SUBSTITUTED HETEROAROMATIC PYRAZOLO-PYRIDINES AND THEIR USE AS GLUN2B RECEPTOR MODULATORS

Cross-Reference to Related Applications

This application claims the priority benefit of U.S. provisional application no. 62/861,665, filed June 14, 2019, the contents of which are incorporated herein in their entireties by reference thereto.

Field of the Invention

The present invention is related to compounds having GluN2B modulating properties, pharmaceutical compositions comprising these compounds, chemical processes for preparing these compounds and their use in the treatment of diseases associated with GluN2B receptor activity in animals, in particular humans.

Background of the Invention

Glutamate is one of the major excitatory neurotransmitters that is widely spread in the brain. First indication of its role as an excitatory messenger was in the 1950's when it was observed that intravenous administration of glutamate induces convulsions. However, the detection of the whole glutamatergic neurotransmitter system with its various receptors did not take place before the 1970's and 1980's when numerous antagonists were developed or, as in the case of PCP and ketamine, were identified as antagonists. Finally, in the 1990's molecular biology provided the tools for the classification of the glutamatergic receptors.

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 GluN2 subunits. The glycine binding site is present on the GluN1 subunit and the glutamate binding site is present on the GluN2 subunit.

The GluNR2 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 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).

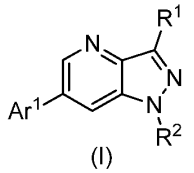
Compounds that modulate GluN2B-containing NMDA receptor function can be useful in treatment of many neurological and psychiatric disorders including but not limited to bipolar disorder (Martucci L et al., *Schizophrenia Res*, **2006**; 84(2-3):214-21),, major depressive disorder (Miller OH et al., *eLife.* **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 ther mood disorders (including schizophrenia (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**; 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 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 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 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 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 autoimmunological 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.* 2**011**;108(48):19407-12).

In view of the clinical importance of GluN2B, the identification of compounds that modulate GluN2B receptor function represents an attractive avenue into the development of new therapeutic agents. Such compounds are provided herein.

Summary of the Invention

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):



(I)

wherein

R^1 is H, halo, or CH_3;

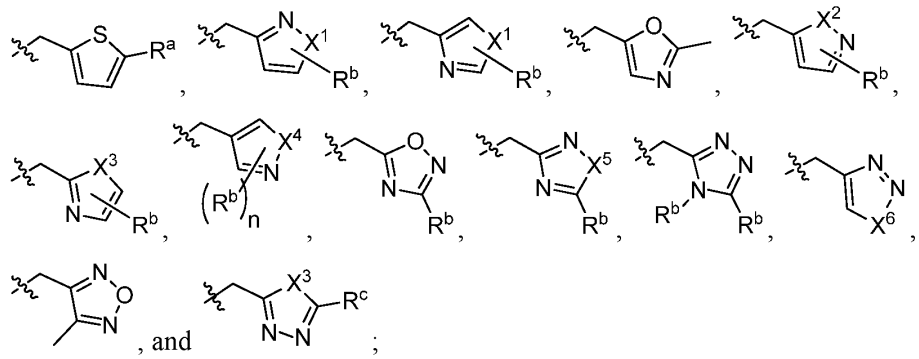
Ar^1 is selected from the group consisting of:

(a) phenyl substituted with one member selected from the group consisting of: halo, $C_{1\text{-}6}$alkyl, $OC_{1\text{-}6}$alkyl, $C_{1\text{-}6}$perhaloalkyl, and $OC_{1\text{-}6}$perhaloalkyl;

(b) phenyl substituted with two or three members each independently selected from the group consisting of: halo, $C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$perhaloalkyl, ~~and~~ $OC_{1\text{-}6}$perhaloalkyl, and CO_2H; and

(c) thienyl substituted with a member selected from the group consisting of: halo, $C_{1\text{-}6}$alkyl, and $C_{1\text{-}6}$perhaloalkyl; and pyridine substituted with CF_3; and

R^2 is selected from the group consisting of:

(d) 

wherein

R^a is halo, $C_{1\text{-}6}$alkyl or CN;

R^b is H or $C_{1\text{-}2}$alkyl;

R^c is selected from the group consisting of: H, $C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$perhaloalkyl, CH_2OH, $OC_{1\text{-}6}$alkyl, OH, NH_2, $NH(CH_3)$, $N(CH_3)_2$, $NH(C{=}O)CH_3$, cyclopropyl, and phenyl;

X^1 is NCH_3, S or O;

X^2 is O, NH or NCH_3;

X^3 is O or S;

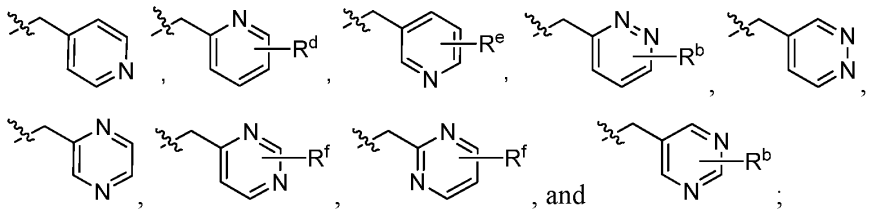
X^4 is NH or O;

X^5 is NCH_3 or O;

X^6 is NCH_3 or S;

and n is 2;

(e) phenyl; phenyl substituted with one or two members independently selected from the group consisting of: halo, OC_{1-6}alkyl, C_{1-6}perhaloalkyl, and CN; and

(f) 

wherein

R^d is H or OC_{1-6}alkyl;

R^e is a member selected from the group consisting of: H, halo, C_{1-6}alkyl, C_{1-6}perhaloalkyl, OC_{1-6}alkyl, OC_{1-6}perhaloalkyl, and CN; and

R^f is H, C_{1-6}alkyl or OC_{1-6}alkyl;

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 GluN2B 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 GluN2B receptor modulators. Thus, the invention is directed to a method for modulating GluN2B receptor activity, including when such receptor is in a subject, comprising exposing GluN2B 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 GluN2B 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}C), reaction kinetic studies (with, for example ^{2}H or ^{3}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}F or ^{11}C labeled compound may be particularly preferred for PET or SPECT studies.

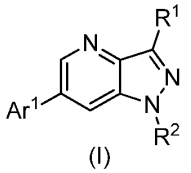
Additional embodiments of this invention include methods of making compounds of Formula (I), pharmaceutically acceptable salts of compounds of Formula (I), pharmaceutically acceptable prodrugs of compounds of Formula (I), and pharmaceutically active metabolites of Formula (I).

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.

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

In one aspect, provided herein are compounds of Formula (I),



(I)

wherein

R^1 is H, halo, or CH_3;

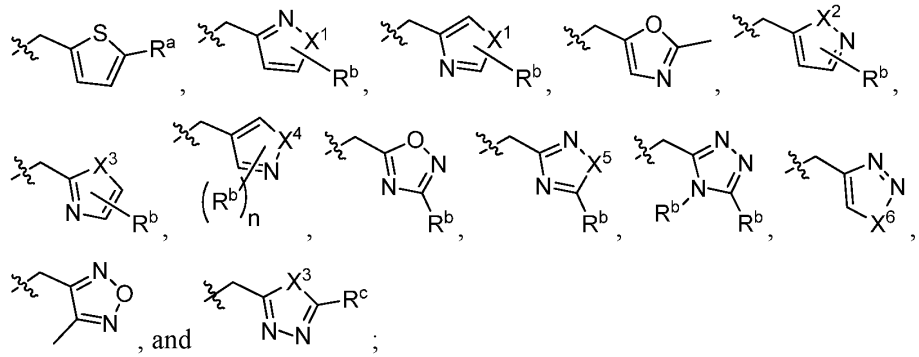
Ar^1 is selected from the group consisting of:

(a) phenyl substituted with one member selected from the group consisting of: halo, $C_{1\text{-}6}$alkyl, $OC_{1\text{-}6}$alkyl, $C_{1\text{-}6}$perhaloalkyl, and $OC_{1\text{-}6}$perhaloalkyl;

(b) phenyl substituted with two or three members each independently selected from the group consisting of: halo, $C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$perhaloalkyl, $OC_{1\text{-}6}$perhaloalkyl, and CO_2H; and

(c) thienyl substituted with a member selected from the group consisting of: halo, $C_{1\text{-}6}$alkyl, and $C_{1\text{-}6}$perhaloalkyl; and pyridine substituted with CF_3; and

R^2 is selected from the group consisting of:

(d) 

wherein

R^a is halo, $C_{1\text{-}6}$alkyl or CN;

R^b is H or $C_{1\text{-}2}$alkyl;

R^c is selected from the group consisting of: H, $C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$perhaloalkyl, CH_2OH, $C_{1\text{-}6}$alkyl, OH, NH_2, $NH(CH_3)$, $N(CH_3)_2$, $NH(C{=}O)CH_3$, cyclopropyl, and phenyl;

X^1 is NCH_3, S or O;

X^2 is O, NH or NCH_3;

X^3 is O or S;

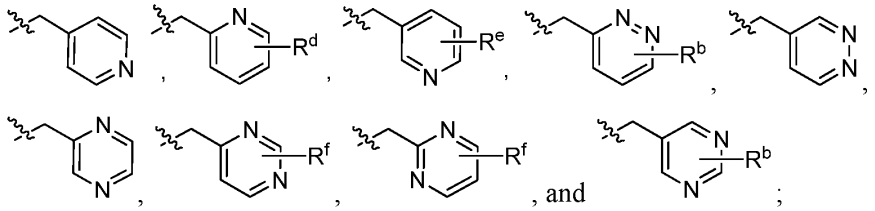
X^4 is NH or O;

X^5 is NCH_3 or O;

X^6 is NCH_3 or S;

and n is 2;

(e) phenyl; phenyl substituted with one or two members independently selected from the group consisting of: halo, OC_{1-6}alkyl, C_{1-6}perhaloalkyl, and CN; and

(f) 

wherein

R^d is H or OC_{1-6}alkyl;

R^e is a member selected from the group consisting of: H, halo, C_{1-6}alkyl, C_{1-6}perhaloalkyl, OC_{1-6}alkyl, OC_{1-6}perhaloalkyl, and CN; and

R^f is H, C_{1-6}alkyl or OC_{1-6}alkyl;

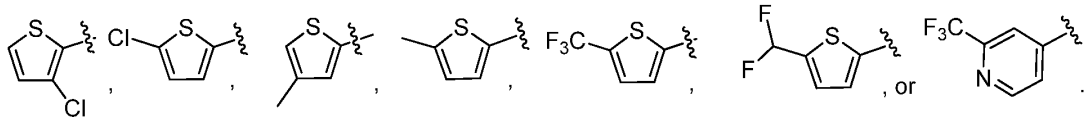
and pharmaceutically acceptable salts, stereoisomers, isotopic variants, N-oxides, or solvates thereof.

An additional embodiment of the invention is a compound of Formula (I) wherein R^1 is H.

An additional embodiment of the invention is a compound of Formula (I) wherein R^1 is F.

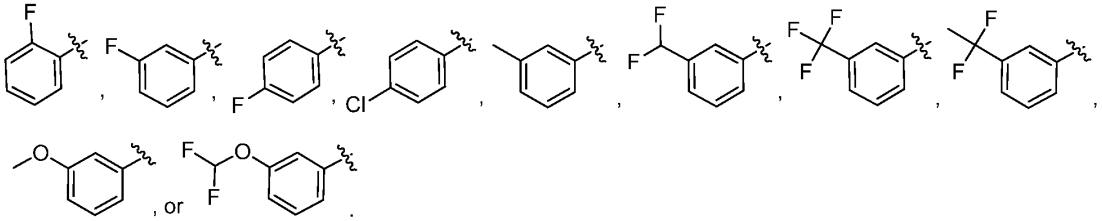
An additional embodiment of the invention is a compound of Formula (I) wherein R^1 is CH_3.

An additional embodiment of the invention is a compound of Formula (I) wherein Ar^1 is



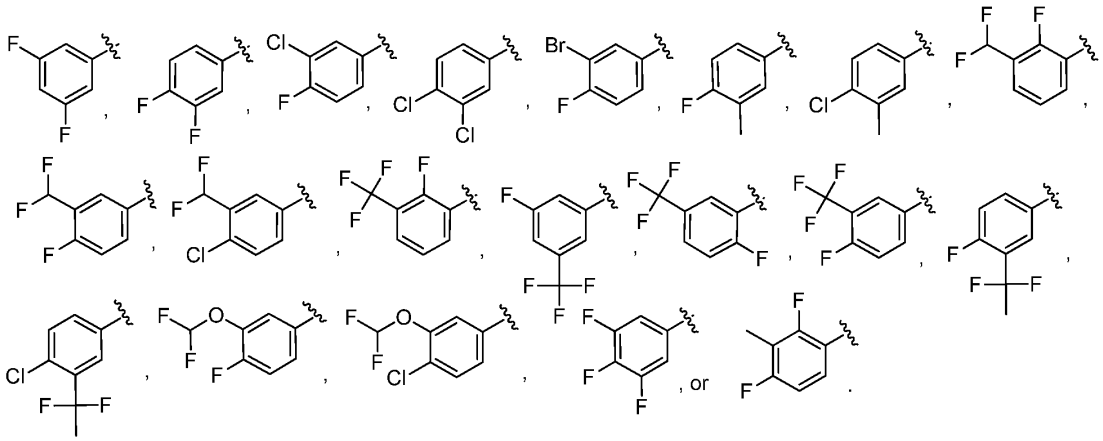
An additional embodiment of the invention is a compound of Formula (I) wherein Ar^1 is phenyl substituted with F, Cl, CH_3, OCH_3, CF_2H, CF_3, CF_2CH_3, or $OCHF_2$.

An additional embodiment of the invention is a compound of Formula (I) wherein Ar^1 is



An additional embodiment of the invention is a compound of Formula (I) wherein Ar^1 is phenyl substituted with two or three members independently selected from the group consisting of: F, Cl, Br, CH_3, CF_2H, CF_3, CF_2CH_3, or $OCHF_2$.

An additional embodiment of the invention is a compound of Formula (I) wherein Ar^1 is



An additional embodiment of the invention is a compound of Formula (I) wherein R^a is F, CH_3 or CN.

An additional embodiment of the invention is a compound of Formula (I) wherein R^b is H, CH_3 or CH_2CH_3.

An additional embodiment of the invention is a compound of Formula (I) wherein R^b is H or CH_3.

An additional embodiment of the invention is a compound of Formula (I) wherein R^c is H, CH_3, CH_2CH_3, CF_3, OCH_3, OH, NH_2, $NH(CH_3)$, $N(CH_3)_2$, $NH(C{=}O)CH_3$, cyclopropyl, or phenyl.

An additional embodiment of the invention is a compound of Formula (I) wherein R^d is H.

An additional embodiment of the invention is a compound of Formula (I) wherein R^d is OCH_3.

An additional embodiment of the invention is a compound of Formula (I) wherein R^e is H, Br, Cl, F, CH_3, CF_2H, CF_3, OCH_3, OCF_2H, or CN.

An additional embodiment of the invention is a compound of Formula (I) wherein R^f is H, CH_3, or OCH_3.

An additional embodiment of the invention is a compound of Formula (I) wherein X^1 is NCH_3.

An additional embodiment of the invention is a compound of Formula (I) wherein X^1 is O.

An additional embodiment of the invention is a compound of Formula (I) wherein X^1 is S.

An additional embodiment of the invention is a compound of Formula (I) wherein X^2 is O.

An additional embodiment of the invention is a compound of Formula (I) wherein X^2 is NH.

An additional embodiment of the invention is a compound of Formula (I) wherein X^2 is NCH_3.

An additional embodiment of the invention is a compound of Formula (I) wherein X^3 is O.

An additional embodiment of the invention is a compound of Formula (I) wherein X^3 is S.

An additional embodiment of the invention is a compound of Formula (I) wherein X^4 is NH.

An additional embodiment of the invention is a compound of Formula (I) wherein X^4 is O.

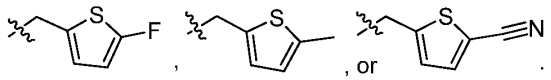
An additional embodiment of the invention is a compound of Formula (I) wherein X^5 is NCH_3.

An additional embodiment of the invention is a compound of Formula (I) wherein X^5 is O.

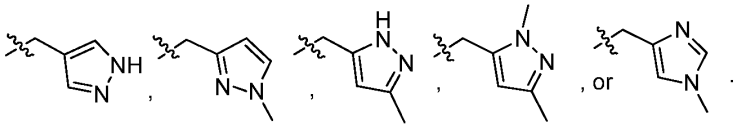
An additional embodiment of the invention is a compound of Formula (I) wherein X^6 is NCH_3.

An additional embodiment of the invention is a compound of Formula (I) wherein X^6 is S.

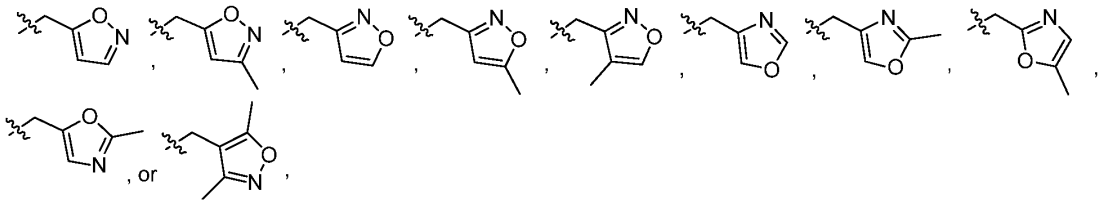
An additional embodiment of the invention is a compound of Formula (I) wherein R^2 is



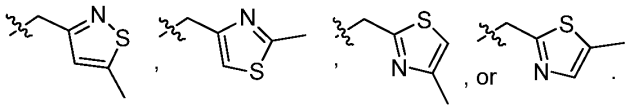
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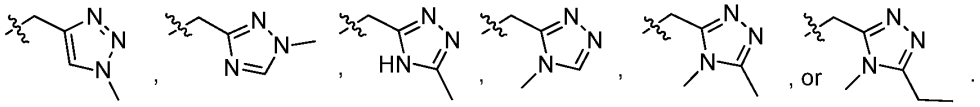
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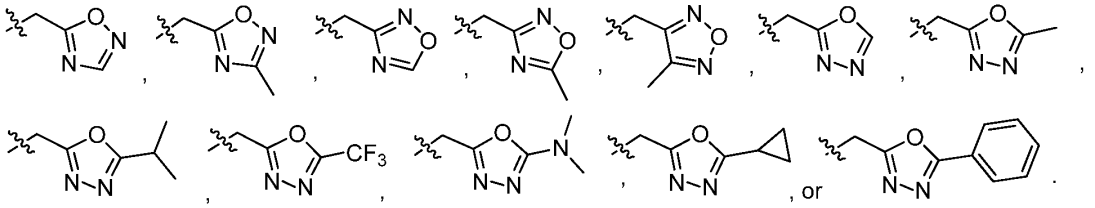
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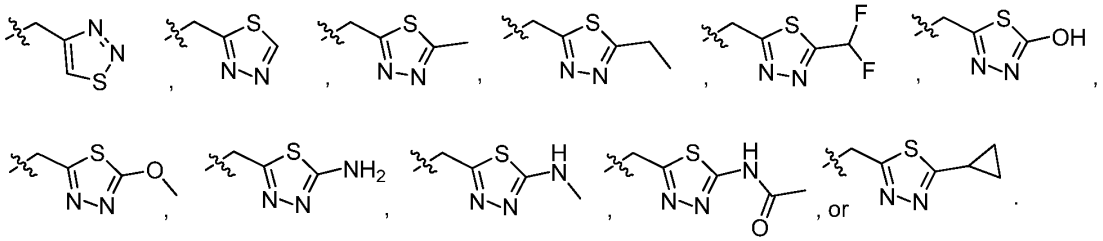
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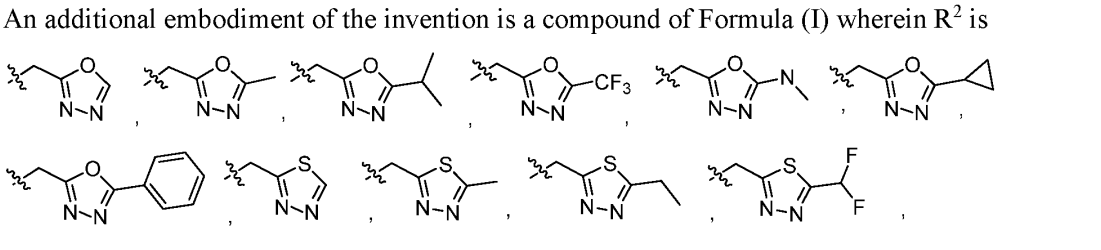
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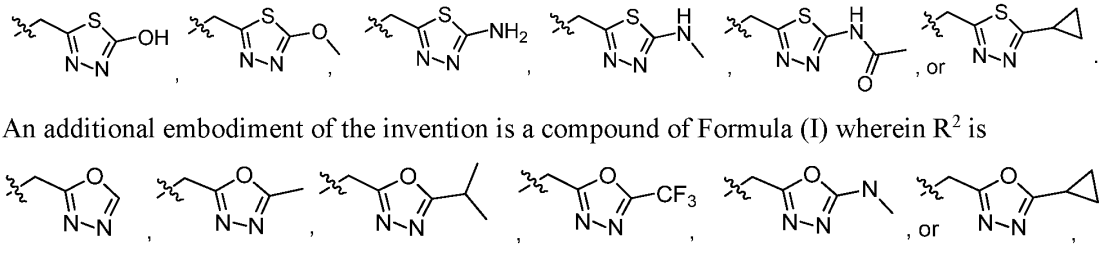
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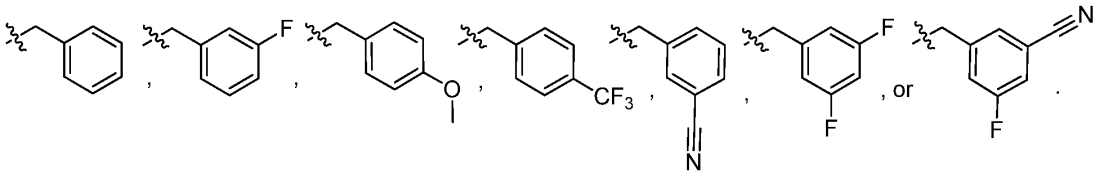
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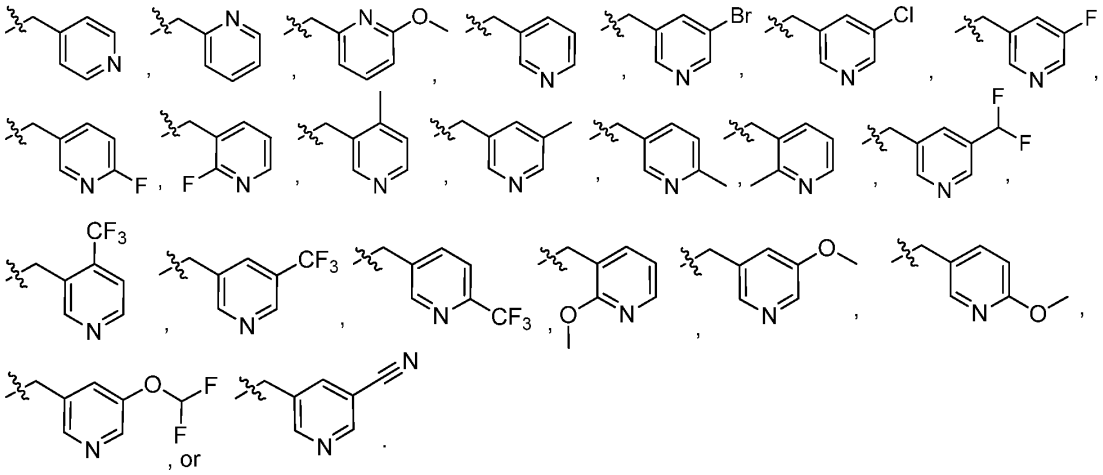
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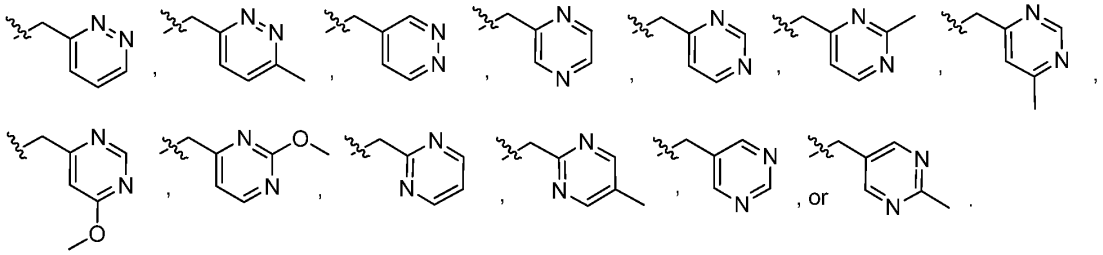
An additional embodiment of the invention is a compound of Formula (I) wherein R^2 is



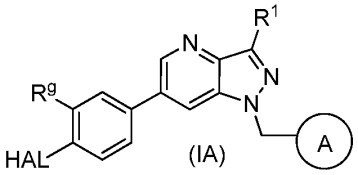
An additional embodiment of the invention is a compound of Formula (I) wherein R^2 is



An additional embodiment of the invention is a compound of Formula (I) wherein R^2 is



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



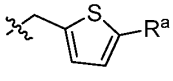
wherein

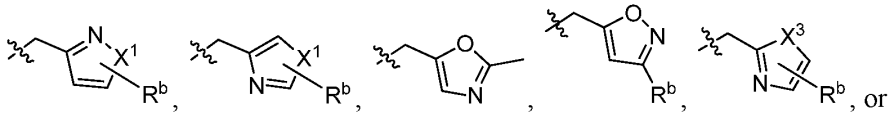
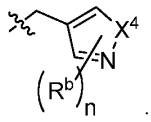
R^1 is H, F, or CH_3;

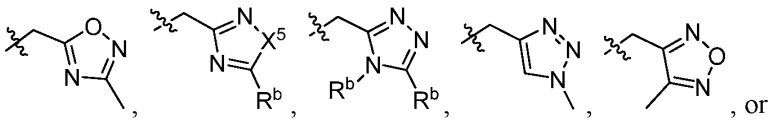
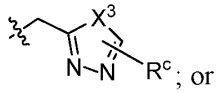
HAL is F or Cl;

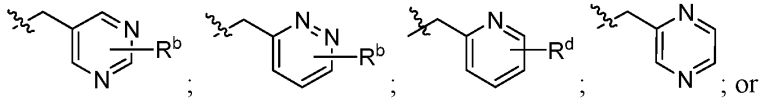
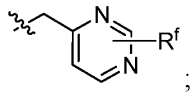
R^g is selected from the group consisting of: H, Cl, CH_3, CF_2H, CF_2CH_3, CF_3, and OCF_2H; and

Ring A is:

(a) , wherein R^a is F, CH_3 or CN;

(b) , or ;

(c) , or ; or

(d) ; or ;

X^1 is O, NCH_3 or S;

X^3 is O or S;

X^4 is NH or O;

X^5 is NCH_3 or O;

R^b is H, CH_3, or CH_2CH_3;

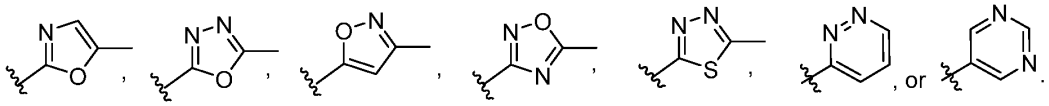
R^c is selected from the group consisting of: H, CH_3, CH_2CH_3, $CH(CH_3)_2$, CF_3, CHF_2, OCH_3, OH, NH_2, $NH(CH_3)$, $N(CH_3)_2$, $NH(C{=}O)CH_3$, cyclopropyl, and phenyl;

R^d is H or OCH_3; and

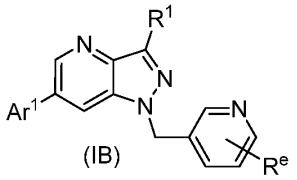
R^f is H, CH_3 or OCH_3;

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

An additional embodiment of the invention is a compound of Formula (IA), wherein ring A is



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



(IB)

wherein

R^1 is H, F, or CH_3;

R^e is a member selected from the group consisting of: H, Br, Cl, F, C_{1-4}alkyl, C_{1-4}perhaloalkyl, OC_{1-4}alkyl, OC_{1-4}perhaloalkyl, and CN; and

Ar^1 is selected from the group consisting of:

(a) phenyl substituted with one member selected from the group consisting of: Cl, F, C_{1-4}alkyl, OC_{1-4}alkyl, C_{1-4}perhaloalkyl, and OC_{1-4}perhaloalkyl;

(b) phenyl substituted with two or three members each independently selected from the group consisting of: Br, Cl, F, C_{1-4}alkyl, C_{1-4}perhaloalkyl, and OC_{1-4}perhaloalkyl; and

(c) thienyl substituted with a member selected from the group consisting of: Cl, CH_3, and CHF_2, CF_3.

An additional embodiment of the invention is a compound of Formula (IB), wherein R^1 is H, and R^e is H or F.

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

Ex #	Compound Name
1	1-(Pyrimidin-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
2	1-[(5-Bromo-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

Ex #	Compound Name
3	5-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;
4	1-[(2-Methylpyrimidin-5-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
5	1-(Pyrazin-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
6	1-(Pyrimidin-4-ylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
7	2-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole;
8	2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-oxazole;
9	2-[[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-oxazole;
10	2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;
11	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(1H-pyrazol-4-ylmethyl)pyrazolo[4,3-b]pyridine;
12	6-[3-(1,1-Difluoroethyl)phenyl]-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;
13	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-methyl-4H-1,2,4-triazol-3-yl)methyl]pyrazolo[4,3-b]pyridine;
14	1-[(3-Methyl-1H-pyrazol-5-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
15	5-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-N-methyl-1,3,4-thiadiazol-2-amine;
16	5-[[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazol-2-amine;
17	5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazol-2-ol;
18	5-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazol-2-amine;
19	N-(5-((6-(3-(Difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-1,3,4-thiadiazol-2-yl)acetamide;
20	3-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,2,4-oxadiazole;
21	1-Benzyl-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

Ex #	Compound Name
22	1-[(3-Fluorophenyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
23	3-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]benzonitrile;
24	1-[(4-Methoxyphenyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
25	6-[3-(Trifluoromethyl)phenyl]-1-[[4-(trifluoromethyl)phenyl]methyl]pyrazolo[4,3-b]pyridine;
26	3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]benzonitrile;
27	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(3,5-difluorophenyl)methyl]pyrazolo[4,3-b]pyridine;
28	3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-fluoro-benzonitrile;
29	3-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]benzonitrile;
30	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(3,5-difluorophenyl)methyl]pyrazolo[4,3-b]pyridine;
31	3-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-fluoro-benzonitrile;
32	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-methyl-2-thienyl)methyl]pyrazolo[4,3-b]pyridine;
33	6-(3-(Difluoromethyl)-4-fluorophenyl)-1-((5-fluorothiophen-2-yl)methyl)-1H-pyrazolo[4,3-b]pyridine;
34	5-((6-(3-(Difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)thiophene-2-carbonitrile;
35	6-[3-(1,1-Difluoroethyl)phenyl]-1-(1H-pyrazol-4-ylmethyl)pyrazolo[4,3-b]pyridine;
36	1-[(1-Methylimidazol-4-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
37	1-[(2,5-Dimethylpyrazol-3-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
38	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(1H-pyrazol-4-ylmethyl)pyrazolo[4,3-b]pyridine;
39	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(1-methylpyrazol-3-yl)methyl]pyrazolo[4,3-b]pyridine;
40	6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-(1H-pyrazol-4-ylmethyl)pyrazolo[4,3-b]pyridine;

Ex #	Compound Name
41	6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-(1H-pyrazol-4-ylmethyl)pyrazolo[4,3-b]pyridine;
42	5-[[6-(4-Fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-isoxazole;
43	3-[[6-(4-Fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-isoxazole;
44	3-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]isoxazole;
45	3-[[6-[3-(1,1-Difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-isoxazole;
46	4-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]oxazole;
47	5-Methyl-3-[[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]isoxazole;
48	5-[[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-2-methyl-oxazole;
49	2-[[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-oxazole;
50	5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]isoxazole;
51	3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]isoxazole;
52	5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-isoxazole;
53	3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-isoxazole;
54	5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-2-methyl-oxazole;
55	4-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-2-methyl-oxazole;
56	3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-4-methyl-isoxazole;
57	4-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3,5-dimethyl-isoxazole;
58	3-[[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-isoxazole;
59	3-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-isoxazole;

Ex #	Compound Name
60	5-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-2-methyl-oxazole;
61	2-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-oxazole;
62	3-[[6-[4-Chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-isoxazole;
63	5-[[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-2-methyl-oxazole;
64	5-Methyl-3-[[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]isothiazole;
65	2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-thiazole;
66	2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-4-methyl-thiazole;
67	4-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-2-methyl-thiazole;
68	2-[[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-thiazole;
69	2-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-thiazole;
70	2-[[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-thiazole;
71	1-[(1-Methyl-1,2,4-triazol-3-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
72	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(1-methyltriazol-4-yl)methyl]pyrazolo[4,3-b]pyridine;
73	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(1-methyl-1,2,4-triazol-3-yl)methyl]pyrazolo[4,3-b]pyridine;
74	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(4-methyl-1,2,4-triazol-3-yl)methyl]pyrazolo[4,3-b]pyridine;
75	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(4,5-dimethyl-1,2,4-triazol-3-yl)methyl]pyrazolo[4,3-b]pyridine;
76	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-ethyl-4-methyl-1,2,4-triazol-3-yl)methyl]pyrazolo[4,3-b]pyridine;
77	2-[[6-(5-Chloro-2-thienyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;
78	2-Methyl-5-[[6-[5-(trifluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole;

Ex #	Compound Name
79	2-[[6-[5-(Difluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;
80	5-[[6-(4-Fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;
81	5-[[6-(3-Methoxyphenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;
82	2-[[6-[3-(1,1-Difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;
83	2-[[6-[3-(1,1-Difluoroethyl)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;
84	3-Methyl-5-[[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,2,4-oxadiazole;
85	2-Methyl-5-[[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole;
86	5-Methyl-3-[[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,2,4-oxadiazole;
87	5-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,2,4-oxadiazole;
88	2-Methyl-5-[[6-[2-(trifluoromethyl)-4-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole;
89	2-[[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;
90	2-[[3-Fluoro-6-(4-fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;
91	2-[[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-(trifluoromethyl)-1,3,4-oxadiazole;
92	2-[[6-(3-Chloro-4-fluoro-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;
93	2-[[6-(3-Chloro-4-fluoro-phenyl)-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;
94	2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole;
95	5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;
96	2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;
97	3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,2,4-oxadiazole;

Ex #	Compound Name
98	3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-4-methyl-1,2,5-oxadiazole;
99	2-Cyclopropyl-5-[[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole;
100	2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-isopropyl-1,3,4-oxadiazole;
101	5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-N,N-dimethyl-1,3,4-oxadiazol-2-amine;
102	2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-(trifluoromethyl)-1,3,4-oxadiazole;
103	2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-phenyl-1,3,4-oxadiazole;
104	2-[[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;
105	2-[[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;
106	2-[[6-[4-Chloro-3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;
107	2-[[6-[4-Chloro-3-(difluoromethyl)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;
108	5-[[6-[3-Fluoro-5-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;
109	5-[[6-[2-Fluoro-5-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;
110	5-[[6-[4-Fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;
111	5-[[6-[2-Fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;
112	5-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;
113	2-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;
114	3-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,2,4-oxadiazole;
115	2-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-(trifluoromethyl)-1,3,4-oxadiazole;
116	2-[[6-[4-Chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

Ex #	Compound Name
117	2-[[6-[4-Chloro-3-(difluoromethoxy)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;
118	2-[[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;
119	2-[[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-(trifluoromethyl)-1,3,4-oxadiazole;
120	4-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]thiadiazole;
121	2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazole;
122	2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;
123	2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;
124	2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-methyl-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;
125	2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-ethyl-1,3,4-thiadiazole;
126	5-((6-(3-(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-N-methyl-1,3,4-thiadiazol-2-amine;
127	2-[[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methoxy-1,3,4-thiadiazole;
128	N-(5-((6-(3-(Difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-1,3,4-thiadiazol-2-yl)acetamide;
129	2-(Difluoromethyl)-5-[[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazole;
130	2-Cyclopropyl-5-[[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazole;
131	2-[[6-[4-Chloro-3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;
132	2-[[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;
133	2-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;
134	2-[[6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methoxy-1,3,4-thiadiazole;
135	2-[[6-[4-Chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;

Ex #	Compound Name
136	2-[[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;
137	6-(4-Methyl-2-thienyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;
138	1-[(5-Methyl-3-pyridyl)methyl]-6-(4-methyl-2-thienyl)pyrazolo[4,3-b]pyridine;
139	6-(5-Methyl-2-thienyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;
140	5-[[6-(5-Chloro-2-thienyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;
141	6-(3-Chloro-2-thienyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;
142	5-[[6-[5-(Difluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;
143	1-((6-fluoropyridin-3-yl)methyl)-6-(5-(trifluoromethyl)thiophen-2-yl)-1H-pyrazolo[4,3-b]pyridine;
144	5-[[6-[5-(Trifluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;
145	1-[(6-Fluoro-3-pyridyl)methyl]-6-(m-tolyl)pyrazolo[4,3-b]pyridine;
146	1-[(5-Fluoro-3-pyridyl)methyl]-6-(m-tolyl)pyrazolo[4,3-b]pyridine;
147	3-Fluoro-1-[(5-fluoro-3-pyridyl)methyl]-6-(m-tolyl)pyrazolo[4,3-b]pyridine;
148	6-(4-Chlorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
149	6-(4-Fluorophenyl)-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;
150	6-(4-Fluorophenyl)-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
151	1-[[5-(Difluoromethoxy)-3-pyridyl]methyl]-6-(4-fluorophenyl)pyrazolo[4,3-b]pyridine;
152	6-(3-Fluorophenyl)-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;
153	6-(2-Fluorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
154	6-(3-Methoxyphenyl)-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;

Ex #	Compound Name
155	1-[(6-Fluoro-3-pyridyl)methyl]-6-(3-methoxyphenyl)pyrazolo[4,3-b]pyridine;
156	6-[3-(Difluoromethyl)phenyl]-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;
157	5-[[6-[3-(Difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;
158	1-[(5-Chloro-3-pyridyl)methyl]-6-[3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
159	6-[3-(Difluoromethoxy)phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
160	6-[3-(1,1-Difluoroethyl)phenyl]-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
161	6-[3-(1,1-Difluoroethyl)phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
162	1-(2-Pyridylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
163	1-(3-Pyridylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
164	1-(4-Pyridylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
165	1-[(6-Methyl-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
166	1-[(2-Methyl-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
167	1-[(5-Methyl-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
168	1-[(4-Methyl-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
169	1-[(6-Fluoro-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
170	1-[(2-Fluoro-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
171	1-[(5-Fluoro-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
172	1-[(2-Methoxy-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
173	1-[(5-Methoxy-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

Ex #	Compound Name
174	6-[3-(Trifluoromethyl)phenyl]-1-[[6-(trifluoromethyl)-3-pyridyl]methyl]pyrazolo[4,3-b]pyridine;
175	6-[3-(Trifluoromethyl)phenyl]-1-[[5-(trifluoromethyl)-3-pyridyl]methyl]pyrazolo[4,3-b]pyridine;
176	6-[3-(Trifluoromethyl)phenyl]-1-[[4-(trifluoromethyl)-3-pyridyl]methyl]pyrazolo[4,3-b]pyridine;
177	6-(4-Fluoro-3-methyl-phenyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;
178	3-Fluoro-6-(4-fluoro-3-methyl-phenyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;
179	6-(4-Fluoro-3-methyl-phenyl)-1-[(2-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
180	6-(4-Fluoro-3-methyl-phenyl)-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
181	6-(4-Fluoro-3-methyl-phenyl)-1-[(4-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
182	6-(4-Fluoro-3-methyl-phenyl)-1-[(6-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
183	6-(4-Fluoro-3-methyl-phenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
184	6-(3,5-Difluorophenyl)-1-[(4-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
185	6-(3,5-Difluorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
186	6-(3,4-Difluorophenyl)-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;
187	6-(3,4-Difluorophenyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;
188	6-(3,4-Difluorophenyl)-1-[(2-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
189	6-(3,4-Difluorophenyl)-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
190	6-(3,4-Difluorophenyl)-1-[(4-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
191	6-(3,4-Difluorophenyl)-1-[(6-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
192	6-(3,4-Difluorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

Ex #	Compound Name
193	6-(3,4-Difluorophenyl)-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
194	1-[[5-(Difluoromethoxy)-3-pyridyl]methyl]-6-(3,4-difluorophenyl)pyrazolo[4,3-b]pyridine;
195	6-(3-Chloro-4-fluoro-phenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
196	6-(3-Chloro-4-fluoro-phenyl)-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
197	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;
198	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;
199	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-methyl-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;
200	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
201	6-(3-(difluoromethyl)-4-fluorophenyl)-1-((6-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine;
202	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
203	5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;
204	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(6-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
205	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(6-methoxy-2-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
206	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(2-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
207	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
208	1-[(5-Chloro-3-pyridyl)methyl]-6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridine;
209	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[[5-(difluoromethyl)-3-pyridyl]methyl]pyrazolo[4,3-b]pyridine;
210	1-[[5-(Difluoromethoxy)-3-pyridyl]methyl]-6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridine;
211	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[[5-(trifluoromethyl)-3-pyridyl]methyl]pyrazolo[4,3-b]pyridine;

