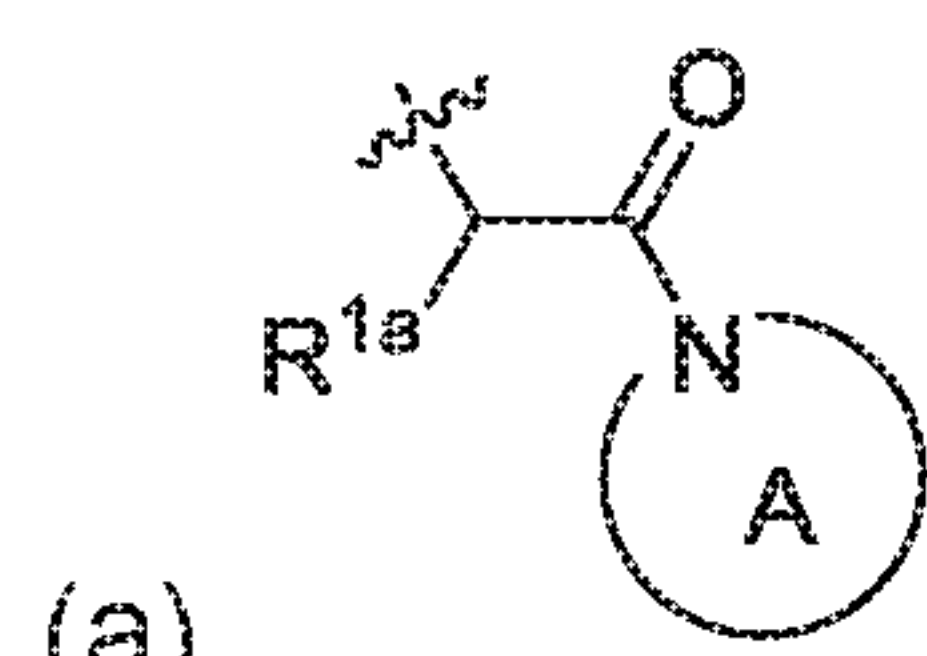
wherein

R<sup>1</sup> is H; CH<sub>2</sub>F; or CH<sub>3</sub>;

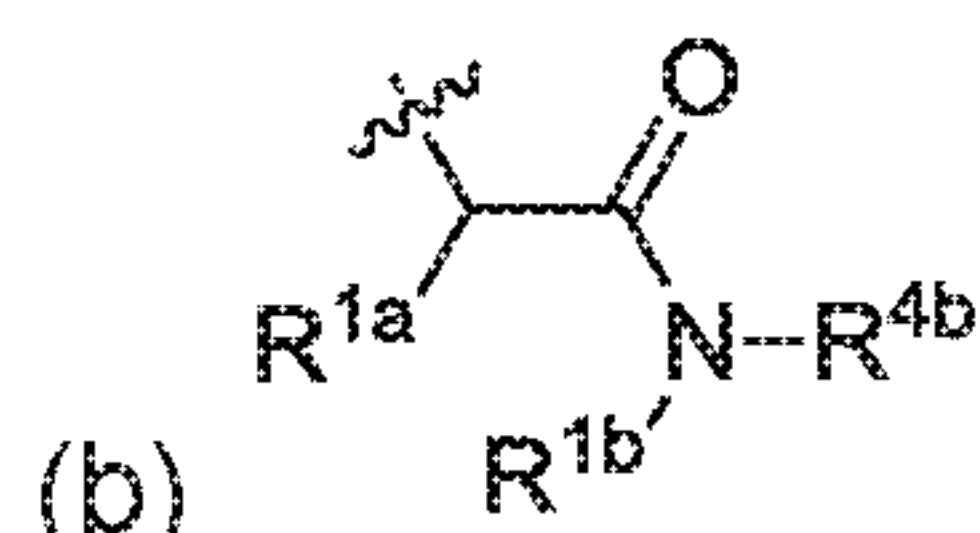
R<sup>2</sup> is selected from the group consisting of: phenyl; phenyl substituted with one, two, or three members each independently selected from the group consisting of: halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>haloalkyl, CN, OC<sub>1-6</sub>alkyl, OC<sub>1-6</sub>haloalkyl, N(CH<sub>3</sub>)<sub>2</sub>, and cyclopropyl; pyridinyl; pyridinyl substituted with F, C<sub>1-4</sub>alkyl, or C<sub>1-4</sub>haloalkyl; thiazolyl; thiazolyl substituted with C<sub>1-6</sub>alkyl or C<sub>1-6</sub>haloalkyl; thienyl; and thienyl substituted with one or two members each independently selected from the group consisting of: halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>haloalkyl, CH<sub>2</sub>OH, CH<sub>2</sub>OCH<sub>3</sub>, and cyclopropyl;

R<sup>3</sup> is H;

R<sup>4</sup> is selected from the group consisting of:



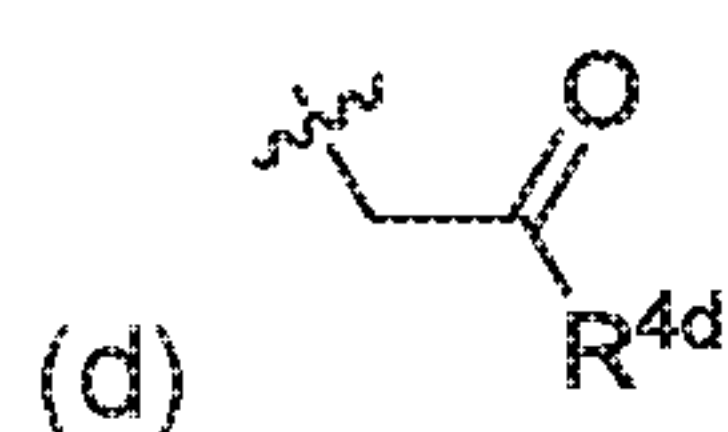
wherein ring A is a 4-6 membered heterocycle optionally containing an additional oxygen heteroatom selected from the group consisting of: azetidiny; azetidiny substituted with one or two members independently selected from the group consisting of: F, OH, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>haloalkyl, CH<sub>2</sub>OCH<sub>3</sub>, CN, and OCH<sub>3</sub>; pyrrolidiny; pyrrolidiny substituted two F members; morpholiny; piperidiny; piperaziny substituted with C<sub>1-6</sub>alkyl; and (2,6-diazaspiro[3.3]heptan-6-yl);



, wherein  $R^{4b}$  is selected from the group consisting of: H;  $C_{1-6}$ alkyl;  $CH_2CH_2OCH_3$ ;  $C_{3-6}$ cycloalkyl;  $C_{3-6}$ cycloalkyl substituted with two or three members independently selected from the group consisting of F or  $CH_3$ ; oxetanyl; oxetanyl substituted with  $CH_3$ ; and pyridinyl;



wherein  $R^{4c}$  is selected from the group consisting of: cyclopropyl; cyclopropyl substituted with one or two F members;  $CH(OH)$ cyclopropyl; azetidiny;  $CH_2$ -azetidiny;  $CH_2$ -azetidiny substituted with one or two members independently selected from: F, OH,  $OCH_3$ , and  $CF_3$ ; oxetanyl; oxetanyl substituted with F or  $CH_3$ ; tetrahydrofuranyl; tetrahydropyranyl;  $CH_2$ pyrrolidinyl;  $CH_2$ pyrrolidinyl substituted with  $CH_3$ , OH, or  $OCH_3$ ;  $CH_2$ piperidinyl;  $CH_2$ piperidinyl substituted with OH, or F; morpholinyl; pyrazolyl substituted with one or two  $CH_3$  members; triazolyl substituted with  $CH_3$ ; tetrazolyl; isoxazolyl substituted with one or two  $CH_3$  members; oxadiazolyl substituted with  $CH_3$ , or  $CH_2OCH_3$ ; thiadiazolyl; pyridinyl; pyridinyl substituted with one or two members independently selected from the group consisting of: Cl, F,  $CH_3$ ,  $OCH_3$ , and  $CF_3$ ; (2-oxo-1H-pyridin-3-yl); 6-oxo-1H-pyridin-3-yl; pyrimidinyl; pyrimidinyl substituted with F or  $CH_3$ ; pyrazinyl; pyridazinyl; pyridazinyl substituted with  $OCH_3$ ; phenyl; phenyl substituted with one or two members independently selected from the group consisting of: halo, CN,  $OCH_3$ ,  $C_{1-6}$ alkyl, and  $CF_3$ ;



wherein  $R^{4d}$  is selected from the group consisting of: OH,  $C_{1-6}$ alkyl,  $O-C_{1-6}$ alkyl,  $C_{3-6}$ cycloalkyl, thienyl, and thiazolyl; and

(e)  $C_{2-6}$ alkyl substituted with one or two members independently selected from OH,  $OC_{1-6}$ alkyl, or cyclopropyl;  $CH_2CH_2NH(C_{1-6}alkyl)$ ;  $CH_2CH_2NH(CH_2CH_2OH)$ ;  $CH_2CH_2NH(C_{3-6}cycloalkyl)$ ; and difluoro(3-pyridyl)methyl; and

$R^{1a}$  and  $R^{1b}$  are each independently H or  $CH_3$ .

2. The compound of claim 1, wherein  $R^1$  is H.

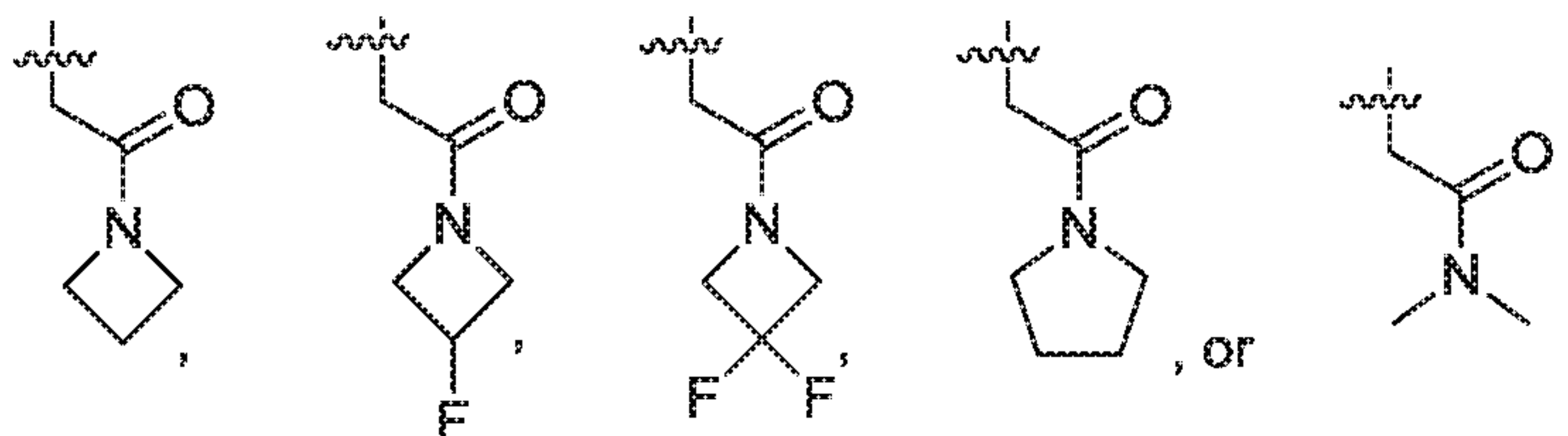
3. The compound of claim 1, wherein R<sup>1</sup> is CH<sub>3</sub> or CH<sub>2</sub>F.

4. The compound of claim 1, wherein R<sup>1a</sup> is H.

5 5. The compound of claim 1, wherein R<sup>2</sup> is phenyl; phenyl substituted with one, two, or three members each independently selected from the group consisting of: Cl, F, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>haloalkyl, CN, OC<sub>1-6</sub>alkyl, OC<sub>1-6</sub>haloalkyl, N(CH<sub>3</sub>)<sub>2</sub>, and cyclopropyl; pyridinyl; or pyridinyl substituted with CF<sub>3</sub>.

10 6. The compound of claim 1, wherein R<sup>2</sup> is thiazolyl substituted with C<sub>1-6</sub>alkyl or CF<sub>3</sub>; thienyl; or thienyl substituted with one or two members each independently selected from the group consisting of: Cl, F, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>haloalkyl, CH<sub>2</sub>OH, CH<sub>2</sub>OCD<sub>3</sub>, and cyclopropyl.

15 7. The compound of claim 1, wherein R<sup>1</sup> is H or CH<sub>3</sub>, R<sup>2</sup> is phenyl, wherein the phenyl is optionally substituted with one, two, or three members independently selected from: halo, C<sub>1-6</sub>alkyl, and C<sub>1-6</sub>haloalkyl; or thienyl, wherein the thienyl is optionally substituted with one or two members independently selected from: halo, C<sub>1-6</sub>alkyl, and C<sub>1-</sub>



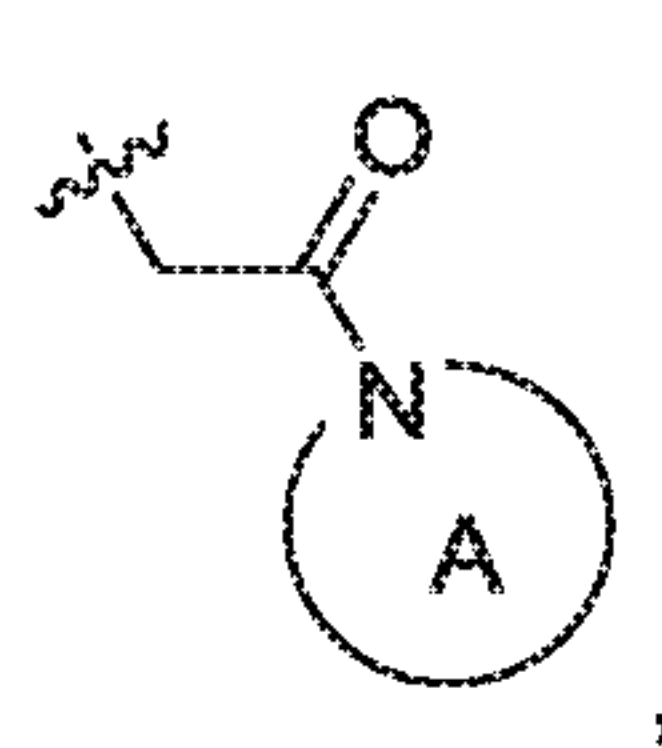
6haloalkyl; R<sup>3</sup> is H, and R<sup>4</sup> is

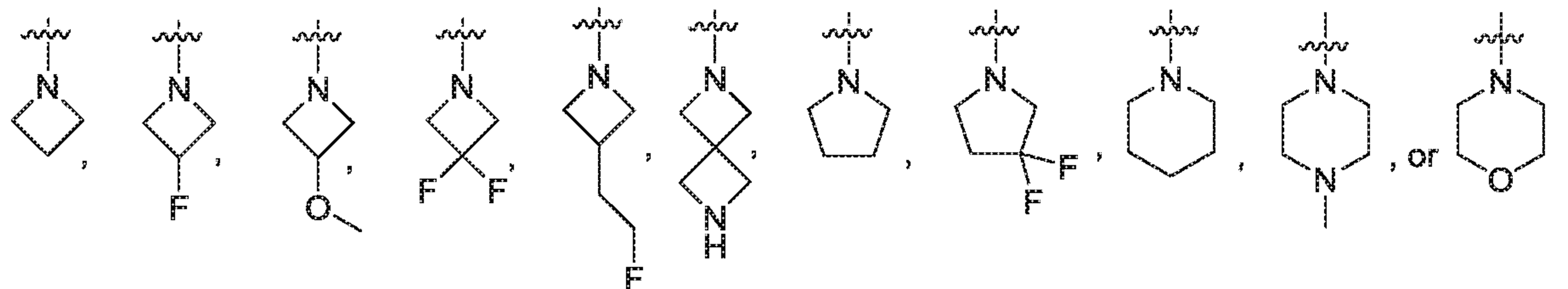
20 8. The compound of claim 1, wherein R<sup>2</sup> is phenyl; o-tolyl; m-tolyl; p-tolyl; 4-tert-butylphenyl; 3-(trifluoromethyl)phenyl; 4-fluorophenyl; 3-fluorophenyl; 3-cyanophenyl; 3-chlorophenyl; 4-chlorophenyl; 3-(difluoromethyl)phenyl; 3-methoxyphenyl; 3-(difluoromethoxy)phenyl; 4-methoxyphenyl; 3-(trifluoromethoxy)phenyl; 2-ethoxyphenyl;  
 25 3-ethoxyphenyl; 3-cyclopropylphenyl; 3-(dimethylamino)phenyl; 2,3-dichlorophenyl; 2,3-difluorophenyl; 2,3-dimethylphenyl; 2-fluoro-3-(trifluoromethyl)phenyl; 2,4-dimethoxyphenyl; 2,3-dimethoxyphenyl; 2,4-difluorophenyl; 3,4-difluorophenyl; 3,4-dichlorophenyl; 3-(difluoromethyl)-4-fluoro-phenyl; 5-(difluoromethyl)-2-fluorophenyl;

- 2,6-dimethylphenyl; 3,5-dimethylphenyl; 3,5-difluorophenyl; 3-fluoro-5-(trifluoromethyl)phenyl; 2-methyl-5-(trifluoromethyl)phenyl; 2-methyl-3-(trifluoromethyl)phenyl; 4-chloro-3-methyl-phenyl; 4-fluoro-3-(trifluoromethyl)phenyl; 4-chloro-3-(trifluoromethyl)phenyl; 2-ethoxy-5-fluoro-phenyl; 3-chloro-2-fluoro-phenyl; 3-chloro-4-fluoro-phenyl; 2-chloro-4-methoxy-phenyl; 4-fluoro-2-methyl-phenyl; 4-fluoro-2-methoxy-phenyl; 2-fluoro-6-methoxy-phenyl; 3-fluoro-4-methoxy-phenyl; 3-fluoro-5-methyl-phenyl; 2-fluoro-3-methyl-phenyl; 4-fluoro-3-methyl-phenyl; 4-methoxy-3-methyl-phenyl; 4-fluoro-2,3-dimethyl-phenyl; 2,4-difluoro-3-methyl-phenyl; 2,3,4-trifluorophenyl; 3,4,5-trifluorophenyl; 3,4-difluoro-5-(trifluoromethyl)phenyl; 3-pyridyl; 2-(trifluoromethyl)-4-pyridyl; 2-thienyl; 5-methyl-2-thienyl; 5-ethyl-2-thienyl; 4-methyl-2-thienyl; 5-(trideuteriomethoxymethyl); 5-(hydroxymethyl)-2-thienyl; 5-fluoro-2-thienyl; 5-chloro-2-thienyl; 5-cyclopropyl-2-thienyl; 5-chloro-4-methyl-2-thienyl; 5-(difluoromethyl)-2-thienyl; 5-(difluoromethyl)-3-thienyl; 5-(trifluoromethyl)-2-thienyl; 5-(trifluoromethyl)-3-thienyl; 2-(trifluoromethyl)-3-thienyl; 4-(difluoromethyl)-2-thienyl; 5-(1,1,2,2,2-pentafluoroethyl)-2-thienyl; 4-methylthiazol-2-yl; 2-methylthiazol-5-yl; 2-(trifluoromethyl)thiazol-5-yl; or 2-(trifluoromethyl)thiazol-4-yl.

9. The compound of claim 1, wherein  $R^3$  is H.

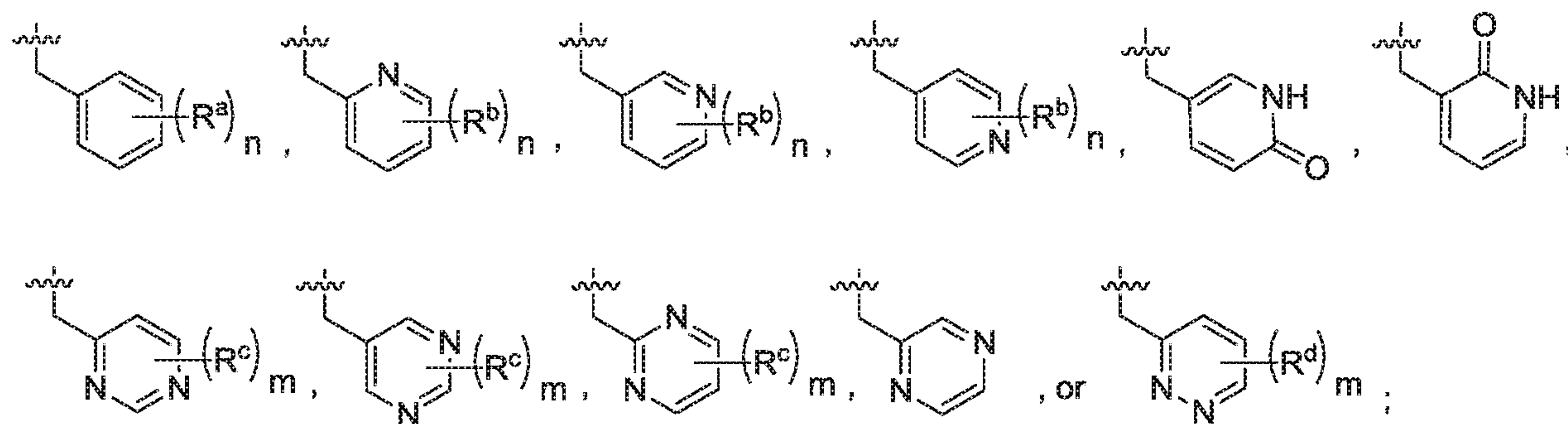
10. The compound of claim 1, wherein  $R^3$  is D or T.

11. The compound of claim 1, wherein  $R^4$  is , wherein ring A is



12. The compound of claim 1, wherein  $R^4$  is

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wherein

$R^a$  is independently selected from: halo, CN,  $\text{OCH}_3$ ,  $\text{C}_{1-6}$ alkyl, and  $\text{CF}_3$ ;

$R^b$  is independently selected from: Cl, F,  $\text{CH}_3$ ,  $\text{OCH}_3$ , and  $\text{CF}_3$ ;

5  $R^c$  is F or  $\text{CH}_3$ ;

$R^d$  is  $\text{OCH}_3$ ;

$m$  is 0 or 1; and

$n$  is 0, 1, or 2.

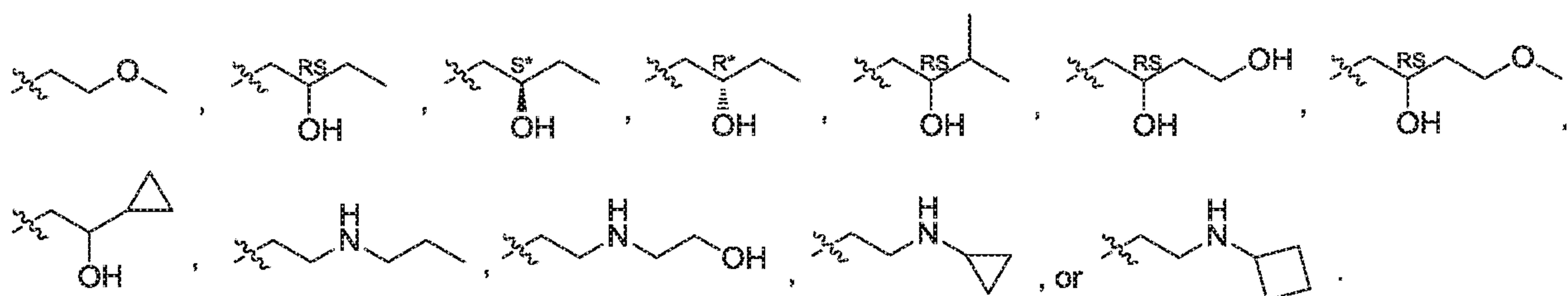
10 16. The compound of claim 1, wherein

$R^1$  is H or  $\text{CH}_3$ ;

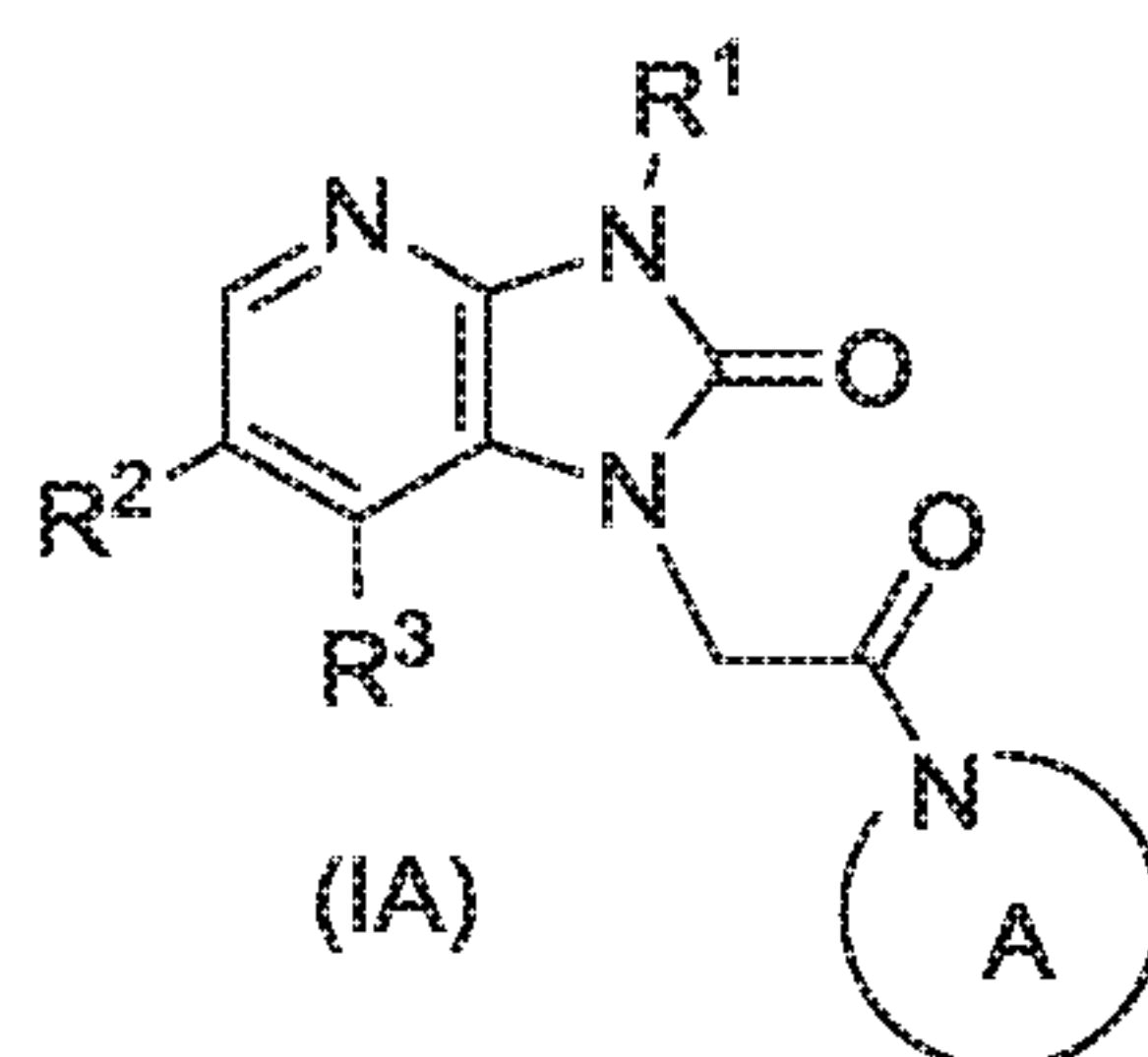
$R^2$  is phenyl substituted with one, two, or three members each independently selected from the group consisting of: halo,  $\text{C}_{1-6}$ alkyl,  $\text{C}_{1-6}$ haloalkyl, and  $\text{OC}_{1-6}$ alkyl;

15  $R^3$  is H; and

$R^4$  is



17. The compound of claim 1, and pharmaceutically acceptable salts, solvates,  
20 stereoisomers, isotopic variants, or N-oxides thereof, having the structure of Formula (IA):

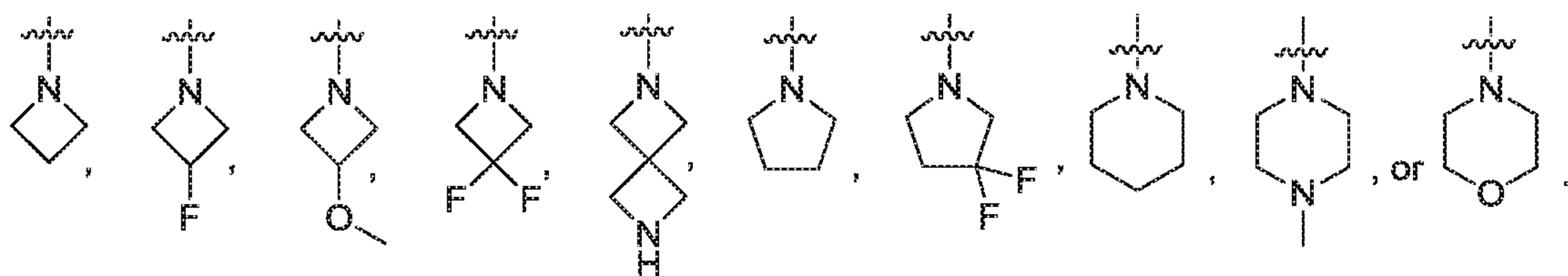


wherein  $R^1$  is H;  $\text{CH}_2\text{F}$ ; or  $\text{CH}_3$ ;

$R^2$  is phenyl substituted with one, two, or three members each independently selected from the group consisting of: halo,  $\text{C}_{1-6}$ alkyl,  $\text{C}_{1-6}$ haloalkyl,  $\text{OC}_{1-6}$ alkyl; thiazolyl substituted with  $\text{C}_{1-6}$ alkyl; and thienyl substituted with one or two members each independently selected from the group consisting of: halo,  $\text{C}_{1-6}$ alkyl,  $\text{C}_{1-6}$ haloalkyl,  $\text{CH}_2\text{OH}$ ,  $\text{CH}_2\text{OCH}_3$ , and cyclopropyl;

$R^3$  is H or T; and

ring A is

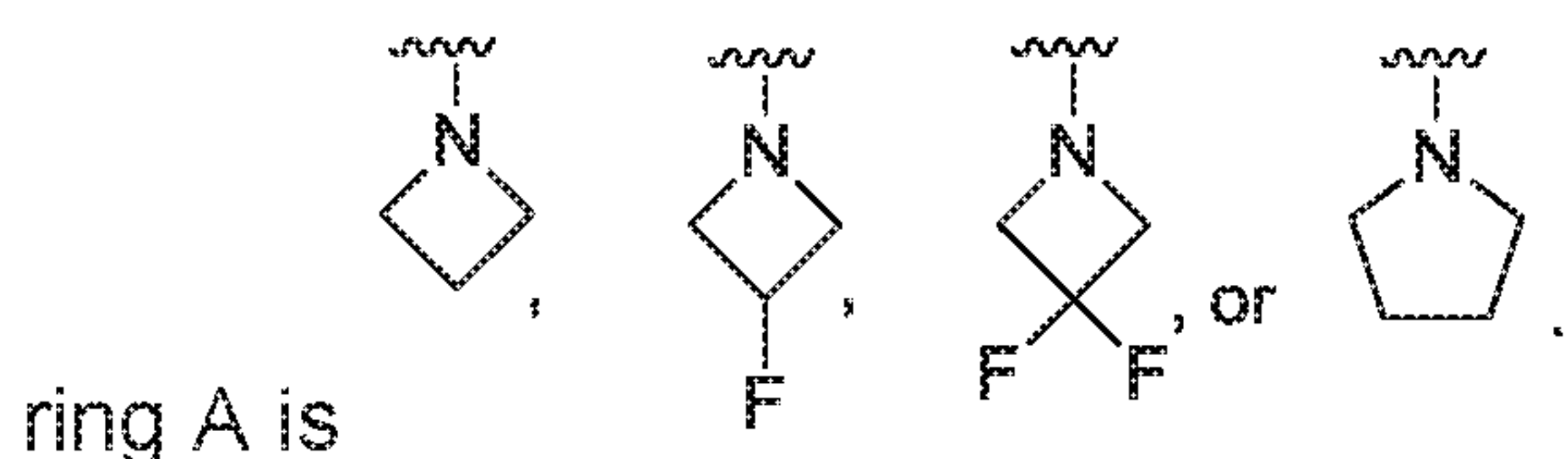


18. The compound of claim 17, wherein

$R^1$  is H;  $\text{CH}_2\text{F}$ ; or  $\text{CH}_3$ ;