Ex #	Compound Name
212	5-[[6-[3-(Difluoromethyl)-2-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;
213	1-[(5-Chloro-3-pyridyl)methyl]-6-[3-(difluoromethyl)-2-fluoro-phenyl]pyrazolo[4,3-b]pyridine;
214	6-(3,4-Dichlorophenyl)-1-[(6-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
215	6-(3,4-Dichlorophenyl)-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
216	6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;
217	6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
218	6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
219	5-[[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;
220	6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
221	1-[(5-Chloro-3-pyridyl)methyl]-6-[3-(1,1-difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridine;
222	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;
223	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;
224	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
225	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
226	5-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;
227	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(6-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
228	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(6-methoxy-2-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
229	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(2-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
230	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

Ex #	Compound Name
231	1-[(5-Chloro-3-pyridyl)methyl]-6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridine;
232	6-[4-Chloro-3-(Difluoromethyl)phenyl]-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
233	1-[(5-Fluoro-3-pyridyl)methyl]-6-[4-fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
234	6-[4-Fluoro-3-(trifluoromethyl)phenyl]-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
235	6-(3-Bromo-4-fluorophenyl)-1-((6-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine;
236	5-[[6-[4-Chloro-3-(1,1-difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;
237	6-[4-Chloro-3-(1,1-difluoroethyl)phenyl]-1-[(5-chloro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
238	6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;
239	6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
240	6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
241	5-[[6-[4-Chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;
242	6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
243	6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-[(5-chloro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
244	6-(2,4-Difluoro-3-methyl-phenyl)-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;
245	6-(2,4-Difluoro-3-methyl-phenyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;
246	6-(2,4-Difluoro-3-methyl-phenyl)-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
247	6-(2,4-Difluoro-3-methyl-phenyl)-1-[(4-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
248	6-(2,4-Difluoro-3-methyl-phenyl)-1-[(6-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
249	6-(2,4-Difluoro-3-methyl-phenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

Ex #	Compound Name
250	1-(2-Pyridylmethyl)-6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridine;
251	1-[(5-Fluoro-3-pyridyl)methyl]-6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridine;
252	1-[(5-Methoxy-3-pyridyl)methyl]-6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridine;
253	1-[[5-(Difluoromethoxy)-3-pyridyl]methyl]-6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridine;
254	1-(Pyridazin-4-ylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
255	6-(m-Tolyl)-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
256	6-(3-Fluorophenyl)-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
257	6-[3-(1,1-Difluoroethyl)phenyl]-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
258	1-(Pyridazin-3-ylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
259	6-(4-Fluoro-3-methyl-phenyl)-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
260	6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
261	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
262	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(6-methylpyridazin-3-yl)methyl]pyrazolo[4,3-b]pyridine;
263	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
264	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(6-methylpyridazin-3-yl)methyl]pyrazolo[4,3-b]pyridine;
265	6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
266	6-(3,4-Difluorophenyl)-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
267	6-(4-Chloro-3-methyl-phenyl)-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
268	1-(Pyridazin-3-ylmethyl)-6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridine;

Ex #	Compound Name
269	6-(2,4-Difluoro-3-methyl-phenyl)-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
270	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(pyrimidin-4-ylmethyl)pyrazolo[4,3-b]pyridine;
271	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(pyrimidin-4-ylmethyl)pyrazolo[4,3-b]pyridine;
272	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(pyrazin-2-ylmethyl)pyrazolo[4,3-b]pyridine;
273	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(pyrazin-2-ylmethyl)pyrazolo[4,3-b]pyridine;
274	6-[3-(1,1-Difluoroethyl)phenyl]-1-(pyrimidin-5-ylmethyl)pyrazolo[4,3-b]pyridine;
275	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(pyrimidin-5-ylmethyl)pyrazolo[4,3-b]pyridine;
276	1-(Pyrimidin-5-ylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
277	6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-(pyrimidin-5-ylmethyl)pyrazolo[4,3-b]pyridine;
278	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(pyrimidin-5-ylmethyl)pyrazolo[4,3-b]pyridine;
279	6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-(pyrimidin-5-ylmethyl)pyrazolo[4,3-b]pyridine;
280	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(6-methylpyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;
281	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(6-methylpyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;
282	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(2-methylpyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;
283	1-[(2-Methylpyrimidin-4-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
284	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(2-methylpyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;
285	6-(3,4-Difluorophenyl)-1-[(2-methylpyrimidin-5-yl)methyl]pyrazolo[4,3-b]pyridine;
286	6-(4-Chloro-3-methyl-phenyl)-1-[(2-methylpyrimidin-5-yl)methyl]pyrazolo[4,3-b]pyridine;
287	1-[(5-Methylpyrimidin-2-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

Ex #	Compound Name
288	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(6-methoxypyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;
289	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(6-methoxypyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;
290	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(2-methoxypyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine; and
291	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(2-methoxypyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;
292	(5-((6-(3-(Difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-1,3,4-oxadiazol-2-yl)methanol;
293	2-Fluoro-5-(1-((5-methyl-1,3,4-oxadiazol-2-yl)methyl)-1H-pyrazolo[4,3-b]pyridin-6-yl)benzoic acid;
294	6-(3-(Difluoromethyl)-4-fluorophenyl)-1-((6-(fluoro-18F)pyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine;
295	2-[[3-Bromo-6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;
296	2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole; and
297	2-[[3-Deuterio-6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

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:

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-oxazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-isoxazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,2,4-oxadiazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

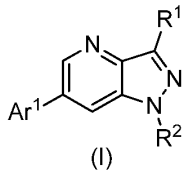
6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(pyrimidin-5-ylmethyl)pyrazolo[4,3-b]pyridine;

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

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

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



(I)

wherein

R^1 is H, halo, or CH_3;

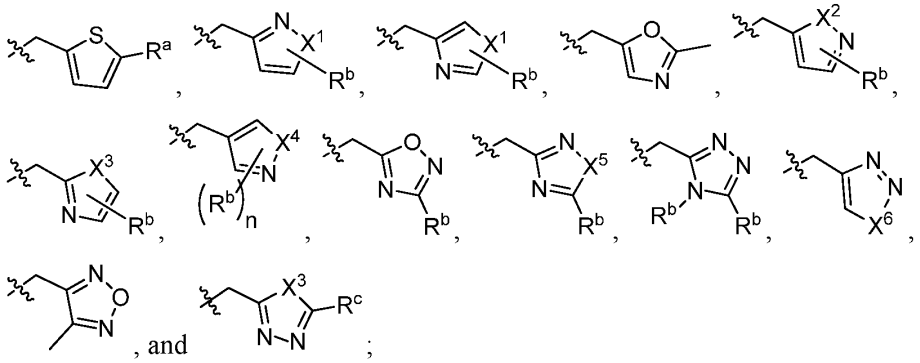
Ar^1 is selected from the group consisting of:

(a) phenyl substituted with one member selected from the group consisting of: halo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{1-6}perhaloalkyl, and OC_{1-6}perhaloalkyl;

(b) phenyl substituted with two or three members each independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}perhaloalkyl, OC_{1-6}perhaloalkyl, and CO_2H; and

(c) thienyl substituted with a member selected from the group consisting of: halo, C_{1-6}alkyl, and C_{1-6}perhaloalkyl; and pyridine substituted with CF_3; and

R^2 is selected from the group consisting of:

(d) 

wherein

R^a is halo, C_{1-6}alkyl or CN;

R^b is H or C_{1-2}alkyl;

R^c is selected from the group consisting of: H, C_{1-6}alkyl, C_{1-6}perhaloalkyl, CH_2OH, OC_{1-6}alkyl, OH, NH_2, $NH(CH_3)$, $N(CH_3)_2$, $NH(C{=}O)CH_3$, cyclopropyl, and phenyl;

X^1 is NCH_3, S or O;

X^2 is O, NH or NCH_3;

X^3 is O or S;

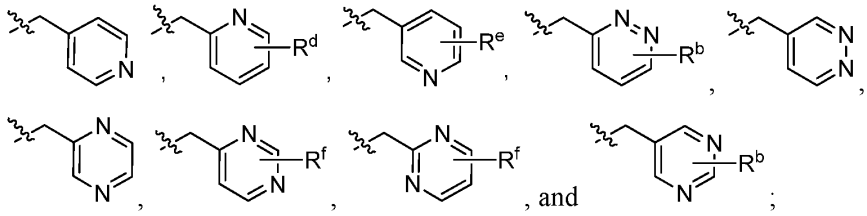
X^4 is NH or O;

X^5 is NCH_3 or O;

X^6 is NCH_3 or S;

and n is 2;

(e) phenyl; phenyl substituted with one or two members independently selected from the group consisting of: halo, OC_{1-6}alkyl, C_{1-6}perhaloalkyl, and CN; and

(f) 

wherein

R^d is H or OC_{1-6}alkyl;

R^e is a member selected from the group consisting of: H, halo, C_{1-6}alkyl, C_{1-6}perhaloalkyl, OC_{1-6}alkyl, OC_{1-6}perhaloalkyl, and CN; and

R^f is H, C_{1-6}alkyl or OC_{1-6}alkyl;

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 and 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 and 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.

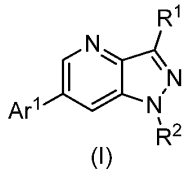
An additional embodiment of the invention is a pharmaceutical composition comprising and effective amount of at least one compound in Table 1, as well as pharmaceutically acceptable salts, N-oxides or solvates of compounds of Table 1, pharmaceutically acceptable prodrugs of compounds of Table 1, and 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), and (IB)). 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), and (IB)). Also within the scope of the invention are the pharmaceutically acceptable prodrugs of compounds of Formula (I) (as well as Formulas (IA), and (IB)), and pharmaceutically active metabolites of the compounds of Formula (I) (as well as Formulas (IA), and (IB)).

Also within the scope of the invention are isotopic variations of compounds of Formula (I) (as well as Formulas (IA), and (IB)), 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), and (IB)). 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), and (IB)), and pharmaceutically active metabolites of the isotopic variations of the compounds of Formula (I) (as well as Formulas (IA), and (IB)).

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 GluN2B 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):



(I)

wherein

R^1 is H, halo, or CH_3;

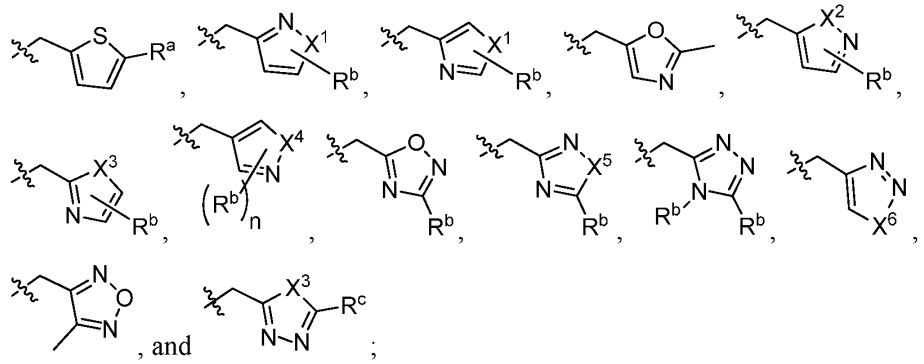
Ar^1 is selected from the group consisting of:

(a) phenyl substituted with one member selected from the group consisting of: halo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{1-6}perhaloalkyl, and OC_{1-6}perhaloalkyl;

(b) phenyl substituted with two or three members each independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}perhaloalkyl, OC_{1-6}perhaloalkyl, and CO_2H; and

(c) thienyl substituted with a member selected from the group consisting of: halo, C_{1-6}alkyl, and C_{1-6}perhaloalkyl; and pyridine substituted with CF_3; and

R^2 is selected from the group consisting of:

(d) 

wherein

R^a is halo, C_{1-6}alkyl or CN;

R^b is H or C_{1-2}alkyl;

R^c is selected from the group consisting of: H, C_{1-6}alkyl, C_{1-6}perhaloalkyl, CH_2OH, OC_{1-6}alkyl, OH, NH_2, $NH(CH_3)$, $N(CH_3)_2$, $NH(C=O)CH_3$, cyclopropyl, and phenyl;

X^1 is NCH_3, S or O;

X^2 is O, NH or NCH_3;

X^3 is O or S;

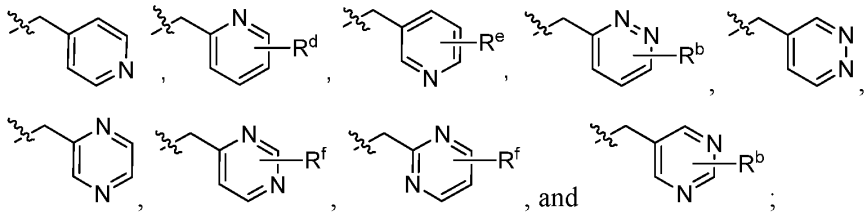
X^4 is NH or O;

X^5 is NCH_3 or O;

X^6 is NCH_3 or S;

and n is 2;

(e) phenyl; phenyl substituted with one or two members independently selected from the group consisting of: halo, OC_{1-6}alkyl, C_{1-6}perhaloalkyl, and CN; and

(f) 

wherein

R^d is H or OC_{1-6}alkyl;

R^e is a member selected from the group consisting of: H, halo, C_{1-6}alkyl, C_{1-6}perhaloalkyl, OC_{1-6}alkyl, OC_{1-6}perhaloalkyl, and CN; and

R^f is H, C_{1-6}alkyl or OC_{1-6}alkyl;

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 GluN2B 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), and (IB)), 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.

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 sever 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 behavioral 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 post encephalitic 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 includes cervical dystonia (torticolli), 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.

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.

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_{1-4}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_{1-6}alkyl as used here refers to a straight- or branched-chain alkyl group having from 1 to 6 carbon atoms in the chain.

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^2 hybridized.)

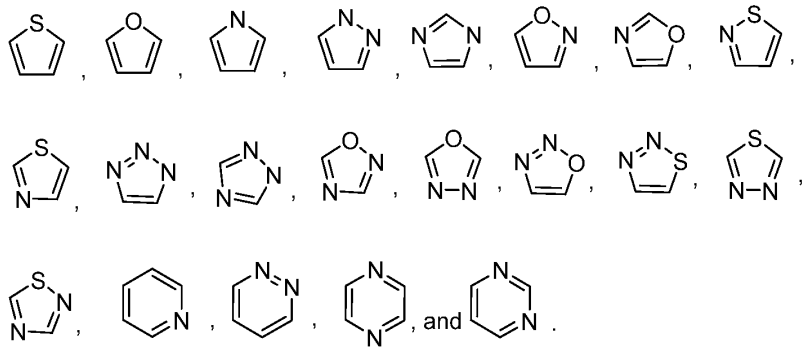
The term "phenyl" represents the following moiety:



The term "thienyl" represents the following moiety:



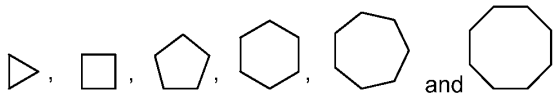
The term "heteroaryl" refers to a monocyclic or fused bicyclic heterocycle (ring structure having ring atoms selected from carbon atoms and up to four heteroatoms selected from nitrogen, oxygen, and sulfur) having from 3 to 9 ring atoms per heterocycle. Illustrative examples of heteroaryl groups include 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.

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:



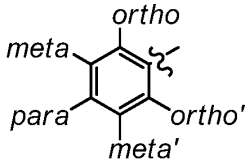
The term "halo" represents chloro, fluoro, bromo or iodo.

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 "$C_{1\text{-}4}$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 "$C_{1\text{-}6}$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_3), difluoromethyl (CF_2H), monofluoromethyl (CH_2F), pentafluoroethyl (CF_2CF_3), tetrafluoroethyl ($CHFCF_3$),monofluoroethyl (CH_2CH_2F), trifluoroethyl (CH_2CF_3), tetrafluorotrifluoromethylethyl ($-CF(CF_3)_2$), 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.

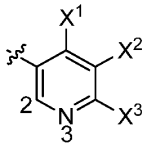
The term “perhaloalkoxy” or “haloalkoxy” refers to a straight- or branched-chain alkoxy group having from 1 to 6 carbon atoms in the chain optionally substituting hydrogens with halogens. Examples of perhaloalkoxy groups include trifluoromethoxy (OCF_3), difluoromethoxy (OCF_2H), monofluoromethoxy (OCH_2F), monofluoroethoxy (OCH_2CH_2F), pentafluoroethoxy (OCF_2CF_3), tetrafluoroethoxy ($OCHFCF_3$), trifluoroethoxy (OCH_2CF_3), tetrafluorotrifluoromethylethoxy (-$OCF(CF_3)_2$), 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 “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^1 substituent in the ortho position, the X^2 substituent in the meta position, and X^3 substituent in the para position:



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 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 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. 261, 5th 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 $MgSO_4$ and $NaHCO_3$ 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." Isomers that differ in the arrangement of their atoms in space are termed "."

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 π 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.

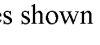
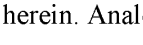
Tautomeric forms may be relevant to the attainment of the optimal chemical reactivity and biological activity of a compound of interest.

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 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.

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*) or (S*) is used in the name to indicate that the absolute stereochemistry of the corresponding stereocenter is unknown. Thus, a compound designated as (R*) refers to an

enantiopure compound with an absolute 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 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), and (IB)), or pharmaceutically acceptable salts of compounds of Formula (I) (as well as Formulas (IA), and (IB)) 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), and (IB)) or pharmaceutically acceptable salts of compounds of Formula (I) (as well as Formulas (IA), and (IB)) 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 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 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-$COOH_{(s)}$, R-$COOH_{(sol)}$, and R-$COO^{-}{}_{(sol)}$. In this example, R-$COOH_{(s)}$ refers to the solid compound, as it could be for example in a tablet or some other solid pharmaceutical composition or preparation; R-$COOH_{(sol)}$ refers to the undissociated form of the compound in a solvent; and R-$COO^{-}{}_{(sol)}$ 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 $R\text{-}COO^-$ upon dissociation in the medium being 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 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 entity is being exposed to species such as $R\text{-}COOH_{(aq)}$ and/or $R\text{-}COO^-_{(aq)}$, 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 H_2NCH_2COOH, and it exists in some media (in this case in neutral media) in the form of the zwitterion $^{+}H_3NCH_2COO^{-}$. 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 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}H, ^{3}H, ^{11}C, ^{13}C, ^{14}C, ^{15}N, ^{18}O, ^{17}O, ^{31}P, ^{32}P, ^{35}S, ^{18}F, ^{36}Cl, ^{125}I, respectively. Such isotopically labeled compounds are useful in metabolic studies (preferably with ^{14}C), reaction kinetic studies (with, for example deuterium (i.e., D or ^{2}H); or tritium (i.e., T or ^{3}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}F or ^{11}C labeled compound may be particularly preferred for PET or SPECT studies. Further, substitution with heavier isotopes such as deuterium (i.e., ^{2}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 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 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 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 $S^1_{example}$ is one of S_1 and S_2, and substituent $S^2_{example}$ is one of S_3 and S_4, then these assignments refer to embodiments of this invention given according to the choices $S^1_{example}$ is S_1 and $S^2_{example}$ is S_3; $S^1_{example}$ is S_1 and $S^2_{example}$ is S_4; $S^1_{example}$ is S_2 and $S^2_{example}$ is S_3; $S^1_{example}$ is S_2 and $S^2_{example}$ is S_4; and equivalents of each one of such choices. The shorter terminology "$S^1_{example}$ is one of S_1 and S_2, and $S^2_{example}$ 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, R^1, Ar^1, R^2, R^a, R^b, R^c, R^d, R^e, R^f, R^g, HAL, X^1, X^2, X^3, X^4, X^5, X^6, L, n, het, 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 $S_{example}$ is one of S_1, S_2, and S_3, this listing refers to embodiments of this invention for which $S_{example}$ is S_1; $S_{example}$ is S_2; $S_{example}$ is S_3; $S_{example}$ is one of S_1 and S_2; $S_{example}$ is one of S_1 and S_3; $S_{example}$ is one of S_2 and S_3; $S_{example}$ is one of S_1, S_2 and S_3; and $S_{example}$ is any equivalent of each one of these choices. The shorter terminology "$S_{example}$ 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, R^1, Ar^1, R^2, R^a, R^b, R^c, R^d, R^e, R^f, R^g, HAL, X^1, X^2, X^3, X^4, X^5, X^6, L, n, het, 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_{1-4} refers independently to embodiments that have one carbon member (C_1), embodiments that have two carbon members (C_2), embodiments that have three carbon members (C_3), and embodiments that have four carbon members (C_4).

The term C_{n-m}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), and (IB)), 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), and (IB)) 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), and (IB)) 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, isobutyrates, 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, γ-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), and (IB)) 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), and (IB)) 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), and (IB)), 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), and (IB)). 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 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), and (IB)) as amides or alkyl esters. Examples of amides include those derived from ammonia, primary C_{1-6}alkyl amines and secondary di(C_{1-6}alkyl) amines. Secondary amines include 5- or 6-membered heterocycloalkyl or heteroaryl ring moieties. Examples of amides include those that are derived from ammonia, C_{1-}

$_{3}$alkyl primary amines, and di(C_{1-2}alkyl)amines. Examples of esters of the invention include C_{1-7}alkyl, C_{5-7}cycloalkyl, phenyl, and phenyl(C_{1-6}alkyl) esters. Preferred esters include methyl esters. Prodrugs may also be prepared by derivatizing free hydroxy groups using 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 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 also be derivatized as amides, sulfonamides or phosphonamides. 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), and (IB)), which may 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), and (IB)) 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 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), and (IB)) and their pharmaceutically acceptable salts, pharmaceutically acceptable prodrugs, and pharmaceutically active metabolites of the present invention are useful as modulators of the GluN2B 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, prevent, inactivate, desensitize, or down-regulate the GluN2B receptor expression or activity, and "activators" are compounds that increase, activate, facilitate, sensitize, or up-regulate GluN2B 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 purpose of affecting a therapeutic or prophylactic benefit through modulation of GluN2B 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 GluN2B receptor activity. The term "subject" refers to a mammalian patient 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 GluN2B receptor activity, such as: 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, 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 anxiety disorders; obsessive compulsive disorder; reaction to sever 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 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 post encephalitic 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; dystonia including but not limited to focal dystonia, multiple-focal or segmental dystonia, torsion dystonia, hemispheric, generalized and tardive dystonia (induced by psychopharmacological drugs). Focal dystonia include cervical dystonia (torticolli), 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) 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; 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 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; 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, 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; glaucoma and other neuropathies; dementias, vascular dementia, 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 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 GluN2B activity, such as another GluN2B 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.

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 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, 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 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, 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, 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), 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 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 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. 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**
Aqueous	aq
Atmosphere	atm
tert-Butylcarbamoyl	Boc
Broad	br
Diatomaceous Earth	Celite®
Electrospray ionization	ESI
Normal-phase silica gel chromatography	FCC
GluNR2B *	$GluN_{2B}$, NMDA-R2B, NR2B, hNR3
Grams	g
Hours	h
High-pressure liquid chromatography	HPLC
Hertz	Hz
Isopropyl alcohol	*i*PrOH, IPA
Liquid chromatography and mass spectrometry	LCMS
Molar	M
Mass to charge ratio	m/z
Milligrams	mg
Minute	min
Milliliter	mL
Microliter	µL
Millimoles	mmol
Mass spectrometry	MS
Normal	N

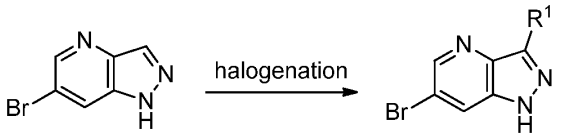
Term	Acronym
Nuclear magnetic resonance	NMR
Parts per million	ppm
Precipitate	ppt
Polytetrafluoroethylene	PTFE
Retention time	R_t
Room temperature	rt
Saturated	sat
Supercritical Fluid Chromatography	SFC
Temperature	T
Thin layer chromatography	TLC
Volume in milliliters of solvent per gram of substrate	V, or volumes

*(Collingridge, G.L, et al, *Neuropharmacology*, **2009**, 56, 2-5)

PREPARATIVE EXAMPLES

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 to follow.

SCHEME 1

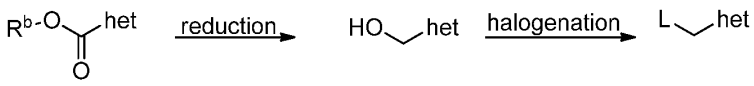


(V)

According to SCHEME 1, commercially available or synthetically accessible 6-bromo-1H-pyrazolo[4,3-b]pyridine is halogenated under conditions known to one skilled in the art, to provide a compound of formula (V). For example, 6-bromo-1H-pyrazolo[4,3-b]pyridine is fluorinated using an electrophilic fluorine source such as, *N*-fluorobenzenesulfonimide (NFSI), *N*-fluoro-*o*-benzenedisulfonimide (NFOBS), or 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) (Selectflor®), preferably Selectflor®; in a

suitable solvent such as acetonitrile (ACN), and the like; at temperatures ranging from 0 to 100 °C; to provide a compound of formula (V), where R^1 is F.

SCHEME 2



(VI) (VII) (VIII)

According to SCHEME 2, a heterocyclic methanol compound of formula (VII) is obtained by reduction of commercially available or synthetically accessible heterocyclic carboxylate derivative, such as an ester of formula (VI), where het is an optionally substituted five or six membered heteroaromatic ring containing one, two, three or four heteroatoms independently selected from N, S, and O; and R^b is $C_{1\text{-}2}$alkyl. For example, a compound of formula (VI) is reacted with a reducing agent such as sodium borohydride, lithium aluminum hydride, diisobutylaluminum hydride, and the like; in a suitable solvent such as ethanol, THF, DCM, and the like; to afford a heterocyclic methanol compound of formula (VII).

A compound of formula (VI), where het is pyridine substituted with OH, is derivatized prior to reduction to the alcohol compound of formula (VII). For example, ethyl 6-methylpyridazine-3-carboxylate is alkylated with sodium chlorodifluoroacetate, a base such as Cs_2CO_3, in a suitable solvent such as DMF, at a temperature of about 100 °C, to provide methyl 5-(difluoromethoxy)pyridine-3-carboxylate. A compound of formula (VI), where het is pyridine substituted with (C=O)H, is derivatized first before reduction to the alcohol. For example, methyl 5-formylnicotinate is reacted with diethylaminosulfur trifluoride, in a suitable solvent such as DCM, to provide methyl 5-(difluoromethyl)pyridine-3-carboxylate.

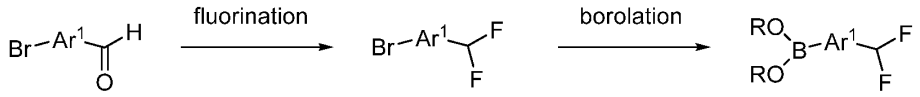
A commercially available or synthetically accessible heterocyclic methanol compound of formula (VII); where het is an optionally substituted five or six membered heteroaromatic ring containing one, two, three or four heteroatoms independently selected from N, S, and O; is halogenated, employing methods known to one skilled in the art, to give a compound of formula (VII) where L is Cl or Br. For example, a compound of formula (VII) is chlorinated with a chlorinating reagent, such as thionyl chloride; neat, or in a suitable solvent such as

dichloromethane (DCM), and the like; at temperatures ranging from 0 to 75 °C; to provide a compound of formula (VII), where L is Cl.

In a further example, a compound of formula (VII) is converted into a pseudo-halide such as a mesylate, triflate, or a para-toluene sulfonate under conditions known to one skilled in the art. For example, a compound of formula (VII) is reacted with methanesulfonyl chloride; in a suitable solvent such as dichloromethane, and the like; a tertiary amine base such as triethylamine, and the like; at temperatures ranging from 0 °C to ambient room temperature; to afford a compound of formula (VIII) where L is OSO_2CH_3.

A compound of formula (VIII), where L is Cl, and het is an optionally substituted five or six membered heteroaromatic ring containing one, two, three or four heteroatoms independently selected from N, S, and O; is protected employing established methodologies. For example, 3-(chloromethyl)pyrazole hydrochloride is reacted with 3,4-dihydro-2H-pyran, in a suitable solvent such as DMF, to provide 4-(chloromethyl)-1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazole, where the protecting group is tetrahydro-2H-pyran-2-yl.

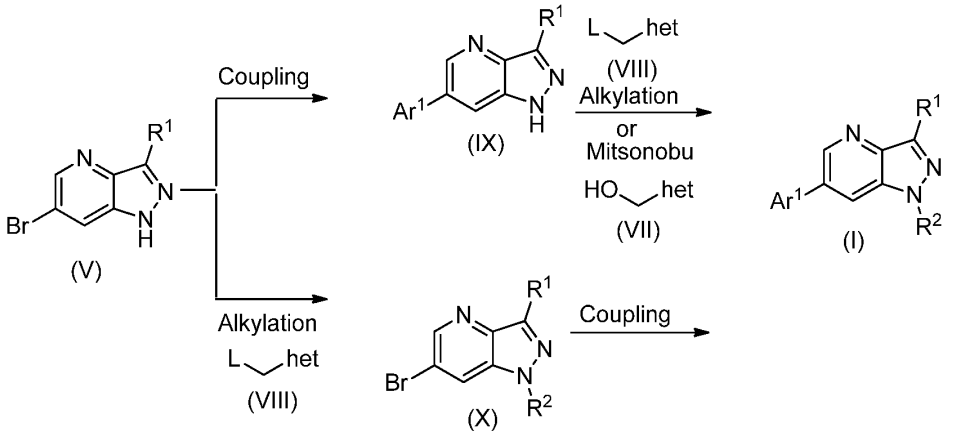
SCHEME 3



Difluorination of a compound of formula (XX) is achieved employing diethylaminosulfur trifluoride (DAST), and the like, in a suitable solvent such as DCM, to provide a compound of formula (XXI) where R^{4a} is CF_2H. A compound of formula (XX), where the Ar^1 substituted with OH, is derivatized by difluoromethylation employing sodium 2-chloro-2,2-difluoroacetate, a suitable base such as NaH, in a solvent such as DMF, and the like, to provide a compound of formula (XXII), where R^{4a} is OCF_2H. For example, 5-bromothiophene-2-carbaldehyde is difluorinated with diethylaminosulfur trifluoride (DAST) in a suitable solvent such as DCM, at a temperature of about 0 °C to ambient room temperature, to provide 2-bromo-5-(difluoromethyl)thiophene. A compound of formula (XXI), is borylated by methods known to those skilled in the art. A compound of formula (XXI) can be treated with a transition metal catalyst, $PdCl_2$dppf for example, in a solvent like DMSO or 1,4-dioxane, and a base like KOAc with bis(pinacolato)diboron to give a compound of formula (XXII). In addition, a compound of formula (XXI), is borylated via a metal halogen exchange of the bromide with organo-lithium or

magnesium reagents, with or without the presence of lithium chloride at a temperature of about -78 °C in a solvent like ether or THF and the like, followed by treatment with 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane to give a compound of formula (XXII).

SCHEME 4



According to SCHEME 4, a compound of formula (V), where R^1 is H, F, or CH_3; is alkylated with a compound of formula (VIII), where L is Cl, Br, or OSO_2CH_3; and het is an optionally substituted five or six membered heteroaromatic ring containing one, two, three or four heteroatoms independently selected from N, S, and O; employing a base such as NaH, K_2CO_3, Cs_2CO_3, and the like; in a suitable solvent such as dimethylformamide (DMF), tetrahydrofuran (THF), dichloromethane (DCM), and the like; to afford a compound of formula (X).

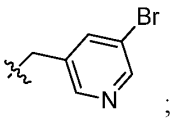
A compound of formula (X) is reacted in a metal-mediated cross coupling reaction; with a suitably substituted aryl or heteroaryl boronic acid, boronic ester, and the like; under Suzuki conditions known to one skilled in the art; to provide a compound of Formula (I). For example, a compound of formula (X), where R^1 is H, F or CH_3; is reacted with a commercially available or synthetically accessible suitably substituted aryl or heteroaryl boronic acid, boronic ester, and the like; in the presence of a palladium catalyst such as (2-dicyclohexylphosphino-2′,6′-diisopropoxy-1,1′-biphenyl)[2-(2′-amino-1,1′-biphenyl)]palladium(II) methanesulfonate (RuPhos-Pd-G3), [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II) ($PdCl_2$(dppf)), tetrakis(triphenylphosphine)palladium(0) ($Pd(PPh_3)_4$), and the like; a base such as K_3PO_4, K_2CO_3, Na_2CO_3, Cs_2CO_3, and the like; potassium fluoride; in a suitable solvent such as 1,4-

dioxane, DMF, ethanol, water, or a mixture thereof; at temperatures ranging from 60 to 150 °C; employing conventional or microwave heating; to afford a compound of Formula (I). A compound of formula (V) is reacted in a metal mediated cross coupling reaction as previously described, with suitably substituted aryl or heteroaryl boronic acid, boronic ester; to provide a compound of formula (IX).

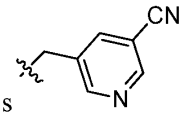
A compound of formula (IX), where R^1 is H, F, or CH_3; is alkylated employing conditions previously described, with a compound of formula (VIII), where L is Cl, Br, or OSO_2CH_3; and het is an optionally substituted five or six membered heteroaromatic ring containing one, two, three or four heteroatoms independently selected from N, S, and O; to provide a compound of Formula (I).

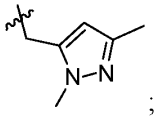
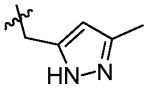
A compound of formula (IX) is reacted with a compound of formula (VII), where het is an optionally substituted five or six membered heteroaromatic ring containing one, two, three or four heteroatoms independently selected from N, S, and O; under Mitsunobu conditions, to provide a compound of Formula (I). For example, using triphenylphosphine, polymer bound triphenylphosphine, and the like; a base such as di-tert-butyl azodicarboxylate (DBAD), di-*tert*-butyl azodicarboxylate (DIAD), diethyl azodicarboxylate (DEAD) and the like; in a solvent such as THF, ACN, dioxane, or a mixture thereof; at a temperature ranging from 25 to 110 °C; to provide a compound of Formula (I).

Wherein when a (VIII) has a protecting group, deprotection employing conditions known to one skilled in the art provides a compound of Formula (I). For example 6-[3-(difluoromethoxy)-4-fluoro-phenyl]-1-(1H-pyrazol-4-ylmethyl)pyrazolo[4,3-b]pyridine, and the protecting group is tetrahydropyranyl. Deprotection is achieved employing a suitable acid such as HCl in dioxane.

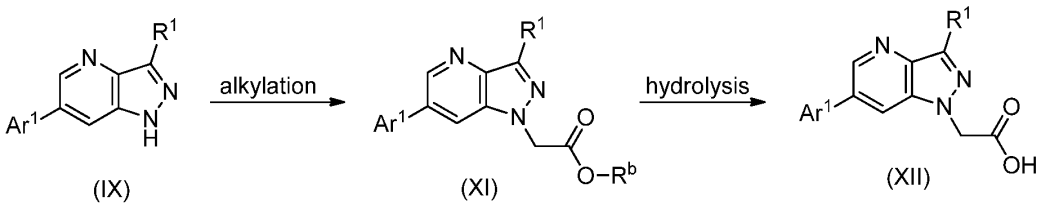
A compound of Formula (I), where R^2 is 

; is reacted in a coupling reaction previously described with zinc cyanide, [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane, in a

suitable solvent such as DMF, DMA, and the like; at temperatures ranging from rt to 150 °C; under microwave irradiation; provides a compound of Formula (I), where R^2 is .

A compound of Formula (I), where R^2 is ; undergoes classic pyridinium hydrochloride (Pyr,HCl) melt demethylation, at a temperature of about 190 °C, for a period of about 24 hr, to provide a compound of Formula (I) where R^2 is .

SCHEME 5

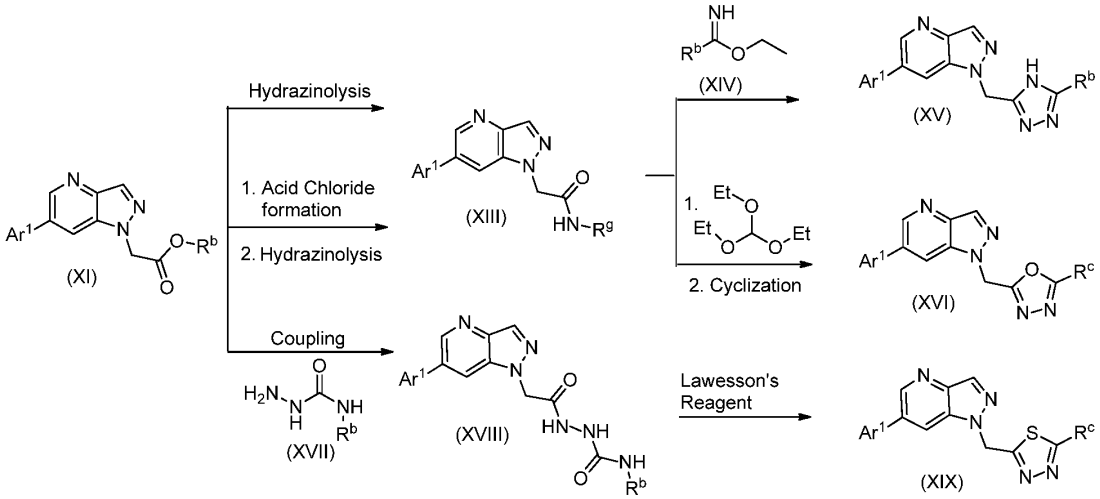


(IX) (XI) (XII)

According to SCHEME 5, a compound of formula (IX) where R^1 is H, F, or CH_3, and Ar^1 is as defined in claim 1; is reacted with an alkylating agent such as ethyl bromoacetate, ethyl chloroacetate, and the like; in a suitable solvent such as DMF, and the like; a base such as Cs_2CO_3, K_2CO_3, and the like; at temperatures ranging from 0 °C to ambient temperature; affords a compound of formula (XI), where R^b is CH_2CH_3. A compound of formula (XI) is hydrolyzed to the acid compound of formula (XII) using a suitable base such as NaOH, LiOH, KOH, and the

like; in a suitable solvent such as MeOH, EtOH, THF, 1,4-dioxane, MeCN, H_2O, or a mixture thereof.

SCHEME 6



A compound of formula (XI), where R^b is CH_2CH_3, is reacted under hydrazinolysis conditions, to provide a compound of formula (XIII), where R^g is NH_2. For example, reaction of a compound of formula (XI), where R^b is CH_2CH_3, and Ar^1 is as defined as in claim 1; with hydrazine hydrate; in a suitable solvent such as EtOH, and the like; at temperatures ranging from rt to 70 °C, for a period of 24-72 hr; provides a compound of formula (XIII) where R^g is NH_2. A 1,2,4-trizole compound of formula (XV), where R^b is CH_3, and Ar^1 is as described in claim 1; is prepared by reaction of a hydrazide compound of formula (XIII); with an imidate compound of formula (XIV), where R^b is CH_3; a base such triethylamine (TEA); in a suitable solvent such as EtOH, and the like; at temperatures of about 70-90 °C.

A hydrazide compound of formula (XIII), where R^g is NH_2, is prepared in two steps from a compound of formula (XI), where R^b is H. In a first step, a compound of formula (XI), where R^b is H; is converted to the corresponding acid chloride using a reagent such as thionyl chloride, oxalyl chloride, and the like; in a suitable solvent such as THF, DMF, or ACN. In a second step, hydrazinolysis of the acid chloride intermediate is achieved employing conditions previously described to provide a hydrazide compound of formula (XIII). A compound of formula (XVI), where R^c is H, and Ar^1 is as described in claim 1; is prepared in two steps form hydrazide compound of formula (XIII). In a first step, a compound of formula (XIII), where R^g is NH_2, is reacted with triethyl orthoformate; at a temperature of about 140 °C; for a period of about 24

hours; to provide the formyl intermediate compound which was used in the next step directly. Cyclodehydration of the formyl intermediate compound employing an acid such as *p*-toluenesulfonic acid monohydrate (TsOH), acetic acid (AcOH), and the like, preferably TsOH; provides the corresponding 1,3,4-oxadiazole compound of formula (XVI), where R^c is H.

A compound of formula (XI) converted to a compound of formula (XVIII) employing conventional amide bond forming techniques such as coupling reactions which are well known to those skilled in the art. For example, reaction of compound of formula (XVII), where R^b is H or CH_3; with an acid compound of formula (XI), where R^b is H; where the acid is activated with an appropriate activating reagent, for example a carbodiimide, such as N,N'-dicyclohexylcarbodiimide (DCC) or 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC, EDAC or EDCI) optionally in the presence of hydroxybenzotriazole (HOBt) and/or a catalyst such as 4-dimethylaminopyridine (DMAP); a halotrisaminophosphonium salt such as (benzotriazol-1-yloxy)tris(dimethylamino)phosphonium hexafluorophosphate (BOP), or bromotripyrrolidinophosphonium hexafluorophosphate (PyBroP®); a suitable pyridinium salt such as 2-chloro-1-methyl pyridinium chloride; or another suitable coupling agent such as *N,N,N',N'*-tetramethyl-*O*-(1*H*-benzotriazol-1-yl)uronium hexafluorophosphate (HBTU), 1-[bis(dimethylamino)methylene]-1*H*-1,2,3-triazolo[4,5-*b*]pyridinium 3-oxid hexafluorophosphate (HATU), 2,4,6-tripropyl-1,3,5,2,4,6-trioxatriphosphorinane-2,4,6-trioxide (T3P®) and the like, provides a compound of formula (XVIII). 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 (XVIII). Thionation followed by spontaneous ring closure through dehydrosulfurization of a compound of formula (XVIII), where R^b is H or CH_3, with 2,4-bis(4-methoxypheny1)-1,2,3,4-dithiadiphosphetane (Lawesson's reagent), in suitable solvent such as toluene, and the like; at temperatures of about 105 °C; for a period of about 24 hr; affords a thiadiazole compound of formula (XIX), where R^c is NH_2 or $NHCH_3$. A thiadiazole compound of formula (XIX), where R^c is NH_2 is acylated employing an acylating reagent selected from an acyl derivative, an acyl halide such as acetyl chloride and the like, and an acid anhydride such as acetic anhydride,

propionic anhydride, and the like; in a suitable solvent such as toluene, and the like; to afford a thiadiazole compound of formula (XIX), where R^c is $NH(C=O)CH_3$.

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 Et_2O, CH_2Cl_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_2SO_4 or $MgSO_4$. 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_2) 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 μM, 30 x 100 or 50 x 150mm) or an XBridge C18 OBD column (5 μM, 30 x 100 or 50 x 150mm), and a mobile phase of 5% ACN in 20mM NH_4OH 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 μm, 30 x 100mm, T = 45 °C), mobile phase of 5% ACN in H_2O (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 μm, 50 x 100mm), mobile phase of 5% ACN in H_2O (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 (5µm, 100 x 50mm), mobile phase of 5-99% ACN in 20 mM NH_4OH over 10 min and then hold at 99 ACN for 2 min, at a flow rate of 80 mL/min.

or

METHOD E. A Wufeng LC100 equipped with a manual Rheodyne 3725i sampler with a Gemini-NX C18 column (5 µM, 30 x 100 mm), and a mobile phase of 0-90% MeCN:8 mM $(NH_4)HCO_3$ (9:1) in 10 mM aqueous $(NH_4)HCO_3$ over 8 min or 21 min, with a flow rate of 40 mL/min.

or

METHOD F. An AccuPrep HPLC with an XBridge C18 column (5µm, 100 x 50mm), mobile phase of 5-99% ACN in 20 mM NH_4OH over 18 min and then hold at 99 ACN for 2 min, at a flow rate of 80 mL/min.

or

METHOD G: An AccuPrep HPLC with an XBridge C18 column (5µm, 100 x 50mm), mobile phase of 5% ACN in H_2O (both with 0.05% TFA) was held for 1 min, then a gradient of 5-99% ACN over 18 min, then held at 99% ACN for 2 min, with 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.

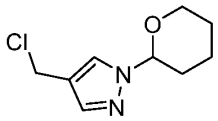
Mass spectra (MS) were obtained on an Agilent series 1100 MSD using electrospray ionization (ESI) in positive mode unless otherwise indicated. Calculated (calcd.) mass corresponds to the exact mass.

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.

Chemical names were generated using ChemDraw Ultra 17.1 (CambridgeSoft Corp., Cambridge, MA) or OEMetaChem V1.4.0.4 (Open Eye).

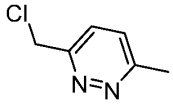
Compounds designated as R* or S* are enantiopure compounds where the absolute configuration was not determined.

Intermediate 1: (Racemic) 4-(Chloromethyl)-1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazole.



To a solution of 3-(chloromethyl)pyrazole hydrochloride (875 mg, 5.72 mmol) in *N,N*-dimethylformamide (DMF) (17 mL) was added 3,4-dihydro-2H-pyran (1.8 mL, 19.7 mmol, 0.922 g/mL). The reaction mixture was stirred at room temperature for 18 h, poured into water (100 mL) and extracted with diethyl ether (Et_2O) (3 x 50 mL). The combined organics were washed with brine (2 x 30 mL), dried over magnesium sulfate ($MgSO_4$), filtered and concentrated. Purification (FCC, SiO_2, 0 to 25% n-heptane/EtOAc) afforded the title compound (760 mg, 3.79 mmol, 66%) as a pale yellow oil. MS (ESI): mass calcd. for $C_9H_{13}ClN_2O$; 200.1 m/z found, 201.1 $[M+H]^+$.

Intermediate 2: 3-(Chloromethyl)-6-methylpyridazine hydrochloride salt.

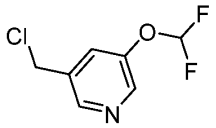


Step A. (6-Methylpyridazin-3-yl)methanol. To a solution of ethyl 6-methylpyridazine-3-carboxylate (200 mg, 1.2 mmol) in methanol (MeOH) (3 mL) and tetrahydrofuran (THF) (1.5 mL) was added sodium borohydride (46 mg, 1.22 mmol) at 0 °C. The reaction mixture was stirred for 10 min at 0 °C then allowed to warm to room temperature and stirred for 1.5 h. 1 M HCl was added (pH~8) and the mixture concentrated. Purification of the residue (FCC, SiO_2, 0 to 10% MeOH in DCM) afforded the title compound (97 mg, 0.781 mmol, 65%) as a yellow crystalline solid. MS (ESI): mass calcd. for $C_6H_8N_2O$; 124.1 m/z found,125.1 $[M+H]^+$.

Step B. 3-(Chloromethyl)-6-methyl-pyridazine hydrochloride. To (6-methylpyridazin-3-yl)methanol (89 mg, 0.717 mmol) was added thionyl chloride (273 µL, 3.76 mmol, 1.64 g/mL) at 0 °C and the reaction was stirred at room temperature for 2 h. The mixture was concentrated and

the residue was taken up in toluene (3 mL) then concentrated again to give the title compound (127 mg, 0.709 mmol, 98%) as a brown powder. MS (ESI): mass calcd. for $C_6H_7ClN_2$; 142.0 m/z found,143.1 $[M+H]^+$.

Intermediate 3: 3-(Chloromethyl)-5-(difluoromethoxy)pyridine hydrochloride salt.



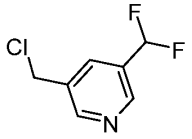
Step A. Methyl 5-(difluoromethoxy)pyridine-3-carboxylate. A mixture of methyl 5-hydroxynicotinate (1.00 g, 6.53 mmol), sodium chlorodifluoroacetate (2.2 g, 14.4 mmol) and cesium carbonate (Cs_2CO_3) (6.40 g, 19.6 mmol) in dry DMF (20 mL) was stirred at 100 °C for 3 h. The reaction mixture was poured into water (80 mL) and diluted with EtOAc (100 mL). The layers were separated, and the aqueous layer was extracted with EtOAc (2 x 80 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated. Purification (FCC, SiO_2, 0 to 30% n-heptane/EtOAc) afforded the title compound (357 mg, 1.76 mmol, 27%) as a pale yellow oil. MS (ESI): mass calcd. for $C_8H_7F_2NO_3$; 203.0 m/z found, 204.1 $[M+H]^+$.

Step B. [5-(Difluoromethoxy)-3-pyridyl]methanol. To a solution of methyl 5-(difluoromethoxy)pyridine-3-carboxylate (265 mg, 1.30 mmol) in MeOH (5.3 mL) and THF (2.7 mL) was added sodium borohydride (99 mg, 2.62 mmol) at 0 °C and the reaction mixture was stirred at room temperature for 20 h. To the reaction mixture was added additional sodium borohydride (99 mg, 2.62 mmol) and the reaction mixture was stirred at room temperature for 2 h. More sodium borohydride (50 mg, 1.32 mmol) was added and the reaction mixture was stirred at room temperature for 2 h. 1 M HCl was added (pH~8) and the mixture concentrated. The residue was taken up in MeOH (15 mL) then filtered and concentrated. Purification (FCC, SiO_2, 0 to 5% DCM/MeOH) afforded the title compound (128 mg, 0.731 mmol, 56%) as a pale yellow oil. MS (ESI): mass calcd. for $C_7H_6F_2NO_2$; 174.0 m/z found, 175.1 $[M+H]^+$.

Step C. 3-(Chloromethyl)-5-(difluoromethoxy)pyridine hydrochloride. To [5-(difluoromethoxy)-3-pyridyl]methanol (118 mg, 0.674 mmol) was added thionyl chloride (257 µL, 3.54 mmol, 1.64 g/mL) at 0 °C and the reaction mixture was stirred at room temperature for 2 h. The reaction mixture was concentrated, and the residue was taken up in toluene (3 mL) and concentrated

again to give the title compound (133 mg, 0.578 mmol, 86%) as an off-white powder. MS (ESI): mass calcd. for $C_7H_6ClF_2NO_2$; 193.0 m/z found, 194.0 $[M+H]^+$.

Intermediate 4: 3-(Chloromethyl)-5-(difluoromethyl)pyridine hydrochloride salt.

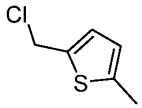


Step A. Methyl 5-(difluoromethyl)pyridine-3-carboxylate. To a solution of methyl 5-formylnicotinate (500 mg, 3.03 mmol) in DCM (10 mL) was added diethylaminosulfur trifluoride (520 µL, 3.94 mmol, 1.22 g/mL) at 0 °C. The reaction mixture was allowed to reach room temperature and stirred for 18 h under argon. The reaction mixture was cooled to 0 °C and quenched with saturated aqueous $NaHCO_3$ (10 mL). The layers were separated and the aqueous layer extracted with DCM (2 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated to afford the title compound (467 mg, 2.49 mmol, 82%) as a yellow crystalline solid. MS (ESI): mass calcd. for $C_8H_7F_2NO_2$; 187.0 m/z found, 188.1 $[M+H]^+$.

Step B. (5-(Difluoromethyl)pyridin-3-yl)methanol. To a solution of methyl 5-(difluoromethyl)pyridine-3-carboxylate (160 mg, 0.855 mmol) in DCM (3.2 mL) cooled to 0 °C was added diisobutylaluminum hydride (1.0 M in DCM, 1.8 mL, 1.80 mmol). The reaction was stirred at 0 °C for 1 h under argon then additional diisobutylaluminum hydride (1.0 M in DCM, 769 µL, 0.769 mmol) was added. The reaction mixture was stirred at 0 °C for another 1 h then quenched with MeOH (5 mL), filtered, and concentrated. Purification (FCC, SiO_2, 0 to 5% DCM/MeOH) afforded the title compound (40 mg) as a yellow oil. MS (ESI): mass calcd. for $C_7H_7F_2NO$; 159.0 m/z found, 160.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.70 – 8.67 (m, 1H), 8.67 – 8.63 (m, 1H), 7.96 – 7.90 (m, 1H), 7.16 (t, J = 55.3 Hz, 1H), 5.45 (t, J = 5.7 Hz, 1H), 4.61 (d, J = 5.7 Hz, 2H).

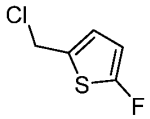
Step C. 3-(Chloromethyl)-5-(difluoromethyl)pyridine hydrochloride. To [5-(difluoromethyl)-3-pyridyl]methanol (37 mg) was added thionyl chloride (89 µL, 1.23 mmol, 1.64 g/mL) at 0 °C. The reaction mixture was stirred at room temperature for 2 h then concentrated. The residue was taken up in DCM (2 mL) and concentrated to afford the title compound (44 mg, 0.206 mmol, 88%) as an off-white powder. MS (ESI): mass calcd. for $C_7H_6ClF_2N$; 177.0 m/z found, 178.0 $[M+H]^+$.

Intermediate 5: 2-(Chloromethyl)-5-methylthiophene.



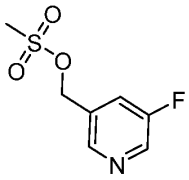
To a solution of (5-methylthiophen-2-yl)methanol (100 mg, 0.78 mmol) in DCM (1.4 mL) was added thionyl chloride (170 µL, 2.34 mmol, 1.64 g/mL) at 0 °C and the reaction mixture was stirred at room temperature for 2 h. The reaction mixture was then concentrated to afford the title compound (108 mg, 0.737 mmol, 94%) as a dark brown oil. Crude title compound was used without further purification. No mass found in MS.

Intermediate 6: 2-(Chloromethyl)-5-fluorothiophene.



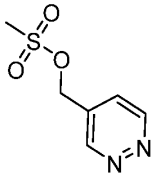
The title compound was made in an analogous manner to Intermediate 5 using (5-fluorothiophen-2-yl)methanol. Crude title compound was used without further purification. No mass found in MS.

Intermediate 7: (5-Fluoropyridin-3-yl)methyl methanesulfonate.



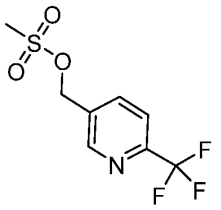
Methanesulfonyl chloride (0.04 mL, 0.5 mmol) was added to a solution of (5-fluoropyridin-3-yl)methanol (50.0 mg, 0.4 mmol) and triethylamine (TEA) (0.8 mL, 0.6 mmol) in DCM (1.7 mL) at 0 °C under a nitrogen atmosphere. After 45 minutes, the reaction mixture was quenched with water (10 mL) and saturated aqueous $NaHCO_3$ (10 mL). The layers were separated and the aqueous layer was extracted with DCM (2 x 35 mL). The combined organics were dried over $MgSO_4$, filtered and concentrated to afford title compound. Crude title compound was used without further purification.

Intermediate 8: Pyridazin-4-ylmethyl methanesulfonate.



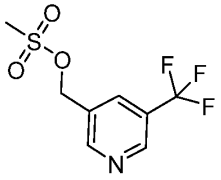
The title compound was prepared in a manner analogous to Intermediate 7 using pyridazin-4-ylmethanol. Crude title compound was used without further purification.

Intermediate 9: (6-(Trifluoromethyl)pyridin-3-yl)methyl methanesulfonate.



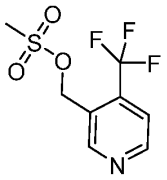
The title compound was prepared in a manner analogous to Intermediate 7 using (6-(trifluoromethyl)pyridin-3-yl)methanol. Crude title compound was used without further purification.

Intermediate 10: (5-(Trifluoromethyl)pyridin-3-yl)methyl methanesulfonate.



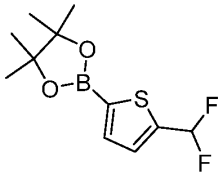
The title compound was prepared in a manner analogous to Intermediate 7 using (5-(trifluoromethyl)pyridin-3-yl)methanol. Crude title compound was used without further purification.

Intermediate 11: (4-(Trifluoromethyl)pyridin-3-yl)methyl methanesulfonate.



The title compound was prepared in a manner analogous to Intermediate 7 using (4-(trifluoromethyl)pyridin-3-yl)methanol. Crude title compound was used without further purification.

Intermediate 12: 2-(5-(Difluoromethyl)thiophen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.

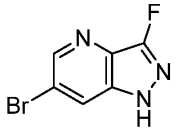


Step A. 2-Bromo-5-(difluoromethyl)thiophene. To dimethylaminosulfur trifluoride (5.6 mL, 42.4 mmol, 1.22 g/mL) was added 5-bromothiophene-2-carbaldehyde (2.00 g, 10.5 mmol) dropwise at 0 °C under argon. The reaction mixture was then stirred at room temperature for 2 h. The reaction was quenched by dropwise addition of 2 M sodium hydroxide (NaOH) (10 mL) at 0 °C. The layers were separated and the aqueous layer was extracted with EtOAc (2 x 20 mL). The combined organics were dried over Na_2SO_4, filtered and concentrated. Purification (FCC, SiO_2, n-heptane) afforded title compound (1.07 g, 5.03 mmol, 48%) as a colorless liquid. No mass ion found in MS.

Step B. 2-(5-(difluoromethyl)thiophen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. To a solution of 2-bromo-5-(difluoromethyl)thiophene (930 mg, 4.37 mmol) in THF (17 mL) was added *n*-butyllithium (1.6 M in hexanes, 3 mL, 4.8 mmol) dropwise at −78 °C under argon and the reaction mixture was stirred at −78 °C for 1 h. To the reaction mixture was added a solution of 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (980 µL, 4.8 mmol, 0.912 g/mL) in THF (2 mL) and the reaction was stirred at −78 °C for 1 h. The reaction mixture was allowed to reach room temperature and then stirred for 16 h. The reaction was diluted with saturated aq. NH_4Cl (30 mL) and ethyl acetate (EtOAc) (40 mL). The layers were separated and the aqueous layer was extracted with EtOAc (1 x 50 mL). The combined organics were dried over Na_2SO_4,

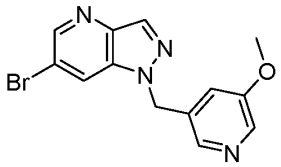
filtered and concentrated to give the title compound (1.00 g) as a brown oil that was used without further purification.

Intermediate 13: 6-Bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridine.



To a solution of 6-bromo-1H-pyrazolo[4,3-b]pyridine (2.5 g, 12.6 mmol) in acetonitrile (62.5 mL) was added 1-chloromethyl-4-fluoro-1,4-diazobicyclo[2.2.2]octane bis(tetrafluoroborate) (Selectflor®) (6.7 g, 18.9 mmol) and the reaction mixture was stirred at 90 °C for 22 h. The reaction mixture was cooled, poured into water (120 mL), and was diluted with EtOAc (80 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 x 60 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated. The residue was purified by basic reverse phase preparative HPLC (METHOD E) to afford the title compound (641 mg, 2.97 mmol, 23%) as a brown powder. MS (ESI): mass calcd. for $C_6H_3BrFN_3$; 214.9 m/z found, 216.0 $[M+H]^+$.

Intermediate 14: 6-Bromo-1-((5-methoxypyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine.

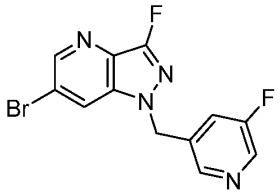


A mixture of 6-bromo-1H-pyrazolo[4,3-b]pyridine (538 mg, 2.72 mmol), 3-(chloromethyl)-5-methoxypyridine hydrochloride (580 mg, 2.99 mmol) and Cs_2CO_3 (2.21 g, 6.78 mmol) in dry DMF (15 mL) was stirred at room temperature for 4 h. The reaction mixture was poured into water (30 mL) and diluted with EtOAc (15 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 x 30 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated. Purification (FCC, SiO_2, 50 to 80% n-heptane/EtOAc) afforded the title compound (508 mg, 1.59 mmol, 59%) as a pale yellow powder. MS (ESI): mass calcd for $C_{13}H_{11}BrN_4O$, 318.0; m/z found, 319.0 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.77 (s, 1H),

8.64 – 8.58 (m, 1H), 8.39 (s, 1H), 8.25 – 8.20 (m, 1H), 8.14 (s, 1H), 7.33 – 7.26 (m, 1H), 5.70 (s, 2H), 3.79 (s, 3H).

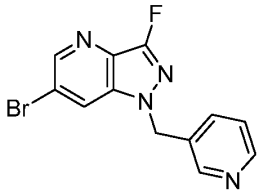
The reaction also produced 6-bromo-2-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine (232 mg, 0.727 mmol, 27%) as a pale yellow powder. MS (ESI): mass calcd for $C_{13}H_{11}BrN_4O$, 318.0; m/z found, 319.0 $[M+H]^+$.

Intermediate 15: 6-Bromo-3-fluoro-1-((5-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine.



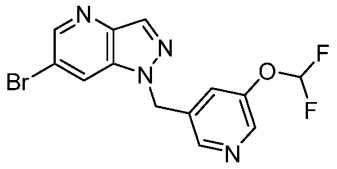
The title compound was made in an analogous manner to Intermediate 14 using 6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridine (Intermediate 13) instead of 6-bromo-1H-pyrazolo[4,3-b]pyridine and using 3-(chloromethyl)-5-fluoropyridine instead of 3-(chloromethyl)-5-methoxypyridine. MS (ESI): mass calcd for $C_{12}H_7BrF_2N_4$, 323.9; m/z found, 325.1 $[M+H]^+$.

Intermediate 16: 6-Bromo-3-fluoro-1-(pyridin-3-ylmethyl)-1H-pyrazolo[4,3-b]pyridine.



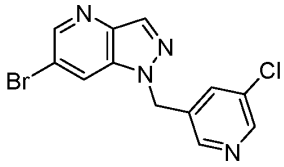
The title compound was made in an analogous manner to Intermediate 14 using 6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridine (Intermediate 13) instead of 6-bromo-1H-pyrazolo[4,3-b]pyridine and using 3-(chloromethyl)pyridine instead of 3-(chloromethyl)-5-methoxypyridine. MS (ESI): mass calcd for $C_{12}H_7BrF_2N_4$, 305.9; m/z found, 307.1 $[M+H]^+$.

Intermediate 17: 6-Bromo-1-((5-(difluoromethoxy)pyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine.



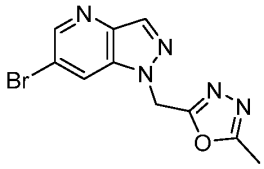
The title compound was made in an analogous manner to Intermediate 14 using 3-(chloromethyl)-5-(difluoromethoxy)pyridine instead of 3-(chloromethyl)-5-methoxypyridine. MS (ESI): mass calcd for $C_{13}H_9BrF_2N_4O$, 353.9; m/z found, 355.0 $[M+H]^+$.

Intermediate 18: 6-Bromo-1-((5-chloropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine.



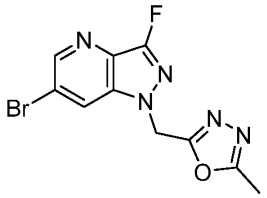
The title compound was made in an analogous manner to Intermediate 14 using 3-chloro-5-(chloromethyl)pyridine instead of 3-(chloromethyl)-5-methoxypyridine. MS (ESI): mass calcd for $C_{12}H_8BrClN_4$, 321.9; m/z found, 323.0 $[M+H]^+$.

Intermediate 19: 2-((6-Bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-5-methyl-1,3,4-oxadiazole.



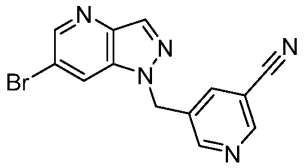
The title compound was made in an analogous manner to Intermediate 14 using 2-(chloromethyl)-5-methyl-1,3,4-oxadiazole instead of 3-(chloromethyl)-5-methoxypyridine. MS (ESI): mass calcd for $C_{10}H_8BrN_5O$, 292.9; m/z found, 294.0 $[M+H]^+$.

Intermediate 20: 2-((6-Bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-5-methyl-1,3,4-oxadiazole.



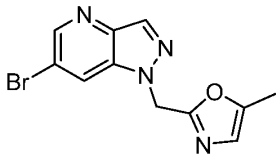
The title compound was made in an analogous manner to Intermediate 14 using 6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridine (Intermediate 13) instead of 6-bromo-1H-pyrazolo[4,3-b]pyridine and using 2-(chloromethyl)-5-methyl-1,3,4-oxadiazole instead of 3-(chloromethyl)-5-methoxypyridine. MS (ESI): mass calcd for $C_{10}H_7BrFN_5O$, 310.9; m/z found, 312.0 $[M+H]^+$.

Intermediate 21: 5-((6-Bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)nicotinonitrile.



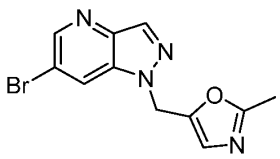
The title compound was made in an analogous manner to Intermediate 14 using 5-(chloromethyl)nicotinonitrile instead of 3-(chloromethyl)-5-methoxypyridine. MS (ESI): mass calcd for $C_{13}H_8BrN_5$, 313.0; m/z found, 314.0 $[M+H]^+$.

Intermediate 22: 2-((6-Bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-5-methyloxazole.



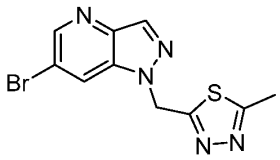
The title compound was made in an analogous manner to Intermediate 14 using 2-(chloromethyl)-5-methyloxazole instead of 3-(chloromethyl)-5-methoxypyridine. MS (ESI): mass calcd. for $C_{11}H_9BrN_4O$, 292.0; m/z found, 293.0 $[M+H]^+$.

Intermediate 23: 5-((6-Bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-2-methyloxazole.



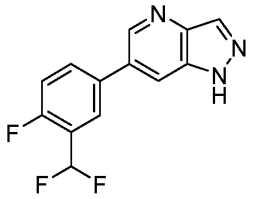
The title compound was prepared in a manner analogous to Intermediate 14 using 5-(chloromethyl)-2-methyloxazole instead of 3-(chloromethyl)-5-methoxypyridine. MS (ESI): mass calcd. for $C_{11}H_9BrN_4O$, 292.0; m/z found, 293.0 $[M+H]^+$.

Intermediate 24: 2-((6-Bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-5-methyl-1,3,4-thiadiazole.



The title compound was prepared in a manner analogous to Intermediate 14 using 2-(chloromethyl)-5-methyl-1,3,4-thiadiazole instead of 3-(chloromethyl)-5-methoxypyridine. MS (ESI): mass calcd. for$C_{10}H_8BrN_5S$, 309.0; m/z found, 309.9 $[M+H]^+$.

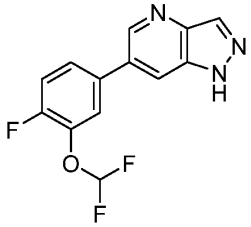
Intermediate 25: 6-(3-(Difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine.



A mixture of 6-bromo-1H-pyrazolo[4,3-b]pyridine (1.40 g, 7.07 mmol), 2-[3-(difluoromethyl)-4-fluoro-phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.31 g, 8.49 mmol), [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (0.673 g, 0.92 mmol) and Na_2CO_3 (2.25 g, 21.2 mmol) in degassed acetonitrile (ACN) (24.4 mL) and water (3.76 mL) was stirred at 120 °C for 4 h under microwave irradiation. The reaction mixture was poured into water (30 mL) and the mixture was extracted with EtOAc (3 x 30 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated. Purification (FCC, SiO_2, 10 to 50% n-heptane/EtOAc)

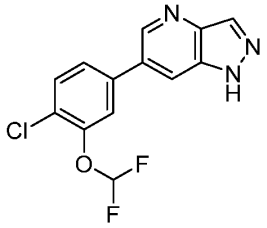
afforded a solid that was triturated with Et_2O (4 mL) to afford the title compound (1.41 g, 5.36 mmol, 76%) as an off-white powder. MS (ESI): mass calcd for $C_{13}H_8F_3N_3$, 263.1; m/z found, 264.2 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 13.48 (br s, 1H), 8.84 (d, J = 2.0 Hz, 1H), 8.41 – 8.30 (m, 1H), 8.30 – 8.20 (m, 1H), 8.13 – 7.99 (m, 2H), 7.60 – 7.49 (m, 1H), 7.27 (t, J = 54.1 Hz, 1H).

Intermediate 26: 6-(3-(Difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine.



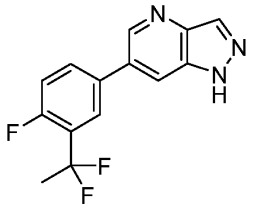
The title compound was made in an analogous manner to Intermediate 25 using 2-(3-(difluoromethoxy)-4-fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane instead of 2-[3-(difluoromethyl)-4-fluoro-phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd for $C_{13}H_8F_3N_3O$, 279.0; m/z found, 280.2 $[M+H]^+$.

Intermediate 27: 6-(4-Chloro-3-(difluoromethoxy)phenyl)-1H-pyrazolo[4,3-b]pyridine.



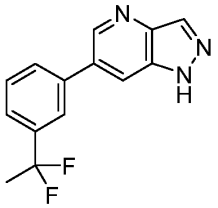
The title compound was made in an analogous manner to Intermediate 25 using 2-(3-(difluoromethoxy)-4-chlorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane instead of 2-[3-(difluoromethyl)-4-fluoro-phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd for $C_{13}H_8ClF_2N_3O$, 295.0; m/z found, 296.0 $[M+H]^+$.

Intermediate 28: 6-(3-(1,1-Difluoroethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine.



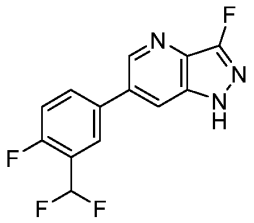
The title compound was made in an analogous manner to Intermediate 25 using 2-(3-(1,1-difluoroethyl)-4-fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane instead of 2-[3-(difluoromethyl)-4-fluoro-phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd for $C_{14}H_{10}F_3N_3$, 277.1; m/z found, 278.1 $[M+H]^+$.

Intermediate 29: 6-(3-(1,1-Difluoroethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine.



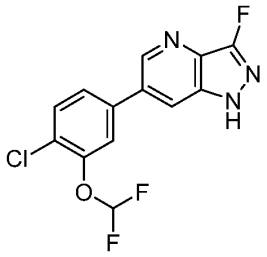
The title compound was made in an analogous manner to Intermediate 25 using 2-(3-(1,1-difluoroethyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane instead of 2-[3-(difluoromethyl)-4-fluoro-phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd for $C_{14}H_{11}F_2N_3$, 259.1; m/z found, 260.1 $[M+H]^+$.

Intermediate 30: 6-(3-(Difluoromethyl)-4-fluorophenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridine.



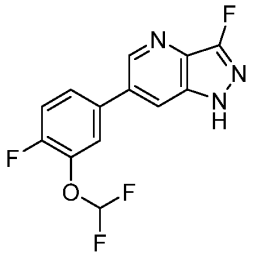
The title compound was made in an analogous manner to Intermediate 25 using 6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridine (Intermediate 13) instead of 6-bromo-1H-pyrazolo[4,3-b]pyridine. MS (ESI): mass calcd for $C_{13}H_7F_4N_3$, 281.1; m/z found, 280.2 $[M-H]^-$.

Intermediate 31: 6-(4-Chloro-3-(difluoromethoxy)phenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridine.



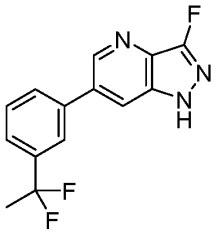
The title compound was made in an analogous manner to Intermediate 25 using 6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridine (Intermediate 13) instead of 6-bromo-1H-pyrazolo[4,3-b]pyridine and 2-(3-(difluoromethoxy)-4-chlorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane instead of 2-[3-(difluoromethyl)-4-fluoro-phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd for $C_{13}H_7ClF_3N_3O$, 313.0; m/z found, 314.1 $[M+H]^+$.

Intermediate 32: 6-(3-(Difluoromethoxy)-4-fluorophenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridine.



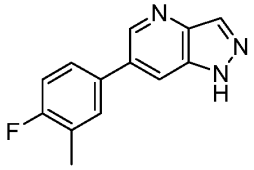
The title compound was made in an analogous manner to Intermediate 25 using 6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridine (Intermediate 13) instead of 6-bromo-1H-pyrazolo[4,3-b]pyridine and using 2-(3-(difluoromethoxy)-4-fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane instead of 2-[3-(difluoromethyl)-4-fluoro-phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd for $C_{13}H_7F_4N_3O$, 297.1; m/z found, 298.0 $[M+H]^+$.

Intermediate 33: 6-(3-(1,1-Difluoroethyl)phenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridine.



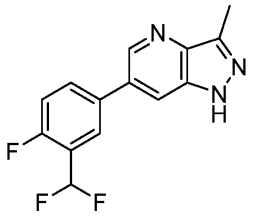
The title compound was made in an analogous manner to Intermediate 25 using 6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridine (Intermediate 13) instead of 6-bromo-1H-pyrazolo[4,3-b]pyridine and using 2-(3-(1,1-difluoroethyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane instead of 2-[3-(difluoromethyl)-4-fluoro-phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd for $C_{14}H_{10}F_3N_3$, 277.1; m/z found, 278.1 $[M+H]^+$.

Intermediate 34: 6-(4-Fluoro-3-methylphenyl)-1H-pyrazolo[4,3-b]pyridine.



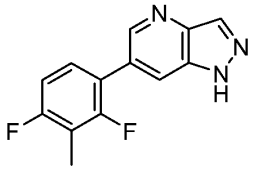
The title compound was made in an analogous manner to Intermediate 25 using (4-fluoro-3-methylphenyl)boronic acid instead of 2-[3-(difluoromethyl)-4-fluoro-phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd for $C_{13}H_{10}FN_3$, 227.1; m/z found, 228.1 $[M+H]^+$.

Intermediate 35: 6-(3-(Difluoromethyl)-4-fluorophenyl)-3-methyl-1H-pyrazolo[4,3-*b*]pyridine.



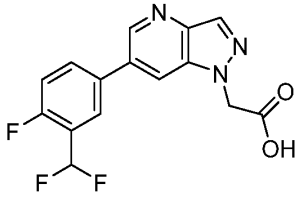
The title compound was made in an analogous manner to Intermediate 25 using 6-bromo-3-methyl-1H-pyrazolo[4,3-b]pyridine instead of 6-bromo-1H-pyrazolo[4,3-b]pyridine. MS (ESI): mass calcd. for $C_{14}H_{10}F_3N_3$, 277.1; m/z found, 278.1 $[M+H]^+$.

Intermediate 36: 6-(2,4-Difluoro-3-methylphenyl)-1H-pyrazolo[4,3-b]pyridine.



The title compound was made in an analogous manner to Intermediate 25 using (2,4-difluoro-3-methylphenyl)boronic acid instead of 2-[3-(difluoromethyl)-4-fluoro-phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd. for $C_{13}H_9F_2N_3$, 245.1; m/z found, 246.1 $[M+H]^+$.

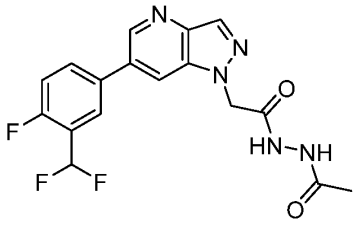
Intermediate 37: 2-(6-(3-(Difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid.



Step A. Ethyl 2-(6-(3-(difluoromethyl)-4-fluoro-phenyl)pyrazolo(4,3-b)pyridin-1-yl)acetate. To a solution of 6-(3-(difluoromethyl)-4-fluoro-phenyl)-1H-pyrazolo(4,3-b)pyridine (Intermediate 25, 2.00 g, 7.6 mmol) in DMF (30 mL) was added Cs_2CO_3 (2.72 g, 8.35 mmol) at 0 °C and the reaction was stirred at 0 °C for 30 min. To the reaction mixture was added ethyl chloroacetate (895 µL, 8.36 mmol, 1.14 g/mL) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 1 h. The reaction mixture was poured into water (50 mL) and the mixture was extracted with EtOAc (3 x 75 mL). The organic layers were combined and concentrated. Purification (FCC, SiO_2, 0 to 75% n-heptane/EtOAc) afforded the title compound (1.60 g, 4.580 mmol, 60%) as a white powder. MS (ESI): mass calcd for $C_{17}H_{14}F_3N_3O_2$, 349.1; m/z found, 350.1 $[M+H]^+$.

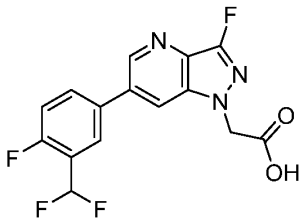
Step B. 2-(6-(3-(Difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid. To a solution of ethyl 2-(6-(3-(difluoromethyl)-4-fluoro-phenyl)pyrazolo(4,3-b)pyridin-1-yl)acetate (1.60 g, 4.58 mmol) in 1,4-dioxane (14 mL) and water (9 mL) was added lithium hydroxide monohydrate (385 mg, 9.17 mmol) and the mixture was stirred at room temperature for 1 h, concentrated to ~9 mL and diluted with water (75 mL). The mixture was acidified to pH 4 with 1 M HCl. The precipitate was collected and washed with water (2 x 10 mL) and Et_2O (3 x 10 mL) to afford the title compound (1.74 g) as a white powder that was used without further purification. MS (ESI): mass calcd for $C_{15}H_{10}F_3N_3O_2$, 321.1; m/z found, 322.1 $[M+H]^+$.

Intermediate 38: N'-Acetyl-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetohydrazide.



A mixture of 2-(6-(3-(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid (Intermediate 37, 71.7 mg, 0.223 mmol), acethydrazide (39.2 mg, 0.529 mmol), *N,N*-diisopropylethylamine (Hünig's base) (0.12 mL, 0.696 mmol), *N*-ethyl-*N'*-(3-dimethylaminopropyl)carbodiimide (EDCI) (68.2 mg, 0.356 mmol), and hydroxybenzotriazole (HOBt) (48.5 mg, 0.359 mmol) was dissolved in DMF (1.5 mL) and stirred at rt overnight. The mixture was then diluted with EtOAc and water, then the layers were separated, and the aqueous layer was extracted with EtOAc (x 3). The combined organic layers were washed with water (x 2) and brine (x 1), then dried (Na_2SO_4) and concentrated under reduced pressure. Purification (FCC, SiO_2, 0 – 10% MeOH in DCM) afforded the title compound as a tan colored solid (58.6 mg, 70%). MS (ESI): mass calcd. for $C_{17}H_{14}F_3N_5O_2$, 377.1; m/z found, 378.1 $[M+H]^+$. ^1H NMR (500 MHz, CD_3OD) δ 8.82 (d, J = 1.8 Hz, 1H), 8.42 (dd, J = 1.8, 1.0 Hz, 1H), 8.27 (d, J = 1.0 Hz, 1H), 8.01 (dd, J = 16.5, 7.4 Hz, 2H), 7.41 (dd, J = 9.9, 8.7 Hz, 1H), 7.08 (t, J = 54.6 Hz, 1H), 5.35 (s, 2H), 1.99 (s, 3H).

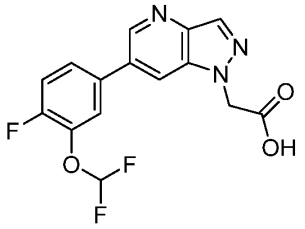
Intermediate 39: 2-(6-(3-(Difluoromethyl)-4-fluorophenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid.



The title compound was made in an analogous manner to Intermediate 37 using Intermediate 30: 6-(3-(difluoromethyl)-4-fluorophenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridine instead of 6-(3-

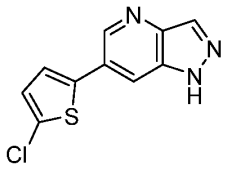
(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine. MS (ESI): mass calcd for $C_{15}H_9F_4N_3O_2$, 339.1; m/z found, 340.1 $[M+H]^+$.

Intermediate 40: 2-(6-(3-(Difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid.



The title compound was made in an analogous manner to Intermediate 37 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) instead of 6-(3-(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine. MS (ESI): mass calcd for $C_{15}H_{10}F_3N_3O_3$, 337.1; m/z found, 338.1 $[M+H]^+$.

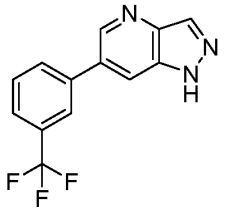
Intermediate 41: 6-(5-Chloro-2-thienyl)-1*H*-pyrazolo[4,3-*b*]pyridine.



To a solution of 6-bromo-1*H*-pyrazolo[4,3-*b*]pyridine (500 mg, 2.52 mmol) in a mixture of degassed 1,4-dioxane (39.4 mL) and water (9.55 mL) was added 5-chlorothiophene-2-boronic acid (431 mg, 2.654 mmol), potassium fluoride (440 mg, 7.57 mmol) and tetrakis(triphenylphosphine)palladium(0) (205 mg, 0.177 mmol) and the reaction mixture was stirred at 80 °C for 1 h under argon. Additional 5-chlorothiophene-2-boronic acid (123 mg, 0.757 mmol) and tetrakis(triphenylphosphine)palladium(0) (87 mg, 0.075 mmol) were introduced and the reaction mixture was stirred at 80 °C for an additional 2 h. The reaction mixture was diluted with water (40 mL) and DCM (30 mL). The layers were separated and the aqueous layer was extracted with DCM (3 x 40 mL). The combined organics were dried over Na_2SO_4, filtered and concentrated. Purification (FCC, SiO_2, 25 to 100% n-heptane/EtOAc) afforded the title compound (419 mg, 1.78 mmol, 70%) as a yellow powder after triturating with diethyl ether (7 mL). MS (ESI): mass calcd. for $C_{10}H_6ClN_3S$, 235.0; m/z found, 236.0 $[M+H]^+$. ^1H NMR (300

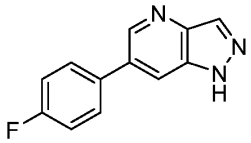
MHz, DMSO-d_6) δ 13.42 (s, 1H), 8.82 (d, J = 2.0 Hz, 1H), 8.35 – 8.29 (m, 1H), 8.17 – 8.09 (m, 1H), 7.64 (d, J = 4.0 Hz, 1H), 7.25 (d, J = 4.0 Hz, 1H).

Intermediate 42: 6-(3-(Trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine.