$R^2$  is 3-(trifluoromethyl)phenyl, 4-fluoro-3-methyl-phenyl, 2,4-difluoro-3-methyl-phenyl, 5-(trifluoromethyl)-2-thienyl, 5-(difluoromethyl)-2-thienyl, or 5-chloro-4-methyl-2-thienyl;

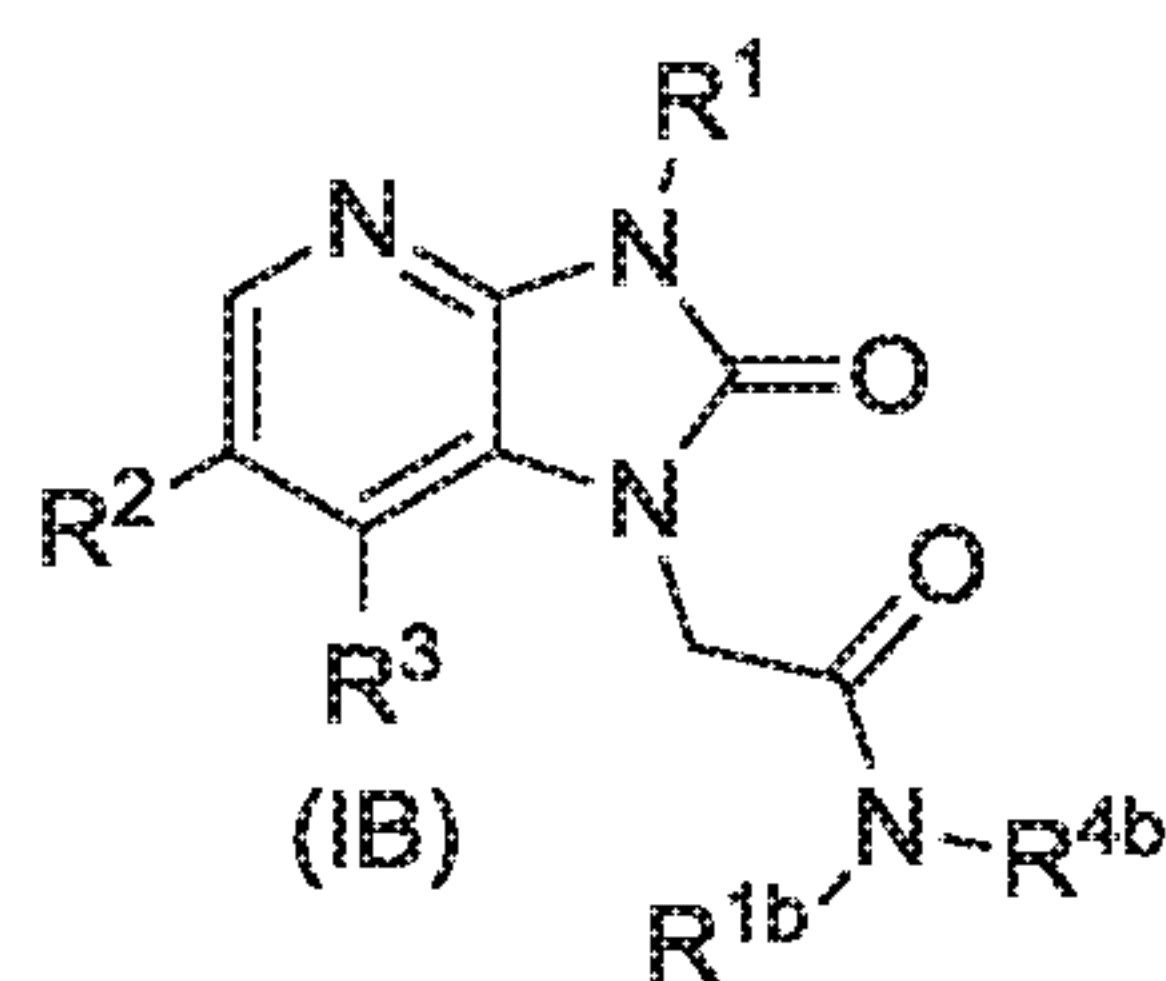
$R^3$  is H; and



19. The compound of claim 17, wherein  $R^2$  is m-tolyl, 3-fluorophenyl, 3-chlorophenyl, 3-(trifluoromethyl)phenyl, 5-methyl-2-thienyl, 5-ethyl-2-thienyl, 5-(hydroxymethyl)-2-thienyl, 5-cyclopropyl-2-thienyl, 5-(trideuteriomethoxymethyl)-2-thienyl, 5-(trifluoromethyl)-2-thienyl, 5-(trifluoromethyl)-3-thienyl, 2-(trifluoromethyl)-3-

thienyl, 5-(1,1,2,2,2-pentafluoroethyl)-2-thienyl, 5-(trifluoromethyl)thiophen-2-yl, 5-fluoro-2-thienyl, 5-chloro-4-methyl-2-thienyl, 5-(difluoromethyl)-2-thienyl, 4-(difluoromethyl)-2-thienyl, 5-(difluoromethyl)-3-thienyl, 4-methylthiazol-2-yl, 2-methylthiazol-5-yl, 4-methoxyphenyl, 4-fluoro-2-methyl-phenyl, 2-fluoro-3-methyl-phenyl, 4-fluoro-3-methyl-phenyl, 3,5-difluorophenyl, 3,4-difluorophenyl, 2,4-difluoro-3-methyl-phenyl, 3,4,5-trifluorophenyl, 2-(trifluoromethyl)thiazol-5-yl, 2-(trifluoromethyl)thiazol-4-yl, 2-methyl-5-(trifluoromethyl)phenyl, 2-methyl-3-(trifluoromethyl)phenyl, 2-fluoro-3-(trifluoromethyl)phenyl, or 4-fluoro-3-(trifluoromethyl)phenyl.

20. The compound of claim 1, and pharmaceutically acceptable salts, solvates, stereoisomers, isotopic variants, or N-oxides thereof, having the structure of Formula (IB):



wherein  $R^1$  and  $R^{1b}$  are each independently H or  $\text{CH}_3$ ;

$R^2$  is selected from the group consisting of: phenyl substituted with one, two, or three members each independently selected from the group consisting of: halo,  $\text{C}_{1-6}$ alkyl,  $\text{C}_{1-6}$ haloalkyl,  $\text{OC}_{1-6}$ alkyl; pyridinyl; thiazolyl substituted with  $\text{C}_{1-6}$ alkyl; and thienyl substituted with one or two members each independently selected from the group consisting of: halo,  $\text{C}_{1-6}$ alkyl,  $\text{C}_{1-6}$ haloalkyl,  $\text{CH}_2\text{OH}$ , and cyclopropyl;

$R^3$  is H; and

$R^{4b}$  is H,  $\text{C}_{1-6}$ alkyl, 2-methoxyethyl,  $\text{C}_{3-6}$ cycloalkyl, 3,3-difluorocyclobutyl, 3,3-difluoro-1-methyl-cyclobutyl, cyclopentyl, oxetan-3-yl, 3-methyloxetan-3-yl, or 2-pyridyl.

21. The compound of claim 20, wherein

$R^1$  is H;  $\text{CH}_2\text{F}$ ; or  $\text{CH}_3$ ;

$R^{1b}$  is  $\text{CH}_3$ ;

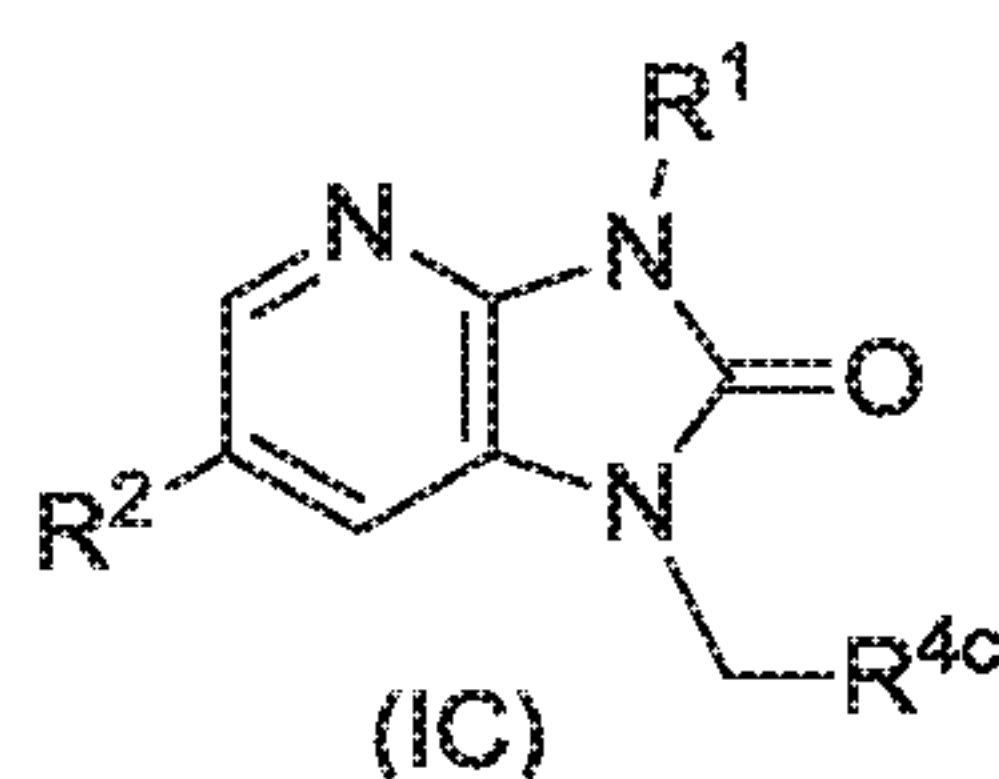
$R^2$  is 3-(trifluoromethyl)phenyl, 4-fluoro-3-methyl-phenyl, 2,4-difluoro-3-methyl-phenyl, 5-(trifluoromethyl)-2-thienyl, 5-(difluoromethyl)-2-thienyl, or 5-chloro-4-methyl-2-thienyl;

$R^3$  is H; and

5  $R^{4b}$  is  $CH_3$ .

22. The compound of claim 20, wherein  $R^2$  is 3-pyridyl, 5-methyl-2-thienyl, 4-methyl-2-thienyl, 5-cyclopropyl-2-thienyl, 5-ethyl-2-thienyl, 5-chloro-2-thienyl, 5-(hydroxymethyl)-2-thienyl, 5-(trifluoromethyl)-2-thienyl, 5-(trifluoromethyl)-3-thienyl, 2-(trifluoromethyl)-3-thienyl, 5-(difluoromethyl)-2-thienyl, 5-(difluoromethyl)-3-thienyl, 5-chloro-4-methyl-2-thienyl, 5-fluoro-2-thienyl, 5-fluoro-2-thienyl, 2-methylthiazol-5-yl, 3,5-dimethylphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 4-fluoro-2-methyl-phenyl, 2-fluoro-3-methyl-phenyl, 4-fluoro-3-methyl-phenyl, 4-chlorophenyl, 2,3-difluorophenyl, 3,5-difluorophenyl, 3,4-difluorophenyl, 2-ethoxyphenyl, 3-ethoxyphenyl, 4-methoxy-3-methyl-phenyl, 4-fluoro-2-methoxy-phenyl, 2-fluoro-6-methoxy-phenyl, 2,4-difluoro-3-methyl-phenyl, 3-(difluoromethyl)phenyl, 3-chloro-4-fluoro-phenyl, 2,4-dimethoxyphenyl, 2-ethoxy-5-fluoro-phenyl, 2-chloro-4-methoxy-phenyl, 3-(trifluoromethyl)phenyl, 2-(trifluoromethyl)thiazol-5-yl, 2-(trifluoromethyl)thiazol-4-yl, 2-fluoro-3-(trifluoromethyl)phenyl, or 3,4-difluoro-5-(trifluoromethyl)phenyl.

23. The compound of claim 1, and pharmaceutically acceptable salts, solvates, stereoisomers, isotopic variants, or N-oxides thereof, having the structure of Formula (IC):



wherein  $R^1$  is H or  $CH_3$ ;

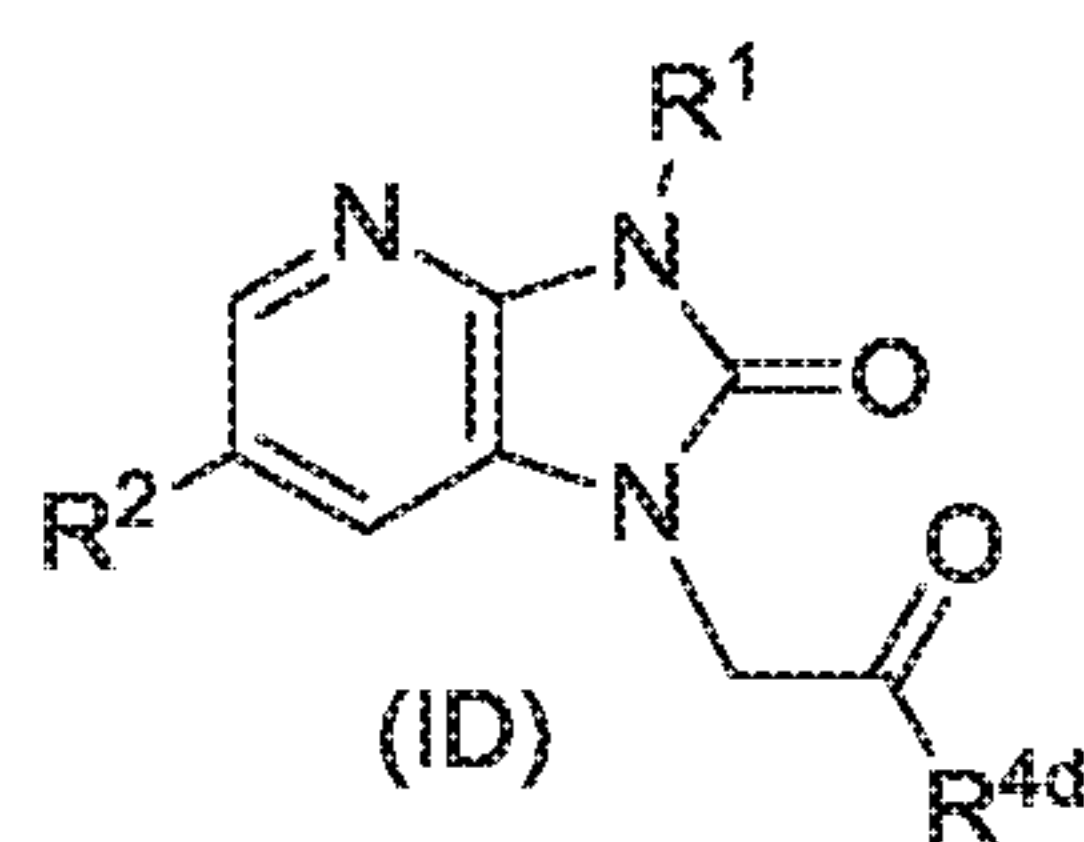
$R^2$  is selected from the group consisting of: phenyl; phenyl substituted with one, two, or three members each independently selected from the group consisting of:

halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>haloalkyl, CN, OC<sub>1-6</sub>alkyl, OC<sub>1-6</sub>haloalkyl, and N(CH<sub>3</sub>)<sub>2</sub>;  
pyridinyl substituted with CF<sub>3</sub>; and thienyl substituted with one or two members  
each independently selected from the group consisting of: halo, C<sub>1-6</sub>alkyl, and C<sub>1-6</sub>  
haloalkyl; and

- 5 R<sup>4c</sup> is selected from the group consisting of: cyclopropyl; cyclopropyl substituted with  
one or two F members; CH(OH)cyclopropyl; azetidiny; CH<sub>2</sub>-azetidiny; CH<sub>2</sub>-  
azetidiny substituted with one or two members independently selected from: F,  
OH, OCH<sub>3</sub>, and CF<sub>3</sub>; oxetanyl; oxetanyl substituted with F or CH<sub>3</sub>;  
tetrahydrofuranyl; tetrahydropyranyl; CH<sub>2</sub>pyrrolidiny; CH<sub>2</sub>pyrrolidiny substituted  
10 with CH<sub>3</sub>, OH, or OCH<sub>3</sub>; CH<sub>2</sub>piperidiny; CH<sub>2</sub>piperidiny substituted with OH, or F;  
morpholiny; pyrazolyl substituted with one or two CH<sub>3</sub> members; triazolyl  
substituted with CH<sub>3</sub>; tetrazolyl; isoxazolyl substituted with one or two CH<sub>3</sub>  
members; oxadiazolyl substituted with CH<sub>3</sub>, or CH<sub>2</sub>OCH<sub>3</sub>; thiadiazolyl; pyridiny;  
pyridiny substituted with one or two members independently selected from the  
15 group consisting of: Cl, F, CH<sub>3</sub>, OCH<sub>3</sub>, and CF<sub>3</sub>; (2-oxo-1H-pyridin-3-yl); 6-oxo-  
1H-pyridin-3-yl; pyrimidinyl; pyrimidinyl substituted with F or CH<sub>3</sub>; pyrazinyl;  
pyridazinyl; pyridazinyl substituted with OCH<sub>3</sub>; phenyl; phenyl substituted with  
one or two members independently selected from the group consisting of: halo,  
CN, OCH<sub>3</sub>, C<sub>1-6</sub>alkyl, and CF<sub>3</sub>.

20

24. The compound of claim 1, and pharmaceutically acceptable salts, solvates,  
stereoisomers, isotopic variants, or N-oxides thereof, having the structure of Formula  
(ID):



- 25 wherein R<sup>1</sup> is H or CH<sub>3</sub>;  
R<sup>2</sup> is m-tolyl, 3-(trifluoromethyl)phenyl, 4-chlorophenyl, 2,4-difluoro-3-methyl-phenyl,  
3,4-difluorophenyl, 4-fluoro-3-methyl-phenyl, 3-cyclopropylphenyl, 3-fluoro-4-

methoxy-phenyl, 2-ethoxyphenyl, 3-ethoxyphenyl, 4-methoxyphenyl, 2-ethoxy-5-fluoro-phenyl, 4-fluoro-2-methoxy-phenyl, or 3-chloro-4-fluoro-phenyl; and R<sup>4d</sup> is OH, C<sub>1-6</sub>alkyl, C<sub>3-6</sub>cycloalkyl, OC<sub>1-6</sub>alkyl, 2-thienyl, or thiazol-2-yl.

- 5 25. A compound selected from the group consisting of:
- 6-(4-Methoxyphenyl)-1-(2-morpholino-2-oxo-ethyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(4-Fluoro-2-methyl-phenyl)-1-(2-methoxyethyl)-3H-imidazo[4,5-b]pyridin-2-one;
- N-Ethyl-2-[6-(4-fluoro-2-methyl-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;
- 10 (S\*)-1-(2-Hydroxybutyl)-6-(4-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-one;
- (R\*)-1-(2-Hydroxybutyl)-6-(4-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(4-Fluoro-3-methyl-phenyl)-3-methyl-1-(2-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-(3-Fluorophenyl)-3-methyl-1-(pyrimidin-4-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 15 6-(3,4-Difluorophenyl)-3-methyl-1-[(5-methylisoxazol-3-yl)methyl]imidazo[4,5-b]pyridin-2-one;
- 2-[6-(5-Chloro-2-thienyl)-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethylacetamide;
- 6-[5-(Difluoromethyl)-2-thienyl]-1-[2-(3-fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-
- 20 imidazo[4,5-b]pyridin-2-one;
- 1-[(5-Methylisoxazol-3-yl)methyl]-6-phenyl-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(4-Fluorophenyl)-1-[(5-methylisoxazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(4-Fluorophenyl)-1-[(5-methyl-1,3,4-oxadiazol-2-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 25 3-Methyl-1-[(5-methylisoxazol-3-yl)methyl]-6-(4-methyl-2-thienyl)imidazo[4,5-b]pyridin-2-one;
- 6-(4-Fluorophenyl)-1-[(1-methylpyrazol-4-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 1-[(1,5-Dimethylpyrazol-3-yl)methyl]-6-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 30 1-[2-(Azetidin-1-yl)ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;

1-[2-(Azetidin-1-yl)ethyl]-3-methyl-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;

1-[(5-Methylisoxazol-3-yl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;

5 N-Cyclopropyl-2-[2-oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;

1-[(3-Chlorophenyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;

10 1-[(2-Methoxy-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;

1-(Pyrimidin-4-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;

(R/S)-1-(Tetrahydrofuran-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;

15 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;

N,N-Dimethyl-2-[2-oxo-6-[5-(trifluoromethyl)-2-thienyl]-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;

1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;

20 N,N-Dimethyl-2-[3-methyl-2-oxo-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-1-yl]acetamide;

1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[2-methyl-5-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;

6-(2,4-Difluoro-3-methyl-phenyl)-1-(2-oxobutyl)-3H-imidazo[4,5-b]pyridin-2-one;

25 (R/S)-1-(2-Cyclopropyl-2-hydroxy-ethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;

1-[(2-Oxo-1H-pyridin-3-yl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;

(R/S)-6-(4-Fluoro-2-methyl-phenyl)-3-methyl-1-(oxetan-2-ylmethyl)imidazo[4,5-

30 b]pyridin-2-one;

- 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;
- 6-(4-Methoxyphenyl)-1-(2-oxo-2-pyrrolidin-1-yl-ethyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 5 N-Cyclopropyl-2-[6-(4-fluoro-2-methyl-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;
- 2-[6-(2-Chloro-4-methoxy-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-cyclopropyl-acetamide;
- N-Cyclopropyl-2-[6-(4-methoxyphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;
- 10 N-Cyclopropyl-2-[6-(3,5-dimethylphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;
- N-Cyclopropyl-2-[6-(4-fluoro-2-methyl-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-methyl-acetamide;
- 15 N-Cyclopropyl-2-[6-(4-methoxyphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-methyl-acetamide;
- N-Cyclopropyl-2-[6-(4-fluoro-2-methyl-phenyl)-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]acetamide;
- (R\*)-6-(4-Fluoro-2-methyl-phenyl)-1-(2-hydroxybutyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 20 (S\*)-6-(4-Fluoro-2-methyl-phenyl)-1-(2-hydroxybutyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(4-Fluoro-3-methyl-phenyl)-3-methyl-1-(3-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;
- 25 6-(4-Fluoro-3-methyl-phenyl)-3-methyl-1-(4-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-(4-Fluoro-3-methyl-phenyl)-3-methyl-1-(pyrazin-2-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 30 6-(4-Fluoro-3-methyl-phenyl)-3-methyl-1-(pyrimidin-5-ylmethyl)imidazo[4,5-b]pyridin-2-one;

- 6-(4-Fluoro-3-methyl-phenyl)-3-methyl-1-(pyrimidin-2-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-(4-Fluoro-3-methyl-phenyl)-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 5 6-(3-Fluorophenyl)-3-methyl-1-(3-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-(3-Fluorophenyl)-3-methyl-1-(4-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-(3-Fluorophenyl)-3-methyl-1-(2-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-(3-Fluorophenyl)-3-methyl-1-(pyrimidin-5-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-(3-Fluorophenyl)-3-methyl-1-(pyrazin-2-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 10 6-(3-Fluorophenyl)-3-methyl-1-(pyrimidin-2-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-(3-Fluorophenyl)-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-(3,4-Difluorophenyl)-3-methyl-1-(4-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-(3,4-Difluorophenyl)-3-methyl-1-(3-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-(3,4-Difluorophenyl)-3-methyl-1-(pyrimidin-5-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 15 6-(3,4-Difluorophenyl)-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-(3,4-difluorophenyl)-3-methyl-1-(2-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-(3,4-Difluorophenyl)-3-methyl-1-(pyrazin-2-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-(3,4-Difluorophenyl)-3-methyl-1-(pyrimidin-2-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-(pyrimidin-2-ylmethyl)imidazo[4,5-
- 20 b]pyridin-2-one;
- 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-(4-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 25 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-(2-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-(pyrimidin-5-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-(3,4-Difluorophenyl)-3-methyl-1-(pyrimidin-4-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 30 6-(4-Fluoro-3-methyl-phenyl)-3-methyl-1-(pyrimidin-4-ylmethyl)imidazo[4,5-b]pyridin-2-one;

- 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-(pyrimidin-4-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-(3,4-Difluorophenyl)-3-methyl-1-[(5-methyl-1,3,4-oxadiazol-2-yl)methyl]imidazo[4,5-b]pyridin-2-one;
- 5 3-Methyl-1-[(5-methylisoxazol-3-yl)methyl]-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;
- 3-Methyl-1-[(5-methyl-1,3,4-oxadiazol-2-yl)methyl]-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;
- 3-Methyl-1-[(3-methyl-1,2,4-oxadiazol-5-yl)methyl]-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;
- 10 6-(3,4-Difluorophenyl)-3-methyl-1-[(3-methyl-1,2,4-oxadiazol-5-yl)methyl]imidazo[4,5-b]pyridin-2-one;
- N,N-Dimethyl-2-[3-methyl-6-(5-methyl-2-thienyl)-2-oxo-imidazo[4,5-b]pyridin-1-yl]acetamide;
- 15 2-[6-(5-Ethyl-2-thienyl)-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethylacetamide;
- N,N-Dimethyl-2-[3-methyl-6-(4-methyl-2-thienyl)-2-oxo-imidazo[4,5-b]pyridin-1-yl]acetamide;
- 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(5-fluoro-2-thienyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 20 2-[6-(5-Fluoro-2-thienyl)-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethylacetamide;
- 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-6-(5-fluoro-2-thienyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 25 3-Methyl-1-(pyridazin-3-ylmethyl)-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;
- 6-(5-Fluoro-2-thienyl)-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-(4-methylthiazol-2-yl)imidazo[4,5-b]pyridin-2-one;
- 30 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(5-ethyl-2-thienyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;

6-(5-Ethyl-2-thienyl)-1-[2-(3-fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;

1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[5-(hydroxymethyl)-2-thienyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;

5 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-6-[5-(hydroxymethyl)-2-thienyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;

2-[6-[5-(Hydroxymethyl)-2-thienyl]-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

10 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[2-(trifluoromethyl)-3-thienyl]imidazo[4,5-b]pyridin-2-one;

1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[5-(difluoromethyl)-2-thienyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;

2-[6-[5-(Difluoromethyl)-2-thienyl]-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

15 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[2-(trifluoromethyl)-3-thienyl]imidazo[4,5-b]pyridin-2-one;

N,N-Dimethyl-2-[3-methyl-2-oxo-6-[2-(trifluoromethyl)-3-thienyl]imidazo[4,5-b]pyridin-1-yl]acetamide;

20 2-[6-[5-(Difluoromethyl)-3-thienyl]-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[5-(difluoromethyl)-3-thienyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;

6-[5-(Difluoromethyl)-3-thienyl]-1-[2-(3-fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;

25 6-[5-(Difluoromethyl)-2-thienyl]-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;

N,N-Dimethyl-2-[3-methyl-2-oxo-6-[5-(trifluoromethyl)-3-thienyl]imidazo[4,5-b]pyridin-1-yl]acetamide;

30 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[5-(trifluoromethyl)-3-thienyl]imidazo[4,5-b]pyridin-2-one;

3-Methyl-1-(pyridazin-3-ylmethyl)-6-[5-(trifluoromethyl)-3-thienyl]imidazo[4,5-b]pyridin-2-one;

1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[5-(trifluoromethyl)-3-thienyl]imidazo[4,5-b]pyridin-2-one;

5 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(5-cyclopropyl-2-thienyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;

6-(5-Cyclopropyl-2-thienyl)-1-[2-(3-fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;

10 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[2-(trifluoromethyl)thiazol-4-yl]imidazo[4,5-b]pyridin-2-one;

N,N-Dimethyl-2-[3-methyl-2-oxo-6-[2-(trifluoromethyl)thiazol-4-yl]imidazo[4,5-b]pyridin-1-yl]acetamide;

1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[2-(trifluoromethyl)thiazol-4-yl]imidazo[4,5-b]pyridin-2-one;

15 2-[6-(5-Cyclopropyl-2-thienyl)-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[5-(1,1,2,2,2-pentafluoroethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;

20 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-(2-methylthiazol-5-yl)imidazo[4,5-b]pyridin-2-one;

1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-(2-methylthiazol-5-yl)imidazo[4,5-b]pyridin-2-one;

N,N-Dimethyl-2-[3-methyl-6-(2-methylthiazol-5-yl)-2-oxo-imidazo[4,5-b]pyridin-1-yl]acetamide;

25 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[2-(trifluoromethyl)thiazol-5-yl]imidazo[4,5-b]pyridin-2-one;

1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[2-(trifluoromethyl)thiazol-5-yl]imidazo[4,5-b]pyridin-2-one;

30 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[4-(difluoromethyl)-2-thienyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;

- 6-[4-(Difluoromethyl)-2-thienyl]-1-[2-(3-fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- N,N-Dimethyl-2-[3-methyl-2-oxo-6-[2-(trifluoromethyl)thiazol-5-yl]imidazo[4,5-b]pyridin-1-yl]acetamide;
- 5 1-(2-(Azetidin-1-yl)-2-oxoethyl)-3-methyl-6-(5-(trifluoromethyl)thiophen-2-yl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one-7-D;
- N,N-Dimethyl-2-[3-methyl-2-oxo-6-[5-(trideuteriomethoxymethyl)-2-thienyl]imidazo[4,5-b]pyridin-1-yl]acetamide;
- 10 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[5-(trideuteriomethoxymethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;
- 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[5-(trideuteriomethoxymethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;
- 1-(2-(Azetidin-1-yl)-2-oxoethyl)-3-methyl-6-(5-(trifluoromethyl)thiophen-2-yl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one-7-T;
- 15 1-[(5-Methylisoxazol-3-yl)methyl]-6-(4-methyl-2-thienyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 1-[(5-Methylisoxazol-3-yl)methyl]-6-(o-tolyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 1-[(3-Methyl-1,2,4-oxadiazol-5-yl)methyl]-6-(4-methyl-2-thienyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 20 6-(4-Fluorophenyl)-1-[(1-methylpyrazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(4-Fluoro-3-methyl-phenyl)-1-[(1-methylpyrazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(3-Chloro-4-fluoro-phenyl)-1-[(1-methylpyrazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 25 6-(3,4-Difluorophenyl)-1-[(1-methylpyrazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(2,4-Difluorophenyl)-1-[(1-methylpyrazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- (R/S)-3-methyl-1-(oxetan-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;
- 30 Ethyl 2-[2-oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-yl]acetate;

2-[2-Oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-yl]acetic acid;

Ethyl 2-[3-methyl-2-oxo-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-1-yl]acetate;

2-[3-Methyl-2-oxo-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-1-yl]acetic acid;

1-[2-(3,3-difluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;

6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-(pyrazin-2-ylmethyl)imidazo[4,5-b]pyridin-2-one;

6-(4-Fluorophenyl)-1-[(3-methyl-1,2,4-oxadiazol-5-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;

6-(4-Fluorophenyl)-1-[(1-methyl-1,2,4-triazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;

6-(4-Fluorophenyl)-1-[(1-methyltriazol-4-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;

6-(3,4-Difluorophenyl)-1-[(3-methyl-1,2,4-oxadiazol-5-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;

6-(3,4-Difluorophenyl)-1-[(5-methyl-1,2,4-oxadiazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;

6-(3,4-Difluorophenyl)-1-[[3-(methoxymethyl)-1,2,4-oxadiazol-5-yl]methyl]-3H-imidazo[4,5-b]pyridin-2-one;

1-(2-Pyrrolidin-1-ylethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;

1-[2-(3-Hydroxyazetidin-1-yl)ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;

1-[2-(Cyclopropylamino)ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;

1-[2-(3-Methoxyazetidin-1-yl)ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;

1-[2-(Cyclobutylamino)ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;

1-[2-(Azetidin-1-yl)ethyl]-6-(4-fluoro-2-methyl-phenyl)-3H-imidazo[4,5-b]pyridin-2-one;