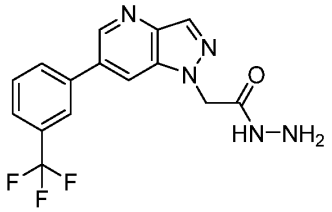
A suspension of 6-bromo-1H-pyrazolo[4,3-b]pyridine (5.0 g, 25.3 mmol), 3-(trifluoromethyl)phenylboronic acid (5.8 g, 30.3 mmol) and palladium-tetrakis(triphenylphosphine) (1.5 g, 1.3 mmol) in aqueous Na_2CO_3 (2M, 32.5 mL, 64.9 mmol) and 1,4-dioxane (96.9 mL) was stirred at 120 °C under a nitrogen atmosphere. After 48 hours, the reaction mixture was cooled and diluted with EtOAc. The resulting mixture was washed with water (2x) and the organic layer was then dried over Na_2SO_4 and concentrated in vacuo. The residue was purified (FCC, SiO_2, n-heptane/EtOAc, 0-50 %) to afford a yellowish solid. The solid was triturated with Et_2O to provide the title compound (2.1 g, 8.0 mmol, 31.6 %). MS (ESI): mass calcd. for $C_{13}H_8F_3N_3$, 263.1; m/z found, 264.1 $[M+H]^+$.

Intermediate 43: 6-(4-Fluorophenyl)-1H-pyrazolo[4,3-b]pyridine.



The title compound was made in an analogous manner to Intermediate 42 using (4-fluorophenyl)boronic acid instead of 3-(trifluoromethyl)phenylboronic acid. MS (ESI): mass calcd for $C_{12}H_8FN_3$, 213.1; m/z found, 214.1 $[M+H]^+$.

Intermediate 44: 2-(6-(3-(Trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetohydrazide.

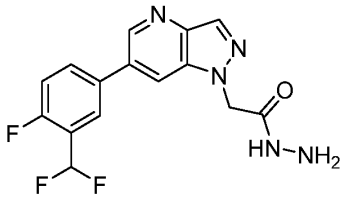


Step A. 2-(6-(3-(Trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid. Sodium hydride (60% dispersion in mineral oil, 387.5 mg, 9.7 mmol) was added to a stirred solution of 6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 42, 850 mg, 3.2 mmol) in DMF (20 mL) at 0 °C, and the reaction mixture was stirred at 0 °C for 10 minutes. Ethyl bromoacetate (0.54 mL, 4.8 mmol) was then added and the reaction mixture was allowed to warm to room temperature and stirred for 16 h. Aqueous potassium hydroxide (1M, 16.1 mL, 16.1 mmol) was added and the reaction mixture stirred for 1 hour. The reaction mixture was then concentrated and the residue was taken up in water and washed with EtOAc. The aqueous layer was acidified with 1M HCl and a precipitate forms. The solid was collected by filtration and washed with water then dried. Trituration of the solid with Et_2O provided the title compound (630 mg, 2.0 mmol, 60.7%). MS (ESI): mass calcd. for $C_{15}H_{10}F_3N_3O_2$, 321.1; m/z found, 322.2 $[M+H]^+$.

Step B. 2-(6-(3-(Trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetyl chloride. A mixture of 2-(6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid (235 mg, 0.7 mmol) and thionyl chloride (5 mL, 68.9 mmol) was stirred at 75 °C for 1 hour. The reaction mixture was then concentrated under vacuum to provide the title compound (134 mg, 0.4 mmol, 53.9%) that was used directly in the following step.

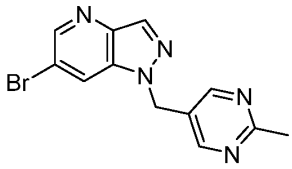
Step C. 2-(6-(3-(Trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetohydrazide. A solution of 2-(6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetyl chloride (Intermediate 5, 134 mg, 0.4 mmol) in hydrazine hydrate (5 mL) was stirred at rt for 30 min. The reaction mixture was then concentrated to afford the title compound that was used without purification. (138 mg, 0.4 mmol). MS (ESI): mass calcd. for $C_{15}H_{12}F_3N_5O$, 335.1; m/z found, 336.3 $[M+H]^+$.

Intermediate 45: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetohydrazide.



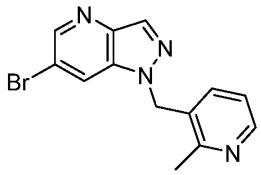
To ethyl 2-(6-(3-(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetate (Step A, Intermediate 37, 217.3 mg, 0.622 mmol) stirring in EtOH (3 mL) was added hydrazine hydrate (0.36 mL, 7.263 mmol). The reaction mixture was warmed to 70 °C until all solid had dissolved, then was removed from the heat, the stir bar was removed, and the mixture was left to cool to rt. The resulting slurry was filtered after standing for 3 days at rt to afford the title compound as a white solid (140 mg, 66%). MS (ESI): mass calcd. for $C_{15}H_{12}F_3N_5O$, 335.1; m/z found, 336.1 $[M+H]^+$. ^1H NMR (400 MHz, CD_3OD) δ 8.80 (s, 1H), 8.38 – 8.32 (m, 1H), 8.26 (d, J = 1.0 Hz, 1H), 8.04 – 7.87 (m, 2H), 7.47 – 7.32 (m, 1H), 7.25 – 6.87 (m, 1H), 5.21 (s, 2H).

Intermediate 46: 6-Bromo-1-((2-methylpyrimidin-5-yl)methyl)-1H-pyrazolo[4,3-b]pyridine.



The title compound was prepared in a manner analogous to Intermediate 44, Step A, using 6-bromo-1H-pyrazolo[4,3-b]pyridine and 5-(chloromethyl)-2-methylpyrimidinehydrochloride. MS (ESI): mass calcd. for $C_{11}H_8BrFN_5$, 289.0; m/z found, 290.0 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 9.19 – 9.15 (m, 1H), 8.73 – 8.70 (m, 1H), 8.65 – 8.62 (m, 1H), 8.42 – 8.39 (m, 1H), 7.70 – 7.65 (m, 1H), 7.52 – 7.47 (m, 1H), 6.02 (s, 2H).

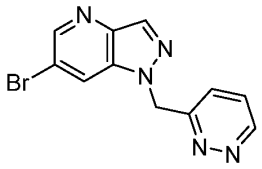
Intermediate 47: 6-Bromo-1-((2-methylpyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine.



The title compound was prepared in a manner analogous to Intermediate 44, Step A, using 6-bromo-1H-pyrazolo[4,3-b]pyridine and 3-(chloromethyl)-2-methylpyridine. MS (ESI): mass

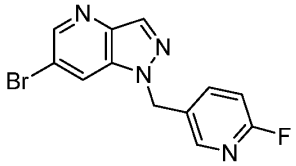
calcd. for $C_{13}H_{11}BrN_4$, 302.0; m/z found, 303.0 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.70 – 8.68 (m, 1H), 8.64 – 8.62 (m, 1H), 8.42 – 8.41 (m, 1H), 8.37 – 8.34 (m, 1H), 7.16 – 7.12 (m, 1H), 7.10 – 7.06 (m, 1H), 5.73 (s, 2H), 2.52 (s, 3H).

Intermediate 48: 6-Bromo-1-(pyridazin-3-ylmethyl)-1H-pyrazolo[4,3-b]pyridine.



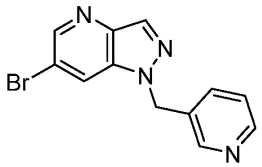
The title compound was prepared in a manner analogous to Intermediate 44, Step A, using 6-bromo-1H-pyrazolo[4,3-b]pyridine and 3-(chloromethyl)pyridazine hydrochloride. MS (ESI): mass calcd. for $C_{11}H_8BrFN_5$, 289.0; m/z found, 290.0 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 9.19 – 9.15 (m, 1H), 8.73 – 8.70 (m, 1H), 8.65 – 8.62 (m, 1H), 8.42 – 8.39 (m, 1H), 7.70 – 7.65 (m, 1H), 7.52 – 7.47 (m, 1H), 6.02 (s, 2H).

Intermediate 49: 6-Bromo-1-((6-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine.



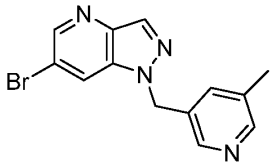
The title compound was prepared in a manner analogous to Intermediate 44, Step A, using 6-bromo-1H-pyrazolo[4,3-b]pyridine and 5-(chloromethyl)-2-fluoropyridine. MS (ESI): mass calcd. for $C_{12}H_8BrFN_4$, 306.0; m/z found, 306.9 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.80 – 8.78 (m, 1H), 8.62 – 8.61 (m, 1H), 8.40 – 8.38 (m, 1H), 8.31 – 8.28 (m, 1H), 7.89 (td, J = 8.2, 2.6 Hz, 1H), 7.15 (dd, J = 8.5, 2.8 Hz, 1H), 5.72 (s, 2H).

Intermediate 50: 6-Bromo-1-(pyridin-3-ylmethyl)-1H-pyrazolo[4,3-b]pyridine.



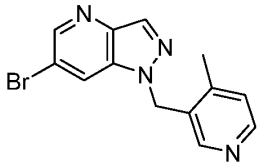
The title compound was prepared in a manner analogous to Intermediate 44, Step A, using 6-bromo-1H-pyrazolo[4,3-b]pyridine and 3-(chloromethyl)pyridine hydrochloride. MS (ESI): mass calcd. for $C_{12}H_9BrN_4$, 288.0; m/z found, 289.0 $[M+H]^+$.

Intermediate 51: 6-Bromo-1-((5-methylpyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine.



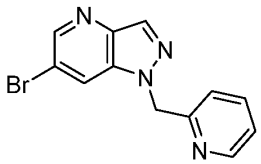
The title compound was prepared in a manner analogous to Intermediate 44, Step A, using 6-bromo-1H-pyrazolo[4,3-b]pyridine and 3-(chloromethyl)-5-methylpyridine hydrochloride. MS (ESI): mass calcd. for $C_{13}H_{11}BrN_4$, 302.0; m/z found, 303.0 $[M+H]^+$.

Intermediate 52: 6-Bromo-1-((4-methylpyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine.



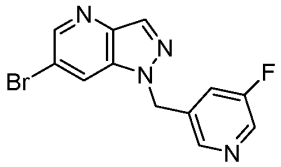
The title compound was prepared in a manner analogous to Intermediate 44, Step A, using 6-bromo-1H-pyrazolo[4,3-b]pyridine and 3-(chloromethyl)-4-methylpyridine hydrochloride. MS (ESI): mass calcd. for $C_{13}H_{11}BrN_4$, 302.0; m/z found, 303.0 $[M+H]^+$.

Intermediate 53: 6-Bromo-1-(pyridin-2-ylmethyl)-1H-pyrazolo[4,3-b]pyridine.



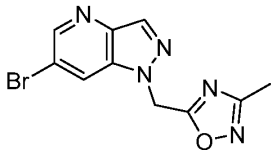
The title compound was prepared in a manner analogous to Intermediate 44, Step A, using 6-bromo-1H-pyrazolo[4,3-b]pyridine and 2-(chloromethyl)pyridine hydrochloride. MS (ESI): mass calcd. for $C_{12}H_9BrFN_4$, 288.0; m/z found, 288.9 $[M+H]^+$.

Intermediate 54: 6-Bromo-1-((5-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine.



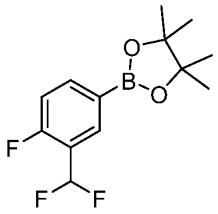
The title compound was prepared in a manner analogous to Intermediate 44, Step A, using 6-bromo-1H-pyrazolo[4,3-b]pyridine and 3-(chloromethyl)-5-fluoropyridine hydrochloride. MS (ESI): mass calcd. for $C_{12}H_8BrFN_4$, 306.0; m/z found, 307.0 $[M+H]^+$.

Intermediate 55: 5-((6-Bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-3-methyl-1,2,4-oxadiazole.



The title compound was prepared in a manner analogous to Intermediate 44, Step A, using 6-bromo-1H-pyrazolo[4,3-b]pyridine and 5-(chloromethyl)-3-methyl-1,2,4-oxadiazole. MS (ESI): mass calcd. for $C_{10}H_8BrN_5O$, 292.9; m/z found, 294.0 $[M+H]^+$.

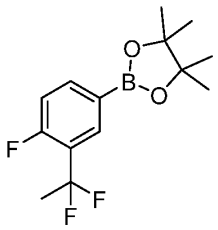
Intermediate 56: 2-(3-(Difluoromethyl)-4-fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.



A solution of 4-bromo-2-(difluoromethyl)-1-fluorobenzene (20 g, 88.9 mmol), bis(pinacolato)diboron (24.8 g, 97.8 mmol), potassium acetate (26.2 g, 267 mmol), and [1,1′-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (3.12 g, 4.44 mmol) in 1,4-dioxane (400 mL) was purged with N_2, and the reaction mixture was stirred at 90 ºC overnight. Upon completion, the reaction mixture was cooled to room temperature, filtered through Celite®, and rinsed with EtOAc. The filtrate was washed with water and brine. The combined organics were dried with Na_2SO_4, filtered and concentrated to yield a clear oil (22.1 g, 81.0 mmol, 91%), which solidified upon standing. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.12 – 8.00 (m, 1H), 7.96 – 7.85

(m, 1H), 7.17 – 7.06 (m, 1H), 6.88 (t, J = 54.9 Hz, 1H), 1.35 (s, 12H). MS (ESI): mass calcd. for $C_{13}H_{16}BF_3O_2$, 272.1; m/z found, 273.0 $[M+H]^+$.

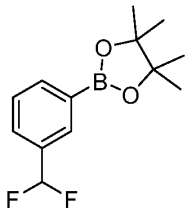
Intermediate 57: 2-(3-(1,1-Difluoroethyl)-4-fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.



Step A: 4-Bromo-2-(1,1-difluoroethyl)-1-fluorobenzene. In a round bottom flask, a mixture of 1-(5-bromo-2-fluorophenyl)-1-ethanone (2.5 g, 11.5 mmol) and DAST (1.9 mL, 14.4 mmol) was heated at 60 °C for 16 h. Then a sat. aq. solution of $NaHCO_3$ was slowly added at 0 °C and extracted with DCM. The organic layers were combined, dried over $MgSO_4$, filtered, and partially concentrated (product is volatile). Purification (FCC, SiO_2, 100% DCM) afforded the title compound (3 g, 7.5 mmol, purity 60%, 65%) as a brown oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.73 – 7.61 (m, 1H), 7.60 – 7.48 (m, 1H), 7.02 (t, J = 9.4 Hz, 1H), 1.98 (t, J = 18.6 Hz, 3H).

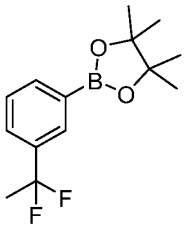
Step B: 2-(3-(1,1-Difluoroethyl)-4-fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. In a round bottom flask, bis(pinacolato)diboron (2.87 g, 11.3 mmol, 1.5 equiv), potassium acetate (2.22 g, 22.6 mmol, 3 equiv), and [1,1′-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (615 mg, 0.75 mmol, 0.1 equiv) were added to a solution of 4-bromo-2-(1,1-difluoroethyl)-1-fluorobenzene (3 g, 7.5 mmol, 1 equiv) in dry 1,4-dioxane (40 mL). The mixture was purged with nitrogen and stirred at 90 °C for 16 h. Then, a sat. aq. solution of $NaHCO_3$ was added and the mixture was extracted with EtOAc. The combined organics were dried with $MgSO_4$, filtered and concentrated to yield a brown oil (2.15 g, 7.53 mmol), which was used in the next step without further purification. MS (ESI): mass calcd. for $C_{14}H_{18}BF_3O_2$, 286.1; m/z found, 287.1 $[M+H]^+$.

Intermediate 58: 2-(3-(Difluoromethyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.



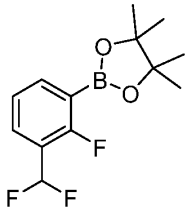
The title compound was prepared in a manner analogous to Intermediate 56 using 1-bromo-3-(difluoromethyl)benzene instead of 4-bromo-2-(difluoromethyl)-1-fluorobenzene. No mass observed.

Intermediate 59: 2-(3-(1,1-Difluoroethyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.



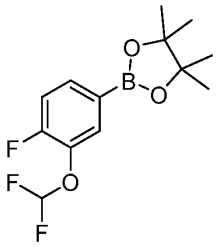
The title compound was prepared in a manner analogous to Intermediate 56 using 1-bromo-3-(1,1-difluoroethyl)benzene instead of 4-bromo-2-(difluoromethyl)-1-fluorobenzene. No mass observed.

Intermediate 60: 2-(3-(Difluoromethyl)-2-fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.



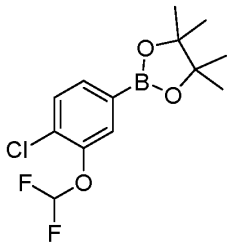
The title compound was prepared in a manner analogous to Intermediate 56 using 1-bromo-3-(difluoromethyl)-2-fluorobenzene instead of 4-bromo-2-(difluoromethyl)-1-fluorobenzene. MS (ESI): mass calcd. for $C_{13}H_{16}BF_3O_2$, 272.1; m/z found, 273.2 $[M+H]^+$.

Intermediate 61: 2-(3-(Difluoromethoxy)-4-fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.



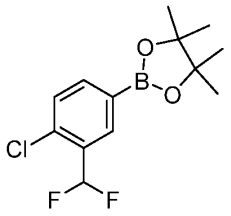
The title compound was prepared in a manner analogous to Intermediate 56 using 4-bromo-2-(difluoromethoxy)-1-fluorobenzene instead of 4-bromo-2-(difluoromethyl)-1-fluorobenzene. MS (ESI): mass calcd. for $C_{13}H_{16}BF_3O_3$, 288.1; m/z found, 289.0 $[M+H]^+$.

Intermediate 62: 2-(4-Chloro-3-(difluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.



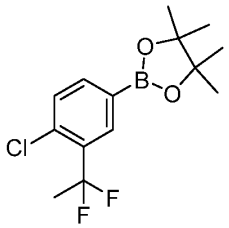
The title compound was prepared in a manner analogous to Intermediate 56 using 4-bromo-1-chloro-2-(difluoromethoxy)benzene instead of 4-bromo-2-(difluoromethyl)-1-fluorobenzene. ^1H NMR (500 MHz, $CDCl_3$) δ 7.62 – 7.56 (m, 2H), 7.44 (d, J = 7.9 Hz, 1H), 6.56 (t, J = 73.6 Hz, 1H), 1.34 (s, 12H).

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



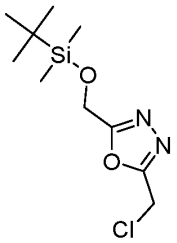
The title compound was prepared in a manner analogous to Intermediate 57 using 5-bromo-2-chlorobenzaldehyde instead of 1-(5-bromo-2-fluorophenyl)-1-ethanone in step A. MS (ESI): mass calcd. for $C_{13}H_{16}BClF_2O_2$, 288.1; m/z found, 289.1 $[M+H]^+$.

Intermediate 64: 2-(4-Chloro-3-(1,1-difluoroethyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.



The title compound was prepared in a manner analogous to Intermediate 57 using 1-(5-bromo-2-chlorophenyl)ethan-1-one instead of 1-(5-bromo-2-fluorophenyl)-1-ethanone in step A. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, J = 1.5 Hz, 1H), 7.79 – 7.71 (m, 1H), 7.47 – 7.39 (m, 1H), 2.03 (t, J = 18.4 Hz, 3H), 1.34 (s, 12H).

Intermediate 65: 2-(((*tert*-Butyldimethylsilyl)oxy)methyl)-5-(chloromethyl)-1,3,4-oxadiazole.



Step A. 2-((*tert*-Butyldimethylsilyl)oxy)acetohydrazide: Ethyl 2-((*tert*-butyldimethylsilyl)oxy)acetate (2.00 g, 9.16 mmol) and hydrazine hydrate (4.5 mL, 92 mmol) were dissolved in ethanol (50 mL). The reaction mixture was allowed to stand at room temperature overnight and then concentrated. The oil thus obtained (1.81 g, 8.86 mmol, 97% yield) was used directly in the next step without further purification. MS (ESI): mass calcd. for $C_{10}H_{22}O_3Si$, 204.1; m/z found, 205.2 $[M+H]^+$.

Step B. Ethyl 2-(2-(2-((*tert*-butyldimethylsilyl)oxy)acetyl)hydrazinyl)-2-oxoacetate: A solution of 2-((*tert*-butyldimethylsilyl)oxy)acetohydrazide (1.81 g, 8.86 mmol) and triethylamine (2.5 mL, 18 mmol) were dissolved in dry DCM (50 mL) and the reaction mixture was cooled to 0 °C. Monoethyl oxalyl chloride (1.0 mL, 8.9 mmol) was added dropwise, and the reaction mixture was stirred at 0 °C for one hour. The mixture was partitioned between DCM and water, the

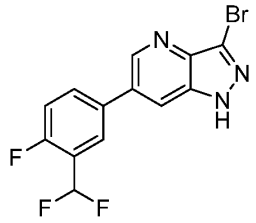
aqueous layer was extracted 3x with DCM, the combined organics were dried ($MgSO_4$), concentrated, and the crude product (3.14 g, 10.3 mmol, >100% measured yield) was used directly in subsequent transformations. MS (ESI): mass calcd. for $C_{12}H_{24}N_2O_5Si$, 304.1; m/z found, 305.2 $[M+H]^+$.

Step C. Ethyl 5-(((*tert*-butyldimethylsilyl)oxy)methyl)-1,3,4-oxadiazole-2-carboxylate: Ethyl 2-(2-(2-((*tert*-butyldimethylsilyl)oxy)acetyl)hydrazinyl)-2-oxoacetate (3.14 g, 10.3 mmol) and triethylamine (1.7 mL, 12 mmol) were dissolved in dry DCM (100 mL). Tosyl chloride (1.97 g, 10.3 mmol) was added in one portion, and the reaction mixture was stirred at r.t. overnight. The mixture was then diluted with water, the aqueous layer was extracted with DCM, and the combined organics were concentrated and purified on silica gel (0-100% ethyl acetate/hexanes) to obtain 1.87 g (6.53 mmol, 63% yield) of the desired product. MS (ESI): mass calcd. for $C_{12}H_{22}N_2O_4Si$, 286.1; m/z found, 287.2 $[M+H]^+$.

Step D. (5-(((*tert*-Butyldimethylsilyl)oxy)methyl)-1,3,4-oxadiazol-2-yl)methanol: A solution of ethyl 5-(((*tert*-butyldimethylsilyl)oxy)methyl)-1,3,4-oxadiazole-2-carboxylate (1.87 g, 6.53 mmol) was dissolved in methanol (40 mL) and the reaction mixture was cooled to 0 °C. Sodium borohydride (988 mg, 26.1 mmol) was added portion wise and the reaction mixture was stirred at r.t. for 2 hours, concentrated to remove volatiles, and partitioned between DCM and water. The aqueous layer was extracted 2x with DCM and the combined organics were concentrated and purified on silica gel (0-100% ethyl acetate/hexanes) to obtain 1.18 g (4.83 mmol, 74% yield) of the desired product. MS (ESI): mass calcd. for $C_{10}H_{20}N_2O_3Si$, 244.1; m/z found, 245.2 $[M+H]^+$.

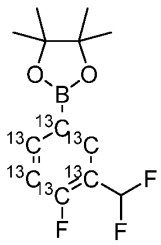
Step E. 2-(((*tert*-butyldimethylsilyl)oxy)methyl)-5-(chloromethyl)-1,3,4-oxadiazole: (5-(((*tert*-Butyldimethylsilyl)oxy)methyl)-1,3,4-oxadiazol-2-yl)methanol (400 mg, 1.64 mmol) and triethylamine (0.68 mL, 4.9 mmol) were dissolved in dry DCM (10 mL). Thionyl chloride (0.24 mL, 3.3 mmol) was added dropwise and the reaction mixture was stirred overnight at r.t. The mixture was partitioned between DCM and sat. aq. Na_2CO_3, the aqueous layer was extracted with DCM, and the combined organics were concentrated and purified on silica gel (0-100% ethyl acetate/hexanes) to obtain 182 mg (0.693 mmol, 42% yield) of the desired product. MS (ESI): mass calcd. for $C_{10}H_{19}ClN_2O_2Si$, 262.1; m/z found, 263.2 $[M+H]^+$.

Intermediate 66: 3-Bromo-6-(3-(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine.



A suspension of 6-(3-(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 25), 1.0 g, 3.8 mmol) and trimethylphenylammonium tribromide (2.9 g, 7.6 mmol) was stirred in ACN (62.5 mL) at room temperature. After 3 days, a saturated aqueous solution of sodium bicarbonate (120 mL) was added to the reaction mixture. The resulting mixture was extracted with EtOAc (3 x 150 mL). The combined organics were dried over $MgSO_4$, filtered and evaporated. Purification (FCC, SiO_2, 0-99% EtOAc in hexanes) afforded the title compound (463 mg, 36%). MS (ESI): mass calcd. for $C_{13}H_7BrF_3N_3$, 341.0; m/z found, 342.0 $[M+H]^+$. ^1H NMR (600 MHz, DMSO-d_6) δ 13.84 (s, 1H), 8.90 (d, J = 1.9 Hz, 1H), 8.31 (d, J = 1.9 Hz, 1H), 8.10 – 8.05 (m, 2H), 7.59 – 7.54 (m, 1H), 7.27 (t, J = 54.1 Hz, 1H).

Intermediate 67: 2-(3-(Difluoromethyl)-4-fluorophenyl-1,2,3,4,5,6-$^{13}C_6$)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.

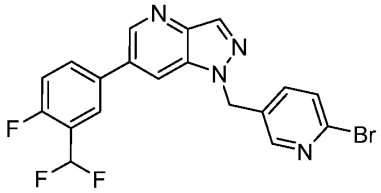


Step A. 5-Bromo-2-fluorobenzaldehyde-1,2,3,4,5,6-$^{13}C_6$. To a solution of di-isopropyl amine (0.58 mL, 4.15 mmol) in THF (10 mL) at -78 °C was added *n*-BuLi (1.59 mL, 2.5 M, 3.97 mmol) dropwise. The solution was stirred at -78 °C for 30 min. To the LDA solution was added 1-bromo-4-fluorobenzene-1,2,3,4,5,6-$^{13}C_6$ (600 mgs, 3.32 mmol) in 1 mL of THF. The resulting solution was stirred at -78 °C for 30 min. DMF was then added and the solution was further stirred at -78°C for an additional 1 h. The reaction mixture was quenched with 2M H_2SO_4 (10 mL) and allowed to warm to rt. The mixture was extracted with Et_2O (5 mL, X3) and the

combined organic extracts were washed with brine (5mL, X 3) and dried over $MgSO_4$. Filtration and concentration provided the title compound (0.856 g, 2.28 mmol) of colorless oil.

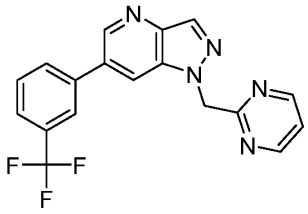
Step B. 2-(3-(Difluoromethyl)-4-fluorophenyl-1,2,3,4,5,6-$^{13}C_6$)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. The title compound was prepared in a manner analogous to Intermediate 57 using 5-bromo-2-fluorobenzaldehyde-1,2,3,4,5,6-$^{13}C_6$ from Step A. MS (ESI): mass calcd. for $C_7{}^{13}C_6H_{16}BF_3O_2$, 278.1; m/z found, 279.1 $[M+H]^+$.

Intermediate 68: 1-((6-Bromopyridin-3-yl)methyl)-6-(3-(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine.



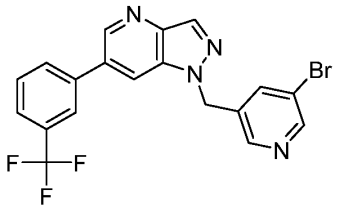
To a solution of Intermediate 25 (40 mg, 0.15 mmol) in 2 mL of DMF was added NaH (60% dispersion in mineral oil, 18 mg, 0.45 mmol). This mixture was stirred at rt for 20 min. The mixture was cooled to -40 °C and 2-bromo-5-(bromomethyl)pyridine was added (38.1 mg, 0.15 mml). The reaction mixture was stirred at --40 °C for 20 min then was quenched by adding 3 g of dry ice. The reaction mixture was warmed to rt and diluted with EtOAc (30 mL). This was then washed with water (3x30 mL), dried over Na_2SO_4 and concentrated. Purification (FCC, SiO_2, 0 to 100% EtOAc/hexanes) afforded the title compound (45 mg, 0.10 mmol, 68%). MS (ESI): mass calcd. for $C_{19}H_{12}BrF_3N_4$, 432.0; m/z found, 455.1 $[M+Na]^+$. ^1H NMR (400 MHz, CDCl3) δ 8.84 (d, J = 1.8 Hz, 1H), 8.40 (t, J = 1.8 Hz, 2H), 7.87 – 7.82 (m, 2H), 7.76-7.71 (m, 1 H), 7.50 – 7.47 (m, 1H), 7.45 – 7.42 (m, 1H), 7.36-7.31 (m, 1H), 7.02 (t, J = 54.8 Hz, 1H), 5.66 (s, 2H).

Example 1: 1-(Pyrimidin-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine.



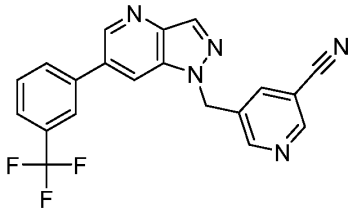
6-(3-(Trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 42, 100 mg, 0.4 mmol) was added to a suspension of NaH (60% dispersion in mineral oil, 36.4 mg, 0.9 mmol) in DMF (4.0 mL) at room temperature under a nitrogen atmosphere. After 10 min, 2-(chloromethyl)pyrimidine hydrochloride (87.8 mg, 0.5 mmol) was added and the reaction mixture was heated to 75 °C. After 3 h, the reaction mixture was cooled to room temperature and water was added. The resulting precipitate was collected by filtration, rinsed with water, and dried under vacuum to provide title compound (72.8 mg, 0.2 mmol, 53.9 %). MS (ESI): mass calcd. for $C_{18}H_{12}F_3N_5$, 355.1; m/z found, 356.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.97 (d, J = 1.9 Hz, 1H), 8.73 (d, J = 4.9 Hz, 2H), 8.67 – 8.65 (m, 1H), 8.39 – 8.37 (m, 1H), 8.18 – 8.14 (m, 2H), 7.83 – 7.74 (m, 2H), 7.42 (t, J = 4.9 Hz, 1H), 6.02 (s, 2H).

Example 2: 1-[(5-Bromo-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine.



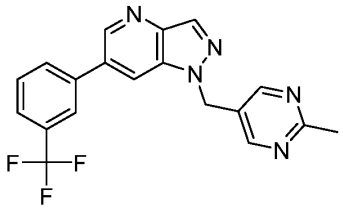
The title compound was prepared in a manner analogous to Example 1, using 3-bromo-5-(chloromethyl)pyridine instead of 2-(chloromethyl)pyrimidine hydrochloride. MS (ESI): mass calcd. for $C_{19}H_{12}BrF_3N_4$, 432.0; m/z found, 432.9 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.97 (d, J = 1.9 Hz, 1H), 8.79 – 8.77 (m, 1H), 8.65 (d, J = 2.2 Hz, 1H), 8.59 – 8.57 (m, 1H), 8.45 – 8.43 (m, 1H), 8.21 – 8.16 (m, 2H), 8.02 (t, J = 2.1 Hz, 1H), 7.85 – 7.78 (m, 2H), 5.82 (s, 2H).

Example 3: 5-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile.



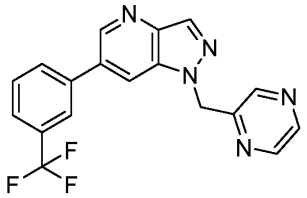
A microwave vial was charged with 1-[(5-bromo-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine (Example 2, 80 mg, 0.2 mmol), zinc cyanide (43.3 mg, 0.4 mmol), [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (9.5 mg, 0.01 mmol) and DMA (1.5 mL). The microwave vial was purged with nitrogen and capped. The reaction mixture was heated to 150 °C under microwave irradiation for 30 min. The mixture was then purified by reverse phase basic HPLC (Method A) to provide title compound (28 mg, 40%). MS (ESI): mass calcd. for $C_{20}H_{12}F_3N_5$, 379.1; m/z found, 380.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.98 – 8.95 (m, 2H), 8.87 (d, J = 2.1 Hz, 1H), 8.77 – 8.75 (m, 1H), 8.45 – 8.43 (m, 1H), 8.26 (t, J = 2.1 Hz, 1H), 8.21 – 8.16 (m, 2H), 7.86 – 7.77 (m, 2H), 5.88 (s, 2H).

Example 4: 1-[(2-Methylpyrimidin-5-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine trifluoroacetate salt.



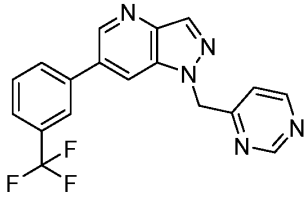
A mixture of 6-bromo-1-((2-methylpyrimidin-5-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 46, 60 mg, 0.2 mmol), (3-(trifluoromethyl)phenyl)boronic acid (56 mg, 0.3 mmol), Cs_2CO_3 (129 mg, 0.4 mmol), and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (10 mg, 0.01 mmol), in 1,4-dioxane (1.8 mL) was heated to 90 °C. After completion, the reaction mixture was concentrated under vacuum and the residue purified by reverse phase HPLC (Method C) to provide title compound (42 mg, 0.09 mmol, 44%). MS (ESI): mass calcd. for $C_{19}H_{14}F_3N_5$, 369.1; m/z found, 370.0 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.96 (d, J = 2.0 Hz, 1H), 8.80 – 8.78 (m, 1H), 8.73 (s, 2H), 8.43 – 8.40 (m, 1H), 8.22 – 8.16 (m, 2H), 7.87 – 7.77 (m, 2H), 5.79 (s, 2H), 2.58 (s, 3H).

Example 5: 1-(Pyrazin-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine dihydrochloride salt.



Di-tert-butyl azodicarboxylate (157.4 mg, 0.7 mmol) was added to a solution of 6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 42, 150 mg, 0.6 mmol), 2-pyrazinylmethanol (75.3 mg, 0.7 mmol) and triphenylphosphine (179.4 mg, 0.7 mmol) in THF (5 mL) at 0 °C. After 21 hours, the solvent was removed and the residue taken up in DCM and washed with water then dried over Na_2SO_4 and concentrated under vacuum. The residue was purified (FCC, SiO_2, 0-10 % DCM/MeOH) to afford the desired product with trace impurities. The material was subjected to ion exchange chromatography using an ISOLUTE SCX2 cartridge eluting with MeOH followed by 7N NH_3/MeOH. The desired fractions were collected and concentrated. The material was then purified by reverse phase HPLC (Method A). The desired fractions were concentrated under vacuum and the residue was treated with HCl in MeOH for 5 min, the solvent was removed under vacuum to provide the title product (33 mg, 0.08 mmol, 13.5%). MS (ESI): mass calcd. for $C_{18}H_{12}F_3N_5$, 355.1; m/z found, 356.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-*d* 6) δ 9.05 (s, 1H), 8.84 (s, 2H), 8.72 – 8.54 (m, 4H), 8.47 (s, 1H), 8.30 – 8.10 (m, 2H), 7.95 – 7.71 (m, 2H), 6.04 (s, 2H).

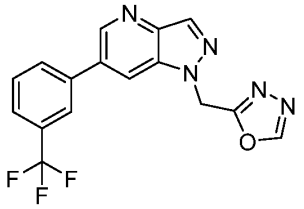
Example 6: 1-(Pyrimidin-4-ylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine hydrochloride salt.



Di-tert-butyl azodicarboxylate (157.5 mg, 0.7 mmol) was added to a solution of 6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 42, 150 mg, 0.6 mmol), 4-

(hydroxymethyl)pyrimidine (75.3 mg, 0.7 mmol) and polymer bound triphenylphosphine (323.0 mg, 0.7 mmol) in THF at 0 °C. The cold bath was removed and the reaction mixture stirred at rt. After 16 hours additional 4-(hydroxymethyl)pyrimidine (37.7 mg, 0.3 mmol), di-tert-butyl azodicarboxylate (78.7 mg, 0.7 mmol) and polymer bound triphenylphosphine (161.5 mg, 0.3 mmol) were added to the reaction mixture. After 2 hours, the reaction mixture was then heated at 50 °C. Upon completion, the mixture was filtered and the filtrate was concentrated. The residue was partitioned between water/DCM and the layers separated. The aqueous layer was extracted with DCM and the combined organics were dried over Na_2SO_4 and concentrated. The residue was purified (FCC, SiO_2, 0-10 % MeOH in DCM) to afford the desired product with trace impurities. The material was further purified (FCC, SiO_2, 50-100 % EtOAc in heptane), the desired fractions were collected and concentrated, and the residue was treated with HCl in MeOH for 5 min. The solvent was removed under vacuum to provide the title compound (58 mg, 0.15 mmol, 26.0%). MS (ESI): mass calcd. for $C_{18}H_{12}F_3N_5$, 355.1; m/z found, 356.2 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-*d* 6) δ 9.03 (d, *J*=1.16 Hz, 1 H), 8.95 (d, *J*=1.85 Hz, 1 H), 8.71 – 8.61 (m, 2 H), 8.40 (d, *J*=0.92 Hz, 1 H), 8.12 – 8.07 (m, 2 H), 7.78 – 7.66 (m, 2 H), 5.89 (s, 2 H) 7.07 (dd, *J*=5.20, 1.27 Hz, 1 H).

Example 7: 2-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole.

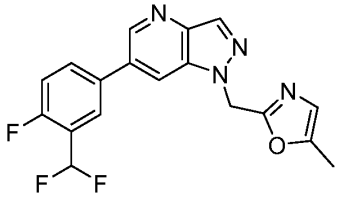


Step A: *N'*-Formyl-2-(6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetohydrazide. A solution of 2-(6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetohydrazide (Intermediate 44, 68 mg, 0.2 mmol) in triethyl orthoformate (4 mL) was stirred at 140 °C. After 22 hours the volatiles were removed under vacuum and the crude product was used in the next step without further purification.

Step B: 2-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole. *N'*-Formyl-2-(6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetohydrazide was

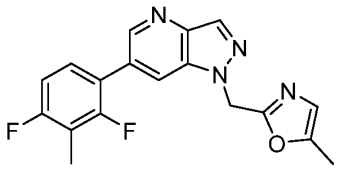
dissolved in toluene (4 mL) and *p*-toluenesulfonic acid monohydrate (3.9 mg, 0.02 mmol) was added. The reaction mixture was then heated to 110 °C. After 24 hours, the solvent was removed and the residue was purified (FCC, SiO_2, 0-10 % EtOAc in heptane) to provide the title compound (8 mg, 0.02 mmol, 11.4 %). MS (ESI): mass calcd. for $C_{16}H_{10}F_3N_5O$, 345.1; m/z found, 346.1 $[M+H]^+$. ^1H NMR (400MHz, $CDCl_3$) δ 8.87 (d, *J*=1.8 Hz, 1H), 8.39 (s, 1H), 8.36 (d, *J*=1.2 Hz, 1H), 8.03 (dd, *J*=0.9, 1.8 Hz, 1H), 7.88 (s, 1H), 7.83 (d, *J*=7.6 Hz, 1H), 7.76 - 7.70 (m, 1H), 7.69 - 7.62 (m, 1H), 5.93 (s, 2H)

Example 8: 2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-oxazole.



To 6-(3-(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 25, 35 mg, 0.133 mmol) stirring in DMF (1 mL) at rt was added Cs_2CO_3 (129.97 mg, 0.399 mmol) followed by 2-(chloromethyl)-5-methyl-1,3-oxazole (26.24 mg, 0.199 mmol). The reaction was stirred at rt for 3 h, then filtered through a 0.45 µM syringe filter and purified by prep HPLC (Method A) to afford the title compound (21.1 mg, 44%). MS (ESI): mass calcd. for $C_{18}H_{13}F_3N_4O$, 358.1; m/z found, 359.1 $[M+H]^+$. ^1H NMR (500 MHz, CD_3OD) δ 8.84 (d, *J* = 1.9 Hz, 1H), 8.45 (dd, *J* = 1.9, 1.0 Hz, 1H), 8.28 (d, *J* = 1.0 Hz, 1H), 8.03 – 7.93 (m, 2H), 7.48 – 7.37 (m, 1H), 7.09 (t, *J* = 54.6 Hz, 1H), 6.76 (d, *J* = 1.3 Hz, 1H), 5.83 (s, 2H), 2.27 (d, *J* = 1.2 Hz, 3H).

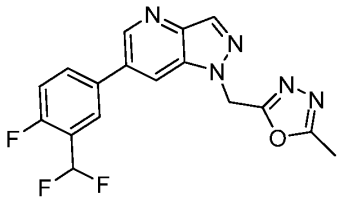
Example 9: 2-[[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-oxazole.



To a microwave vial was added 2-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-5-methyloxazole (Intermediate 22, 25 mg, 0.0853 mmol), (2,4-difluoro-3-methylphenyl)boronic

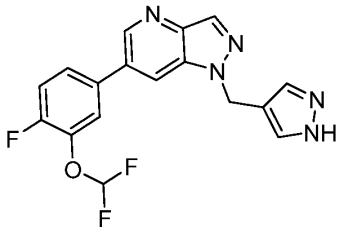
acid (17.597 mg, 0.102 mmol), Cs_2CO_3 (83.366 mg, 0.256 mmol), RuPhos Pd G3 (3.567 mg, 0.00426 mmol), and 1,4-dioxane (1 mL). The vial was purged with N_2, sealed, and stirred at 80 °C overnight. The reaction was removed from the heat, cooled to rt, then filtered through a 0.45 µM syringe filter. Purification (Method A) afforded the title compound (13.0 mg, 45%). MS (ESI): mass calcd. for $C_{18}H_{14}F_2N_4O$, 340.1; m/z found, 341.1 $[M+H]^+$. ^1H NMR (400 MHz, CD_3OD) δ 8.69 (s, 1H), 8.34 – 8.23 (m, 2H), 7.56 – 7.41 (m, 1H), 7.19 – 7.03 (m, 1H), 6.75 (d, *J* = 1.2 Hz, 1H), 5.80 (s, 2H), 2.34 – 2.20 (m, 6H).

Example 10: 2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole.



2-((6-Bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-5-methyl-1,3,4-oxadiazole (Intermediate 19, 445.6 mg, 1.515 mmol), 2-(3-(difluoromethyl)-4-fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (541.8 mg, 1.991 mmol), Na_2CO_3 (319.3 mg, 3.013 mmol), (1,1'-bis(diphenylphosphino)ferrocene)dichloropalladium(II) (55.1 mg, 0.0748 mmol), 1,4-dioxane (5 mL), and water (1.25 mL) were placed in a microwave vial. The vial was sealed and stirred at 100 °C for 1 h. The reaction mixture was cooled to rt, diluted with EtOAc and water, then the layers were separated and the aqueous layer was extracted with EtOAc (x 3). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified (FCC, SiO_2, 0 – 8% MeOH in DCM), then re-purified (FCC, SiO_2, 50 – 100% EtOAc in hexanes) to afford the title compound (370 mg, 68%). MS (ESI): mass calcd. for $C_{17}H_{12}F_3N_5O$, 359.1; m/z found, 360.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.94 (d, *J* = 1.9 Hz, 1H), 8.67 – 8.61 (m, 1H), 8.47 – 8.42 (m, 1H), 8.12 – 8.05 (m, 2H), 7.64 – 7.54 (m, 1H), 7.31 (t, *J* = 54.1 Hz, 1H), 6.10 (s, 2H), 2.44 (s, 3H).

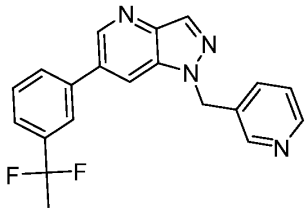
Example 11: 6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(1H-pyrazol-4-ylmethyl)pyrazolo[4,3-b]pyridine.



Step A. 6-(3-(Difluoromethoxy)-4-fluorophenyl)-1-((1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazol-4-yl)methyl)-1H-pyrazolo[4,3-b]pyridine. To a suspension of sodium hydride (60% in mineral oil, 12.0 mg, 0.300 mmol) in DMF (500 µL) was added a solution of 6-[3-(difluoromethoxy)-4-fluoro-phenyl]-1*H*-pyrazolo[4,3-*b*]pyridine (Intermediate 26, 80 mg, 0.287 mmol) in DMF (600 µL) at 0 °C under argon and the reaction was stirred at 0 °C for 30 min. To the reaction mixture was added a solution of 4-(chloromethyl)-1-tetrahydropyran-2-yl-pyrazole (Intermediate 1, 60 mg, 0.299 mmol) in DMF (500 µL) at 0 °C and the reaction mixture was stirred at room temperature for 18 h. The reaction mixture was poured into water (10 mL) and extracted with EtOAc (3 x 5 mL). The combined organics were dried over $MgSO_4$, filtered and concentrated. Purification (FCC, SiO_2, 0 to 100% EtOAc in n-heptane) afforded the title compound (82 mg, 0.185 mmol, 64%) as a yellow oil. MS (ESI): mass calcd. for $C_{22}H_{20}F_3N_5O2$, 443.2; m/z found, 444.2 $[M+H]^+$.

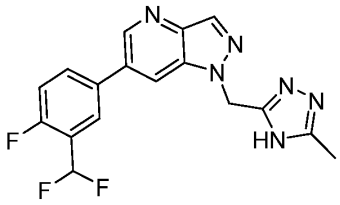
Step B. 6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(1H-pyrazol-4-ylmethyl)pyrazolo[4,3-b]pyridine. To 6-(3-(difluoromethoxy)-4-fluorophenyl)-1-((1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazol-4-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (80 mg, 0.180 mmol) was added hydrogen chloride (4.90 M in 1,4-dioxane, 3 mL, 14.7 mmol) and the reaction mixture was stirred at room temperature for 18 h. The reaction mixture was concentrated and the residue was purified by preparative HPLC (METHOD E) to afford the title compound (32 mg, 0.089 mmol, 49%) as a white powder. MS (ESI): mass calcd. for $C_{17}H_{12}F_3N_5O$, 359.1; m/z found, 360.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 12.74 (br s, 1H), 8.92 – 8.83 (m, 1H), 8.54 – 8.47 (m, 1H), 8.33 (s, 1H), 7.89 – 7.81 (m, 1H), 7.81 – 7.71 (m, 1H), 7.68 – 7.55 (m, 2H), 7.39 (t, J = 73.2 Hz, 1H), 6.17 – 6.09 (m, 1H), 5.71 (s, 2H).

Example 12: 6-[3-(1,1-Difluoroethyl)phenyl]-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine.



A mixture of 6-(3-(1,1-difluoroethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 29, 70 mg, 0.270 mmol), 3-(chloromethyl)pyridine hydrochloride (49 mg, 0.299 mmol) and Cs_2CO_3 (220 mg, 0.675 mmol) in dry DMF (1.4 mL) was stirred at 80 °C for 18 h. The reaction mixture was poured into water (10 mL) and extracted with EtOAc (3 x 5 mL). The combined organics were dried over $MgSO_4$, filtered and concentrated. Purification (FCC, SiO_2, 0 to 5% MeOH in DCM) afforded the title compound (45 mg, 0.128 mmol, 47%) as a yellow oil. MS (ESI): mass calcd. for $C_{20}H_{16}F_2N_4$, 350.1; m/z found, 351.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.93 (d, J = 1.9 Hz, 1H), 8.71 – 8.67 (m, 1H), 8.64 – 8.59 (m, 1H), 8.49 (dd, J = 4.8, 1.7 Hz, 1H), 8.42 – 8.39 (m, 1H), 8.01 – 7.92 (m, 2H), 7.71 – 7.62 (m, 3H), 7.37 – 7.31 (m, 1H), 5.82 (s, 2H), 2.06 (t, J = 18.9 Hz, 3H).

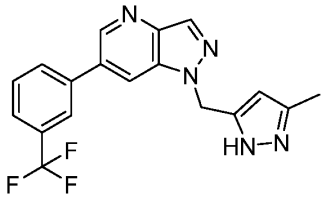
Example 13: 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-methyl-4H-1,2,4-triazol-3-yl)methyl]pyrazolo[4,3-b]pyridine.



To a suspension of 2-(6-(3-(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetohydrazide (Intermediate 45, 35 mg, 0.0857 mmol) and ethyl acetimidate hydrochloride (32 mg, 0.259 mmol) in ethanol (1.05 mL) was added triethylamine (72 µL, 0.516 mmol, 0.726 g/mL). The reaction mixture was stirred at 70 °C for 1 h then cooled and evaporated to dryness. The residue was taken up in DCM (5 mL) and the organic layer was washed with water (1 x 5 mL). The aqueous washing was extracted with DCM (2 x 5 mL) and the combined organics were dried over Na_2SO_4, filtered and concentrated. Purification (FCC, SiO_2, 0 to 5% MeOH in DCM) afforded the title compound (13 mg, 0.036 mmol, 42%) as a white powder. MS (ESI): mass calcd. for $C_{17}H_{13}F_3N_6$, 358.1; m/z found, 359.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 13.50

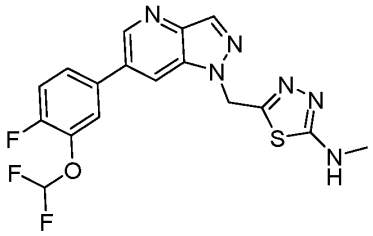
(br s, 1H), 8.89 (d, J = 2.0 Hz, 1H), 8.59 – 8.52 (m, 1H), 8.37 – 8.27 (m, 1H), 8.12 – 8.02 (m, 2H), 7.62 – 7.54 (m, 1H), 7.30 (t, J = 54.1 Hz, 1H), 5.72 (s, 2H), 2.25 (s, 3H).

Example 14: 1-[(3-Methyl-1H-pyrazol-5-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine.



A microwave vial was charged with 1-[(2,5-dimethylpyrazol-3-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine (Example 37, 48 mg, 0.13 mmol) and pyridine hydrochloride (600 mg, 5.2 mmol). The vial was flushed with N_2, sealed and heated to 190 °C overnight. The reaction mixture was cooled and methanol was added to the melt and the resulting residue was purified by prep HPLC (Method A) to give the title compound as a solid (10 mg, 22%). MS (ESI): mass calcd. for $C_{18}H_{14}F_3N_5$, 357.1; m/z found, 358.1 $[M+H]^+$. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.80 – 8.77 (m, 1H), 8.30 – 8.27 (m, 1H), 7.98 – 7.95 (m, 1H), 7.87 – 7.78 (m, 2H), 7.71 – 7.59 (m, 2H), 5.97 (s, 1H), 5.63 (s, 2H), 2.25 (s, 3H).

Example 15: 5-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-N-methyl-1,3,4-thiadiazol-2-amine.

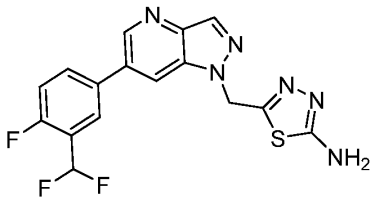


Step A. 2-(2-(6-(3-(Difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetyl)-N-methylhydrazine-1-carboxamide. To a solution of 2-[6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetic acid (Intermediate 40, 150 mg, 0.445 mmol) and triethylamine (186 µL, 1.33 mmol, 0.726 g/mL) in DCM (4.2 mL) was added 3-amino-1-methylurea (48 mg, 0.539 mmol), N-(3-dimethylaminopropyl)-N′-ethylcarbodiimide

hydrochloride (102 mg, 0.532 mmol) and 1-hydroxybenzotriazole hydrate (82 mg, 0.535 mmol). The reaction mixture was stirred at room temperature for 18 h. The reaction mixture was diluted with DCM (10 mL) and washed with 20% Na_2CO_3 (1 x 10 mL). The aqueous layer was then extracted with DCM (3 x 10 mL). The combined organics were dried over Na_2SO4, filtered and concentrated to give the title compound (304 mg) as an off-white powder. MS (ESI): mass calcd. for $C_{17}H_{15}F_3N_6O_3$, 408.1; m/z found, 409.1 $[M+H]^+$.

Step B. 5-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-N-methyl-1,3,4-thiadiazol-2-amine. A mixture of 1-[[2-[6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]amino]-3-methyl-urea (150 mg, 0.367 mmol) and 2,4-bis(4-methoxyphenyl)-2,4-dithioxo-1,3,2,4-dithiadiphosphetane (Lawesson's reagent) (297 mg, 0.735 mmol) in toluene (3.75 mL) was stirred at 105 °C for 20 h. The reaction mixture was concentrated, and the residue was purified. Purification (FCC, SiO_2, 0 to 10% MeOH in DCM) afforded the title compound (15 mg, 0.037 mmol, 10%) as a white powder. MS (ESI): mass calcd. for $C_{17}H_{13}F_3N_6OS$, 406.1; m/z found, 407.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.92 (d, J = 1.9 Hz, 1H), 8.62 – 8.58 (m, 1H), 8.43 (d, J = 1.0 Hz, 1H), 7.88 – 7.83 (m, 1H), 7.81 – 7.75 (m, 1H), 7.66 – 7.59 (m, 1H), 7.61 (dd, J = 10.5, 8.8 Hz, 1H), 7.39 (t, J = 73.2 Hz, 1H), 5.98 (s, 2H), 2.80 (d, J = 4.8 Hz, 3H).

Example 16: 5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazol-2-amine.



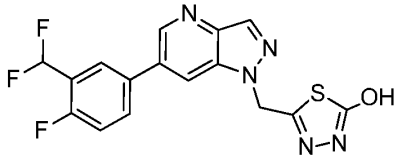
Step A. [[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]amino]urea. To a solution of 2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetic acid (Intermediate 37, 1.50 g, 4.67 mmol) in DCM (40 mL) was added semicarbazide hydrochloride (625 mg, 5.60 mmol), N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (1.07 g, 5.58 mmol), 1-hydroxybenzotriazole hydrate (858 mg, 5.60 mmol) and triethylamine (2.6 mL, 18.6 mmol) and the mixture was stirred at room temperature for 74 h. DMF (10 mL) was added and the reaction was stirred for 45 h. Additional

DMF was added (30 mL) and the reaction was stirred for 24 h. The reaction mixture was concentrated to 40 mL under vacuum and stirred for an additional 24 h. The reaction mixture was then diluted with dichloromethane (120 mL) and washed with 20% aq. Na_2CO_3 (1 x 120 mL). The aqueous layer was then extracted with $CHCl_3$:2-propanol (3:1, 4 x 105 mL). The combined organic layers were concentrated. The residue was purified by preparative HPLC (Method E) to give the title compound (793 mg, 2.10 mmol, 45%) as a white powder. MS (ESI): mass calcd. for $C_{16}H_{13}F_3N_6O_2$, 378.1; m/z found, 379.1 $[M+H]^+$.

Step B. 5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazol-2-amine. A mixture of [[2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]amino]urea (765 mg, 2.02 mmol) and 4-methoxyphenylthionophosphine sulfide dimer (Lawesson's reagent) (1.63 g, 4.04 mmol) in THF (23 mL) was stirred at 100 °C for 2 h under argon and microwave irradiation. The reaction mixture was concentrated, and the residue was purified. Purification (FCC, SiO_2, 0 to 10% DCM/MeOH-NH_3), afforded the title compound. Further purification by preparative HPLC (Method E) afforded the title compound (19 mg, 0.050 mmol, 2%) as a white powder. MS (ESI): mass calcd. for $C_{16}H_{11}F_3N_6S$, 376.1; m/z found, 377.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.92 (d, J = 1.9 Hz, 1H), 8.66 – 8.61 (m, 1H), 8.44 – 8.40 (m, 1H), 8.12 – 8.05 (m, 2H), 7.62 – 7.55 (m, 1H), 7.30 (t, J = 54.2 Hz, 1H), 7.18 (br s, 2H), 5.97 (s, 2H).

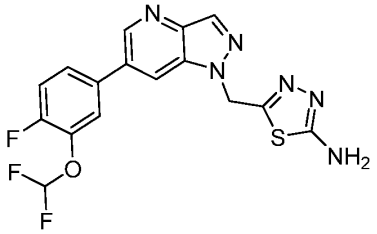
Also isolated from the reaction mixture was 5-[[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazol-2-ol (147 mg, 0.390 mmol, 19%) as a white powder. MS (ESI): mass calcd. for $C_{16}H_{10}F_3N_6OS$, 377.1; m/z found, 378.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 12.87 (br s, 1H), 8.98 – 8.88 (m, 1H), 8.67 – 8.58 (m, 1H), 8.51 – 8.40 (m, 1H), 8.17 – 8.01 (m, 2H), 7.65 – 7.53 (m, 1H), 7.30 (t, J = 54.1 Hz, 1H), 5.88 (s, 2H).

Example 17: 5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazol-2-ol.



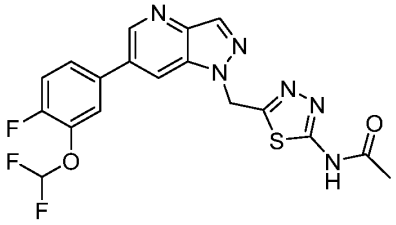
The title compound was also isolated from Example 16. MS (ESI): mass calcd. for $C_{16}H_{10}F_3N_6OS$, 377.1; m/z found, 378.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 12.87 (br s, 1H), 8.98 – 8.88 (m, 1H), 8.67 – 8.58 (m, 1H), 8.51 – 8.40 (m, 1H), 8.17 – 8.01 (m, 2H), 7.65 – 7.53 (m, 1H), 7.30 (t, J = 54.1 Hz, 1H), 5.88 (s, 2H).

Example 18: 5-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazol-2-amine.



The title compound was prepared in a manner analogous to Example 16 using 2-(6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid (Intermediate 40) in Step A. MS (ESI): mass calcd. for $C_{16}H_{11}F_3N_6OS$, 392.1; m/z found, 393.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.92 (d, J = 2.0 Hz, 1H), 8.62 – 8.57 (m, 1H), 8.43 (d, J = 1.0 Hz, 1H), 7.86 (dd, J = 7.6, 2.3 Hz, 1H), 7.80 – 7.75 (m, 1H), 7.61 (dd, J = 10.5, 8.6 Hz, 1H), 7.38 (t, J = 73.2 Hz, 1H), 7.18 (s, 2H), 5.96 (s, 2H).

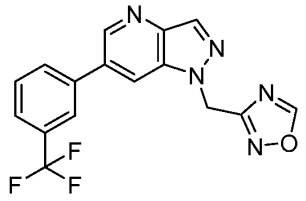
Example 19: N-(5-((6-(3-(Difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-1,3,4-thiadiazol-2-yl)acetamide.



To a solution of 5-[[6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazol-2-amine (Example 18, 18.0 mg, 0.0459 mmol) in toluene (840 µL) was added acetic anhydride (9 µL, 0.0954 mmol) and the reaction mixture was stirred at 60 °C for 13 h. The reaction mixture was washed with 10% aq. Na_2CO_3 (1 x 5 mL) and the aqueous layer was extracted with EtOAc (1 x 5 mL). The combined organics were dried over Na_2SO_4,

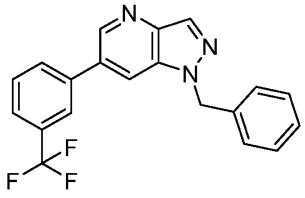
filtered and concentrated. Purification (FCC, SiO_2, 0 to 10% MeOH in DCM) afforded the title compound (18 mg, 0.041 mmol, 89%) as a white powder. MS (ESI): mass calcd. for $C_{18}H_{13}F_3N_6O_2S$, 434.1; m/z found, 435.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 12.51 (br s, 1H), 8.93 (d, J = 2.0 Hz, 1H), 8.68 – 8.63 (m, 1H), 8.46 (d, J = 1.0 Hz, 1H), 7.86 (dd, J = 7.5, 2.3 Hz, 1H), 7.82 – 7.74 (m, 1H), 7.61 (dd, J = 10.5, 8.6 Hz, 1H), 7.38 (t, J = 73.2 Hz, 1H), 6.16 (s, 2H), 2.13 (s, 3H)

Example 20: 3-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,2,4-oxadiazole.



A mixture of 6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 42, 200 mg, 0.76 mmol), 3-(chloromethyl)-1,2,4-oxadiazole (0.13 mL, 1.5 mmol) and Cs_2CO_3 (495 mg, 1.5 mmol) in DMF (1.5 mL) were stirred at 50 °C for 6h. The mixture was cooled, the solids filtered off, and the solvent evaporated. The residue was purified (FCC, SiO_2, 0-6 % MeOH in DCM) and the desired fractions were collected. The material was further purified by reverse phase HPLC (Method A) to provide the title compound (31 mg, 0.09 mmol, 11.8%). MS (ESI): mass calcd. for $C_{16}H_{10}F_3N_5O$, 345.1; m/z found, 346.1$[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.85 (d, J=1.85 Hz, 1H), 8.71 (s, 1H), 8.36 (d, J=0.69 Hz, 1H), 8.03 (s, 1H), 7.89 (s, 1H), 7.84 (d, J=7.63 Hz, 1H), 7.76 – 7.69 (m, 1H), 7.69 – 7.61 (m, 1H), 5.85 (s, 2H).

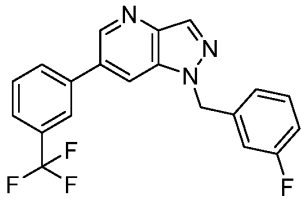
Example 21: 1-Benzyl-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine hydrochloride salt.



The title compound was prepared in a manner analogous to Example 8, using 6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 42) and benzyl bromide. MS

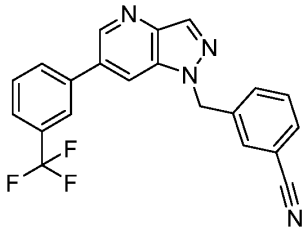
(ESI): mass calcd. for $C_{20}H_{14}F_3N_3$, 353.1; m/z found, 354.3 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.97 (d, *J*=1.85 Hz, 1H), 8.75 (dd, *J*=1.97, 1.04 Hz, 1H), 8.41 (d, *J*=0.92 Hz, 1H), 8.25 – 8.05 (m, 2H), 7.97 – 7.68 (m, 2H), 7.46 – 7.06 (m, 5H), 5.79 (s, 2H).

Example 22: 1-[(3-Fluorophenyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine hydrochloride salt.



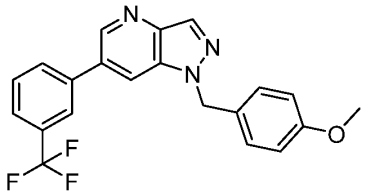
The title compound was prepared in a manner analogous to Example 8, using 6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 42) and 3-fluorobenzyl bromide. MS (ESI): mass calcd. for $C_{20}H_{13}F_4N_3$, 371.1; m/z found, 372.3 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.98 (d, *J*=2.08 Hz, 1 H), 8.76 (dd, *J*=1.85, 0.92 Hz, 1 H), 8.44 (d, *J*=0.92 Hz, 1 H), 8.28 – 8.09 (m, 2 H), 7.93 – 7.71 (m, 2 H), 7.51 – 7.29 (m, 1 H), 7.25 – 6.95 (m, 3 H), 5.81 (s, 2 H).

Example 23: 3-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]benzonitrile.



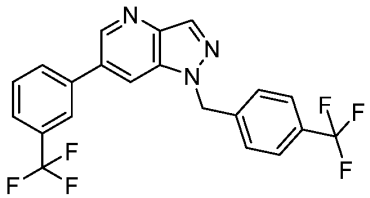
The title compound was prepared in a manner analogous to Example 8, using 6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 42) and 3-cyanobenzyl bromide. MS (ESI): mass calcd. for $C_{21}H_{13}F_3N_4$, 378.1; m/z found, 379.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.86 (d, *J*=2.02 Hz, 1H), 8.39 (d, *J*=1.16 Hz, 1H), 7.85 (s, 1H), 7.75 - 7.82 (m, 2H), 7.69 - 7.74 (m, 1H), 7.56 - 7.69 (m, 2H), 7.40 - 7.52 (m, 3H), 5.70 (s, 2H).

Example 24: 1-[(4-Methoxyphenyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine hydrochloride salt.



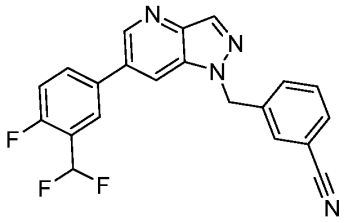
The title compound was prepared in a manner analogous to Example 8, using 6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 42) and 4-methoxybenzyl chloride. MS (ESI): mass calcd. for $C_{21}H_{16}F_3N_3O$, 383.1; m/z found, 384.3 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-*d* 6) δ 8.95 (d, *J*=2.08 Hz, 1H), 8.74 (dd, *J*=1.85, 0.92 Hz, 1H), 8.38 (d, *J*=0.92 Hz, 1H), 8.10 - 8.26 (m, 2H), 7.72 - 7.96 (m, 2H), 7.18 - 7.42 (m, 2H), 6.77 - 6.97 (m, 2H), 5.70 (s, 2H), 3.70 (s, 4H).

Example 25: 6-[3-(Trifluoromethyl)phenyl]-1-[[4-(trifluoromethyl)phenyl]methyl]pyrazolo[4,3-b]pyridine hydrochloride salt.



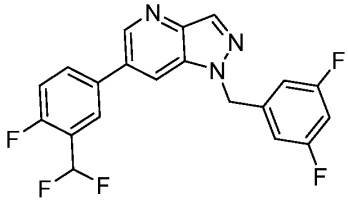
The title compound was prepared in a manner analogous to Example 8, using 6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 42) and 4-(trifluoromethyl)benzyl bromide. MS (ESI): mass calcd. for $C_{21}H_{13}F_6N_3$, 421.1; m/z found, 422.3 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.99 (d, *J*=2.08 Hz, 1H), 8.77 (dd, *J*=1.97, 1.04 Hz, 1H), 8.45 (d, *J*=0.92 Hz, 1H), 8.08 - 8.28 (m, 2H), 7.76 - 7.92 (m, 2H), 7.71 (d, *J*=8.32 Hz, 2H), 7.47 (d, *J*=8.09 Hz, 2H), 5.91 (s, 2H).

Example 26: 3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]benzonitrile.



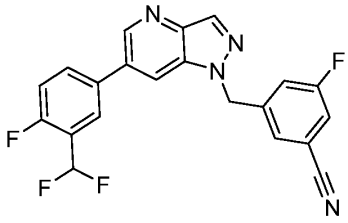
The title compound was made in an analogous manner to Example 8 using 3-(chloromethyl)benzonitrile instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{21}H_{13}F_3N_4$, 378.1; m/z found, 379.3 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.91 (d, J = 1.9 Hz, 1H), 8.73 – 8.64 (m, 1H), 8.42 (s, 1H), 8.15 – 8.02 (m, 2H), 7.83 – 7.72 (m, 2H), 7.63 – 7.50 (m, 3H), 7.30 (t, J = 54.1 Hz, 1H), 5.83 (s, 2H).

Example 27: 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(3,5-difluorophenyl)methyl]pyrazolo[4,3-b]pyridine.



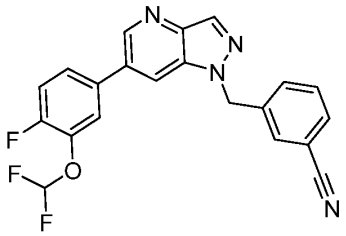
The title compound was made in an analogous manner to Example 8 using 3-(chloromethyl)-3,5-difluorobenzene instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{20}H_{12}F_5N_3$, 389.1; m/z found, 390.3 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.91 (d, J = 1.9 Hz, 1H), 8.71 – 8.60 (m, 1H), 8.43 (s, 1H), 8.13 – 8.02 (m, 2H), 7.64 – 7.53 (m, 1H), 7.30 (t, J = 54.1 Hz, 1H), 7.22 – 7.11 (m, 1H), 7.06 – 6.91 (m, 2H), 5.79 (s, 2H).

Example 28: 3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-fluoro-benzonitrile.



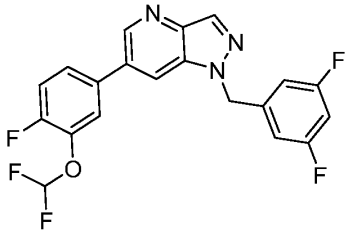
The title compound was made in an analogous manner to Example 8 using 3-(chloromethyl)-5-fluorobenzonitrile instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{21}H_{12}F_4N_4$, 396.1; m/z found, 397.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.91 (d, J = 1.9 Hz, 1H), 8.68 – 8.65 (m, 1H), 8.44 (s, 1H), 8.12 – 8.05 (m, 2H), 7.82 – 7.77 (m, 1H), 7.66 – 7.62 (m, 1H), 7.61 – 7.55 (m, 1H), 7.54 – 7.48 (m, 1H), 7.30 (t, J = 54.1 Hz, 1H), 5.83 (s, 2H).

Example 29: 3-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]benzonitrile.



The title compound was made in an analogous manner to Example 8 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 3-(chloromethyl)benzonitrile. MS (ESI): mass calcd. for $C_{21}H_{13}F_3N_4O$, 394.1; m/z found, 395.3 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.91 (d, J = 1.9 Hz, 1H), 8.68 – 8.60 (m, 1H), 8.42 (s, 1H), 7.91 – 7.82 (m, 1H), 7.83 – 7.71 (m, 3H), 7.68 – 7.47 (m, 3H), 7.37 (t, J = 73.2 Hz, 1H), 5.82 (s, 2H).

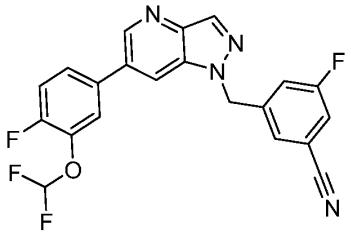
Example 30: 6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(3,5-difluorophenyl)methyl]pyrazolo[4,3-b]pyridine.



The title compound was made in an analogous manner to Example 8 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 1-(chloromethyl)-3,5-difluorobenzene. MS (ESI): mass calcd. for $C_{20}H_{12}F_5N_3O$, 405.1; m/z found, 406.2 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.91 (d, J = 1.9 Hz, 1H), 8.67 – 8.59 (m, 1H),

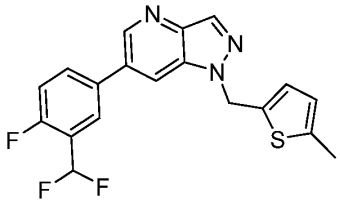
8.43 (s, 1H), 7.90 – 7.82 (m, 1H), 7.82 – 7.74 (m, 1H), 7.57 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.38 (t, *J* = 73.5 Hz, 1H), 7.23 – 7.10 (m, 1H), 7.03 – 6.93 (m, 2H), 5.78 (s, 2H).

Example 31: 3-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-fluoro-benzonitrile.



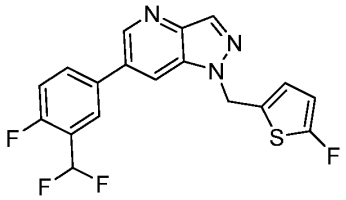
The title compound was made in an analogous manner to Example 8 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 3-(chloromethyl)-5-fluorobenzonitrile. MS (ESI): mass calcd. for $C_{21}H_{12}F_4N_4O$, 412.3; m/z found, 413.2 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.92 (d, *J* = 1.9 Hz, 1H), 8.68 – 8.61 (m, 1H), 8.44 (s, 1H), 7.91 – 7.83 (m, 1H), 7.85 – 7.74 (m, 2H), 7.68 – 7.58 (m, 2H), 7.56 – 7.46 (m, 1H), 7.38 (t, *J* = 73.2 Hz, 1H), 5.82 (s, 2H).

Example 32: 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-methyl-2-thienyl)methyl]pyrazolo[4,3-b]pyridine.



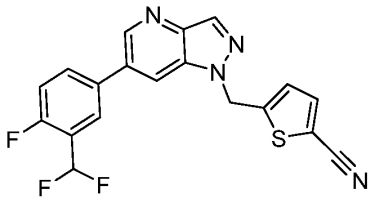
The title compound was made in an analogous manner to Example 8 using 2-(chloromethyl)-5-methylthiophene instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{19}H_{14}F_3N_3S$, 373.1; m/z found, 374.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.88 (d, *J* = 1.9 Hz, 1H), 8.70 – 8.61 (m, 1H), 8.43 – 8.31 (m, 1H), 8.16 – 8.00 (m, 2H), 7.64 – 7.54 (m, 1H), 7.30 (t, *J* = 54.1 Hz, 1H), 7.01 (d, *J* = 3.4 Hz, 1H), 6.67 – 6.58 (m, 1H), 5.86 (s, 2H), 2.33 (s, 3H).

Example 33: 6-(3-(Difluoromethyl)-4-fluorophenyl)-1-((5-fluorothiophen-2-yl)methyl)-1H-pyrazolo[4,3-b]pyridine.



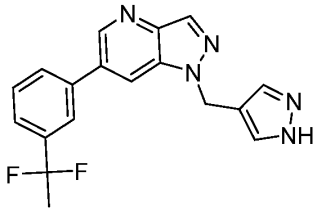
The title compound was made in an analogous manner to Example 8 using 2-(chloromethyl)-5-fluorothiophene instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{18}H_{11}F_4N_3S$, 377.1; m/z found, 378.1 $[M+H]^+$.

Example 34: 5-((6-(3-(Difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)thiophene-2-carbonitrile.



The title compound was made in an analogous manner to Example 8 using 5-(chloromethyl)thiophene-2-carbonitrile instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{19}H_{11}F_3N_4S$, 384.1; m/z found, 385.1 $[M+H]^+$.

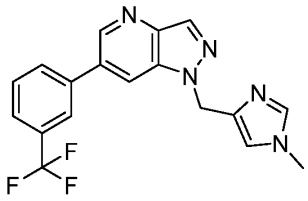
Example 35: 6-[3-(1,1-Difluoroethyl)phenyl]-1-(1H-pyrazol-4-ylmethyl)pyrazolo[4,3-b]pyridine.



The title compound was prepared in a manner analogous to Example 11 using 6-(3-(1,1-difluoroethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 29) instead of 6-[3-(difluoromethoxy)-4-fluoro-phenyl]-1*H*-pyrazolo[4,3-*b*]pyridine (Intermediate 26) in Step A.

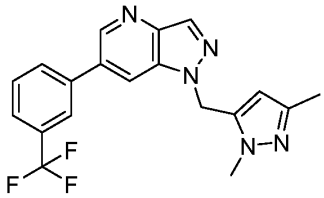
MS (ESI): mass calcd. for $C_{18}H_{15}F_2N_5$, 339.3; m/z found, 340.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 12.72 (br s, 1H), 8.89 (d, J = 1.9 Hz, 1H), 8.54 – 8.48 (m, 1H), 8.32 (s, 1H), 8.00 – 7.90 (m, 2H), 7.71 – 7.55 (m, 3H), 6.17 – 6.09 (m, 1H), 5.73 (s, 2H), 2.07 (t, J = 18.9 Hz, 3H).

Example 36: 1-[(1-Methylimidazol-4-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine.



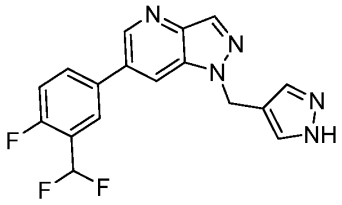
The title compound was prepared in a manner analogous to Example 1, using 4-(chloromethyl)-1-methyl-1H-imidazole instead of 2-(chloromethyl)pyrimidine hydrochloride. MS (ESI): mass calcd. for $C_{18}H_{14}F_3N_5$, 357.1; m/z found, 358.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.79 (d, J = 1.9 Hz, 1H), 8.28 (d, J = 1.0 Hz, 1H), 8.14 (dd, J = 1.9, 1.0 Hz, 1H), 7.90-7.87 (m, 1H), 7.84 (d, J = 7.7 Hz, 1H), 7.71 – 7.61 (m, 2H), 7.38 – 7.34 (m, 1H), 6.83 (s, 1H), 5.61 – 5.56 (m, 2H), 3.62 (s, 3H).

Example 37: 1-[(2,5-Dimethylpyrazol-3-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine.



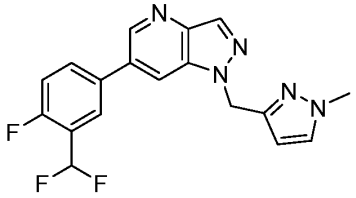
The title compound was prepared in a manner analogous to Example 1, using 5-(chloromethyl)-1,3-dimethyl-1H-pyrazole instead of 2-(chloromethyl)pyrimidine hydrochloride. MS (ESI): mass calcd. for $C_{19}H_{16}F_3N_5$, 371.1; m/z found, 372.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.81-8.78 (m, 1H), 8.29-8.27 (m, 1H), 8.04 – 8.00 (m, 1H), 7.88 – 7.81 (m, 2H), 7.72 – 7.60 (m, 2H), 5.92 – 5.88 (m, 1H), 5.58 (m, 2H), 3.74 (s, 3H), 2.23 – 2.17 (m, 3H), 2.00 (s, 3H).

Example 38: 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(1H-pyrazol-4-ylmethyl)pyrazolo[4,3-b]pyridine.



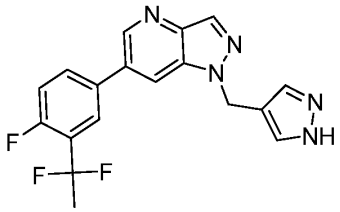
The title compound was prepared in a manner analogous to Example 11 using 6-(3-(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 25) instead of 6-[3-(difluoromethoxy)-4-fluoro-phenyl]-1*H*-pyrazolo[4,3-*b*]pyridine (Intermediate 26) in Step A. MS (ESI): mass calcd. for $C_{17}H_{12}F_3N_5$, 343.1; m/z found, 344.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 12.73 (br s, 1H), 8.87 (d, J = 1.9 Hz, 1H), 8.59 – 8.50 (m, 1H), 8.33 (s, 1H), 8.11 – 8.02 (m, 2H), 7.68 – 7.50 (m, 2H), 7.29 (t, J = 54.1 Hz, 1H), 6.19 – 6.11 (m, 1H), 5.72 (s, 2H).

Example 39: 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(1-methylpyrazol-3-yl)methyl]pyrazolo[4,3-b]pyridine.



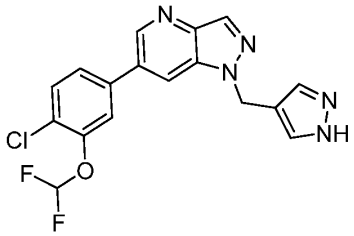
The title compound was prepared in a manner analogous to Example 8 using 3-(chloromethyl)-1-methyl-1H-pyrazole hydrochloride instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{18}H_{14}F_3N_5$, 357.1; m/z found, 358.0 $[M+H]^+$. ^1H NMR (500 MHz, CD_3OD) δ 8.78 (d, J = 1.9 Hz, 1H), 8.36 (dd, J = 2.0, 1.0 Hz, 1H), 8.23 (d, J = 1.0 Hz, 1H), 8.03 – 7.89 (m, 2H), 7.49 (d, J = 2.3 Hz, 1H), 7.41 (dd, J = 9.9, 8.7 Hz, 1H), 7.08 (t, J = 54.6 Hz, 1H), 6.20 (d, J = 2.3 Hz, 1H), 5.67 (s, 2H), 3.84 (s, 3H).

Example 40: 6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-(1H-pyrazol-4-ylmethyl)pyrazolo[4,3-b]pyridine.



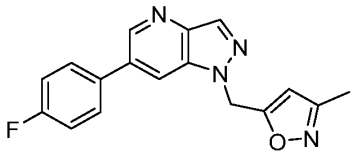
The title compound was prepared in a manner analogous to Example 11 using Intermediate 28: 6-(3-(1,1-Difluoroethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine. MS (ESI): mass calcd. for $C_{18}H_{14}F_3N_5$, 357.1; m/z found, 358.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 12.73 (s, 1H), 8.93 – 8.82 (m, 1H), 8.55 – 8.48 (m, 1H), 8.32 (s, 1H), 8.06 – 7.89 (m, 2H), 7.69 – 7.58 (m, 1H), 7.59 – 7.50 (m, 1H), 6.17 – 6.08 (m, 1H), 5.72 (s, 2H), 2.10 (t, J = 19.2 Hz, 3H).

Example 41: 6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-(1H-pyrazol-4-ylmethyl)pyrazolo[4,3-b]pyridine.



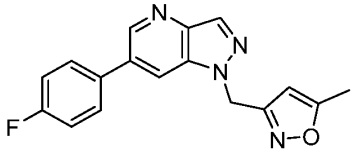
The title compound was prepared in a manner analogous to Example 11 using 6-(4-chloro-3-(difluoromethoxy)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 27) instead of 6-[3-(difluoromethoxy)-4-fluoro-phenyl]-1*H*-pyrazolo[4,3-*b*]pyridine (Intermediate 26) in Step A. MS (ESI): mass calcd. for $C_{17}H_{12}ClF_2N_5O$, 375.1; m/z found, 376.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 12.73 (br s, 1H), 8.89 (d, J = 1.9 Hz, 1H), 8.60 – 8.50 (m, 1H), 8.34 (s, 1H), 7.86 – 7.71 (m, 3H), 7.66 – 7.54 (m, 1H), 7.45 (t, J = 73.2 Hz, 1H), 6.19 – 6.09 (m, 1H), 5.72 (s, 2H).

Example 42: 5-[[6-(4-Fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-isoxazole.



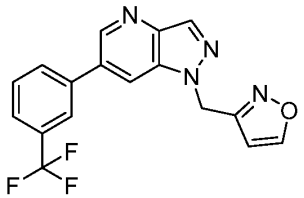
The title compound was prepared in a manner analogous to Example 1, using 6-(4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 43) and 5-(chloromethyl)-3-methylisoxazole. MS (ESI): mass calcd. for $C_{17}H_{13}FN_4O$, 308.1; m/z found, 309.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.81 (d, J = 1.9 Hz, 1H), 8.31-8.29 (m, 1H), 7.92-7.89 (m, 1H), 7.64 – 7.58 (m, 2H), 7.25 – 7.16 (m, 2H), 5.98 (s, 1H), 5.70 – 5.67 (m, 2H), 2.25 (s, 3H).

Example 43: 3-[[6-(4-Fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-isoxazole.