- 1-[2-(Azetidin-1-yl)ethyl]-6-(o-tolyl)-3H-imidazo[4,5-b]pyridin-2-one;  
 1-[2-(Azetidin-1-yl)ethyl]-6-phenyl-3H-imidazo[4,5-b]pyridin-2-one;  
 1-[2-(Azetidin-1-yl)ethyl]-6-(m-tolyl)-3H-imidazo[4,5-b]pyridin-2-one;  
 1-[2-(Azetidin-1-yl)ethyl]-6-[2-(trifluoromethyl)-4-pyridyl]-3H-imidazo[4,5-b]pyridin-2-  
 5 one;  
 1-[2-(Azetidin-1-yl)ethyl]-6-(4-fluoro-3-methyl-phenyl)-3H-imidazo[4,5-b]pyridin-2-  
 one;  
 1-[2-(Azetidin-1-yl)ethyl]-6-(2,6-dimethylphenyl)-3H-imidazo[4,5-b]pyridin-2-one;  
 1-[2-(Azetidin-1-yl)ethyl]-6-(3-chlorophenyl)-3H-imidazo[4,5-b]pyridin-2-one;  
 10 1-[2-(Azetidin-1-yl)ethyl]-6-(3,5-difluorophenyl)-3H-imidazo[4,5-b]pyridin-2-one;  
 1-[2-(Azetidin-1-yl)ethyl]-6-[3-(trifluoromethoxy)phenyl]-3H-imidazo[4,5-b]pyridin-2-  
 one;  
 1-[2-(1-Piperidyl)ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;  
 1-[2-(4-Fluoro-1-piperidyl)ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-  
 15 b]pyridin-2-one;  
 1-[2-(3-Fluoroazetidin-1-yl)ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-  
 b]pyridin-2-one;  
 1-[2-(3-Methylpyrrolidin-1-yl)ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-  
 b]pyridin-2-one;  
 20 1-[2-(4-Hydroxy-1-piperidyl)ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-  
 b]pyridin-2-one;  
 1-[2-[3-(Trifluoromethyl)azetidin-1-yl]ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-  
 imidazo[4,5-b]pyridin-2-one;  
 1-[2-(3,3-Difluoroazetidin-1-yl)ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-  
 25 b]pyridin-2-one;  
 1-[2-(Azetidin-1-yl)ethyl]-6-[2-methyl-3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-  
 b]pyridin-2-one;  
 1-[2-(Azetidin-1-yl)ethyl]-6-(2,3-dimethylphenyl)-3H-imidazo[4,5-b]pyridin-2-one;  
 1-[2-(Azetidin-1-yl)ethyl]-6-(3,5-dimethylphenyl)-3H-imidazo[4,5-b]pyridin-2-one;  
 30 1-[2-(Azetidin-1-yl)ethyl]-6-(4-fluoro-2,3-dimethyl-phenyl)-3H-imidazo[4,5-b]pyridin-2-  
 one;

- 1-[2-(Azetidin-1-yl)ethyl]-6-[2-methyl-5-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(3,5-Difluorophenyl)-1-[2-(2-hydroxyethylamino)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 5 6-(3,5-Difluorophenyl)-1-(2-pyrrolidin-1-ylethyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(3,5-Difluorophenyl)-1-[2-(3-hydroxypyrrolidin-1-yl)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(3,5-Difluorophenyl)-1-[2-(3-methoxypyrrolidin-1-yl)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 10 6-(4-Fluoro-2-methyl-phenyl)-1-(2-pyrrolidin-1-ylethyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(2,6-Dimethylphenyl)-1-(2-pyrrolidin-1-ylethyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(o-Tolyl)-1-(2-pyrrolidin-1-ylethyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 6-Phenyl-1-(2-pyrrolidin-1-ylethyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 15 1-[2-(3-Fluoroazetidin-1-yl)ethyl]-6-[2-methyl-3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(2,3-Dimethylphenyl)-1-[2-(3-fluoroazetidin-1-yl)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(3,5-Dimethylphenyl)-1-[2-(3-fluoroazetidin-1-yl)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 20 1-[2-(3-Fluoroazetidin-1-yl)ethyl]-6-(4-fluoro-2,3-dimethyl-phenyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 1-[2-(3-Fluoroazetidin-1-yl)ethyl]-6-[2-methyl-5-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 25 1-[2-(3-Fluoroazetidin-1-yl)ethyl]-6-(o-tolyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 1-[2-(3-Fluoroazetidin-1-yl)ethyl]-6-(4-fluoro-2-methyl-phenyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 1-[2-(3-Fluoroazetidin-1-yl)ethyl]-6-phenyl-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(3,5-Difluorophenyl)-1-[2-(propylamino)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 30 N-Cyclobutyl-2-[2-oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;

1-[2-(3-Methoxyazetidin-1-yl)-2-oxo-ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;

N-(Oxetan-3-yl)-2-[2-oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;

5 1-[2-(4-Methylpiperazin-1-yl)-2-oxo-ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;

1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;

10 N-(3,3-Difluorocyclobutyl)-2-[2-oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;

1-[2-(3,3-Difluoropyrrolidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;

3-Methyl-1-(2-oxo-2-pyrrolidin-1-yl-ethyl)-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;

15 N-(3,3-Difluoro-1-methyl-cyclobutyl)-2-[3-methyl-2-oxo-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-1-yl]acetamide;

N-(3-Methyloxetan-3-yl)-2-[3-methyl-2-oxo-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-1-yl]acetamide;

20 N-(3,3-Difluorocyclobutyl)-2-[3-methyl-2-oxo-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-1-yl]acetamide;

1-(2-Oxo-2-pyrrolidin-1-yl-ethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;

(R/S)-N-Cyclopropyl-2-[2-oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-yl]propanamide;

25 (R/S)-1-[2-(Azetidin-1-yl)-1-methyl-2-oxo-ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;

1-(2-Morpholino-2-oxo-ethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;

30 N-Cyclopentyl-2-[2-oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;

- 1-[2-Oxo-2-(1-piperidyl)ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 1-[2-(2,6-Diazaspiro[3.3]heptan-6-yl)-2-oxo-ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 5 2-[2-Oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-yl]-N-(2-pyridyl)acetamide;
- N-(3,3-Difluoro-1-methyl-cyclobutyl)-2-[2-oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;
- 10 1-[(6-Methoxy-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 1-(Cyclopropylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 3-[[2-Oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;
- 2-[[2-Oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;
- 15 1-[2-Oxo-2-(2-thienyl)ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 1-(2-Oxo-2-thiazol-2-yl-ethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 20 (R/S)-1-(Oxetan-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- (R/S)-1-(Morpholin-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- (R/S)-1-(Tetrahydropyran-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 25 6-[3-(Trifluoromethyl)phenyl]-1-[[4-(trifluoromethyl)phenyl]methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 1-[(3-Fluoro-4-methoxy-phenyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 30 1-[(4-Fluoro-3-methyl-phenyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;

- 1-[(3-Fluorophenyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- (R\*)-1-(Oxetan-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 5 (S\*)-1-(Oxetan-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- (R/S)-1-[(2,2-Difluorocyclopropyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 1-[(3-Fluorooxetan-3-yl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 10 1-(Pyrimidin-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 1-(2-Pyridylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 1-(4-Pyridylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 1-(3-Pyridylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 15 1-[(2-Methylpyrimidin-5-yl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 1-(Pyridazin-3-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 1-[(3-Methoxy-2-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 20 1-[(3-Fluoro-5-methyl-2-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 1-[(6-Methyl-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 1-(2H-Tetrazol-5-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 25 1-[Difluoro(3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 1-[(6-Fluoro-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 30 1-(2-Cyclopropyl-2-oxo-ethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;

- 1-(2-Oxobutyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;  
 1-(3-Methyl-2-oxo-butyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;  
 1-[(5-Methyl-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-  
 5 2-one;  
 1-(Thiadiazol-4-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;  
 1-[(6-Oxo-1H-pyridin-3-yl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;  
 10 (R/S)-1-(Azetidin-2-ylmethyl)-3-methyl-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;  
 3-Methyl-1-(pyrimidin-4-ylmethyl)-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;  
 3-Methyl-1-(pyrimidin-5-ylmethyl)-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-  
 15 2-one;  
 3-Methyl-1-[(2-methylpyrimidin-4-yl)methyl]-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;  
 3-Methyl-1-(pyrazin-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;  
 20 3-Methyl-1-(4-pyridylmethyl)-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;  
 3-Methyl-1-(2-pyridylmethyl)-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;  
 1-[(6-Methoxypyridazin-3-yl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;  
 1-(Pyrazin-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;  
 25 1-[(2-Methylpyrimidin-4-yl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;  
 1-(Pyrimidin-5-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;  
 1-[(5-Fluoropyrimidin-2-yl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;  
 30 6-[3-(Trifluoromethyl)phenyl]-1-[[6-(trifluoromethyl)-3-pyridyl]methyl]-3H-imidazo[4,5-b]pyridin-2-one;

- 1-[(5-Fluoro-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 6-[3-(Trifluoromethyl)phenyl]-1-[[5-(trifluoromethyl)-3-pyridyl]methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 5 6-[3-(Trifluoromethyl)phenyl]-1-[[4-(trifluoromethyl)-3-pyridyl]methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 3-Methyl-1-(pyrimidin-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;
- 1-(2-cyclobutyl-2-oxo-ethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 10 (R/S)-1-(Azetidin-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- (R/S)-1-(Azetidin-2-ylmethyl)-6-[2-fluoro-3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 15 (R/S)-1-(Azetidin-2-ylmethyl)-6-phenyl-3H-imidazo[4,5-b]pyridin-2-one;
- (R/S)-1-(Azetidin-2-ylmethyl)-6-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-one;
- (R/S)-1-(Azetidin-2-ylmethyl)-6-[4-fluoro-3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- (R/S)-1-(Azetidin-2-ylmethyl)-6-(2,3-dichlorophenyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 20 6-(4-Fluoro-3-methyl-phenyl)-1-[(5-methyl-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(2,4-Difluoro-3-methyl-phenyl)-1-[(5-methyl-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- (R/S)-6-[4-Fluoro-3-(trifluoromethyl)phenyl]-1-(oxetan-2-ylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 25 6-(3,4-Difluorophenyl)-1-[(5-methyl-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(3-Chlorophenyl)-1-[(5-methyl-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(3-Fluorophenyl)-1-[(5-methyl-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(3,4-Difluorophenyl)-1-[(4-methyl-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 30 6-(3-Fluorophenyl)-1-[(4-methyl-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;

- 6-(4-Fluoro-3-methyl-phenyl)-1-[(4-methyl-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(2,4-Difluoro-3-methyl-phenyl)-1-[(4-methyl-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 5 6-(3,4-Difluorophenyl)-1-(2-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(2,4-Difluoro-3-methyl-phenyl)-1-(2-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(3-Fluorophenyl)-1-(2-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(3-Chlorophenyl)-1-(2-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(4-Fluoro-3-methyl-phenyl)-1-(2-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 10 6-(3,4-Difluorophenyl)-1-[(3-methyl-2-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(3-Fluorophenyl)-1-[(3-methyl-2-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(4-Fluorophenyl)-1-(2-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 6-[3-(Difluoromethyl)phenyl]-1-(2-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(3-Methoxyphenyl)-1-(2-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 15 6-(p-Tolyl)-1-(2-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(3-fluorophenyl)-1-(3-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 6-[3-(Difluoromethyl)phenyl]-1-(3-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(3,4-Difluorophenyl)-1-(3-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(2,4-Difluoro-3-methyl-phenyl)-1-(3-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 20 6-(4-Fluoro-3-methyl-phenyl)-1-(3-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(4-Fluorophenyl)-1-(3-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(3-Chlorophenyl)-1-(3-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(m-Tolyl)-1-(3-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(3,4-Difluorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 25 6-(4-Fluoro-3-methyl-phenyl)-1-[(5-fluoro-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 6-[3-(Difluoromethoxy)phenyl]-1-(3-pyridylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(2,4-Difluoro-3-methyl-phenyl)-1-[(5-fluoro-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 30 6-[3-(Difluoromethyl)phenyl]-1-[(5-fluoro-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;

6-(2,3-Difluorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;

6-[3-(Difluoromethoxy)phenyl]-1-[(5-fluoro-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;

6-(3-Chlorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;

5 6-(4-Chloro-3-methyl-phenyl)-1-[(5-fluoro-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;

1-[(5-Fluoro-3-pyridyl)methyl]-6-[3-(trifluoromethoxy)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;

10 1-[(5-Methyl-3-pyridyl)methyl]-6-(3,4,5-trifluorophenyl)-3H-imidazo[4,5-b]pyridin-2-one;

6-[4-Fluoro-3-(trifluoromethyl)phenyl]-1-[(5-methyl-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;

6-(2,3-Difluorophenyl)-1-[(5-methyl-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;

6-(3,5-Difluorophenyl)-1-[(5-methyl-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;

15 1-[(4-Methyl-3-pyridyl)methyl]-6-(3,4,5-trifluorophenyl)-3H-imidazo[4,5-b]pyridin-2-one;

1-[(4-Methyl-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;

20 6-[4-Fluoro-3-(trifluoromethyl)phenyl]-1-[(4-methyl-3-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;

1-[(3-Methyl-2-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;

6-(4-Fluoro-3-methyl-phenyl)-1-[(3-methyl-2-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;

25 6-(2,4-Difluoro-3-methyl-phenyl)-1-[(3-methyl-2-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;

6-(3,5-Difluorophenyl)-1-[(3-methyl-2-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;

6-(2,3-Difluorophenyl)-1-[(3-methyl-2-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;

30 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(4-fluoro-2-methyl-phenyl)-3H-imidazo[4,5-b]pyridin-2-one;

2-[6-(5-Chloro-4-methyl-2-thienyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

2-[6-(5-Chloro-4-methyl-2-thienyl)-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

5 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[5-(trifluoromethyl)-2-thienyl]-3H-imidazo[4,5-b]pyridin-2-one;

1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(5-chloro-4-methyl-2-thienyl)-3H-imidazo[4,5-b]pyridin-2-one;

10 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(5-chloro-4-methyl-2-thienyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;

1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-(5-methyl-2-thienyl)imidazo[4,5-b]pyridin-2-one;

1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;

15 3-Methyl-1-(2-oxo-2-pyrrolidin-1-yl-ethyl)-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;

1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[2-methyl-3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;

6-(3,4-Difluorophenyl)-1-(2-oxobutyl)-3H-imidazo[4,5-b]pyridin-2-one;

20 6-(4-Fluoro-3-methyl-phenyl)-1-(2-oxobutyl)-3H-imidazo[4,5-b]pyridin-2-one;

6-(m-Tolyl)-1-(2-oxobutyl)-3H-imidazo[4,5-b]pyridin-2-one;

(R/S)-6-(3,4-Difluorophenyl)-1-(2-hydroxybutyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;

25 (R/S)-6-(4-Fluoro-3-methyl-phenyl)-1-(2-hydroxybutyl)-3H-imidazo[4,5-b]pyridin-2-one;

(R/S)-1-(2-Hydroxybutyl)-6-(m-tolyl)-3H-imidazo[4,5-b]pyridin-2-one;

(R/S)-6-(2,4-difluoro-3-methyl-phenyl)-1-(2-hydroxybutyl)-3H-imidazo[4,5-b]pyridin-2-one;

30 (R/S)-1-(2-Hydroxybutyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;

- (R/S)-1-(2-Hydroxy-3-methyl-butyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-(3-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;
- 5 6-(4-Fluoro-3-methyl-phenyl)-1-[(5-fluoro-3-pyridyl)methyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 6-(2,4-Difluoro-3-methyl-phenyl)-1-[(5-fluoro-3-pyridyl)methyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 10 6-[3-(Difluoromethoxy)phenyl]-1-[(5-fluoro-3-pyridyl)methyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 6-(3,4-Difluorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 1-[(5-Fluoro-3-pyridyl)methyl]-3-methyl-6-(3,4,5-trifluorophenyl)imidazo[4,5-b]pyridin-2-one;
- 15 1-[(5-Fluoro-3-pyridyl)methyl]-3-methyl-6-[3-(trifluoromethoxy)phenyl]imidazo[4,5-b]pyridin-2-one;
- 6-(2,3-Difluorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 1-[(5-Fluoro-3-pyridyl)methyl]-3-methyl-6-(2,3,4-trifluorophenyl)imidazo[4,5-b]pyridin-2-one;
- 20 6-(3-Chlorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 6-(3-Chloro-2-fluoro-phenyl)-1-[(5-fluoro-3-pyridyl)methyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 25 1-[(5-Fluoro-3-pyridyl)methyl]-3-methyl-6-(m-tolyl)imidazo[4,5-b]pyridin-2-one;
- 6-(3,4-Dichlorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 6-(2-Fluoro-3-methyl-phenyl)-1-[(5-fluoro-3-pyridyl)methyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 30 3-Methyl-1-(3-pyridylmethyl)-6-(3,4,5-trifluorophenyl)imidazo[4,5-b]pyridin-2-one;
- 6-(3,5-Difluorophenyl)-3-methyl-1-(3-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;

- 6-(3-Chloro-4-fluoro-phenyl)-3-methyl-1-(3-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;
- 3-Methyl-6-(m-tolyl)-1-(3-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-(2-Fluoro-3-methyl-phenyl)-3-methyl-1-(3-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;
- 5 6-[2-Fluoro-3-(trifluoromethyl)phenyl]-3-methyl-1-(3-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-(3-Chloro-2-fluoro-phenyl)-3-methyl-1-(3-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;
- 10 6-[4-Fluoro-3-(trifluoromethyl)phenyl]-3-methyl-1-(3-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;
- 3-Methyl-1-(3-pyridylmethyl)-6-(2,3,4-trifluorophenyl)imidazo[4,5-b]pyridin-2-one;
- 3-Methyl-1-(3-pyridylmethyl)-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;
- 6-[3-(Difluoromethyl)phenyl]-3-methyl-1-(3-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;
- 15 3-Methyl-1-(3-pyridylmethyl)-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;
- 6-(5-Chloro-4-methyl-2-thienyl)-3-methyl-1-(3-pyridylmethyl)imidazo[4,5-b]pyridin-2-one;
- 20 1-[(5-Chloro-3-pyridyl)methyl]-3-methyl-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;
- 1-[(5-Chloro-3-pyridyl)methyl]-6-(4-fluoro-3-methyl-phenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 1-[(5-Chloro-3-pyridyl)methyl]-6-(2,4-difluoro-3-methyl-phenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 25 1-[(5-Chloro-3-pyridyl)methyl]-6-(3,4-difluorophenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 1-[(5-Chloro-3-pyridyl)methyl]-3-methyl-6-(3,4,5-trifluorophenyl)imidazo[4,5-b]pyridin-2-one;
- 30 1-[(5-Chloro-3-pyridyl)methyl]-6-(2-fluoro-3-methyl-phenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;

- 6-(5-Chloro-4-methyl-2-thienyl)-1-[(5-chloro-3-pyridyl)methyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 1-[(5-Chloro-3-pyridyl)methyl]-3-methyl-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;
- 5 1-[(5-Chloro-3-pyridyl)methyl]-3-methyl-6-(m-tolyl)imidazo[4,5-b]pyridin-2-one;
- 1-[(5-Chloro-3-pyridyl)methyl]-6-(2,3-difluorophenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 6-(3-Chlorophenyl)-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-[3-(Difluoromethyl)phenyl]-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 10 3-Methyl-1-(pyridazin-3-ylmethyl)-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;
- 3-Methyl-6-(m-tolyl)-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-(3-Chloro-4-fluoro-phenyl)-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 15 6-(3-Fluoro-5-methyl-phenyl)-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-[4-Fluoro-3-(trifluoromethyl)phenyl]-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 20 6-[3-Fluoro-5-(trifluoromethyl)phenyl]-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-[4-Chloro-3-(trifluoromethyl)phenyl]-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-[3,4-Difluoro-5-(trifluoromethyl)phenyl]-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 25 3-Methyl-1-(2-oxobutyl)-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;
- 6-(4-Fluoro-3-methyl-phenyl)-3-methyl-1-(2-oxobutyl)imidazo[4,5-b]pyridin-2-one;
- 6-(3,4-Difluorophenyl)-3-methyl-1-(2-oxobutyl)imidazo[4,5-b]pyridin-2-one;
- 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-(2-oxobutyl)imidazo[4,5-b]pyridin-2-one;
- 30 6-(3-Cyclopropylphenyl)-3-methyl-1-(2-oxobutyl)imidazo[4,5-b]pyridin-2-one;

- (R/S)-6-(4-Fluoro-3-methyl-phenyl)-1-(2-hydroxy-4-methoxy-butyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;
- (R/S)-6-[3-(Difluoromethyl)phenyl]-3-methyl-1-(oxetan-2-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 5 (R/S)-6-(4-Fluoro-3-methyl-phenyl)-3-methyl-1-(oxetan-2-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- (R/S)-6-[2-Fluoro-3-(trifluoromethyl)phenyl]-3-methyl-1-(oxetan-2-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- (R/S)-6-(3-Chlorophenyl)-3-methyl-1-(oxetan-2-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 10 (R/S)-3-Methyl-6-[2-methyl-3-(trifluoromethyl)phenyl]-1-(oxetan-2-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- (R/S)-1-(2,4-Dihydroxybutyl)-3-methyl-6-[2-methyl-3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;
- 6-(2,4-Difluoro-3-methyl-phenyl)-1-[2-(3-fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 15 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-6-(4-fluoro-3-methyl-phenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-(3,4,5-trifluorophenyl)imidazo[4,5-b]pyridin-2-one;
- 20 6-(3,4-Difluorophenyl)-1-[2-(3-fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-(m-tolyl)imidazo[4,5-b]pyridin-2-one;
- 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-6-(2-fluoro-3-methyl-phenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 25 6-(3-Chlorophenyl)-1-[2-(3-fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-6-[4-fluoro-3-(trifluoromethyl)phenyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 30 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;

- 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(2,4-difluoro-3-methyl-phenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(4-fluoro-3-methyl-phenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 5 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-(3,4,5-trifluorophenyl)imidazo[4,5-b]pyridin-2-one;
- 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(3,5-difluorophenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 10 1-(2-(3,3-Difluoroazetidin-1-yl)-2-oxoethyl)-6-(4-fluoro-3-methylphenyl)-3-methyl-1H-imidazo[4,5-b]pyridin-2(3H)-one;
- 1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]-6-(2,4-difluoro-3-methyl-phenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]-6-[2-fluoro-3-(trifluoromethyl)phenyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 15 1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]-6-(3,4-difluorophenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]-6-(3-fluorophenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]-6-(2-fluoro-3-methyl-phenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 20 N,N-Dimethyl-2-[3-methyl-2-oxo-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-1-yl]acetamide;
- 2-[6-(4-Fuoro-3-methyl-phenyl)-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
- 25 2-[6-(3,4-Difluorophenyl)-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
- 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(3,4-difluorophenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 2-[6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
- 30

2-[6-[2-Fluoro-3-(trifluoromethyl)phenyl]-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-  
N,N-dimethyl-acetamide;

2-[6-(2,3-Difluorophenyl)-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-  
acetamide;

5 2-[6-[3-(Difluoromethyl)phenyl]-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-  
dimethyl-acetamide;

2-[6-(2-Fluoro-3-methyl-phenyl)-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-  
dimethyl-acetamide;

10 2-[6-(3,5-Difluorophenyl)-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-  
acetamide;

N,N-Dimethyl-2-[3-methyl-2-oxo-6-(3-pyridyl)imidazo[4,5-b]pyridin-1-yl]acetamide;

1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[5-(trifluoromethyl)-2-  
thienyl]imidazo[4,5-b]pyridin-2-one;

15 2-[6-[3,4-Difluoro-5-(trifluoromethyl)phenyl]-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-  
yl]-N,N-dimethyl-acetamide;

2-[2-Oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;

2-[6-(4-Fluoro-2-methoxy-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;

2-[6-(3-Chloro-4-fluoro-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;

20 N-Methyl-2-[2-oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-  
yl]acetamide;

2-[6-(4-Chlorophenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-methyl-acetamide;

2-[6-(4-Fluoro-2-methyl-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-methyl-  
acetamide;

2-[6-(3,5-Dimethylphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-methyl-acetamide;

25 2-[6-(4-Methoxy-3-methyl-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-methyl-  
acetamide;

2-[6-(4-Fluoro-2-methoxy-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-methyl-  
acetamide;

2-[6-(2-Ethoxyphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-methyl-acetamide;

30 N-(2-Methoxyethyl)-2-[2-oxo-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-1-  
yl]acetamide;

- 2-[6-(2-Ethoxy-5-fluoro-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-(2-methoxyethyl)acetamide;
- N-(2-Methoxyethyl)-2-[6-(4-methoxyphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;
- 5 N-(2-Methoxyethyl)-2-[2-oxo-6-(3-pyridyl)-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;
- 2-[6-(4-Fluoro-2-methoxy-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-(2-methoxyethyl)acetamide;
- N-Cyclopropyl-2-[6-(3,5-difluorophenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;
- 10 2-[6-(3-Chloro-4-fluoro-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-cyclopropyl-acetamide;
- N-Cyclopropyl-2-[6-(3-ethoxyphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;
- N-Cyclopropyl-2-[6-(3-methoxyphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;
- 15 N-Cyclopropyl-2-[6-(4-methoxy-3-methyl-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;
- N-Cyclopropyl-2-[6-(4-fluoro-2-methoxy-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;
- 2-[6-(4-Chlorophenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-cyclopropyl-acetamide;
- 20 N-Cyclopropyl-2-[6-(2,4-dimethoxyphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;
- N-Cyclopropyl-2-[6-(2-fluoro-6-methoxy-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;
- N-Cyclopropyl-2-[6-(2-ethoxyphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;
- 25 6-(3-Fluoro-4-methoxy-phenyl)-1-[2-oxo-2-(2-thienyl)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(2-Ethoxyphenyl)-1-[2-oxo-2-(2-thienyl)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(4-Chlorophenyl)-1-[2-oxo-2-(2-thienyl)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(2-Ethoxy-5-fluoro-phenyl)-1-[2-oxo-2-(2-thienyl)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 30 one;
- 6-(4-Methoxyphenyl)-1-[2-oxo-2-(2-thienyl)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;

- 6-(4-Fluoro-2-methoxy-phenyl)-1-[2-oxo-2-(2-thienyl)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(3-Ethoxyphenyl)-1-[2-oxo-2-(2-thienyl)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(3-Chloro-4-fluoro-phenyl)-1-[2-oxo-2-(2-thienyl)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 1-(Cyclopropylmethyl)-6-(2,4-dimethoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 1-(Cyclopropylmethyl)-6-(2-ethoxy-5-fluoro-phenyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 1-(Cyclopropylmethyl)-6-(4-fluoro-2-methoxy-phenyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 1-(Cyclopropylmethyl)-6-(4-methoxy-3-methyl-phenyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 1-(Cyclopropylmethyl)-6-(3-fluoro-4-methoxy-phenyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 1-(Cyclopropylmethyl)-6-(3,5-difluorophenyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 1-(Cyclopropylmethyl)-6-(4-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 1-(Cyclopropylmethyl)-6-(2-thienyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 1-(Cyclopropylmethyl)-6-[3-(dimethylamino)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 1-(Cyclopropylmethyl)-6-(3,5-dimethylphenyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(3-Methoxyphenyl)-1-(tetrahydrofuran-2-ylmethyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 4-[[6-(4-Methoxyphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;
- 3-[[6-(4-Methoxyphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;
- 3-[[6-(4-Fluoro-2-methoxy-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;
- 3-[[6-(4-Fluoro-2-methyl-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;
- 3-[[6-(3-Chloro-4-fluoro-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;
- 2-[[6-(2-Fluoro-6-methoxy-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;
- 2-[[6-(4-Chlorophenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;

- 2-[[6-(4-Fluoro-2-methyl-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;
- 2-[[6-(2-Ethoxyphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;
- 2-[[6-(3-Methoxyphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;
- 5 2-[[6-(3-Cyanophenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;
- 2-[[6-(2,4-Dimethoxyphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;
- 2-[[6-(3,5-Dimethylphenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;
- 2-[[6-(2-Ethoxy-5-fluoro-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;
- 10 2-[[6-(4-Fluoro-2-methoxy-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;
- 2-[[6-(3-Fluoro-4-methoxy-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;
- 6-(4-Fluoro-2-methyl-phenyl)-1-[(4-fluorophenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 15 6-(2,3-Dimethoxyphenyl)-1-[(4-fluorophenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(2-Ethoxy-5-fluoro-phenyl)-1-[(3-fluorophenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(3,5-Dimethylphenyl)-1-[(3-fluorophenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 20 6-(2,4-Dimethoxyphenyl)-1-[(3-fluorophenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(2-Ethoxyphenyl)-1-[(3-fluorophenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 1-[(3-Fluorophenyl)methyl]-6-(4-methoxy-3-methyl-phenyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(4-Fluoro-2-methoxy-phenyl)-1-[(3-fluorophenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 25 6-[3-(Dimethylamino)phenyl]-1-[(3-fluorophenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(4-Fluoro-2-methoxy-phenyl)-1-[(4-fluorophenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 30 6-(3-Chloro-4-fluoro-phenyl)-1-[(4-fluorophenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;

- 6-(2-Ethoxyphenyl)-1-[(2-fluorophenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;  
 1-[(3-Chlorophenyl)methyl]-6-(3,5-difluorophenyl)-3H-imidazo[4,5-b]pyridin-2-one;  
 6-(4-Fluoro-2-methoxy-phenyl)-1-[(3-methoxyphenyl)methyl]-3H-imidazo[4,5-  
 b]pyridin-2-one;  
 5 1-[(3-Methoxyphenyl)methyl]-6-(3-pyridyl)-3H-imidazo[4,5-b]pyridin-2-one;  
 1-[(3-Methoxyphenyl)methyl]-6-(4-methyl-2-thienyl)-3H-imidazo[4,5-b]pyridin-2-one;  
 6-(3,5-Difluorophenyl)-1-[(4-methoxyphenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;  
 1-[(3,5-Dimethoxyphenyl)methyl]-6-(2-fluoro-6-methoxy-phenyl)-3H-imidazo[4,5-  
 b]pyridin-2-one;  
 10 1-[(3,5-Dimethoxyphenyl)methyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-  
 b]pyridin-2-one;  
 6-(4-Chlorophenyl)-1-[(4-isopropylphenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;  
 6-(4-tert-Butylphenyl)-1-[(3,4-dimethoxy-2-pyridyl)methyl]-3H-imidazo[4,5-b]pyridin-  
 2-one;  
 15 3-[1-[(3,5-Dimethylisoxazol-4-yl)methyl]-2-oxo-3H-imidazo[4,5-b]pyridin-6-  
 yl]benzonitrile;  
 1-[(3,5-Dimethylisoxazol-4-yl)methyl]-6-(2-ethoxy-5-fluoro-phenyl)-3H-imidazo[4,5-  
 b]pyridin-2-one;  
 6-(4-Methoxy-3-methyl-phenyl)-1-[(5-methylisoxazol-3-yl)methyl]-3H-imidazo[4,5-  
 b]pyridin-2-one;  
 20 6-(3,5-Dimethylphenyl)-1-[(5-methylisoxazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-  
 one;  
 6-(2-Ethoxyphenyl)-1-[(5-methylisoxazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-  
 one;  
 25 6-(2,4-Dimethoxyphenyl)-1-[(5-methylisoxazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-  
 2-one;  
 6-(3-Fluoro-4-methoxy-phenyl)-1-[(5-methylisoxazol-3-yl)methyl]-3H-imidazo[4,5-  
 b]pyridin-2-one;  
 6-(4-Fluoro-2-methoxy-phenyl)-1-[(5-methylisoxazol-3-yl)methyl]-3H-imidazo[4,5-  
 b]pyridin-2-one;  
 30

6-(2-Ethoxy-5-fluoro-phenyl)-1-[(5-methylisoxazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;

6-(4-Fluoro-2-methyl-phenyl)-1-[(5-methylisoxazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one; and

5 6-(3,5-Difluorophenyl)-1-[(5-methylisoxazol-3-yl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;

and pharmaceutically acceptable salts, solvates, or N-oxides or N-oxides thereof.

26. A compound selected from the group consisting of:

10 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;

N,N-Dimethyl-2-[3-methyl-2-oxo-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-1-yl]acetamide;

15 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[5-(trifluoromethyl)-2-thienyl]-3H-imidazo[4,5-b]pyridin-2-one;

1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(5-chloro-4-methyl-2-thienyl)-3H-imidazo[4,5-b]pyridin-2-one;

1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-6-(4-fluoro-3-methyl-phenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;

20 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(2,4-difluoro-3-methyl-phenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;

1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(4-fluoro-3-methyl-phenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one;

25 1-(2-(3,3-Difluoroazetidin-1-yl)-2-oxoethyl)-6-(4-fluoro-3-methylphenyl)-3-methyl-1H-imidazo[4,5-b]pyridin-2(3H)-one;

1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]-6-(2,4-difluoro-3-methyl-phenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one; and

2-[6-(4-Fuoro-3-methyl-phenyl)-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

30 and pharmaceutically acceptable salts, solvates, or N-oxides thereof.