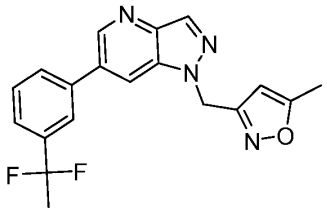
The title compound was prepared in a manner analogous to Example 1, using 6-(4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 43) and 3-(chloromethyl)-5-methylisoxazole. MS (ESI): mass calcd. for $C_{17}H_{13}FN_4O$, 308.1; m/z found, 309.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.81 (d, J = 1.9 Hz, 1H), 8.33 (d, J = 1.0 Hz, 1H), 7.94 (dd, J = 1.9, 1.0 Hz, 1H), 7.86-7.84 (m, 1H), 7.82-7.79 (m, 1H), 7.72 – 7.60 (m, 2H), 6.77-7.76 (m, 1H), 5.72 (s, 2H), 2.49 (d, J = 1.0 Hz, 3H).

Example 44: 3-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]isoxazole.



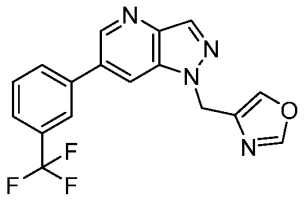
The title compound was prepared in a manner analogous to Example 1, using 3-(chloromethyl)isoxazole instead of 2-(chloromethyl)pyrimidine hydrochloride. MS (ESI): mass calcd. for $C_{17}H_{11}F_3N_4O$, 344.1; m/z found, 345.1 $[M+H]^+$. 1H NMR (500 MHz, $CDCl_3$) δ 8.84-8.82 (m, 1H), 8.37-8.32 (m, 2H), 7.97-7.95 (m, 1H), 7.88-7.85 (m, 1H), 7.83 – 7.79 (m, 1H), 7.72-7.69 (m, 1H), 7.67-7.62 (m, 1H), 6.32-6.29 (m, 1H), 5.76 (s, 2H).

Example 45: 3-[[6-[3-(1,1-Difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-isoxazole.



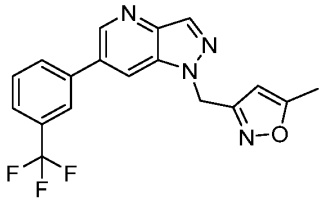
The title compound was made in an analogous manner to Example 11, Step A, using 6-(3-(1,1-difluoroethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 29) instead of 6-[3-(difluoromethoxy)-4-fluoro-phenyl]-1*H*-pyrazolo[4,3-*b*]pyridine (Intermediate 26) and 3-(chloromethyl)-5-methylisoxazole instead of 4-(chloromethyl)-1-tetrahydropyran-2-yl-pyrazole (Intermediate 1). MS (ESI): mass calcd. for $C_{19}H_{16}F_2N_4O$, 354.1; m/z found, 355.2 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.94 (d, J = 1.9 Hz, 1H), 8.67 – 8.57 (m, 1H), 8.44 – 8.36 (m, 1H), 8.03 – 7.92 (m, 2H), 7.73 – 7.60 (m, 2H), 6.07 (s, 1H), 5.84 (s, 2H), 2.32 (s, 3H), 2.07 (t, J = 18.9 Hz, 3H).

Example 46: 4-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]oxazole.



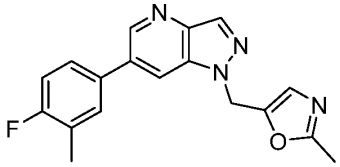
The title compound was prepared in a manner analogous to Example 1, using 4-(chloromethyl)oxazole instead of 2-(chloromethyl)pyrimidine hydrochloride. MS (ESI): mass calcd. for $C_{17}H_{11}F_3N_4O$, 344.1; m/z found, 345.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.84 – 8.81 (m, 1H), 8.32 – 8.29 (m, 1H), 8.09 – 8.12 (m, 1H), 7.92 – 7.83 (m, 3H), 7.73 – 7.63 (m, 3H), 5.62 – 5.58 (m, 2H).

Example 47: 5-Methyl-3-[[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]isoxazole.



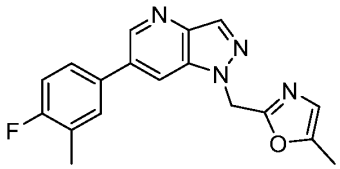
The title compound was prepared in a manner analogous to Example 8, using 6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 42) and 3-(chloromethyl)-5-methylisoxazole. MS (ESI): mass calcd. for $C_{18}H_{13}F_3N_4O$, 358.1; m/z found, 359.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.83 (d, *J*=2.02 Hz, 1 H), 8.33 (d, *J*=0.87 Hz, 1 H), 7.97 (dd, *J*=1.88, 1.01 Hz, 1 H), 7.87 (s, 1 H), 7.82 (d, *J*=7.80 Hz, 1 H), 7.75 – 7.69 (m, 1 H), 7.68 – 7.57 (m, 1 H), 5.91 (s, 1 H), 5.68 (s, 2 H), 2.37 (d, *J*=0.87 Hz, 3 H).

Example 48: 5-[[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-2-methyl-oxazole.



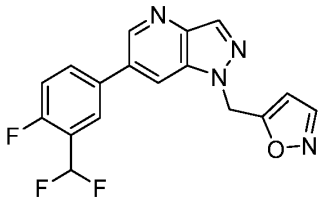
The title compound was prepared in a manner analogous to Example 9 using 5-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-2-methyloxazole (Intermediate 23) and (4-fluoro-3-methylphenyl)boronic acid. MS (ESI): mass calcd. for $C_{18}H_{15}FN_4O$, 322.1; m/z found, 323.1 $[M+H]^+$. ^1H NMR (400 MHz, CD_3OD) δ 8.79 (d, *J* = 1.8 Hz, 1H), 8.43 – 8.33 (m, 1H), 8.23 (d, *J* = 1.0 Hz, 1H), 7.70 – 7.61 (m, 1H), 7.61 – 7.55 (m, 1H), 7.24 – 7.15 (m, 1H), 7.10 (s, 1H), 5.76 (s, 2H), 2.44 – 2.31 (m, 6H).

Example 49: 2-[[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-oxazole.



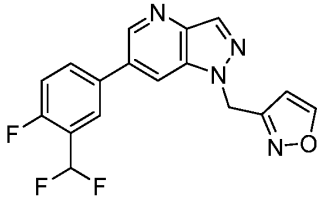
The title compound was prepared in a manner analogous to Example 9 using 5-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-2-methyloxazole (Intermediate 23) and (4-fluoro-3-methylphenyl)boronic acid. MS (ESI): mass calcd. for $C_{18}H_{15}FN_4O$, 322.1; m/z found, 323.1 $[M+H]^+$. ^1H NMR (400 MHz, CD_3OD) δ 8.81 (d, J = 1.9 Hz, 1H), 8.35 (dd, J = 1.9, 1.0 Hz, 1H), 8.25 (d, J = 1.0 Hz, 1H), 7.70 – 7.63 (m, 1H), 7.63 – 7.55 (m, 1H), 7.24 – 7.12 (m, 1H), 6.76 (d, J = 1.2 Hz, 1H), 5.81 (s, 2H), 2.38 (d, J = 2.0 Hz, 3H), 2.27 (d, J = 1.2 Hz, 3H).

Example 50: 5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]isoxazole.



The title compound was prepared in a manner analogous to Example 8 using 5-(chloromethyl)isoxazole instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{17}H_{11}F_3N_4O$, 344.1; m/z found, 345.0 $[M+H]^+$. ^1H NMR (500 MHz, CD_3OD) δ 8.83 (d, J = 1.9 Hz, 1H), 8.45 (dd, J = 1.9, 1.0 Hz, 1H), 8.32 (d, J = 1.6 Hz, 1H), 8.29 (d, J = 1.0 Hz, 1H), 8.03 – 7.91 (m, 2H), 7.46 – 7.34 (m, 1H), 7.07 (t, J = 54.6 Hz, 1H), 6.39 – 6.33 (m, 1H), 5.95 (s, 2H).

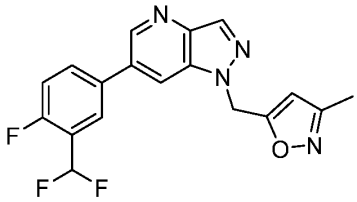
Example 51: 3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]isoxazole.



The title compound was prepared in a manner analogous to Example 8 using 3-(chloromethyl)isoxazole instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{17}H_{11}F_3N_4O$, 344.1; m/z found, 345.0 $[M+H]^+$. ^1H NMR (500 MHz, CD_3OD) δ 8.82 (d, J = 1.9 Hz, 1H), 8.61 (d, J = 1.7 Hz, 1H), 8.40 (dd, J = 1.9, 1.0 Hz, 1H), 8.29 (d, J = 1.0 Hz,

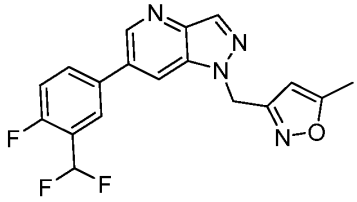
1H), 8.02 – 7.91 (m, 2H), 7.41 (ddt, *J* = 9.8, 8.7, 1.1 Hz, 1H), 7.07 (t, *J* = 54.6 Hz, 1H), 6.41 (d, *J* = 1.7 Hz, 1H), 5.87 (s, 2H).

Example 52: 5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-isoxazole.



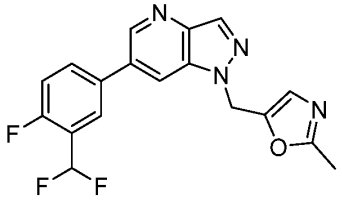
The title compound was prepared in a manner analogous to Example 8 using 5-(chloromethyl)-3-methylisoxazole instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{18}H_{13}F_3N_4O$, 358.1; m/z found, 359.1 $[M+H]^+$. ^1H NMR (500 MHz, CD_3OD) δ 8.84 (d, *J* = 1.9 Hz, 1H), 8.45 (dd, *J* = 1.9, 1.0 Hz, 1H), 8.30 (d, *J* = 1.0 Hz, 1H), 8.07 – 7.90 (m, 2H), 7.42 (dd, *J* = 10.1, 8.6 Hz, 1H), 7.08 (t, *J* = 54.6 Hz, 1H), 6.21 (s, 1H), 5.88 (s, 2H), 2.22 (s, 3H).

Example 53: 3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-isoxazole.



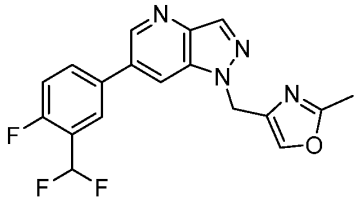
The title compound was made in an analogous manner to Example 11, Step A, using 6-(3-(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 25) instead of 6-[3-(difluoromethoxy)-4-fluoro-phenyl]-1*H*-pyrazolo[4,3-*b*]pyridine (Intermediate 26) and 3-(chloromethyl)-5-methylisoxazole instead of 4-(chloromethyl)-1-tetrahydropyran-2-yl-pyrazole (Intermediate 1). MS (ESI): mass calcd. for $C_{18}H_{13}F_3N_4O$, 358.1; m/z found, 359.2 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.92 (d, *J* = 1.9 Hz, 1H), 8.67 – 8.59 (m, 1H), 8.44 – 8.37 (m, 1H), 8.14 – 8.04 (m, 2H), 7.64 – 7.53 (m, 1H), 7.30 (t, *J* = 54.1 Hz, 1H), 6.07 (s, 1H), 5.82 (s, 2H), 2.32 (s, 3H).

Example 54: 5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-2-methyl-oxazole.



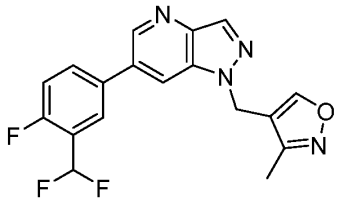
The title compound was prepared in a manner analogous to Example 8 using 5-(chloromethyl)-2-methyloxazole instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{18}H_{13}F_3N_4O$, 358.1; m/z found, 359.1 $[M+H]^+$. ^1H NMR (500 MHz, CD_3OD) δ 8.83 (d, J = 1.9 Hz, 1H), 8.48 (dd, J = 1.9, 1.0 Hz, 1H), 8.27 (d, J = 1.0 Hz, 1H), 8.07 – 7.90 (m, 2H), 7.44 (dd, J = 10.0, 8.7 Hz, 1H), 7.25 – 6.93 (m, 2H), 5.79 (s, 2H), 2.37 (s, 3H).

Example 55: 4-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-2-methyl-oxazole.



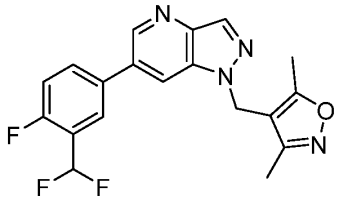
The title compound was prepared in a manner analogous to Example 8 using 4-(chloromethyl)-2-methyloxazole instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{18}H_{13}F_3N_4O$, 358.1; m/z found, 359.1 $[M+H]^+$. ^1H NMR (500 MHz, CD_3OD) δ 8.81 (d, J = 1.9 Hz, 1H), 8.47 (dd, J = 1.9, 1.0 Hz, 1H), 8.24 (d, J = 1.0 Hz, 1H), 8.07 – 7.93 (m, 2H), 7.89 – 7.80 (m, 1H), 7.42 (t, J = 9.3 Hz, 1H), 7.09 (t, J = 54.6 Hz, 1H), 5.60 (d, J = 0.9 Hz, 2H), 2.37 (s, 3H).

Example 56: 3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-4-methyl-isoxazole.



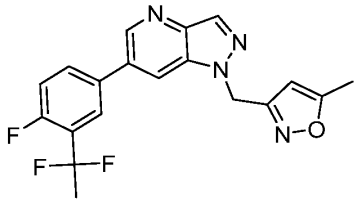
The title compound was prepared in a manner analogous to Example 8 using 4-(chloromethyl)-3-methylisoxazole instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{18}H_{13}F_3N_4O$, 358.1; m/z found, 359.1 $[M+H]^+$. ^1H NMR (400 MHz, CD_3OD) δ 8.81 (d, J = 1.9 Hz, 1H), 8.40 – 8.35 (m, 2H), 8.27 (d, J = 1.0 Hz, 1H), 8.03 – 7.87 (m, 2H), 7.48 – 7.36 (m, 1H), 7.27 – 6.88 (m, 1H), 5.83 (d, J = 0.6 Hz, 2H), 1.92 (d, J = 1.1 Hz, 3H).

Example 57: 4-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3,5-dimethyl-isoxazole.



The title compound was prepared in a manner analogous to Example 8 using 4-(chloromethyl)-3,5-dimethylisoxazole instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{19}H_{15}F_3N_4O$, 372.1; m/z found, 373.0 $[M+H]^+$. ^1H NMR (500 MHz, CD_3OD) δ 8.80 (d, J = 1.9 Hz, 1H), 8.41 (dd, J = 1.9, 1.0 Hz, 1H), 8.24 (d, J = 1.0 Hz, 1H), 8.06 – 7.90 (m, 2H), 7.48 – 7.37 (m, 1H), 7.08 (t, J = 54.6 Hz, 1H), 5.52 (s, 2H), 2.45 (s, 3H), 2.15 (s, 3H).

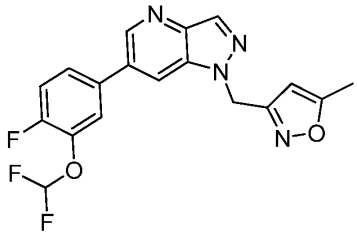
Example 58: 3-[[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-isoxazole.



The title compound was made in a manner analogous to Example 11, Step A, using 6-(3-(1,1-difluoroethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 28) instead of 6-[3-

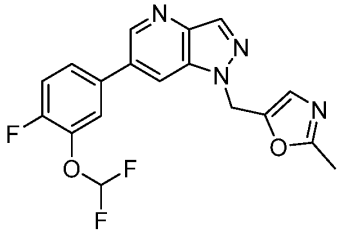
(difluoromethoxy)-4-fluoro-phenyl]-1*H*-pyrazolo[4,3-*b*]pyridine (Intermediate 26) and 3-(chloromethyl)-5-methylisoxazole instead of 4-(chloromethyl)-1-tetrahydropyran-2-yl-pyrazole (Intermediate 1). MS (ESI): mass calcd. for $C_{19}H_{15}F_3N_4O$, 372.1; m/z found, 373.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.92 (d, J = 1.9 Hz, 1H), 8.65 – 8.57 (m, 1H), 8.44 – 8.36 (m, 1H), 8.08 – 8.00 (m, 1H), 7.97 (dd, J = 7.2, 2.3 Hz, 1H), 7.56 (dd, J = 11.0, 8.6 Hz, 1H), 6.10 – 6.02 (m, 1H), 5.83 (s, 2H), 2.32 (s, 3H), 2.10 (t, J = 19.1 Hz, 3H).

Example 59: 3-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-isoxazole.



The title compound was made in an analogous manner to Example 11, Step A, using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 3-(chloromethyl)-5-methylisoxazole instead of 4-(chloromethyl)-1-tetrahydropyran-2-yl-pyrazole (Intermediate 1). MS (ESI): mass calcd. for $C_{18}H_{13}F_3N_4O_2$, 374.1; m/z found, 375.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.91 (d, J = 1.9 Hz, 1H), 8.59 – 8.55 (m, 1H), 8.41 – 8.37 (m, 1H), 7.85 (dd, J = 7.6, 2.3 Hz, 1H), 7.80 – 7.76 (m, 1H), 7.60 (dd, J = 10.5, 8.6 Hz, 1H), 7.37 (t, J = 73.2 Hz, 1H), 6.07 (s, 1H), 5.81 (s, 2H), 2.33 (s, 3H).

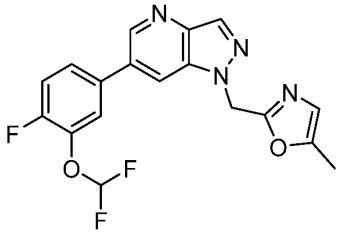
Example 60: 5-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-2-methyl-oxazole.



The title compound was prepared in a manner analogous to Example 8 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 5-

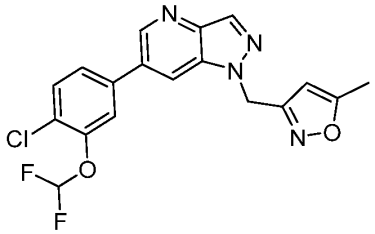
(chloromethyl)-2-methyloxazole. MS (ESI): mass calcd. for $C_{18}H_{13}F_3N_4O_2$, 374.1; m/z found, 375.1 $[M+H]^+$. ^1H NMR (600 MHz, CD_3OD) δ 8.82 (s, 1H), 8.45 (dd, J = 1.9, 1.0 Hz, 1H), 8.26 (d, J = 1.0 Hz, 1H), 7.78 – 7.62 (m, 2H), 7.45 (dd, J = 10.3, 8.6 Hz, 1H), 7.17 – 6.81 (m, 2H), 5.78 (d, J = 0.8 Hz, 2H), 2.37 (s, 3H).

Example 61: 2-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-oxazole.



The title compound was prepared in a manner analogous to Example 8 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{18}H_{13}F_3N_4O_2$, 374.1; m/z found, 375.1 $[M+H]^+$. ^1H NMR (600 MHz, CD_3OD) δ 8.83 (d, J = 1.9 Hz, 1H), 8.42 (dd, J = 1.8, 1.0 Hz, 1H), 8.28 (d, J = 1.1 Hz, 1H), 7.78 – 7.64 (m, 2H), 7.44 (dd, J = 10.3, 8.5 Hz, 1H), 6.99 (t, J = 73.3 Hz, 1H), 6.76 (d, J = 1.6 Hz, 1H), 5.83 (s, 2H), 2.27 (d, J = 1.2 Hz, 3H).

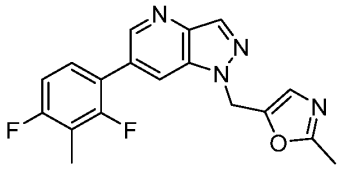
Example 62: 3-[[6-[4-Chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-isoxazole.



The title compound was made in an analogous manner to Example 11, Step A, using 6-(4-chloro-3-(difluoromethoxy)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 27) instead of 6-[3-(difluoromethoxy)-4-fluoro-phenyl]-1*H*-pyrazolo[4,3-*b*]pyridine (Intermediate 26) and 3-(chloromethyl)-5-methylisoxazole instead of 4-(chloromethyl)-1-tetrahydropyran-2-yl-pyrazole (Intermediate 1). MS (ESI): mass calcd. for $C_{18}H_{13}ClF_2N_4O_2$, 390.1; m/z found, 391.2 $[M+H]^+$.

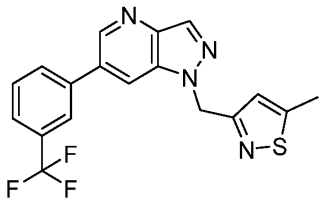
^{1}H NMR (500 MHz, DMSO-d_6) δ 8.94 (d, J = 1.9 Hz, 1H), 8.63 – 8.60 (m, 1H), 8.43 – 8.39 (m, 1H), 7.85 – 7.82 (m, 1H), 7.80 – 7.75 (m, 2H), 7.44 (t, J = 73.2 Hz, 1H), 6.09 – 6.05 (m, 1H), 5.82 (s, 2H), 2.33 (s, 3H).

Example 63: 5-[[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-2-methyl-oxazole.



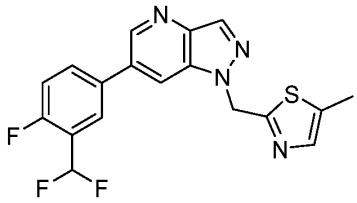
The title compound was prepared in a manner analogous to Example 9 using 5-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-2-methyloxazole (Intermediate 22) and (2,4-difluoro-3-methylphenyl)boronic acid. MS (ESI): mass calcd. for $C_{18}H_{14}F_2N_4O$, 340.1; m/z found, 341.1 $[M+H]^+$. ^{1}H NMR (400 MHz, CD_3OD) δ 8.72 – 8.64 (m, 1H), 8.34 (d, J = 1.5 Hz, 1H), 8.26 (d, J = 1.0 Hz, 1H), 7.56 – 7.41 (m, 1H), 7.16 – 7.06 (m, 2H), 5.76 (d, J = 0.9 Hz, 2H), 2.37 (s, 3H), 2.30 (t, J = 2.0 Hz, 3H).

Example 64: 5-Methyl-3-[[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]isothiazole.



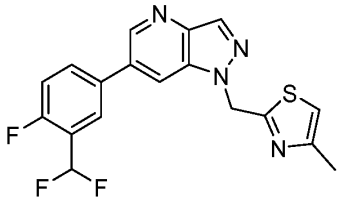
The title compound was prepared in a manner analogous to Example 1, using 3-(chloromethyl)-5-methylisothiazole instead of 2-(chloromethyl)pyrimidine hydrochloride. MS (ESI): mass calcd. for $C_{18}H_{13}F_3N_4S$, 374.1; m/z found, 375.0 $[M+H]^+$. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.81 (d, J = 1.9 Hz, 1H), 8.33 (d, J = 1.0 Hz, 1H), 7.94 (dd, J = 1.9, 1.0 Hz, 1H), 7.86-7.84 (m, 1H), 7.82-7.79 (m, 1H), 7.72 – 7.60 (m, 2H), 6.77-7.76 (m, 1H), 5.72 (s, 2H), 2.49 (d, J = 1.0 Hz, 3H).

Example 65: 2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-thiazole.



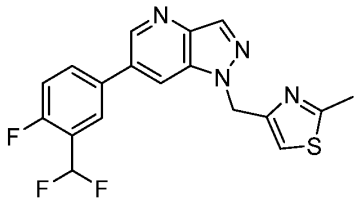
The title compound was prepared in a manner analogous to Example 8 using 2-(chloromethyl)-5-methylthiazole instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{18}H_{13}F_3N_4S$, 374.1; m/z found, 375.0 $[M+H]^+$. ^1H NMR (500 MHz, CD_3OD) δ 8.83 (d, J = 1.9 Hz, 1H), 8.43 (dd, J = 1.9, 1.0 Hz, 1H), 8.30 (d, J = 1.0 Hz, 1H), 8.07 – 7.88 (m, 2H), 7.49 – 7.32 (m, 2H), 7.07 (t, J = 54.6 Hz, 1H), 5.97 (s, 2H), 2.41 (d, J = 1.2 Hz, 3H).

Example 66: 2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-4-methyl-thiazole.



The title compound was prepared in a manner analogous to Example 8 using 4-(chloromethyl)-2-methylthiazole instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{18}H_{13}F_3N_4S$, 374.1; m/z found, 375.0 $[M+H]^+$. ^1H NMR (500 MHz, CD_3OD) δ 8.83 (d, J = 1.9 Hz, 1H), 8.46 (dd, J = 1.9, 1.0 Hz, 1H), 8.30 (d, J = 1.0 Hz, 1H), 8.06 – 7.88 (m, 2H), 7.48 – 7.33 (m, 1H), 7.23 – 6.90 (m, 2H), 6.00 (s, 2H), 2.39 (d, J = 1.0 Hz, 3H).

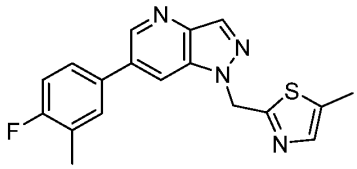
Example 67: 4-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-2-methyl-thiazole.



The title compound was prepared in a manner analogous to Example 8 using 4-(chloromethyl)-2-methylthiazole instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for

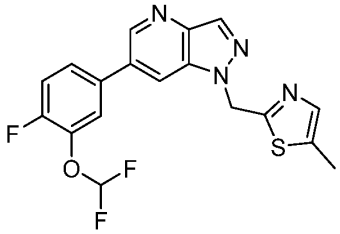
$C_{18}H_{13}F_3N_4S$, 374.1; m/z found, 375.0 $[M+H]^+$. ^1H NMR (500 MHz, CD_3OD) δ 8.81 (d, J = 1.9 Hz, 1H), 8.47 – 8.40 (m, 1H), 8.26 (d, J = 1.0 Hz, 1H), 8.05 – 7.91 (m, 2H), 7.47 – 7.36 (m, 1H), 7.30 – 7.25 (m, 1H), 7.23 – 6.94 (m, 1H), 5.76 (d, J = 0.8 Hz, 2H), 2.64 (s, 3H).

Example 68: 2-[[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-thiazole.



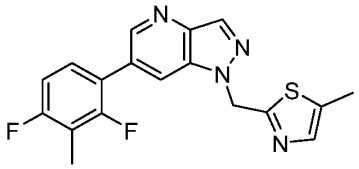
The title compound was prepared in a manner analogous to Example 8 using 6-(4-fluoro-3-methylphenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 34) and 2-(chloromethyl)-5-methyl-1,3-thiazole. MS (ESI): mass calcd. for $C_{18}H_{15}FN_4S$, 338.1; m/z found, 339.1 $[M+H]^+$. ^1H NMR (500 MHz, CD_3OD) δ 8.79 (d, J = 1.9 Hz, 1H), 8.35 (dd, J = 1.8, 1.0 Hz, 1H), 8.27 (d, J = 1.0 Hz, 1H), 7.64 (ddd, J = 7.2, 2.4, 1.0 Hz, 1H), 7.60 – 7.52 (m, 1H), 7.40 (d, J = 1.2 Hz, 1H), 7.18 (dd, J = 9.6, 8.5 Hz, 1H), 5.96 (s, 2H), 2.40 (d, J = 1.2 Hz, 3H), 2.37 (d, J = 1.9 Hz, 3H).

Example 69: 2-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-thiazole.



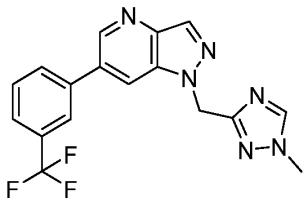
The title compound was prepared in a manner analogous to Example 8 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 2-(chloromethyl)-5-methyl-1,3-thiazole. MS (ESI): mass calcd. for $C_{18}H_{13}F_3N_4OS$, 390.1; m/z found, 391.0 $[M+H]^+$. ^1H NMR (500 MHz, CD_3OD) δ 8.81 (d, J = 1.9 Hz, 1H), 8.40 (dd, J = 2.0, 1.0 Hz, 1H), 8.29 (d, J = 0.9 Hz, 1H), 7.70 (dd, J = 7.4, 2.3 Hz, 1H), 7.66 (ddd, J = 8.6, 4.3, 2.3 Hz, 1H), 7.49 – 7.34 (m, 2H), 6.97 (t, J = 73.3 Hz, 1H), 5.97 (s, 2H), 2.41 (d, J = 1.2 Hz, 3H).

Example 70: 2-[[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-thiazole.



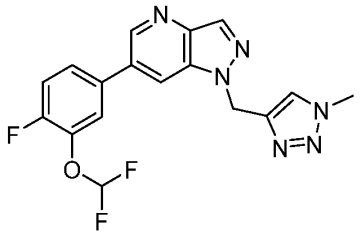
The title compound was prepared in a manner analogous to Example 8 using 6-(2,4-difluoro-3-methylphenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 36) and 2-(chloromethyl)-5-methyl-1,3-thiazole. MS (ESI): mass calcd. for $C_{18}H_{14}F_2N_4S$, 356.1; m/z found, 357.0 $[M+H]^+$. ^1H NMR (500 MHz, CD_3OD) δ 8.68 (t, J = 1.8 Hz, 1H), 8.36 – 8.19 (m, 2H), 7.46 (td, J = 8.7, 6.4 Hz, 1H), 7.40 (q, J = 1.2 Hz, 1H), 7.10 (td, J = 8.7, 1.5 Hz, 1H), 5.96 (s, 2H), 2.41 (d, J = 1.2 Hz, 3H), 2.29 (t, J = 2.0 Hz, 3H).

Example 71: 1-[(1-Methyl-1,2,4-triazol-3-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine.



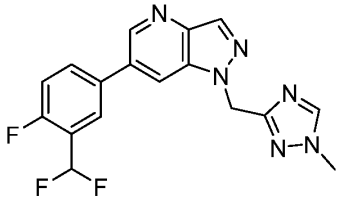
The title compound was prepared in a manner analogous to Example 1, using 3-(chloromethyl)-1-methyl-1H-1,2,4-triazole instead of 2-(chloromethyl)pyrimidine hydrochloride. MS (ESI): mass calcd. for $C_{17}H_{13}F_3N_6$, 358.1; m/z found, 359.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.85 – 8.81 (m, 1H), 8.31 – 8.28 (m, 1H), 8.12 – 8.10 (m, 1H), 7.88 – 7.80 (m, 3H), 7.74 – 7.62 (m, 2H), 5.83-5.81 (m, 2H), 3.98-3.96 (m, 3H).

Example 72: 6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(1-methyltriazol-4-yl)methyl]pyrazolo[4,3-b]pyridine.



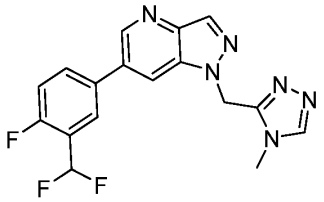
The title compound was prepared in a manner analogous to Example 8 using Intermediate 26, 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine and 4-(chloromethyl)-1-methyl-1H-1,3,4-triazole hydrochloride. MS (ESI): mass calcd. for $C_{17}H_{13}F_3N_6O$, 374.1; m/z found, 375.1 $[M+H]^+$.

Example 73: 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(1-methyl-1,2,4-triazol-3-yl)methyl]pyrazolo[4,3-b]pyridine.



The title compound was prepared in a manner analogous to Example 8 using 3-(chloromethyl)-1-methyl-1H-1,2,4-triazole instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{17}H_{13}F_3N_6$, 358.1; m/z found, 359.1 $[M+H]^+$. ^1H NMR (500 MHz, CD_3OD) δ 8.83 (s, 1H), 8.45 (d, J = 1.8 Hz, 1H), 8.32 (d, J = 38.1 Hz, 2H), 8.05 – 7.90 (m, 2H), 7.42 (dd, J = 9.9, 8.7 Hz, 1H), 7.09 (t, J = 54.6 Hz, 1H), 5.77 (s, 2H), 3.88 (s, 3H).

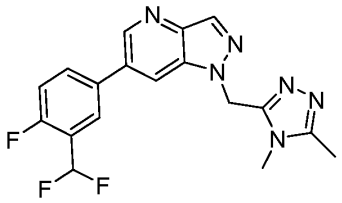
Example 74: 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(4-methyl-1,2,4-triazol-3-yl)methyl]pyrazolo[4,3-b]pyridine.



The title compound was made in an analogous manner to Example 8 using 3-(chloromethyl)-4-methyl-4H-1,2,4-triazole instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass

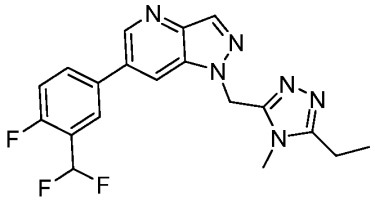
calcd. for $C_{17}H_{13}F_3N_6$, 358.1; m/z found, 359.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.91 (d, J = 1.9 Hz, 1H), 8.61 – 8.56 (m, 1H), 8.45 (s, 1H), 8.40 (s, 1H), 8.11 – 8.03 (m, 2H), 7.64 – 7.56 (m, 1H), 7.31 (t, J = 54.1 Hz, 1H), 6.00 (s, 2H), 3.66 (s, 3H).

Example 75: 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(4,5-dimethyl-1,2,4-triazol-3-yl)methyl]pyrazolo[4,3-b]pyridine.



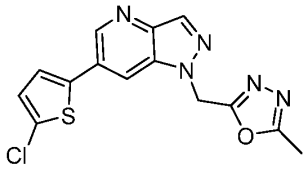
The title compound was made in an analogous manner to Example 8 using 3-(chloromethyl)-4,5-dimethyl-4H-1,2,4-triazole instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{18}H_{15}F_3N_6$, 372.1; m/z found, 373.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.90 (d, J = 1.9 Hz, 1H), 8.61 – 8.53 (m, 1H), 8.39 (s, 1H), 8.13 – 8.00 (m, 2H), 7.65 – 7.55 (m, 1H), 7.31 (t, J = 54.1 Hz, 1H), 5.95 (s, 2H), 3.54 (s, 3H), 2.30 (s, 3H).

Example 76: 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-ethyl-4-methyl-1,2,4-triazol-3-yl)methyl]pyrazolo[4,3-b]pyridine.



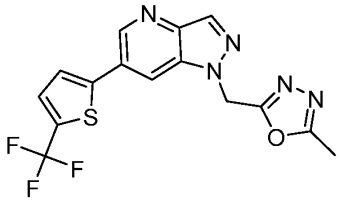
The title compound was made in an analogous manner to Example 8 using 3-(chloromethyl)-5-ethyl-4-methyl-4H-1,2,4-triazole instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{19}H_{17}F_3N_6$, 386.2; m/z found, 387.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.90 (d, J = 2.0 Hz, 1H), 8.58 – 8.55 (m, 1H), 8.39 (d, J = 1.0 Hz, 1H), 8.10 – 8.03 (m, 2H), 7.63 – 7.55 (m, 1H), 7.31 (t, J = 54.1 Hz, 1H), 5.95 (s, 2H), 3.55 (s, 3H), 2.67 (q, J = 7.5 Hz, 2H), 1.20 (t, J = 7.5 Hz, 3H).

Example 77: 2-[[6-(5-Chloro-2-thienyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole.



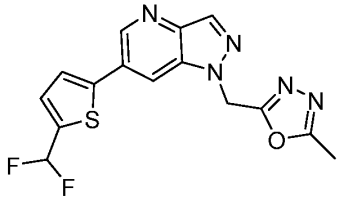
The title compound was made in an analogous manner to Intermediate 41 using 2-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-5-methyl-1,3,4-oxadiazole (Intermediate 19) and (5-chlorothiophen-2-yl)boronic acid. MS (ESI): mass calcd. for $C_{14}H_{10}ClN_5OS$, 331.1; m/z found, 332.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.92 (d, J = 2.0 Hz, 1H), 8.51 – 8.48 (m, 1H), 8.42 – 8.40 (m, 1H), 7.64 (d, J = 4.0 Hz, 1H), 7.28 (d, J = 4.0 Hz, 1H), 6.06 (s, 2H), 2.45 (s, 3H).

Example 78: 2-Methyl-5-[[6-[5-(trifluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole.



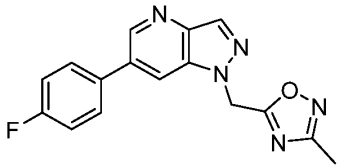
The title compound was made in an analogous manner to Intermediate 41 using 2-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-5-methyl-1,3,4-oxadiazole (Intermediate 19) and (5-(trifluoromethyl)thiophen-2-yl)boronic acid. MS (ESI): mass calcd. for $C_{15}H_{10}F_3N_5OS$, 365.1; m/z found, 366.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 9.03 (d, J = 2.0 Hz, 1H), 8.74 – 8.65 (m, 1H), 8.51 – 8.40 (m, 1H), 7.90 – 7.79 (m, 2H), 6.09 (s, 2H), 2.45 (s, 3H).

Example 79: 2-[[6-[5-(Difluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole.



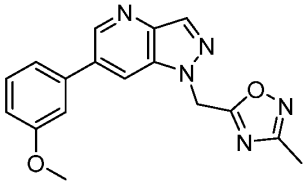
The title compound was made in an analogous manner to Intermediate 41 using 2-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-5-methyl-1,3,4-oxadiazole (Intermediate 19) and 2-(5-(difluoromethyl)thiophen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Intermediate 12). MS (ESI): mass calcd. for $C_{15}H_{11}F_2N_5OS$, 347.1; m/z found, 348.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 9.00 (d, J = 1.9 Hz, 1H), 8.70 – 8.57 (m, 1H), 8.49 – 8.38 (m, 1H), 7.81 – 7.71 (m, 1H), 7.62 – 7.56 (m, 1H), 7.38 (t, J = 55.2 Hz, 1H), 6.09 (s, 2H), 2.45 (s, 3H).

Example 80: 5-[[6-(4-Fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole.



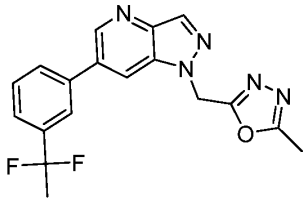
The title compound was prepared in a manner analogous to Intermediate 42 using 5-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-3-methyl-1,2,4-oxadiazole (Intermediate 55) and (4-fluorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{16}H_{12}FN_5O$, 309.1; m/z found, 310.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.83 (d, J = 1.9 Hz, 1H), 8.34 (d, J = 1.1 Hz, 1H), 7.89 (dd, J = 1.9, 1.0 Hz, 1H), 7.65 – 7.59 (m, 2H), 7.25 – 7.19 (m, 2H), 5.83 (s, 2H), 2.38 (s, 3H).

Example 81: 5-[[6-(3-Methoxyphenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole.



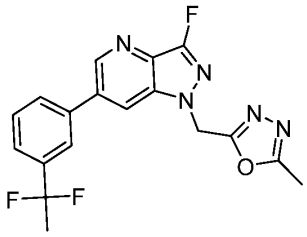
The title compound was prepared in a manner analogous to Intermediate 42 using 5-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-3-methyl-1,2,4-oxadiazole (Intermediate 55) and (3-methoxyphenyl)boronic acid. MS (ESI): mass calcd. for $C_{17}H_{15}N_5O_2$, 321.1; m/z found, 322.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.98 – 8.92 (m, 1H), 8.61 – 8.58 (m, 1H), 8.46 – 8.42 (m, 1H), 7.51 – 7.43 (m, 1H), 7.43 – 7.34 (m, 2H), 7.07 – 7.01 (m, 1H), 6.20 (s, 2H), 3.86 (s, 3H), 2.28 (s, 3H).

Example 82: 2-[[6-[3-(1,1-Difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole.



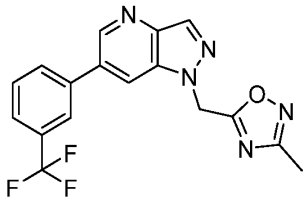
The title compound was made in an analogous manner to Intermediate 25 using 2-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-5-methyl-1,3,4-oxadiazole (Intermediate 19) and 2-(3-(1,1-difluoroethyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd. for $C_{18}H_{15}F_2N_5O$, 355.1; m/z found, 356.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.97 (d, J = 1.9 Hz, 1H), 8.63 (dd, J = 2.0, 1.0 Hz, 1H), 8.44 (d, J = 0.9 Hz, 1H), 8.01 – 7.95 (m, 2H), 7.72 – 7.64 (m, 2H), 6.11 (s, 2H), 2.44 (s, 3H), 2.07 (t, J = 18.9 Hz, 3H).

Example 83: 2-[[6-[3-(1,1-Difluoroethyl)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole.



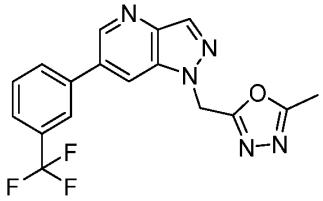
The title compound was made in an analogous manner to Example 8 using 6-(3-(1,1-Difluoroethyl)phenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridine (Intermediate 33) and 2-(chloromethyl)-5-methyl-1,3,4-oxadiazole. MS (ESI): mass calcd. for $C_{18}H_{14}F_3N_5O$, 373.1; m/z found, 374.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 9.03 (d, J = 1.8 Hz, 1H), 8.74 – 8.65 (m, 1H), 8.03 – 7.94 (m, 2H), 7.75 – 7.64 (m, 2H), 6.01 (s, 2H), 2.46 (s, 3H), 2.07 (t, J = 18.9 Hz, 3H).