27. A compound selected from the group consisting of:

1-(2-Oxo-2-(pyrrolidin-1-yl)ethyl)-6-(thiazol-5-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one;

1-(2-(3-hydroxy-3-methylazetidin-1-yl)-2-oxoethyl)-6-(5-methylpyridin-3-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one;

5 1-(2-(Azetidin-1-yl)-2-oxoethyl)-6-(6-fluoropyridin-3-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one;

1-(2-(2-Oxo-6-(3-(trifluoromethyl)phenyl)-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)acetyl)azetidine-3-carbonitrile;

1-Benzyl-6-(4-fluoro-3-(trifluoromethyl)phenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one;

10 1-(2-(3-Methylazetidin-1-yl)-2-oxoethyl)-6-(3-(trifluoromethyl)phenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one;

1-(2-(3-(Methoxymethyl)azetidin-1-yl)-2-oxoethyl)-6-(3-(trifluoromethyl)phenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one; and

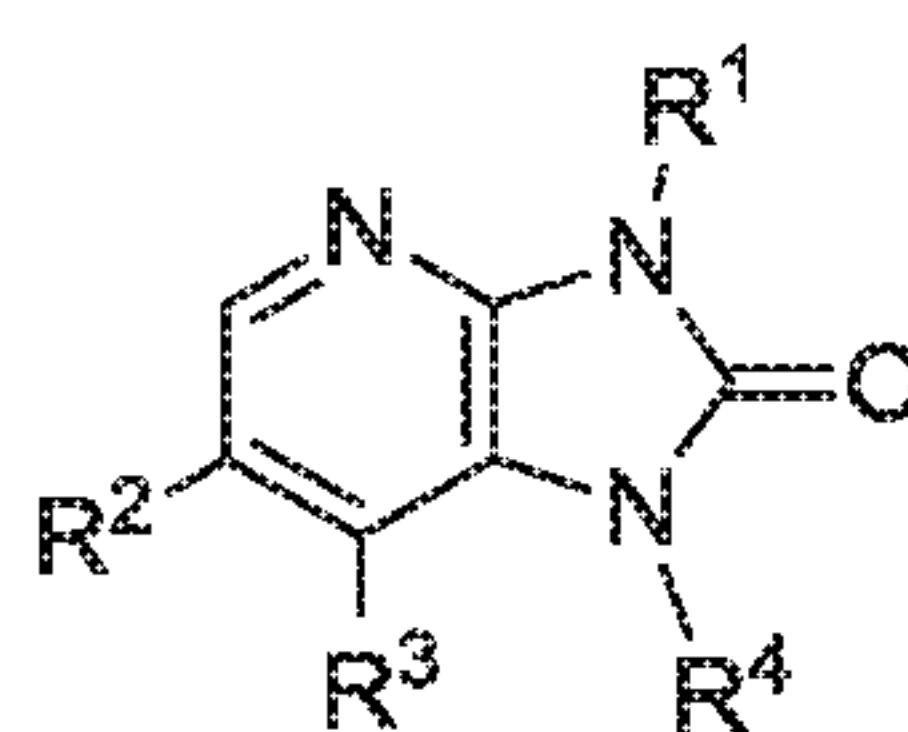
15 6-(2-Fluoro-3-methylphenyl)-1-(2-oxo-2-(3-(trifluoromethyl)azetidin-1-yl)ethyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one; and

pharmaceutically acceptable salts, solvates, or N-oxides thereof.

28. A pharmaceutical composition comprising:

(A) an effective amount of at least one compound selected from compounds of

20 Formula (I) wherein:



(I)

wherein

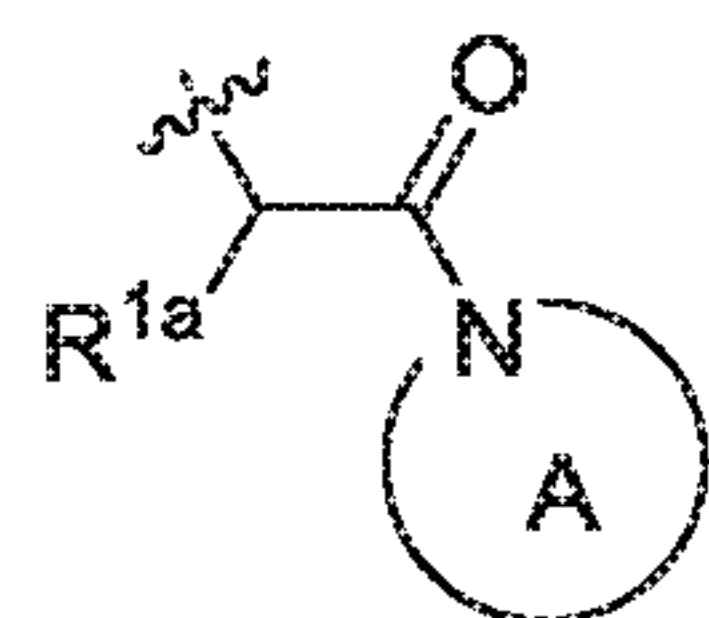
R<sup>1</sup> is H; CH<sub>2</sub>F; or CH<sub>3</sub>;

R<sup>2</sup> is selected from the group consisting of: phenyl; phenyl substituted with one, two,  
25 or three members each independently selected from the group consisting of:  
halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>haloalkyl, CN, OC<sub>1-6</sub>alkyl, OC<sub>1-6</sub>haloalkyl, N(CH<sub>3</sub>)<sub>2</sub>, and  
cyclopropyl; pyridinyl; pyridinyl substituted with F, C<sub>1-4</sub>alkyl, or C<sub>1-4</sub>haloalkyl;

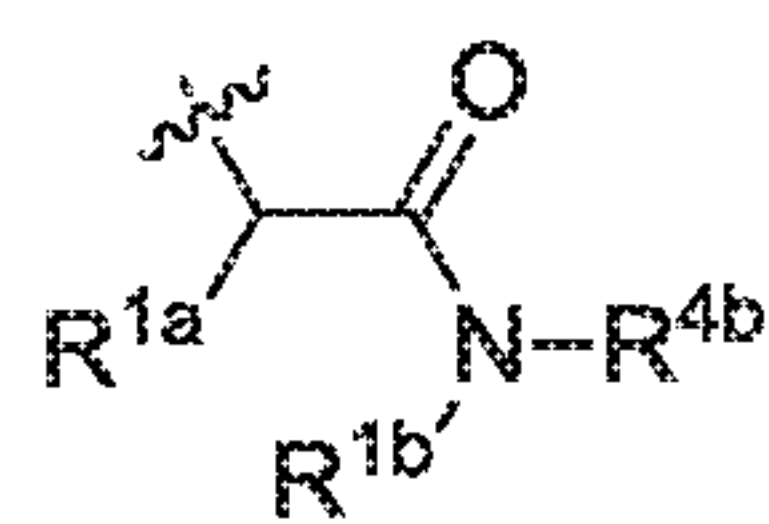
thiazolyl; thiazolyl substituted with C<sub>1-6</sub>alkyl or C<sub>1-6</sub>haloalkyl; thienyl; and thienyl substituted with one or two members each independently selected from the group consisting of: halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>haloalkyl, CH<sub>2</sub>OH, CH<sub>2</sub>OCH<sub>3</sub>, and cyclopropyl;

5 R<sup>3</sup> is H;

R<sup>4</sup> is selected from the group consisting of:



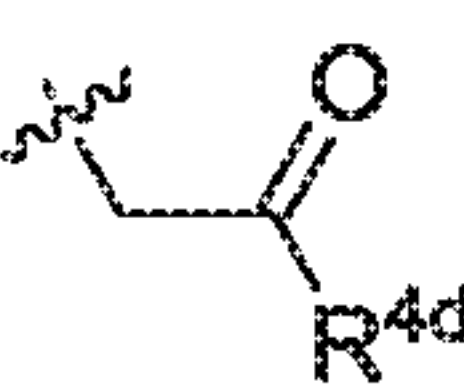
(a) wherein ring A is a 4-6 membered heterocycle optionally containing an additional oxygen heteroatom selected from the group consisting of: azetidiny; azetidiny substituted with one or two members independently selected from the group consisting of: F, OH, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>haloalkyl, CH<sub>2</sub>OCH<sub>3</sub>, CN, and OCH<sub>3</sub>; pyrrolidiny; pyrrolidiny substituted two F members; morpholiny; piperidiny; piperaziny substituted with C<sub>1-6</sub>alkyl; and (2,6-diazaspiro[3.3]heptan-6-yl);



(b) , wherein R<sup>4b</sup> is selected from the group consisting of: H; C<sub>1-6</sub>alkyl; CH<sub>2</sub>CH<sub>2</sub>OCH<sub>3</sub>; C<sub>3-6</sub>cycloalkyl; C<sub>3-6</sub>cycloalkyl substituted substituted with two or three members independently selected from the group consisting of F or CH<sub>3</sub>; oxetany; oxetany substituted with CH<sub>3</sub>; and pyridiny;

(c) wherein R<sup>4c</sup> is selected from the group consisting of: cyclopropyl; cyclopropyl substituted with one or two F members; CH(OH)cyclopropyl; azetidiny; CH<sub>2</sub>-azetidiny; CH<sub>2</sub>-azetidiny substituted with one or two members independently selected from: F, OH, OCH<sub>3</sub>, and CF<sub>3</sub>; oxetany; oxetany substituted with F or CH<sub>3</sub>; tetrahydrofurany; tetrahydropyrany; CH<sub>2</sub>pyrrolidiny; CH<sub>2</sub>pyrrolidiny substituted with CH<sub>3</sub>, OH, or OCH<sub>3</sub>; CH<sub>2</sub>piperidiny; CH<sub>2</sub>piperidiny substituted with OH, or F; morpholiny; pyrazolyl substituted with one or two CH<sub>3</sub> members; triazolyl substituted with CH<sub>3</sub>; tetrazolyl; isoxazolyl substituted with one or two CH<sub>3</sub> members; oxadiazolyl substituted with CH<sub>3</sub>, or CH<sub>2</sub>OCH<sub>3</sub>; thiadiazolyl; pyridiny; pyridiny substituted with one or two members

independently selected from the group consisting of: Cl, F, CH<sub>3</sub>, OCH<sub>3</sub>, and CF<sub>3</sub>; (2-oxo-1H-pyridin-3-yl); 6-oxo-1H-pyridin-3-yl; pyrimidinyl; pyrimidinyl substituted with F or CH<sub>3</sub>; pyrazinyl; pyridazinyl; pyridazinyl substituted with OCH<sub>3</sub>; phenyl; phenyl substituted with one or two members independently selected from the group consisting of: halo, CN, OCH<sub>3</sub>, C<sub>1-6</sub>alkyl, and CF<sub>3</sub>;

(d)  wherein R<sup>4d</sup> is selected from the group consisting of: OH, C<sub>1-6</sub>alkyl, O-C<sub>1-6</sub>alkyl, C<sub>3-6</sub>cycloalkyl, thienyl, and thiazolyl; and

(e) C<sub>2-6</sub>alkyl substituted with one or two members independently selected from OH, OC<sub>1-6</sub>alkyl, or cyclopropyl; CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>1-6</sub>alkyl); CH<sub>2</sub>CH<sub>2</sub>NH(CH<sub>2</sub>CH<sub>2</sub>OH); CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>3-6</sub>cycloalkyl); and difluoro(3-pyridyl)methyl; and

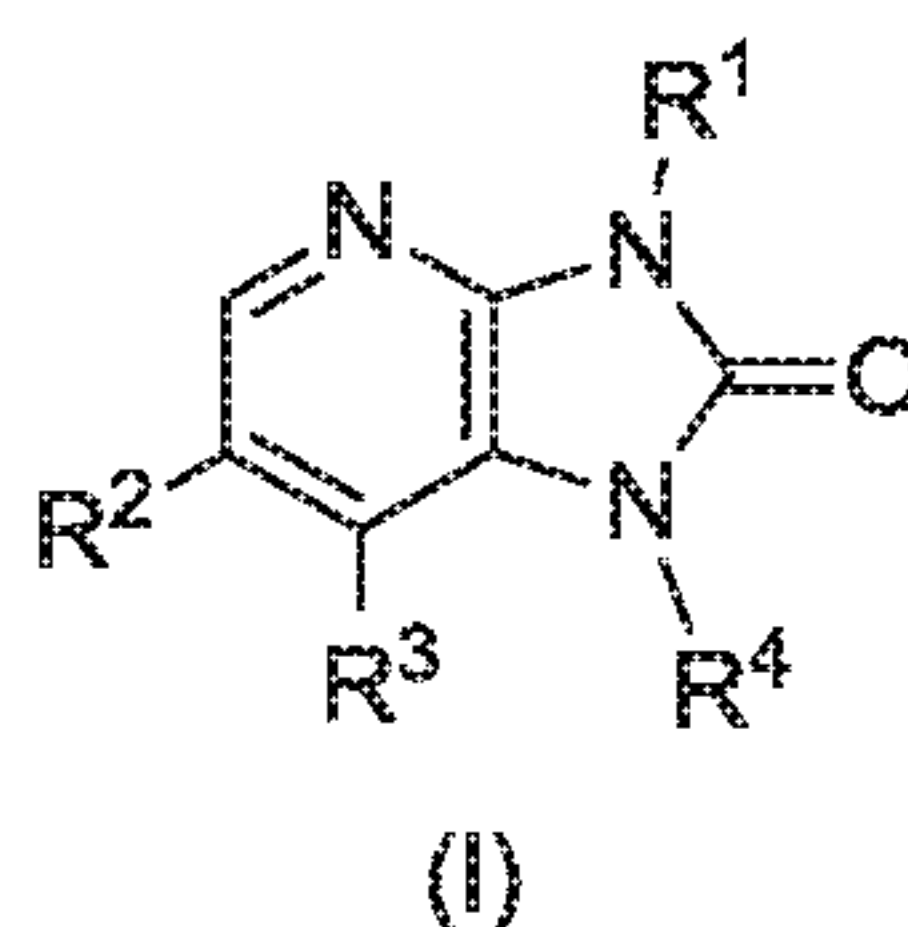
R<sup>1a</sup> and R<sup>1b</sup> are each independently H or CH<sub>3</sub>;

and pharmaceutically acceptable salts, solvates, stereoisomers, isotopic variants, or N-oxides of compounds of Formula (I); and

(B) at least one pharmaceutically acceptable excipient.

29. A pharmaceutical composition comprising an effective amount of at least one compound of claim 25 and at least one pharmaceutically acceptable excipient.

30. A method of treating a subject suffering from or diagnosed with a disease, disorder, or medical condition mediated by NR2B receptor activity, comprising administering to a subject in need of such treatment an effective amount of at least one compound selected from compounds of Formula (I):



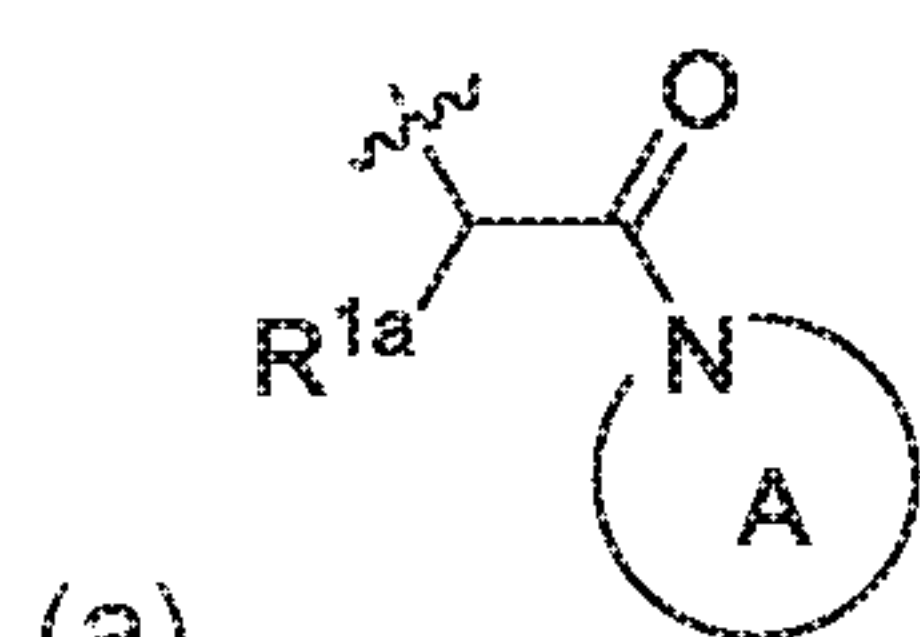
wherein

R<sup>1</sup> is H; CH<sub>2</sub>F; or CH<sub>3</sub>;