Example 84: 3-Methyl-5-[[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,2,4-oxadiazole.



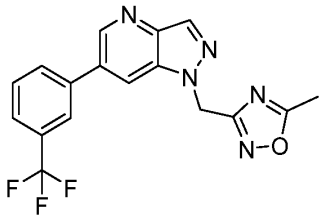
The title compound was prepared in a manner analogous to Example 8, using 6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 42) and 5-(chloromethyl)-3-methyl-1,2,4-oxadiazole. MS (ESI): mass calcd. for $C_{17}H_{12}F_3N_5O$, 359.1; m/z found, 360.6 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.87 (d, *J*=1.73 Hz, 1 H), 8.37 (s, 1 H), 8.07 – 7.92 (m, 1 H), 7.89 (s, 1 H), 7.84 (d, *J*=7.80 Hz, 1 H), 7.76 – 7.69 (m, 1 H), 7.69 – 7.59 (m, 1 H), 5.86 (s, 2 H), 2.38 (s, 3 H).

Example 85: 2-Methyl-5-[[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole.



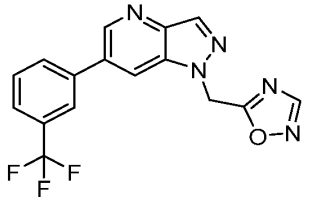
The title compound was prepared in a manner analogous to Example 8, using 6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 42) and 2-(chloromethyl)-5-methyl-1,3,4-oxadiazole. MS (ESI): mass calcd. for $C_{17}H_{12}F_3N_5O$, 359.1; m/z found, 360.3 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.87 (d, *J*=1.73 Hz, 1 H), 8.36 (d, *J*=0.87 Hz, 1 H), 8.12 – 7.98 (m, 1 H), 7.89 (s, 1 H), 7.84 (d, *J*=7.80 Hz, 1 H), 7.77 – 7.70 (m, 1 H), 7.69 – 7.63 (m, 1 H), 5.85 (s, 2 H), 2.67 – 2.30 (m, 3 H).

Example 86: 5-Methyl-3-[[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,2,4-oxadiazole.



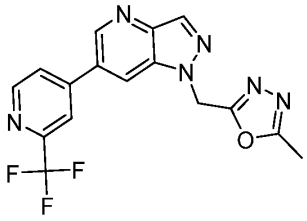
The title compound was prepared in a manner analogous to Example 8, using 6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 42) and 3-(chloromethyl)-5-methyl-1,2,4-oxadiazole. MS (ESI): mass calcd. for $C_{17}H_{12}F_3N_5O$, 359.1; m/z found, 360.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.85 (d, *J*=1.73 Hz, 1 H), 8.36 (d, *J*=1.16 Hz, 1 H), 8.02 (dd, *J*=1.88, 1.01 Hz, 1 H), 7.90 (s, 1 H), 7.85 (d, *J*=7.51 Hz, 1 H), 7.75 – 7.70 (m, 1 H), 7.69 – 7.63 (m, 1 H), 5.75 (s, 2 H), 2.56 (s, 3 H).

Example 87: 5-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,2,4-oxadiazole.



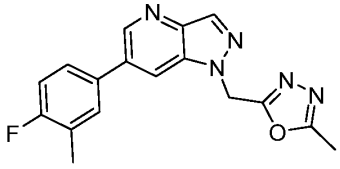
The title compound was prepared in a manner analogous to Example 20, using 6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 42) and 5-(chloromethyl)-1,2,4-oxadiazole. MS (ESI): mass calcd. for $C_{16}H_{10}F_3N_5O$, 345.1; m/z found, 346.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.88 (d, *J*=1.73 Hz, 1 H), 8.42 (s, 1 H), 8.39 (d, *J*=0.87 Hz, 1 H), 8.02 – 7.94 (m, 1 H), 7.89 (s, 1 H), 7.84 (d, *J*=7.80 Hz, 1 H), 7.77 – 7.70 (m, 1 H), 7.69 – 7.61 (m, 1 H), 5.95 (s, 2 H).

Example 88: 2-Methyl-5-[[6-[2-(trifluoromethyl)-4-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole.



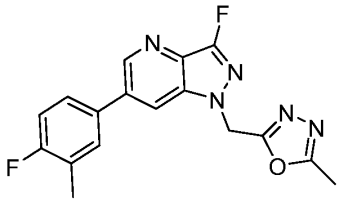
The title compound was made in an analogous manner to Intermediate 25 using 2-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-5-methyl-1,3,4-oxadiazole (Intermediate 19) and (2-(trifluoromethyl)pyridin-4-yl)boronic acid. MS (ESI): mass calcd. for $C_{16}H_{11}F_3N_6O$, 360.1; m/z found, 361.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 9.14 (d, J = 1.9 Hz, 1H), 9.00 – 8.85 (m, 2H), 8.51 (s, 1H), 8.44 – 8.35 (m, 1H), 8.30 – 8.20 (m, 1H), 6.12 (s, 2H), 2.45 (s, 3H).

Example 89: 2-[[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole.



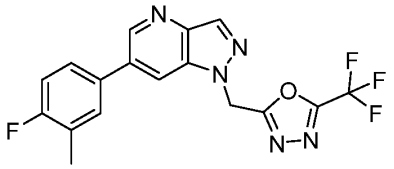
The title compound was made in an analogous manner to Intermediate 25 using 2-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-5-methyl-1,3,4-oxadiazole (Intermediate 19) and (4-fluoro-3-methylphenyl)boronic acid. MS (ESI): mass calcd. for $C_{17}H_{14}FN_5O$, 323.1; m/z found, 324.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.96 – 8.82 (m, 1H), 8.57 – 8.50 (m, 1H), 8.45 – 8.36 (m, 1H), 7.82 – 7.74 (m, 1H), 7.71 – 7.64 (m, 1H), 7.37 – 7.29 (m, 1H), 6.08 (s, 2H), 2.44 (s, 3H), 2.35 (s, 3H).

Example 90: 2-[[3-Fluoro-6-(4-fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole.



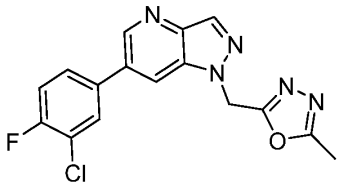
The title compound was made in an analogous manner to Intermediate 25 using 2-((6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-5-methyl-1,3,4-oxadiazole (Intermediate 20) and (4-fluoro-3-methylphenyl)boronic acid. MS (ESI): mass calcd. for $C_{17}H_{13}F_2N_5O$, 341.1; m/z found, 342.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.95 (d, J = 1.9 Hz, 1H), 8.61 – 8.56 (m, 1H), 7.80 (dd, J = 7.3, 2.4 Hz, 1H), 7.73 – 7.68 (m, 1H), 7.38 – 7.31 (m, 1H), 6.01 – 5.92 (m, 2H), 2.45 (s, 3H), 2.35 (d, J = 1.9 Hz, 3H).

Example 91: 2-[[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-(trifluoromethyl)-1,3,4-oxadiazole.



The title compound was prepared in a manner analogous to Example 8 using 6-(4-fluoro-3-methylphenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 34) and 2-(chloromethyl)-5-(trifluoromethyl)-1,3,4-oxadiazole. MS (ESI): mass calcd. for $C_{17}H_{11}F_4N_5O$, 377.1; m/z found, 378.0 $[M+H]^+$. ^1H NMR (500 MHz, CD_3OD) δ 8.84 (d, J = 1.9 Hz, 1H), 8.41 (dd, J = 1.9, 1.0 Hz, 1H), 8.31 (d, J = 1.0 Hz, 1H), 7.66 (ddd, J = 7.3, 2.5, 1.0 Hz, 1H), 7.59 (ddd, J = 7.8, 4.8, 2.5 Hz, 1H), 7.20 (dd, J = 9.5, 8.5 Hz, 1H), 6.17 (s, 2H), 2.37 (d, J = 1.9 Hz, 3H).

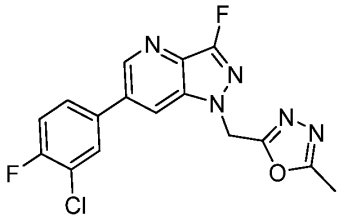
Example 92: 2-[[6-(3-Chloro-4-fluoro-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole.



The title compound was made in an analogous manner to Intermediate 25 using 2-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-5-methyl-1,3,4-oxadiazole (Intermediate 19) and (3-chloro-4-fluorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{16}H_{11}ClFN_5O$, 343.1; m/z found, 344.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.99 – 8.91 (m, 1H), 8.67 – 8.61 (m, 1H), 8.47 – 8.40

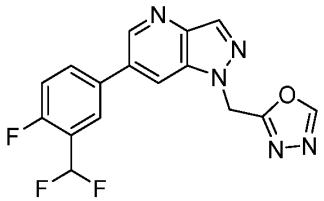
(m, 1H), 8.15 – 8.06 (m, 1H), 7.92 – 7.84 (m, 1H), 7.62 (t, *J* = 9.0 Hz, 1H), 6.08 (s, 2H), 2.44 (s, 3H).

Example 93: 2-[[6-(3-Chloro-4-fluoro-phenyl)-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole.



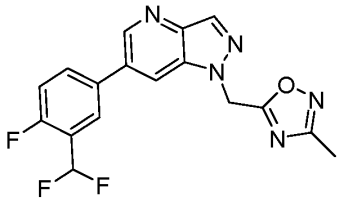
The title compound was made in an analogous manner to Intermediate 25 using 2-((6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-5-methyl-1,3,4-oxadiazole (Intermediate 20) and (3-chloro-4-fluorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{16}H_{10}ClF_2N_5O$, 361.1; m/z found, 362.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 9.00 (d, *J* = 1.9 Hz, 1H), 8.71 – 8.67 (m, 1H), 8.13 (dd, *J* = 7.1, 2.4 Hz, 1H), 7.94 – 7.86 (m, 1H), 7.64 (t, *J* = 8.9 Hz, 1H), 5.97 (s, 2H), 2.46 (s, 3H).

Example 94: 2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole.



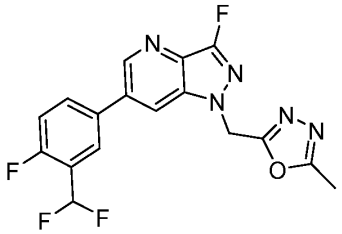
The title compound was prepared in a manner analogous to Example 8 using 2-(chloromethyl)-1,3,4-oxadiazole instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{16}H_{10}F_3N_5O$, 345.1; m/z found, 346.0 $[M+H]^+$. ^1H NMR (500 MHz, CD_3OD) δ 8.92 (s, 1H), 8.87 (d, *J* = 1.9 Hz, 1H), 8.50 (dd, *J* = 1.9, 1.0 Hz, 1H), 8.32 (d, *J* = 1.0 Hz, 1H), 8.02 (d, *J* = 6.1 Hz, 1H), 7.98 (dd, *J* = 8.8, 4.5 Hz, 1H), 7.43 (t, *J* = 9.3 Hz, 1H), 7.08 (t, *J* = 54.6 Hz, 1H), 6.11 (s, 2H).

Example 95: 5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole.



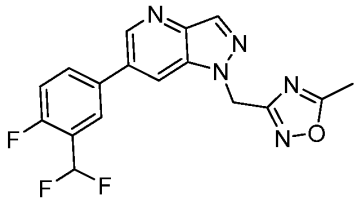
The title compound was made in an analogous manner to Example 8 using 5-(chloromethyl)-3-methyl-1,2,4-oxadiazole instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{17}H_{12}F_3N_5O$, 359.1; m/z found, 360.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.96 (d, J = 1.9 Hz, 1H), 8.69 – 8.63 (m, 1H), 8.50 – 8.43 (m, 1H), 8.13 – 8.04 (m, 2H), 7.64 – 7.53 (m, 1H), 7.30 (t, J = 54.1 Hz, 1H), 6.21 (s, 2H), 2.28 (s, 3H).

Example 96: 2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole.



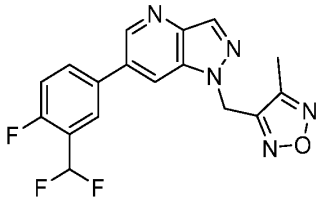
The title compound was made in an analogous manner to Example 8 using 6-(3-(difluoromethyl)-4-fluorophenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridine (Intermediate 30) and 2-(chloromethyl)-5-methyl-1,3,4-oxadiazole. MS (ESI): mass calcd. for $C_{17}H_{11}F_4N_5O$, 377.1; m/z found, 378.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 9.00 (d, J = 1.8 Hz, 1H), 8.75 – 8.65 (m, 1H), 8.17 – 8.04 (m, 2H), 7.69 – 7.54 (m, 1H), 7.32 (t, J = 54.1 Hz, 1H), 5.99 (s, 2H), 2.46 (s, 3H).

Example 97: 3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,2,4-oxadiazole.



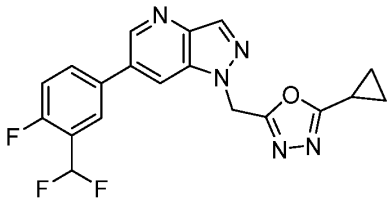
The title compound was made in an analogous manner to Example 8 using 3-(chloromethyl)-5-methyl-1,2,4-oxadiazole instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{17}H_{12}F_3N_5O$, 359.1; m/z found, 360.3 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.93 (d, J = 2.1 Hz, 1H), 8.66 – 8.60 (m, 1H), 8.43 – 8.37 (m, 1H), 8.12 – 8.05 (m, 2H), 7.65 – 7.53 (m, 1H), 7.30 (t, J = 54.2 Hz, 1H), 5.95 (s, 2H), 2.52 (s, 3H).

Example 98: 3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-4-methyl-1,2,5-oxadiazole.



The title compound was prepared in a manner analogous to Example 8 using 3-(chloromethyl)-4-methyl-1,2,5-oxadiazole instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{17}H_{12}F_3N_5O$, 359.1; m/z found, 360.0 $[M+H]^+$. ^1H NMR (500 MHz, CD_3OD) δ 8.84 (d, J = 1.9 Hz, 1H), 8.44 (dd, J = 1.9, 1.0 Hz, 1H), 8.29 (d, J = 1.0 Hz, 1H), 8.05 – 7.88 (m, 2H), 7.42 (ddt, J = 9.8, 8.6, 1.1 Hz, 1H), 7.08 (t, J = 54.6 Hz, 1H), 5.97 (s, 2H), 2.29 (s, 3H).

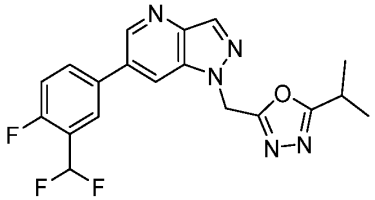
Example 99: 2-Cyclopropyl-5-[[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole.



The title compound was prepared in a manner analogous to Example 8 using 2-(chloromethyl)-5-cyclopropyl-1,3,4-oxadiazole instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass

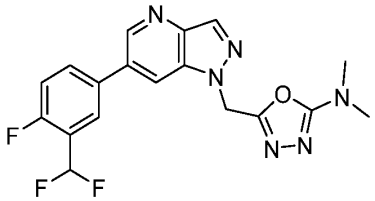
calcd. for $C_{19}H_{14}F_3N_5O$, 385.1; m/z found, 386.1 $[M+H]^+$. ^1H NMR (500 MHz, CD_3OD) δ 8.84 (s, 1H), 8.53 – 8.37 (m, 1H), 8.34 – 8.22 (m, 1H), 8.07 – 7.86 (m, 2H), 7.41 (t, *J* = 9.2 Hz, 1H), 7.08 (t, *J* = 54.6 Hz, 1H), 5.98 (s, 2H), 2.24 – 2.07 (m, 1H), 1.21 – 1.09 (m, 2H), 1.09 – 0.95 (m, 2H).

Example 100: 2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-isopropyl-1,3,4-oxadiazole.



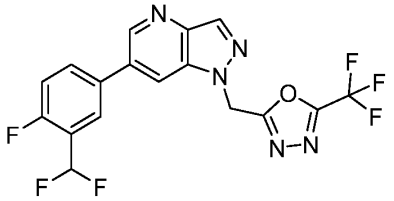
The title compound was prepared in a manner analogous to Example 8 using 2-(chloromethyl)-5-isopropyl-1,3,4-oxadiazole instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{19}H_{16}F_3N_5O$, 387.1; m/z found, 388.1 $[M+H]^+$. ^1H NMR (500 MHz, CD_3OD) δ 8.87 (d, *J* = 1.9 Hz, 1H), 8.50 (dd, *J* = 1.8, 1.0 Hz, 1H), 8.32 (d, *J* = 1.0 Hz, 1H), 8.06 – 7.92 (m, 2H), 7.43 (dd, *J* = 9.9, 8.7 Hz, 1H), 7.09 (t, *J* = 54.6 Hz, 1H), 6.04 (s, 2H), 3.17 (dt, *J* = 14.0, 7.0 Hz, 1H), 1.32 (d, *J* = 7.0 Hz, 6H).

Example 101: 5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-*N*,*N*-dimethyl-1,3,4-oxadiazol-2-amine.



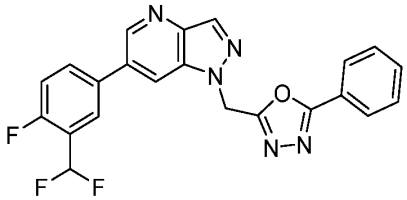
The title compound was prepared in a manner analogous to Example 8 using 5-(chloromethyl)-*N*,*N*-dimethyl-1,3,4-oxadiazol-2-amine instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{18}H_{15}F_3N_6O$, 388.1; m/z found, 389.1 $[M+H]^+$. ^1H NMR (400 MHz, CD_3OD) δ 8.85 (d, *J* = 1.9 Hz, 1H), 8.59 – 8.41 (m, 1H), 8.30 (d, *J* = 1.0 Hz, 1H), 8.07 – 7.89 (m, 2H), 7.52 – 7.35 (m, 1H), 7.26 – 6.92 (m, 1H), 5.86 (s, 2H), 3.00 (s, 6H).

Example 102: 2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-(trifluoromethyl)-1,3,4-oxadiazole.



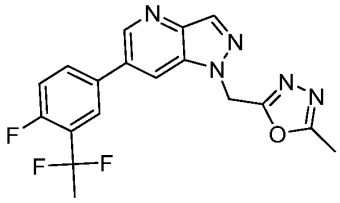
The title compound was prepared in a manner analogous to Example 8 using 2-(chloromethyl)-5-(trifluoromethyl)-1,3,4-oxadiazole instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{17}H_9F_6N_5O$, 413.1; m/z found, 414.1 $[M+H]^+$. ^1H NMR (600 MHz, CD_3OD) δ 8.88 (s, 1H), 8.51 (dt, *J* = 1.8, 0.9 Hz, 1H), 8.35 (d, *J* = 1.0 Hz, 1H), 8.02 (d, *J* = 6.3 Hz, 1H), 7.98 (dt, *J* = 7.7, 3.3 Hz, 1H), 7.43 (dd, *J* = 10.0, 8.7 Hz, 1H), 7.09 (t, *J* = 54.6 Hz, 1H), 6.19 (s, 2H).

Example 103: 2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-phenyl-1,3,4-oxadiazole.



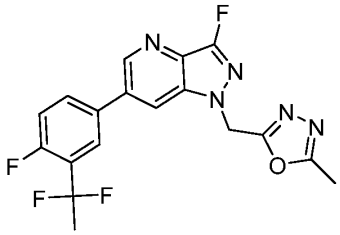
The title compound was prepared in a manner analogous to Example 8 using 2-(chloromethyl)-5-phenyl-1,3,4-oxadiazole instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{22}H_{14}F_3N_5O$, 421.1; m/z found, 422.1 $[M+H]^+$. ^1H NMR (500 MHz, CD_3OD) δ 8.88 (d, *J* = 1.9 Hz, 1H), 8.56 (dd, *J* = 1.9, 1.0 Hz, 1H), 8.35 (d, *J* = 1.0 Hz, 1H), 8.04 (d, *J* = 6.1 Hz, 1H), 8.02 – 7.95 (m, 3H), 7.64 – 7.56 (m, 1H), 7.56 – 7.50 (m, 2H), 7.43 (dd, *J* = 10.1, 8.6 Hz, 1H), 7.09 (t, *J* = 54.6 Hz, 1H), 6.15 (s, 2H).

Example 104: 2-[[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole.



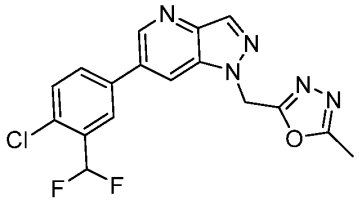
The title compound was made in an analogous manner to Intermediate 25 using 2-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-5-methyl-1,3,4-oxadiazole (Intermediate 19) and 2-(3-(1,1-difluoroethyl)-4-fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd. for $C_{18}H_{14}F_3N_5O$, 373.1; m/z found, 374.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.94 (d, J = 1.9 Hz, 1H), 8.62 (dd, J = 2.0, 1.0 Hz, 1H), 8.44 (d, J = 1.0 Hz, 1H), 8.05 – 8.00 (m, 1H), 7.97 (dd, J = 7.2, 2.4 Hz, 1H), 7.57 (dd, J = 11.0, 8.5 Hz, 1H), 6.10 (s, 2H), 2.44 (s, 3H), 2.10 (t, J = 19.3 Hz, 3H).

Example 105: 2-[[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole.



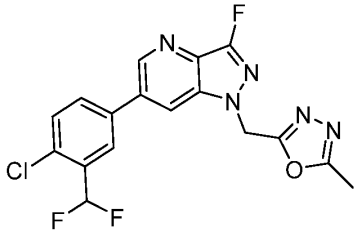
The title compound was made in an analogous manner to Intermediate 25 using 2-((6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-5-methyl-1,3,4-oxadiazole (Intermediate 20) and 2-(3-(1,1-difluoroethyl)-4-fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd. for $C_{18}H_{13}F_4N_5O$, 391.1; m/z found, 392.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 9.00 (d, J = 1.8 Hz, 1H), 8.70 – 8.65 (m, 1H), 8.08 – 8.02 (m, 1H), 8.02 – 7.97 (m, 1H), 7.59 (dd, J = 11.0, 8.6 Hz, 1H), 5.99 (s, 2H), 2.45 (s, 3H), 2.10 (t, J = 19.1 Hz, 3H).

Example 106: 2-[[6-[4-Chloro-3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole.



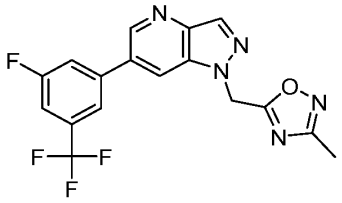
The title compound was made in an analogous manner to Intermediate 25 using 2-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-5-methyl-1,3,4-oxadiazole (Intermediate 19) and 2-(4-chloro-3-(difluoromethyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd. for $C_{17}H_{12}ClF_2N_5O$, 375.1; m/z found, 376.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.97 (d, J = 1.9 Hz, 1H), 8.74 – 8.64 (m, 1H), 8.45 (s, 1H), 8.17 – 8.09 (m, 1H), 8.10 – 8.02 (m, 1H), 7.80 (d, J = 8.4 Hz, 1H), 7.31 (t, J = 54.1 Hz, 1H), 6.11 (s, 2H), 2.44 (s, 3H).

Example 107: 2-[[6-[4-Chloro-3-(difluoromethyl)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole.



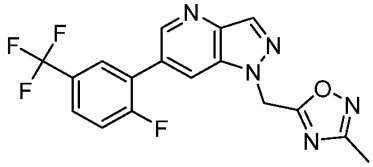
The title compound was made in an analogous manner to Intermediate 25 using 2-((6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-5-methyl-1,3,4-oxadiazole (Intermediate 20) and 2-(4-chloro-3-(difluoromethyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd. for $C_{17}H_{11}ClF_3N_5O$, 393.1; m/z found, 394.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 9.02 (d, J = 1.8 Hz, 1H), 8.77 – 8.71 (m, 1H), 8.18 – 8.12 (m, 1H), 8.12 – 8.03 (m, 1H), 7.82 (d, J = 8.4 Hz, 1H), 7.32 (t, J = 54.0 Hz, 1H), 6.01 (s, 2H), 2.46 (s, 3H).

Example 108: 5-[[6-[3-Fluoro-5-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole.



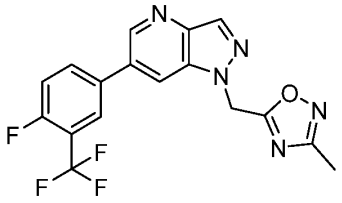
The title compound was prepared in a manner analogous to Intermediate 42 using 5-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-3-methyl-1,2,4-oxadiazole (Intermediate 55) and (3-fluoro-5-(trifluoromethyl)phenyl)boronic acid. MS (ESI): mass calcd. for $C_{17}H_{11}F_4N_5O$, 377.1; m/z found, 378.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 9.06 (d, J = 2.0 Hz, 1H), 8.80 – 8.78 (m, 1H), 8.49 (d, J = 1.0 Hz, 1H), 8.16 – 8.07 (m, 2H), 7.82 – 7.77 (m, 1H), 6.21 (s, 2H), 2.28 (s, 3H).

Example 109: 5-[[6-[2-Fluoro-5-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole.



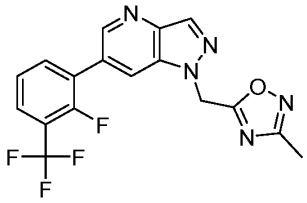
The title compound was prepared in a manner analogous to Intermediate 42 using 5-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-3-methyl-1,2,4-oxadiazole (Intermediate 55) and (2-fluoro-5-(trifluoromethyl)phenyl)boronic acid. MS (ESI): mass calcd. for $C_{17}H_{11}F_4N_5O$, 377.1; m/z found, 378.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.84 – 8.81 (m, 1H), 8.61 – 8.58 (m, 1H), 8.51 – 8.49 (m, 1H), 8.10 – 8.06 (m, 1H), 7.97 – 7.91 (m, 1H), 7.71 – 7.65 (m, 1H), 6.21 (s, 2H), 2.28 (s, 3H).

Example 110: 5-[[6-[4-Fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole.



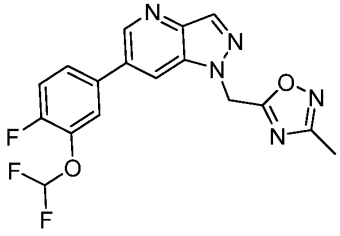
The title compound was prepared in a manner analogous to Intermediate 42 using 5-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-3-methyl-1,2,4-oxadiazole (Intermediate 55) and (4-fluoro-3-(trifluoromethyl)phenyl)boronic acid. MS (ESI): mass calcd. for $C_{17}H_{11}F_4N_5O$, 377.1; m/z found, 378.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.82 (d, J = 1.9 Hz, 1H), 8.37 (d, J = 1.0 Hz, 1H), 7.93 (dd, J = 1.9, 1.1 Hz, 1H), 7.88 – 7.79 (m, 2H), 7.38 (t, J = 9.2 Hz, 1H), 5.85 (s, 2H), 2.38 (s, 3H).

Example 111: 5-[[6-[2-Fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole.



The title compound was prepared in a manner analogous to Intermediate 42 using 5-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-3-methyl-1,2,4-oxadiazole (Intermediate 55) and (2-fluoro-3-(trifluoromethyl)phenyl)boronic acid. MS (ESI): mass calcd. for $C_{17}H_{11}F_4N_5O$, 377.1; m/z found, 378.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.81 – 8.78 (m, 1H), 8.60 – 8.58 (m, 1H), 8.53 – 8.49 (m, 1H), 8.07 – 8.01 (m, 1H), 7.94 – 7.88 (m, 1H), 7.64 – 7.58 (m, 1H), 6.22 (s, 2H), 2.28 (s, 3H).

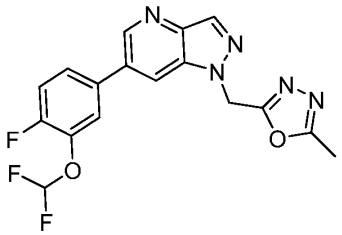
Example 112: 5-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole.



The title compound was made in an analogous manner to Example 8 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 5-(chloromethyl)-3-methyl-1,2,4-oxadiazole. MS (ESI): mass calcd. for $C_{17}H_{12}F_3N_5O_2$, 375.1; m/z

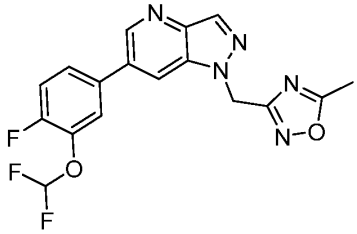
found, 376.2 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.96 (d, J = 1.9 Hz, 1H), 8.66 – 8.59 (m, 1H), 8.49 – 8.43 (m, 1H), 7.89 – 7.82 (m, 1H), 7.82 – 7.74 (m, 1H), 7.61 (dd, J = 10.4, 8.6 Hz, 1H), 7.38 (t, J = 73.2 Hz, 1H), 6.20 (s, 2H), 2.28 (s, 3H).

Example 113: 2-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole.



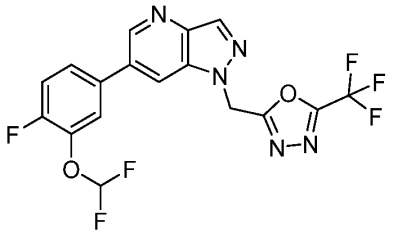
The title compound was made in an analogous manner to Example 8 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 2-(chloromethyl)-5-methyl-1,3,4-oxadiazole. MS (ESI): mass calcd. for $C_{17}H_{12}F_3N_5O_2$, 375.1; m/z found, 376.2 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.94 (d, J = 1.9 Hz, 1H), 8.64 – 8.57 (m, 1H), 8.49 – 8.41 (m, 1H), 7.89 – 7.82 (m, 1H), 7.82 – 7.74 (m, 1H), 7.62 (dd, J = 10.5, 8.7 Hz, 1H), 7.38 (t, J = 73.2 Hz, 1H), 6.09 (s, 2H), 2.45 (s, 3H).

Example 114: 3-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,2,4-oxadiazole.



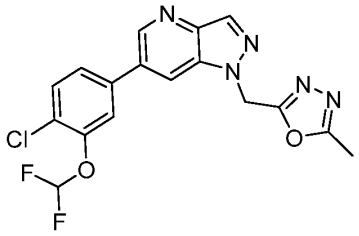
The title compound was made in an analogous manner to Example 8 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 3-(chloromethyl)-5-methyl-1,2,4-oxadiazole. MS (ESI): mass calcd. for $C_{17}H_{12}F_3N_5O_2$, 375.1; m/z found, 376.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.93 (d, J = 2.0 Hz, 1H), 8.65 – 8.54 (m, 1H), 8.40 (s, 1H), 7.92 – 7.82 (m, 1H), 7.82 – 7.73 (m, 1H), 7.62 (dd, J = 10.4, 8.8 Hz, 1H), 7.39 (t, J = 73.2 Hz, 1H), 5.94 (s, 2H), 2.52 (s, 3H).

Example 115: 2-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-(trifluoromethyl)-1,3,4-oxadiazole.



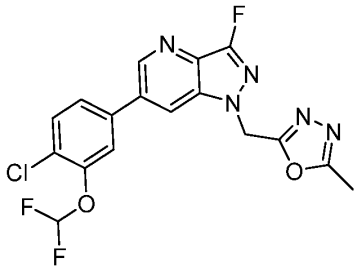
The title compound was prepared in a manner analogous to Example 8 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 2-(chloromethyl)-5-(trifluoromethyl)-1,3,4-oxadiazole. MS (ESI): mass calcd. for $C_{17}H_9F_6N_5O_2$, 429.1; m/z found, 430.1 $[M+H]^+$. ^1H NMR (600 MHz, CD_3OD) δ 8.86 (s, 1H), 8.48 (t, J = 1.4 Hz, 1H), 8.35 (d, J = 1.0 Hz, 1H), 7.73 (dd, J = 7.3, 2.3 Hz, 1H), 7.69 (ddd, J = 8.5, 4.3, 2.3 Hz, 1H), 7.45 (dd, J = 10.3, 8.6 Hz, 1H), 6.98 (t, J = 73.3 Hz, 1H), 6.19 (s, 2H).

Example 116: 2-[[6-[4-Chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole.



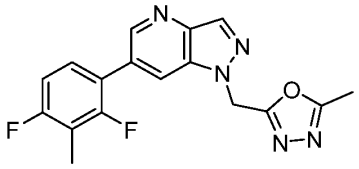
The title compound was made in an analogous manner to Intermediate 25 using 2-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-5-methyl-1,3,4-oxadiazole (Intermediate 19) and 2-(4-chloro-3-(difluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd. for $C_{17}H_{12}ClF_2N_5O_2$, 391.1; m/z found, 392.0 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.97 (d, J = 1.9 Hz, 1H), 8.68 – 8.60 (m, 1H), 8.46 (s, 1H), 7.86 – 7.82 (m, 1H), 7.80 (d, J = 8.4 Hz, 1H), 7.76 (dd, J = 8.4, 1.9 Hz, 1H), 7.44 (t, J = 73.2 Hz, 1H), 6.10 (s, 2H), 2.45 (s, 3H).

Example 117: 2-[[6-[4-Chloro-3-(difluoromethoxy)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole.



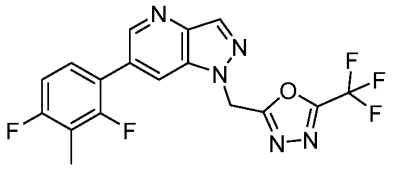
The title compound was made in an analogous manner to Example 8 using 6-(4-chloro-3-(difluoromethoxy)phenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridine (Intermediate 31) and 2-(chloromethyl)-5-methyl-1,3,4-oxadiazole. MS (ESI): mass calcd. for $C_{17}H_{11}ClF_3N_5O_2$, 409.1; m/z found, 410.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 9.02 (d, J = 1.8 Hz, 1H), 8.72 – 8.66 (m, 1H), 7.88 – 7.84 (m, 1H), 7.82 (d, J = 8.4 Hz, 1H), 7.77 (dd, J = 8.5, 1.9 Hz, 1H), 7.44 (t, J = 73.1 Hz, 1H), 5.99 (s, 2H), 2.46 (s, 3H).

Example 118: 2-[[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole.



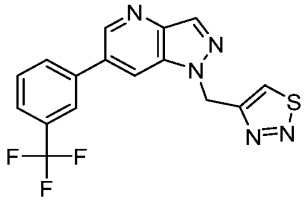
The title compound was prepared in a manner analogous to Example 8 using 6-(2,4-difluoro-3-methylphenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 36) and 2-(chloromethyl)-5-methyl-1,3,4-oxadiazole. MS (ESI): mass calcd. for $C_{17}H_{13}F_2N_5O$, 341.1; m/z found, 342.1 $[M+H]^+$. ^1H NMR (500 MHz, CD_3OD) δ 8.71 (t, J = 1.9 Hz, 1H), 8.41 – 8.32 (m, 1H), 8.31 (d, J = 1.0 Hz, 1H), 7.55 – 7.42 (m, 1H), 7.11 (td, J = 8.7, 1.5 Hz, 1H), 6.00 (s, 2H), 2.48 (s, 3H), 2.30 (t, J = 2.0 Hz, 3H).

Example 119: 2-[[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-(trifluoromethyl)-1,3,4-oxadiazole.



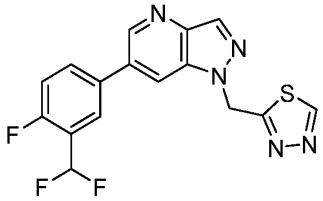
The title compound was prepared in a manner analogous to Example 8 using 6-(2,4-difluoro-3-methylphenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 36) and 2-(chloromethyl)-5-(trifluoromethyl)-1,3,4-oxadiazole. MS (ESI): mass calcd. for $C_{17}H_{10}F_5N_5O$, 395.1; m/z found, 396.0 $[M+H]^+$. ^1H NMR (500 MHz, CD_3OD) δ 8.71 (t, J = 1.9 Hz, 1H), 8.38 – 8.34 (m, 1H), 8.33 (d, J = 1.0 Hz, 1H), 7.46 (td, J = 8.6, 6.2 Hz, 1H), 7.09 (td, J = 8.7, 1.5 Hz, 1H), 6.16 (s, 2H), 2.29 (t, J = 2.0 Hz, 3H).

Example 120: 4-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]thiadiazole.



The title compound was prepared in a manner analogous to Example 1, using 4-(chloromethyl)-1,2,3-thiadiazole instead of 2-(chloromethyl)pyrimidine hydrochloride. MS (ESI): mass calcd. for $C_{16}H_{10}F_3N_5S$, 361.1; m/z found, 362.0 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 9.15 (s, 1H), 8.98 (d, J = 1.9 Hz, 1H), 8.83 – 8.81 (m, 1H), 8.42 – 8.40 (m, 1H), 8.21 – 8.17 (m, 2H), 7.86 – 7.77 (m, 2H), 6.30 (s, 2H).

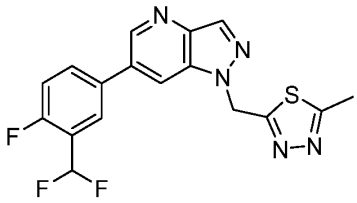
Example 121: 2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazole.



The title compound was prepared in a manner analogous to Example 8 using 2-(chloromethyl)-1,3,4-thiadiazole instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for

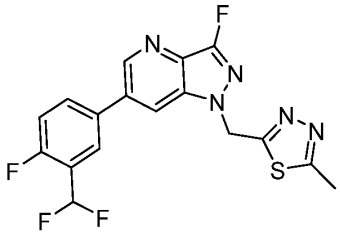
$C_{16}H_{10}F_3N_5S$, 361.1; m/z found, 362.0 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 9.10 (s, 1H), 8.81 (d, J = 1.9 Hz, 1H), 8.37 (d, J = 1.0 Hz, 1H), 8.00 (dd, J = 1.8, 1.0 Hz, 1H), 7.88 – 7.81 (m, 1H), 7.72 (dt, J = 7.5, 2.5 Hz, 1H), 7.33 – 7.27 (m, 1H), 6.98 (t, J = 54.8 Hz, 1H), 6.13 (s, 2H).

Example 122: 2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole.



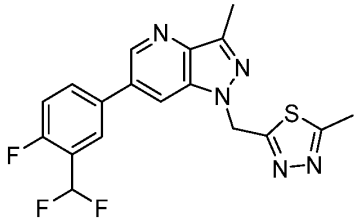
The title compound was prepared in a manner analogous to Example 8 using 2-(chloromethyl)-5-methyl-1,3,4-thiadiazole instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{17}H_{12}F_3N_5S$, 375.1; m/z found, 376.0 $[M+H]^+$. ^1H NMR (500 MHz, CD_3OD) δ 8.85 (d, J = 1.9 Hz, 1H), 8.49 (dd, J = 1.9, 1.0 Hz, 1H), 8.33 (d, J = 1.0 Hz, 1H), 8.07 – 7.91 (m, 2H), 7.42 (t, J = 9.3 Hz, 1H), 7.08 (t, J = 54.6 Hz, 1H), 6.17 (s, 2H), 2.71 (s, 3H).

Example 123: 2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole.



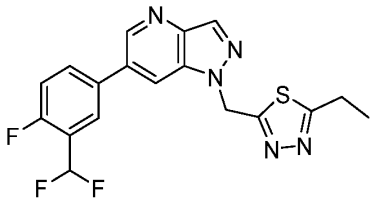
The title compound was made in an analogous manner to Example 8 using 6-(3-(difluoromethyl)-4-fluorophenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridine (Intermediate 30) and 2-(chloromethyl)-5-methyl-1,3,4-thiadiazole. MS (ESI): mass calcd. for $C_{17}H_{11}F_4N_5S$, 393.1; m/z found, 394.0 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.99 (d, J = 1.9 Hz, 1H), 8.77 – 8.73 (m, 1H), 8.13 – 8.07 (m, 2H), 7.64 – 7.57 (m, 1H), 7.31 (t, J = 54.1 Hz, 1H), 6.13 (s, 2H), 2.66 (s, 3H).

Example 124: 2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-methyl-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole.



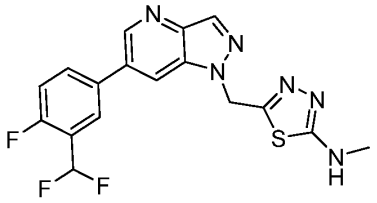
The title compound was prepared in a manner analogous to Example 8 using 6-(3-(difluoromethyl)-4-fluorophenyl)-3-methyl-1H-pyrazolo[4,3-b]pyridine (Intermediate 35) and 2-(chloromethyl)-5-methyl-1,3,4-thiadiazole. MS (ESI): mass calcd. for $C_{18}H_{14}F_3N_5S$, 389.1; m/z found, 390.0 $[M+H]^+$. ^1H NMR (400 MHz, CD_3OD) δ 8.78 (d, J = 1.9 Hz, 1H), 8.39 (d, J = 1.9 Hz, 1H), 8.05 – 7.85 (m, 2H), 7.47 – 7.29 (m, 1H), 7.26 – 6.84 (m, 1H), 6.06 (s, 2H), 2.70 (s, 3H), 2.63 (s, 3H).