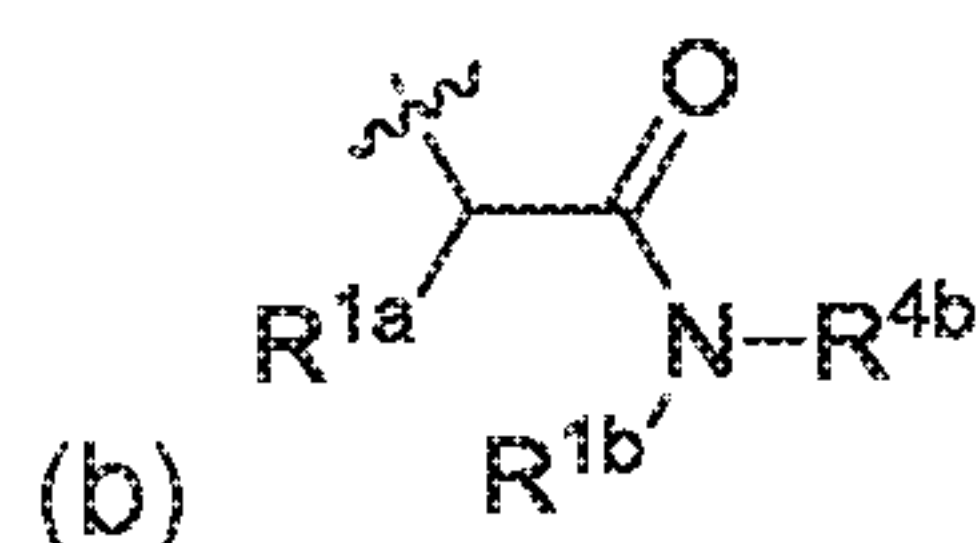
R<sup>2</sup> is selected from the group consisting of: phenyl; phenyl substituted with one, two, or three members each independently selected from the group consisting of: halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>haloalkyl, CN, OC<sub>1-6</sub>alkyl, OC<sub>1-6</sub>haloalkyl, N(CH<sub>3</sub>)<sub>2</sub>, and cyclopropyl; pyridinyl; pyridinyl substituted with F, C<sub>1-4</sub>alkyl, or C<sub>1-4</sub>haloalkyl; thiazolyl; thiazolyl substituted with C<sub>1-6</sub>alkyl or C<sub>1-6</sub>haloalkyl; thienyl; and thienyl substituted with one or two members each independently selected from the group consisting of: halo, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>haloalkyl, CH<sub>2</sub>OH, CH<sub>2</sub>OCH<sub>3</sub>, and cyclopropyl;

R<sup>3</sup> is H;

R<sup>4</sup> is selected from the group consisting of:



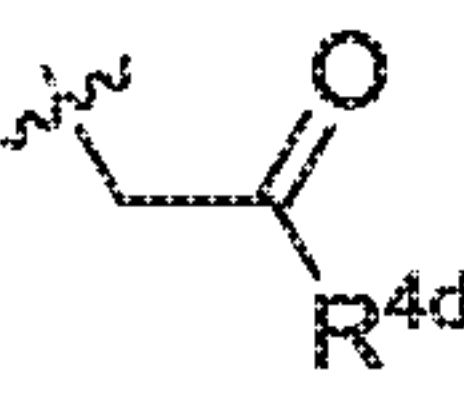
(a) wherein ring A is a 4-6 membered heterocycle optionally containing an additional oxygen heteroatom selected from the group consisting of: azetidiny; azetidiny substituted with one or two members independently selected from the group consisting of: F, OH, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>haloalkyl, CH<sub>2</sub>OCH<sub>3</sub>, CN, and OCH<sub>3</sub>; pyrrolidiny; pyrrolidiny substituted two F members; morpholiny; piperidiny; piperaziny substituted with C<sub>1-6</sub>alkyl; and (2,6-diazaspiro[3.3]heptan-6-yl);



(b) , wherein R<sup>4b</sup> is selected from the group consisting of: H; C<sub>1-6</sub>alkyl; CH<sub>2</sub>CH<sub>2</sub>OCH<sub>3</sub>; C<sub>3-6</sub>cycloalkyl; C<sub>3-6</sub>cycloalkyl substituted substituted with two or three members independently selected from the group consisting of F or CH<sub>3</sub>; oxetany; oxetany substituted with CH<sub>3</sub>; and pyridinyl;

(c) wherein R<sup>4c</sup> is selected from the group consisting of: cyclopropyl; cyclopropyl substituted with one or two F members; CH(OH)cyclopropyl; azetidiny; CH<sub>2</sub>-azetidiny; CH<sub>2</sub>-azetidiny substituted with one or two members independently selected from: F, OH, OCH<sub>3</sub>, and CF<sub>3</sub>; oxetany; oxetany substituted with F or CH<sub>3</sub>; tetrahydrofurany; tetrahydropyrany; CH<sub>2</sub>pyrrolidiny; CH<sub>2</sub>pyrrolidiny substituted with CH<sub>3</sub>, OH, or OCH<sub>3</sub>; CH<sub>2</sub>piperidiny;

CH<sub>2</sub>piperidinyl substituted with OH, or F; morpholinyl; pyrazolyl substituted with one or two CH<sub>3</sub> members; triazolyl substituted with CH<sub>3</sub>; tetrazolyl; isoxazolyl substituted with one or two CH<sub>3</sub> members; oxadiazolyl substituted with CH<sub>3</sub>, or CH<sub>2</sub>OCH<sub>3</sub>; thiadiazolyl; pyridinyl; pyridinyl substituted with one or two members independently selected from the group consisting of: Cl, F, CH<sub>3</sub>, OCH<sub>3</sub>, and CF<sub>3</sub>; (2-oxo-1H-pyridin-3-yl); 6-oxo-1H-pyridin-3-yl; pyrimidinyl; pyrimidinyl substituted with F or CH<sub>3</sub>; pyrazinyl; pyridazinyl; pyridazinyl substituted with OCH<sub>3</sub>; phenyl; phenyl substituted with one or two members independently selected from the group consisting of: halo, CN, OCH<sub>3</sub>, C<sub>1-6</sub>alkyl, and CF<sub>3</sub>;

(d)  wherein R<sup>4d</sup> is selected from the group consisting of: OH, C<sub>1-6</sub>alkyl, O-C<sub>1-6</sub>alkyl, C<sub>3-6</sub>cycloalkyl, thienyl, and thiazolyl; and

(e) C<sub>2-6</sub>alkyl substituted with one or two members independently selected from OH, OC<sub>1-6</sub>alkyl, or cyclopropyl; CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>1-6</sub>alkyl); CH<sub>2</sub>CH<sub>2</sub>NH(CH<sub>2</sub>CH<sub>2</sub>OH); CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>3-6</sub>cycloalkyl); and difluoro(3-pyridyl)methyl; and

R<sup>1a</sup> and R<sup>1b</sup> are each independently H or CH<sub>3</sub>;

and pharmaceutically acceptable salts, solvates, stereoisomers, isotopic variants, or N-oxides of compounds of Formula (I).

31. The method of claim 30, wherein the disorder, disease or condition mediated by the NR2B receptor is selected from the group consisting of: bipolar disorder, major depressive disorder, treatment-resistant depression, post-partum depression, seasonal affective disorder, Alzheimer's disease, Parkinson's disease, Huntington's chorea, multiple sclerosis, cognitive impairment, head injury, spinal cord injury, stroke, epilepsy, dyskinesias, amyotrophic lateral sclerosis, neurodegeneration associated with bacterial or chronic infections, pain, diabetic neuropathy, migraine, cerebral ischemia, schizophrenia, encephalitis, autism and autism spectrum disorders, memory and learning disorders, obsessive compulsive disorder, attention deficit hyperactivity disorder (ADHD) and addictive illnesses.

32. The method of claim 31, wherein the disorder, disease or condition is selected from the group consisting of treatment-resistant depression, major depressive disorder and bipolar disorder.

- 5 33. A compound selected from the group consisting of:
- 6-(5-(Difluoromethyl)-2-fluorophenyl)-3-methyl-1-(pyridazin-3-ylmethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one;
- 6-(5-(Difluoromethyl)-2-fluorophenyl)-3-methyl-1-(pyridin-3-ylmethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one;
- 10 N-(3-Chloropropyl)-2-[3-methyl-2-oxo-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-1-yl]acetamide;
- 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
- 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-(fluoromethyl)-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;
- 15 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-3-(2-fluoroethyl)-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;
- 1-[2-[3-(2-Fluoroethyl)azetidin-1-yl]-2-oxo-ethyl]-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 20 6-(6-Fluoro-2-pyridyl)-1-(2-oxobutyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[4-(2-fluoroethoxy)-3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[3-(2-fluoroethoxy)-5-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 25 1-[2-(3-<sup>18</sup>F-Fluoranylazetidin-1-yl)-2-oxo-ethyl]-6-(4-fluoro-3-methyl-phenyl)-3-methyl-imidazo[4,5-b]pyridin-2-one
- 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 30

- 6-[4-Chloro-3-(difluoromethoxy)phenyl]-3-methyl-1-(pyridazin-3-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-[(5-fluoro-3-pyridyl)methyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 5 6-(3,4-Difluorophenyl)-3-methyl-1-(thiadiazol-4-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-fluoro-3-pyridyl)methyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(5-fluoro-3-pyridyl)methyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 10 3-Methyl-1-(thiadiazol-4-ylmethyl)-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;
- 6-(3,4-Difluorophenyl)-3-methyl-1-[(1-methyltriazol-4-yl)methyl]imidazo[4,5-b]pyridin-2-one;
- 6-(3,4-Difluorophenyl)-3-methyl-1-[(1-methylpyrazol-4-yl)methyl]imidazo[4,5-b]pyridin-2-one;
- 15 3-Methyl-1-[(1-methylpyrazol-4-yl)methyl]-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;
- 3-Methyl-1-[(1-methyltriazol-4-yl)methyl]-6-[3-(trifluoromethyl)phenyl]imidazo[4,5-b]pyridin-2-one;
- 20 3-Methyl-6-(5-methyl-2-thienyl)-1-[(1-methyltriazol-4-yl)methyl]imidazo[4,5-b]pyridin-2-one;
- 3-Methyl-1-[(5-methyl-1,3,4-oxadiazol-2-yl)methyl]-6-(5-methyl-2-thienyl)imidazo[4,5-b]pyridin-2-one;
- 3-Methyl-1-[(1-methylpyrazol-4-yl)methyl]-6-(5-methyl-2-thienyl)imidazo[4,5-b]pyridin-2-one;
- 25 3-Methyl-6-(5-methyl-2-thienyl)-1-(thiadiazol-4-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 3-Methyl-1-[(3-methyl-1,2,4-oxadiazol-5-yl)methyl]-6-(5-methyl-2-thienyl)imidazo[4,5-b]pyridin-2-one;
- 3-Methyl-1-[(5-methylisoxazol-3-yl)methyl]-6-(5-methyl-2-thienyl)imidazo[4,5-b]pyridin-2-one;
- 30

- 6-[5-(Difluoromethyl)-2-thienyl]-3-methyl-1-[(1-methyltriazol-4-yl)methyl]imidazo[4,5-b]pyridin-2-one;
- 6-[5-(Difluoromethyl)-2-thienyl]-3-methyl-1-[(5-methyl-1,3,4-oxadiazol-2-yl)methyl]imidazo[4,5-b]pyridin-2-one;
- 5 6-[5-(Difluoromethyl)-2-thienyl]-3-methyl-1-[(1-methylpyrazol-4-yl)methyl]imidazo[4,5-b]pyridin-2-one;
- 6-[5-(Difluoromethyl)-2-thienyl]-3-methyl-1-(thiadiazol-4-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- 6-[5-(Difluoromethyl)-2-thienyl]-3-methyl-1-[(3-methyl-1,2,4-oxadiazol-5-yl)methyl]imidazo[4,5-b]pyridin-2-one;
- 10 6-[5-(Difluoromethyl)-2-thienyl]-3-methyl-1-[(5-methylisoxazol-3-yl)methyl]imidazo[4,5-b]pyridin-2-one;
- 3-Methyl-1-[(1-methylpyrazol-4-yl)methyl]-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;
- 15 3-Methyl-1-[(1-methyltriazol-4-yl)methyl]-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;
- 3-Methyl-1-[(5-methyl-1,3,4-oxadiazol-2-yl)methyl]-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;
- 3-Methyl-1-(thiadiazol-4-ylmethyl)-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;
- 20 3-Methyl-1-[(3-methyl-1,2,4-oxadiazol-5-yl)methyl]-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;
- 3-Methyl-1-[(5-methylisoxazol-3-yl)methyl]-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;
- 25 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-[(5-methylisoxazol-3-yl)methyl]imidazo[4,5-b]pyridin-2-one;
- 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-[(1-methylpyrazol-4-yl)methyl]imidazo[4,5-b]pyridin-2-one;
- 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-[(3-methyl-1,2,4-oxadiazol-5-yl)methyl]imidazo[4,5-b]pyridin-2-one;
- 30

- 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-[(1-methyltriazol-4-yl)methyl]imidazo[4,5-b]pyridin-2-one;
- 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-[(5-methyl-1,3,4-oxadiazol-2-yl)methyl]imidazo[4,5-b]pyridin-2-one;
- 5 6-(2,4-Difluoro-3-methyl-phenyl)-3-methyl-1-(thiadiazol-4-ylmethyl)imidazo[4,5-b]pyridin-2-one;
- N-(2-Fluoroethyl)-N-methyl-2-[3-methyl-2-oxo-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-1-yl]acetamide;
- 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-6-[5-(trifluoromethyl)-2-thienyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 10 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(2,4-difluoro-3-methyl-phenyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]-6-(m-tolyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 15 1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-6-(m-tolyl)imidazo[4,5-b]pyridin-2-one;
- 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[3-(2-fluoroethoxy)-5-(trifluoromethyl)phenyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- N,N-Dimethyl-2-[3-methyl-6-(m-tolyl)-2-oxo-imidazo[4,5-b]pyridin-1-yl]acetamide;
- 20 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[3-(difluoromethyl)-4-fluoro-phenyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[2-(3-fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]-6-[3-(difluoromethyl)-4-fluoro-phenyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 25 2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
- 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[3-(difluoromethoxy)-4-fluoro-phenyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 30 6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[2-(3-fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;

- 1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]-6-[3-(difluoromethoxy)-4-fluoro-phenyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 2-[6-[4-Chloro-3-(difluoromethoxy)phenyl]-3-methyl-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
- 5 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-[4-chloro-3-(difluoromethoxy)phenyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-[2-(3-fluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-[2-(3,3-difluoroazetidin-1-yl)-2-oxo-ethyl]-3-methyl-imidazo[4,5-b]pyridin-2-one;
- 10 1-[2-(Azetidin-1-yl)-2-oxo-ethyl]-6-(2,4-difluoro-3-methyl-phenyl)-3-(fluoromethyl)imidazo[4,5-b]pyridin-2-one;
- 2-[3-(Fluoromethyl)-2-oxo-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
- 15 1-[2-(3-Fluoroazetidin-1-yl)-2-oxo-ethyl]-3-(fluoromethyl)-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;
- 3-(Fluoromethyl)-1-(2-oxo-2-pyrrolidin-1-yl-ethyl)-6-[5-(trifluoromethyl)-2-thienyl]imidazo[4,5-b]pyridin-2-one;
- 2-[6-(2,4-Difluoro-3-methyl-phenyl)-3-(fluoromethyl)-2-oxo-imidazo[4,5-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
- 20 6-(2,4-Difluoro-3-methyl-phenyl)-1-[2-(3-fluoroazetidin-1-yl)-2-oxo-ethyl]-3-(fluoromethyl)imidazo[4,5-b]pyridin-2-one;
- 1-(3,3-Dimethyl-2-oxo-butyl)-6-(4-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(3-Methoxyphenyl)-1-[2-oxo-2-(2-thienyl)ethyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 25 1-(3,3-Dimethyl-2-oxo-butyl)-6-(4-methoxy-3-methyl-phenyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 1-Isobutyl-6-(4-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(2-Ethoxyphenyl)-1-[(3-methoxyphenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 6-(2-Ethoxyphenyl)-1-[(4-fluorophenyl)methyl]-3H-imidazo[4,5-b]pyridin-2-one;
- 30 N-Cyclopropyl-2-[6-(2-ethoxy-5-fluoro-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]acetamide;

2-[[6-(4-Methoxy-3-methyl-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]methyl]benzonitrile;

1-(3,3-Dimethyl-2-oxo-butyl)-6-(3-fluoro-4-methoxy-phenyl)-3H-imidazo[4,5-b]pyridin-2-one;

5 2-[6-(3,5-Difluorophenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-(2-methoxyethyl)acetamide;

1-(3,3-Dimethyl-2-oxo-butyl)-6-[3-(trifluoromethyl)phenyl]-3H-imidazo[4,5-b]pyridin-2-one; and

10 2-[6-(3-Chloro-4-fluoro-phenyl)-2-oxo-3H-imidazo[4,5-b]pyridin-1-yl]-N-(2-methoxyethyl)acetamide;

and pharmaceutically acceptable salts, solvates, or N-oxides thereof.