Example 125: 2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-ethyl-1,3,4-thiadiazole.



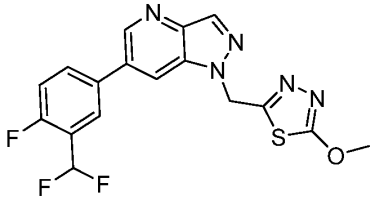
The title compound was prepared in a manner analogous to Example 8 using 2-(chloromethyl)-5-ethyl-1,3,4-thiadiazole instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{18}H_{14}F_3N_5S$, 389.1; m/z found, 390.0 $[M+H]^+$. ^1H NMR (500 MHz, CD_3OD) δ 8.85 (d, J = 1.9 Hz, 1H), 8.50 (dd, J = 1.9, 1.0 Hz, 1H), 8.33 (d, J = 1.0 Hz, 1H), 8.06 – 7.90 (m, 2H), 7.42 (dd, J = 10.0, 8.6 Hz, 1H), 7.08 (t, J = 54.6 Hz, 1H), 6.18 (s, 2H), 3.08 (q, J = 7.6 Hz, 2H), 1.34 (t, J = 7.6 Hz, 3H).

Example 126: 5-((6-(3-(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-N-methyl-1,3,4-thiadiazol-2-amine.



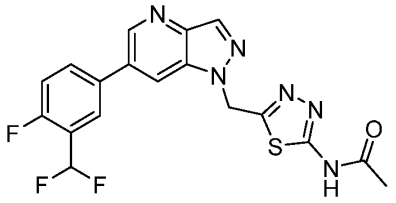
The title compound was prepared in a manner analogous to Example 15 using 2-(6-(3-(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid (Intermediate 37). MS (ESI): mass calcd. for $C_{17}H_{13}F_3N_6S$, 390.1; m/z found, 391.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.92 (d, J = 1.9 Hz, 1H), 8.66 – 8.62 (m, 1H), 8.44 – 8.42 (m, 1H), 8.11 – 8.06 (m, 2H), 7.63 (q, J = 4.8 Hz, 1H), 7.61 – 7.56 (m, 1H), 7.30 (t, J = 54.1 Hz, 1H), 5.99 (s, 2H), 2.80 (d, J = 4.8 Hz, 3H).

Example 127: 2-[[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methoxy-1,3,4-thiadiazole.



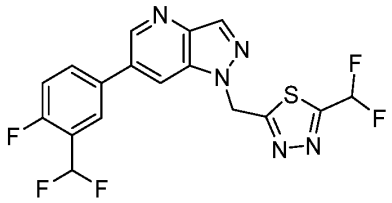
The title compound was made in an analogous manner to Example 8 using 2-(chloromethyl)-5-methoxy-1,3,4-thiadiazole instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{17}H_{12}F_3N_5OS$, 391.1; m/z found, 392.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.94 (d, J = 2.0 Hz, 1H), 8.73 – 8.63 (m, 1H), 8.47 (s, 1H), 8.15 – 8.01 (m, 2H), 7.66 – 7.52 (m, 1H), 7.31 (t, J = 54.1 Hz, 1H), 6.12 (s, 2H), 4.07 (s, 3H).

Example 128: N-(5-((6-(3-(Difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-1,3,4-thiadiazol-2-yl)acetamide.



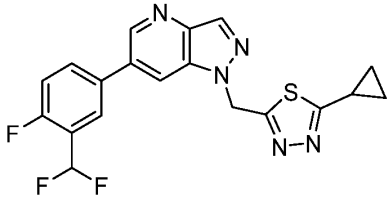
The title compound was prepared in a manner analogous to Example 19 using 5-[[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazol-2-amine (Example 16). MS (ESI): mass calcd. for $C_{18}H_{13}F_3N_6OS$, 418.1; m/z found, 419.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 12.51 (br s, 1H), 8.93 (d, J = 2.0 Hz, 1H), 8.72 – 8.67 (m, 1H), 8.48 – 8.44 (m, 1H), 8.12 – 8.05 (m, 2H), 7.62 – 7.54 (m, 1H), 7.30 (t, J = 54.1 Hz, 1H), 6.17 (s, 2H), 2.13 (s, 3H).

Example 129: 2-(Difluoromethyl)-5-[[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazole.



The title compound was prepared in a manner analogous to Example 8 using 2-(chloromethyl)-5-(difluoromethyl)-1,3,4-thiadiazole instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{17}H_{10}F_5N_5S$, 411.1; m/z found, 412.0 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.83 (d, J = 1.9 Hz, 1H), 8.39 (d, J = 1.0 Hz, 1H), 7.99 (dd, J = 1.9, 1.0 Hz, 1H), 7.85 (dd, J = 6.4, 2.4 Hz, 1H), 7.77 – 7.69 (m, 1H), 7.31 (ddt, J = 9.6, 8.6, 1.1 Hz, 1H), 7.13 – 6.82 (m, 2H), 6.11 (s, 2H).

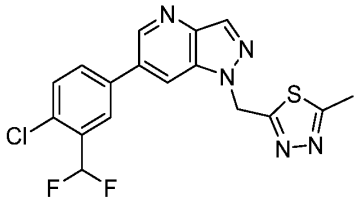
Example 130: 2-Cyclopropyl-5-[[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazole.



The title compound was prepared in a manner analogous to Example 8 using 2-(chloromethyl)-5-cyclopropyl-1,3,4-thiadiazole instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{19}H_{14}F_3N_5S$, 401.1; m/z found, 402.0 $[M+H]^+$. ^1H NMR (500 MHz, CD_3OD) δ 8.82 (d, J = 1.9 Hz, 1H), 8.46 (dd, J = 1.8, 1.0 Hz, 1H), 8.30 (d, J = 1.0 Hz, 1H), 8.06 – 7.87 (m, 2H),

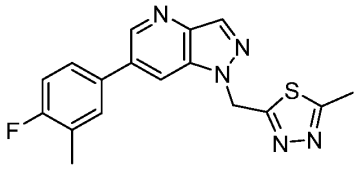
7.40 (dd, J = 9.9, 8.7 Hz, 1H), 7.07 (t, J = 54.6 Hz, 1H), 6.12 (s, 2H), 2.39 (tt, J = 8.4, 4.8 Hz, 1H), 1.29 – 1.16 (m, 2H), 1.02 (dt, J = 7.2, 4.5 Hz, 2H).

Example 131: 2-[[6-[4-Chloro-3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole.



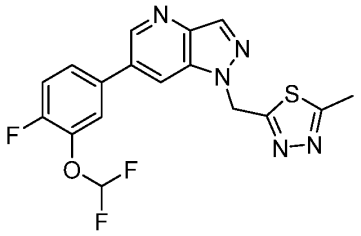
The title compound was prepared in a manner analogous to Example 9 using Intermediate 24, 2-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-5-methyl-1,3,4-thiadiazole and 2-(4-chloro-3-(difluoromethyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd. for $C_{17}H_{12}ClF_2N_5S$, 391.0; m/z found, 392.0 $[M+H]^+$. ^1H NMR (500 MHz, CD_3OD) δ 8.87 (d, J = 1.9 Hz, 1H), 8.53 (dd, J = 1.9, 1.0 Hz, 1H), 8.33 (d, J = 1.0 Hz, 1H), 8.07 (d, J = 2.2 Hz, 1H), 7.93 (ddd, J = 8.3, 2.2, 1.1 Hz, 1H), 7.69 (dt, J = 8.3, 1.1 Hz, 1H), 7.14 (t, J = 54.6 Hz, 1H), 6.18 (s, 2H), 2.71 (s, 3H).

Example 132: 2-[[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole.



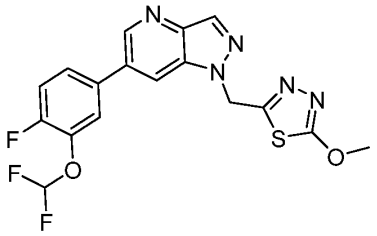
The title compound was prepared in a manner analogous to Example 9 using 2-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-5-methyl-1,3,4-thiadiazole (Intermediate 24) and 4-fluoro-3-methylphenylboronic acid. MS (ESI): mass calcd. for $C_{17}H_{14}FN_5S$, 339.1; m/z found, 340.0 $[M+H]^+$. ^1H NMR (400 MHz, CD_3OD) δ 8.82 (d, J = 1.9 Hz, 1H), 8.45 – 8.36 (m, 1H), 8.30 (d, J = 1.0 Hz, 1H), 7.66 (d, J = 7.2 Hz, 1H), 7.63 – 7.55 (m, 1H), 7.26 – 7.14 (m, 1H), 6.15 (s, 2H), 2.71 (s, 3H), 2.38 (d, J = 2.0 Hz, 3H).

Example 133: 2-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole.



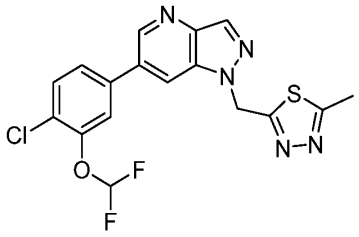
The title compound was prepared in a manner analogous to Example 8 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 2-(chloromethyl)-5-methyl-1,3,4-thiadiazole. MS (ESI): mass calcd. for $C_{17}H_{12}F_3N_5OS$, 391.1; m/z found, 392.1 $[M+H]^+$. ^1H NMR (600 MHz, CD_3OD) δ 8.85 (d, J = 1.9 Hz, 1H), 8.48 (dd, J = 1.9, 1.0 Hz, 1H), 8.34 (d, J = 1.1 Hz, 1H), 7.77 – 7.66 (m, 2H), 7.45 (dd, J = 10.3, 8.6 Hz, 1H), 7.00 (t, J = 73.3 Hz, 1H), 6.18 (s, 2H), 2.72 (s, 3H).

Example 134: 2-[[6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methoxy-1,3,4-thiadiazole.



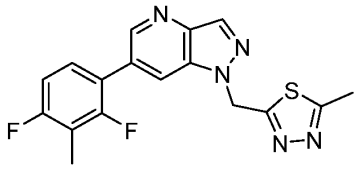
The title compound was made in an analogous manner to Example 8 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 2-(chloromethyl)-5-methoxy-1,3,4-thiadiazole. MS (ESI): mass calcd. for $C_{17}H_{12}F_3N_5O_2S$, 407.1; m/z found, 408.1 $[M+H]^+$.

Example 135: 2-[[6-[4-Chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole.



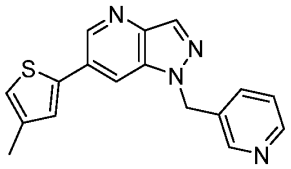
The title compound was prepared in a manner analogous to Example 9 using 2-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-5-methyl-1,3,4-thiadiazole (Intermediate 24) and 2-(4-chloro-3-(difluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd. for $C_{17}H_{12}ClF_2N_5OS$, 407.0; m/z found, 408.0 $[M+H]^+$. ^1H NMR (500 MHz, CD_3OD) δ 8.85 (d, J = 1.9 Hz, 1H), 8.49 (dd, J = 1.9, 1.0 Hz, 1H), 8.33 (d, J = 1.0 Hz, 1H), 7.76 – 7.61 (m, 3H), 7.02 (t, J = 73.3 Hz, 1H), 6.17 (s, 2H), 2.71 (s, 3H).

Example 136: 2-[[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole.



The title compound was prepared in a manner analogous to Example 9 using 2-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-5-methyl-1,3,4-thiadiazole (Intermediate 24) and (2,4-difluoro-3-methylphenyl)boronic acid. MS (ESI): mass calcd. for $C_{17}H_{13}F_2N_5S$, 357.1; m/z found, 358.0 $[M+H]^+$. ^1H NMR (400 MHz, CD_3OD) δ 8.70 (s, 1H), 8.39 – 8.28 (m, 2H), 7.52 – 7.42 (m, 1H), 7.15 – 7.04 (m, 1H), 6.15 (s, 2H), 2.71 (s, 3H), 2.30 (t, J = 2.0 Hz, 3H).

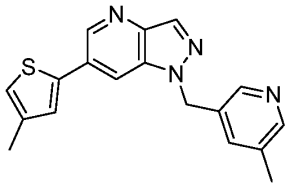
Example 137: 6-(4-Methyl-2-thienyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine.



The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-(pyridin-3-ylmethyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 50) and 4-methylthiophene-2-

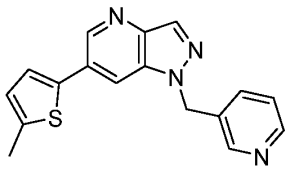
boronic acid. MS (ESI): mass calcd. for $C_{17}H_{14}N_4S$, 306.1; m/z found, 307.1 $[M+H]^+$. ^1H NMR (600 MHz, DMSO-d_6) δ 8.85 (d, J = 1.9 Hz, 1H), 8.61 – 8.59 (m, 1H), 8.54 – 8.52 (m, 1H), 8.49 (dd, J = 4.8, 1.7 Hz, 1H), 8.35 – 8.34 (m, 1H), 7.67 – 7.64 (m, 1H), 7.60 – 7.58 (m, 1H), 7.36 – 7.33 (m, 1H), 7.27 – 7.25 (m, 1H), 5.78 (s, 2H), 2.29 – 2.27 (m, 3H).

Example 138: 1-[(5-Methyl-3-pyridyl)methyl]-6-(4-methyl-2-thienyl)pyrazolo[4,3-b]pyridine.



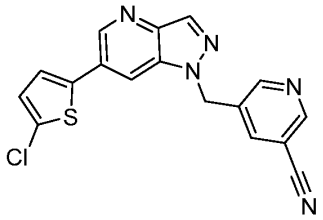
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((5-methylpyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 51) and 4-methylthiophene-2-boronic acid. MS (ESI): mass calcd. for $C_{18}H_{16}N_4S$, 320.1; m/z found, 321.0 $[M+H]^+$. ^1H NMR (600 MHz, DMSO-d_6) δ 8.85 (d, J = 1.9 Hz, 1H), 8.52 – 8.50 (m, 1H), 8.41 – 8.39 (m, 1H), 8.35 – 8.32 (m, 2H), 7.60 – 7.58 (m, 1H), 7.49 – 7.47 (m, 1H), 7.28 – 7.25 (m, 1H), 5.74 (s, 2H), 2.29 – 2.27 (m, 3H), 2.24 (s, 3H).

Example 139: 6-(5-Methyl-2-thienyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine.



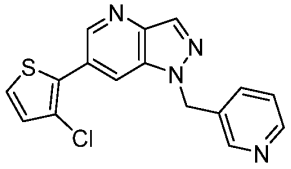
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-(pyridin-3-ylmethyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 50) and using 4,4,5,5-tetramethyl-2-(5-methylthiophen-2-yl)-1,3,2-dioxaborolane. MS (ESI): mass calcd. for $C_{17}H_{14}N_4S$, 306.1; m/z found, 307.0 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.83 (d, J = 1.9 Hz, 1H), 8.61 – 8.58 (m, 1H), 8.49 (dd, J = 4.8, 1.6 Hz, 1H), 8.46 – 8.44 (m, 1H), 8.34 – 8.32 (m, 1H), 7.68 – 7.63 (m, 1H), 7.55 (d, J = 3.6 Hz, 1H), 7.35 (ddd, J = 7.9, 4.8, 0.9 Hz, 1H), 6.93 – 6.90 (m, 1H), 5.77 (s, 2H).

Example 140: 5-[[6-(5-Chloro-2-thienyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile.



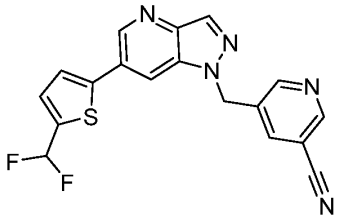
The title compound was made in an analogous manner to Intermediate 41 using 5-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)nicotinonitrile (Intermediate 21) and (5-chlorothiophen-2-yl)boronic acid. MS (ESI): mass calcd. for $C_{17}H_{10}ClN_5S$, 351.0; m/z found, 352.0 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.97 (d, J = 2.0 Hz, 1H), 8.88 (d, J = 1.9 Hz, 1H), 8.85 (d, J = 1.9 Hz, 1H), 8.60 – 8.53 (m, 1H), 8.40 (s, 1H), 8.29 – 8.18 (m, 1H), 7.65 (d, J = 4.0 Hz, 1H), 7.28 (d, J = 4.0 Hz, 1H), 5.83 (s, 2H).

Example 141: 6-(3-Chloro-2-thienyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine.



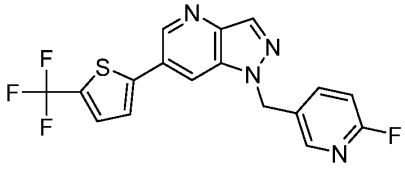
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-(pyridin-3-ylmethyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 50) and (3-chlorothiophen-2-yl)boronic acid. MS (ESI): mass calcd. for $C_{16}H_{11}ClN_4S$, 326.0; m/z found, 327.0 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.75 (d, J = 1.9 Hz, 1H), 8.63 – 8.60 (m, 1H), 8.56 – 8.54 (m, 1H), 8.49 (dd, J = 4.8, 1.6 Hz, 1H), 8.44 – 8.42 (m, 1H), 7.86 (d, J = 5.4 Hz, 1H), 7.71 – 7.66 (m, 1H), 7.38 – 7.33 (m, 1H), 7.28 (d, J = 5.4 Hz, 1H), 5.81 (s, 2H).

Example 142: 5-[[6-[5-(Difluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile.



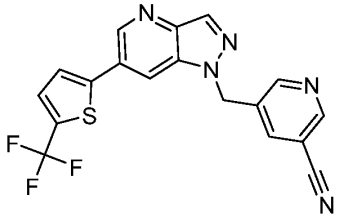
The title compound was made in an analogous manner to Intermediate 41 using 5-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)nicotinonitrile (Intermediate 21) and 2-(5-(difluoromethyl)thiophen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Intermediate 12). MS (ESI): mass calcd. for $C_{18}H_{11}F_2N_5S$, 367.1; m/z found, 368.0 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.99 – 8.93 (m, 2H), 8.87 (d, J = 2.2 Hz, 1H), 8.72 – 8.67 (m, 1H), 8.42 (d, J = 1.0 Hz, 1H), 8.28 – 8.22 (m, 1H), 7.79 – 7.75 (m, 1H), 7.61 – 7.56 (m, 1H), 7.38 (t, J = 55.2 Hz, 1H), 5.85 (s, 2H).

Example 143: 1-((6-Fluoropyridin-3-yl)methyl)-6-(5-(trifluoromethyl)thiophen-2-yl)-1H-pyrazolo[4,3-b]pyridine.



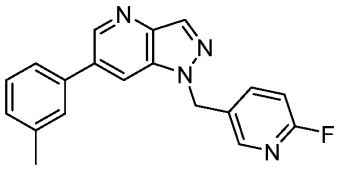
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((6-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 49) and (5-(trifluoromethyl)thiophen-2-yl)boronic acid. MS (ESI): mass calcd. for $C_{17}H_{10}F_4FN_4S$, 378.1; m/z found, 379.1 $[M+H]^+$.

Example 144: 5-[[6-[5-(Trifluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile.



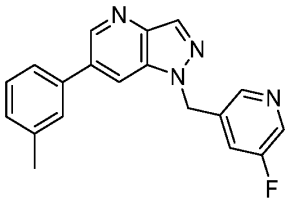
The title compound was made in an analogous manner to Intermediate 41 using 5-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)nicotinonitrile (Intermediate 21) and (5-(trifluoromethyl)thiophen-2-yl)boronic acid. MS (ESI): mass calcd. for $C_{18}H_{10}F_3N_5S$, 385.1; m/z found, 386.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.99 (d, J = 1.9 Hz, 1H), 8.97 (d, J = 2.0 Hz, 1H), 8.87 (d, J = 2.2 Hz, 1H), 8.79 – 8.72 (m, 1H), 8.50 – 8.38 (m, 1H), 8.29 – 8.22 (m, 1H), 7.92 – 7.78 (m, 2H), 5.85 (s, 2H).

Example 145: 1-[(6-Fluoro-3-pyridyl)methyl]-6-(m-tolyl)pyrazolo[4,3-b]pyridine.



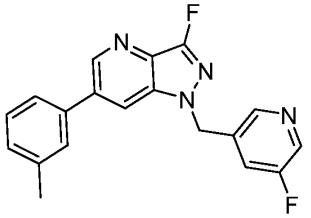
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((6-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 49) and *m*-tolylboronic acid. MS (ESI): mass calcd. for $C_{19}H_{15}FN_4$, 318.1; m/z found, 319.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.87 (d, J = 1.9 Hz, 1H), 8.63 – 8.60 (m, 1H), 8.38 – 8.36 (m, 1H), 8.33 – 8.31 (m, 1H), 7.92 (td, J = 8.3, 2.6 Hz, 1H), 7.68 – 7.66 (m, 1H), 7.65 – 7.61 (m, 1H), 7.44 (t, J = 7.6 Hz, 1H), 7.30 – 7.26 (m, 1H), 7.17 – 7.12 (m, 1H), 5.80 (s, 2H), 2.43 (s, 3H).

Example 146: 1-[(5-Fluoro-3-pyridyl)methyl]-6-(m-tolyl)pyrazolo[4,3-b]pyridine.



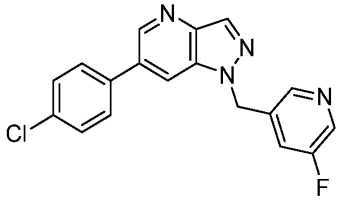
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((5-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 54) and *m*-tolylboronic acid. MS (ESI): mass calcd. for $C_{19}H_{15}FN_4$, 318.1; m/z found, 319.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.88 (d, J = 1.9 Hz, 1H), 8.62 – 8.60 (m, 1H), 8.52 (d, J = 2.8 Hz, 1H), 8.47 (t, J = 1.8 Hz, 1H), 8.40 – 8.39 (m, 1H), 7.68 – 7.61 (m, 3H), 7.44 (t, J = 7.6 Hz, 1H), 7.30 – 7.26 (m, 1H), 5.85 (s, 2H), 2.43 (s, 3H).

Example 147: 3-Fluoro-1-[(5-fluoro-3-pyridyl)methyl]-6-(m-tolyl)pyrazolo[4,3-b]pyridine.



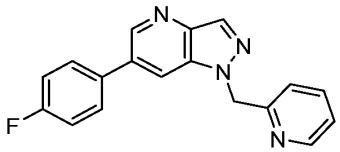
The title compound was made in an analogous manner to Intermediate 25 using 6-bromo-3-fluoro-1-((5-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 15) and *m*-tolylboronic acid. MS (ESI): mass calcd. for $C_{19}H_{14}F_2N_4$, 336.1; m/z found, 337.3 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.92 (d, J = 1.8 Hz, 1H), 8.70 – 8.62 (m, 1H), 8.57 – 8.51 (m, 1H), 8.52 – 8.44 (m, 1H), 7.75 – 7.60 (m, 3H), 7.45 (t, J = 7.6 Hz, 1H), 7.36 – 7.25 (m, 1H), 5.72 (s, 2H), 2.43 (s, 3H).

Example 148: 6-(4-Chlorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine trifluoroacetate salt.



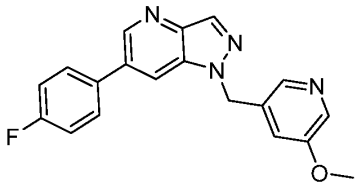
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((5-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 54) and (4-chlorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{18}H_{12}ClFN_4$, 338.1; m/z found, 339.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.90 (d, J = 1.9 Hz, 1H), 8.68 – 8.66 (m, 1H), 8.52 (d, J = 2.7 Hz, 1H), 8.48 (t, J = 1.8 Hz, 1H), 8.42 – 8.40 (m, 1H), 7.92 – 7.87 (m, 2H), 7.69 – 7.65 (m, 1H), 7.64 – 7.60 (m, 2H), 5.84 (s, 2H).

Example 149: 6-(4-Fluorophenyl)-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine.



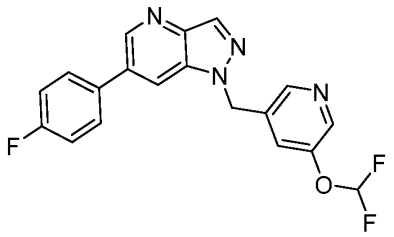
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-(pyridin-2-ylmethyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 53) and (4-fluorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{18}H_{13}FN_4$, 304.1; m/z found, 305.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.87 (d, J = 1.9 Hz, 1H), 8.51 – 8.48 (m, 2H), 8.37 – 8.36 (m, 1H), 7.90 – 7.85 (m, 2H), 7.74 (td, J = 7.7, 1.8 Hz, 1H), 7.41 – 7.35 (m, 2H), 7.30 – 7.27 (m, 1H), 7.11 – 7.08 (m, 1H), 5.86 (s, 2H).

Example 150: 6-(4-Fluorophenyl)-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



The title compound was made in an analogous manner to Intermediate 25 using 6-bromo-1-((5-methoxypyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 14) and (4-fluorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{19}H_{15}FN_4O$, 334.1; m/z found, 335.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.87 (d, J = 1.9 Hz, 1H), 8.61 (dd, J = 2.0, 1.0 Hz, 1H), 8.38 (d, J = 1.0 Hz, 1H), 8.24 – 8.19 (m, 1H), 8.19 – 8.14 (m, 1H), 7.93 – 7.86 (m, 2H), 7.43 – 7.36 (m, 2H), 7.34 – 7.30 (m, 1H), 5.77 (s, 2H), 3.78 (s, 3H).

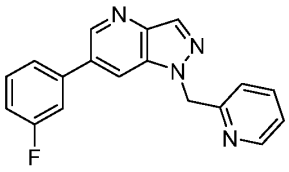
Example 151: 1-[[5-(Difluoromethoxy)-3-pyridyl]methyl]-6-(4-fluorophenyl)pyrazolo[4,3-b]pyridine.



The title compound was made in an analogous manner to Intermediate 25 using 6-bromo-1-((5-(difluoromethoxy)pyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 17) and (4-fluorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{19}H_{13}F_3N_4O$, 370.1; m/z found, 371.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.88 (d, J = 1.9 Hz, 1H), 8.66 – 8.61 (m, 1H), 8.51 –

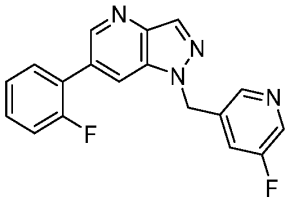
8.46 (m, 1H), 8.44 – 8.41 (m, 1H), 8.41 – 8.38 (m, 1H), 7.93 – 7.85 (m, 2H), 7.65 – 7.60 (m, 1H), 7.43 – 7.36 (m, 2H), 7.27 (t, *J* = 73.3 Hz, 1H), 5.83 (s, 2H).

Example 152: 6-(3-Fluorophenyl)-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine.



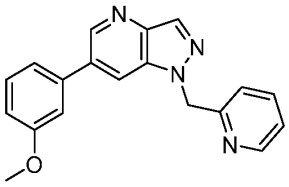
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-(pyridin-2-ylmethyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 53) and (3-fluorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{18}H_{13}FN_4$, 304.1; m/z found, 305.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.93 (d, *J* = 1.9 Hz, 1H), 8.60 – 8.58 (m, 1H), 8.50 – 8.48 (m, 1H), 8.39 – 8.38 (m, 1H), 7.77 – 7.68 (m, 3H), 7.61 – 7.55 (m, 1H), 7.31 – 7.26 (m, 2H), 7.12 – 7.09 (m, 1H), 5.87 (s, 2H).

Example 153: 6-(2-Fluorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



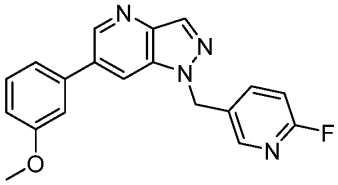
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((5-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 54) and (2-fluorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{18}H_{12}F_2N_4$, 322.1; m/z found, 323.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.73 (t, *J* = 1.9 Hz, 1H), 8.57 – 8.55 (m, 1H), 8.52 (d, *J* = 2.8 Hz, 1H), 8.48 – 8.46 (m, 1H), 8.44 – 8.42 (m, 1H), 7.73 – 7.65 (m, 2H), 7.56 – 7.50 (m, 1H), 7.44 – 7.37 (m, 2H), 5.84 (s, 2H).

Example 154: 6-(3-Methoxyphenyl)-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine.



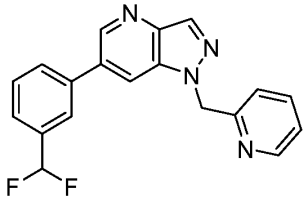
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-(pyridin-2-ylmethyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 53) and (3-methoxyphenyl)boronic acid. MS (ESI): mass calcd. for $C_{19}H_{16}N_4O$, 316.1; m/z found, 317.0 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.90 (d, J = 1.9 Hz, 1H), 8.51 – 8.48 (m, 2H), 8.37 – 8.36 (m, 1H), 7.74 (td, J = 7.7, 1.8 Hz, 1H), 7.47 – 7.42 (m, 1H), 7.40 – 7.35 (m, 2H), 7.30 – 7.27 (m, 1H), 7.11 – 7.08 (m, 1H), 7.04 – 7.00 (m, 1H), 5.87 (s, 2H), 3.86 (s, 3H).

Example 155: 1-[(6-Fluoro-3-pyridyl)methyl]-6-(3-methoxyphenyl)pyrazolo[4,3-b]pyridine.



The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((6-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 49) and (3-methoxyphenyl)boronic acid. MS (ESI): mass calcd. for $C_{19}H_{15}FN_4O$, 334.1; m/z found, 335.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.90 (d, J = 1.9 Hz, 1H), 8.64 – 8.62 (m, 1H), 8.39 – 8.37 (m, 1H), 8.33 – 8.31 (m, 1H), 7.92 (td, J = 8.2, 2.6 Hz, 1H), 7.49 – 7.44 (m, 1H), 7.42 – 7.38 (m, 2H), 7.16 – 7.13 (m, 1H), 7.04 (ddd, J = 8.2, 2.6, 1.0 Hz, 1H), 5.80 (s, 2H), 3.87 (s, 3H).

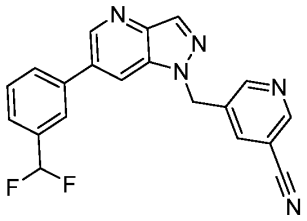
Example 156: 6-[3-(Difluoromethyl)phenyl]-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine.



The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-(pyridin-2-ylmethyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 53) and (3-

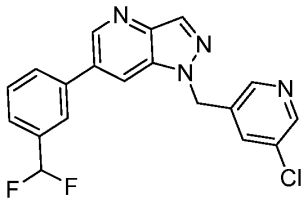
(difluoromethyl)phenyl)boronic acid. MS (ESI): mass calcd. for $C_{19}H_{14}F_2N_4$, 336.1; m/z found, 337.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.92 (d, J = 1.9 Hz, 1H), 8.61 – 8.59 (m, 1H), 8.50 – 8.48 (m, 1H), 8.40 – 8.38 (m, 1H), 8.04 – 7.99 (m, 2H), 7.75 (td, J = 7.7, 1.8 Hz, 1H), 7.72 – 7.64 (m, 2H), 7.31 – 7.27 (m, 1H), 7.13 (t, J = 55.8 Hz, 1H), 7.11 – 7.08 (m, 1H), 5.89 (s, 2H).

Example 157: 5-[[6-[3-(Difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile.



The title compound was made in an analogous manner to Intermediate 25 using 5-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)nicotinonitrile (Intermediate 21) and (3-(difluoromethyl)phenyl)boronic acid. MS (ESI): mass calcd. for $C_{20}H_{13}F_2N_5$, 361.1; m/z found, 362.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.96 (d, J = 2.0 Hz, 1H), 8.93 (d, J = 1.9 Hz, 1H), 8.87 (d, J = 2.1 Hz, 1H), 8.76 – 8.67 (m, 1H), 8.43 (s, 1H), 8.31 – 8.21 (m, 1H), 8.12 – 7.98 (m, 2H), 7.78 – 7.60 (m, 2H), 7.14 (t, J = 55.8 Hz, 1H), 5.88 (s, 2H).

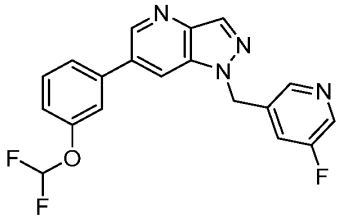
Example 158: 1-[(5-Chloro-3-pyridyl)methyl]-6-[3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridine.



The title compound was made in an analogous manner to Intermediate 25 using 6-bromo-1-((5-chloropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 18) and (3-(difluoromethyl)phenyl)boronic acid. MS (ESI): mass calcd. for $C_{19}H_{13}ClF_2N_4$, 370.1; m/z found, 371.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.93 (d, J = 1.9 Hz, 1H), 8.80 – 8.67

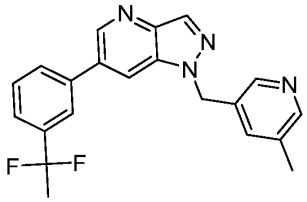
(m, 1H), 8.63 – 8.48 (m, 2H), 8.43 (s, 1H), 8.12 – 7.98 (m, 2H), 7.93 – 7.81 (m, 1H), 7.77 – 7.63 (m, 2H), 7.14 (t, J = 55.8 Hz, 1H), 5.84 (s, 2H).

Example 159: 6-[3-(Difluoromethoxy)phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



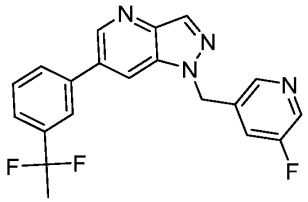
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((5-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 54) and (3-(difluoromethoxy)phenyl)boronic acid. MS (ESI): mass calcd. for $C_{19}H_{13}F_3N_4O$, 370.1; m/z found, 371.1 $[M+H]^+$. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.93 (d, J = 1.9 Hz, 1H), 8.70 – 8.68 (m, 1H), 8.52 (d, J = 2.8 Hz, 1H), 8.48 (t, J = 1.8 Hz, 1H), 8.42 (d, J = 1.0 Hz, 1H), 7.76 – 7.73 (m, 1H), 7.70 – 7.64 (m, 2H), 7.61 (t, J = 8.0 Hz, 1H), 7.38 (t, J = 74.0 Hz, 1H), 7.30 – 7.26 (m, 1H), 5.85 (s, 2H).

Example 160: 6-[3-(1,1-Difluoroethyl)phenyl]-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



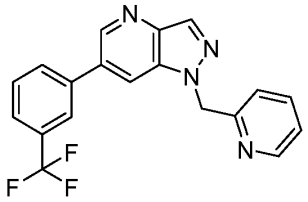
The title compound was made in an analogous manner to Example 8 using 6-(3-(1,1-difluoroethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 29) and 3-(chloromethyl)-5-methylpyridine. MS (ESI): mass calcd. for $C_{21}H_{18}F_2N_4$, 364.2; m/z found, 365.2 $[M+H]^+$. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.93 (d, J = 1.9 Hz, 1H), 8.69 (dd, J = 2.0, 1.0 Hz, 1H), 8.43 – 8.40 (m, 1H), 8.40 (d, J = 0.9 Hz, 1H), 8.35 – 8.32 (m, 1H), 8.01 – 7.95 (m, 2H), 7.70 – 7.63 (m, 2H), 7.53 – 7.50 (m, 1H), 5.78 (s, 2H), 2.24 (s, 3H), 2.07 (t, J = 18.9 Hz, 3H).

Example 161: 6-[3-(1,1-Difluoroethyl)phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



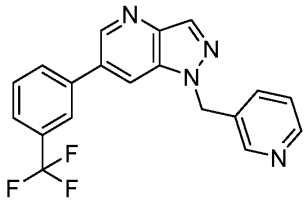
The title compound was made in an analogous manner to Example 8 using 6-(3-(1,1-difluoroethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 29) and 3-(chloromethyl)-5-fluoropyridine. MS (ESI): mass calcd. for $C_{20}H_{15}F_3N_4$, 368.1; m/z found, 369.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.94 (d, J = 1.9 Hz, 1H), 8.71 (dd, J = 2.0, 1.0 Hz, 1H), 8.52 (d, J = 2.8 Hz, 1H), 8.49 – 8.45 (m, 1H), 8.43 (d, J = 1.0 Hz, 1H), 8.02 – 7.95 (m, 2H), 7.72 – 7.62 (m, 3H), 5.86 (s, 2H), 2.06 (t, J = 18.9 Hz, 3H).

Example 162: 1-(2-Pyridylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine.



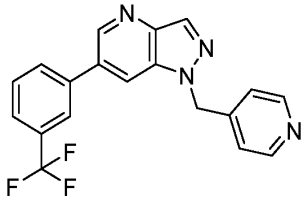
The title compound was prepared in a manner analogous to Example 8, using 6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 42) and 2-(bromomethyl)pyridine hydrobromide. MS (ESI): mass calcd. for $C_{19}H_{13}F_3N_4$, 354.1; m/z found, 355.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.82 (d, J=2.02 Hz, 1H), 8.59 (dt, J=4.84, 1.19 Hz, 1H), 8.36 (d, J=1.16 Hz, 1H), 7.97 (dd, J=1.88, 1.01 Hz, 1H), 7.85 (s, 1H), 7.81 (d, J=7.51 Hz, 1H), 7.74 – 7.67 (m, 1H), 7.66 – 7.56 (m, 2H), 7.23 (ddd, J=7.51, 4.91, 0.87 Hz, 1H), 7.07 (d, J=7.80 Hz, 1H), 5.79 (s, 2H).

Example 163: 1-(3-Pyridylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine hydrochloride salt.



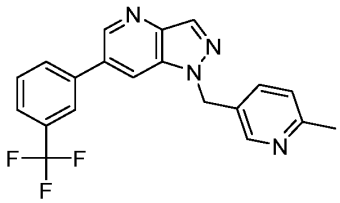
The title compound was prepared in a manner analogous to Example 8, using 6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 42) and 3-(bromomethyl)pyridine hydrobromide. MS (ESI): mass calcd. for $C_{19}H_{13}F_3N_4$, 354.1; m/z found, 355.0 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-*d* 6) δ 9.01 (d, *J*=2.02 Hz, 1 H), 8.92 (s, 1 H), 8.86 – 8.76 (m, 2 H), 8.49 (d, *J*=0.87 Hz, 1 H), 8.31 (d, *J*=8.09 Hz, 1 H), 8.25 – 8.14 (m, 2 H), 7.90 (dd, *J*=7.95, 5.64 Hz, 1 H), 7.88 – 7.76 (m, 2 H), 6.00 (s, 2 H).

Example 164: 1-(4-Pyridylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine hydrochloride salt.



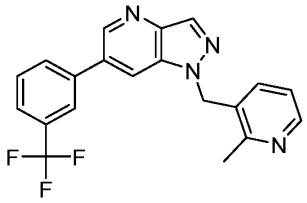
The title compound was prepared in a manner analogous to Example 8, using 6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 42) and 4-(bromomethyl)pyridine hydrobromide. MS (ESI): mass calcd. for $C_{19}H_{13}F_3N_4$, 354.1; m/z found, 355.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.86 (d, *J*=1.73 Hz, 1 H), 8.66 – 8.46 (m, 2 H), 8.40 (d, *J*=0.87 Hz, 1 H), 7.84 (s, 1 H), 7.78 (d, *J*=7.80 Hz, 1 H), 7.76 – 7.73 (m, 1 H), 7.73 – 7.68 (m, 1 H), 7.67 – 7.61 (m, 1 H), 7.06 (d, *J*=6.07 Hz, 2 H), 5.69 (s, 2 H).

Example 165: 1-[(6-Methyl-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine.



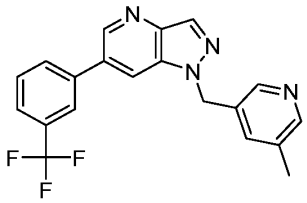
The title compound was prepared in a manner analogous to Example 1, using 5-(chloromethyl)-2-methylpyridine hydrochloride instead of 2-(chloromethyl)pyrimidine hydrochloride. MS (ESI): mass calcd. for $C_{20}H_{15}F_3N_4$, 368.1; m/z found, 369.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.95 (d, J = 1.9 Hz, 1H), 8.76 – 8.74 (m, 1H), 8.51 – 8.49 (m, 1H), 8.40 – 8.38 (m, 1H), 8.20 – 8.14 (m, 2H), 7.85 – 7.76 (m, 2H), 7.59 (dd, J = 8.0, 2.4 Hz, 1H), 7.21 – 7.17 (m, 1H), 5.76 (s, 2H), 2.41 (s, 3H).

Example 166: 1-[(2-Methyl-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine.



The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((2-methylpyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 47) and (3-(trifluoromethyl)phenyl)boronic acid. MS (ESI): mass calcd. for $C_{20}H_{15}F_3N_4$, 368.1; m/z found, 369.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.97 (d, J = 1.9 Hz, 1H), 8.70 – 8.66 (m, 1H), 8.45 – 8.43 (m, 1H), 8.36 – 8.34 (m, 1H), 8.18 – 8.14 (m, 2H), 7.87 – 7.75 (m, 2H), 7.16 – 7.09 (m, 2H), 5.83 (s, 2H), 2.56 (s, 3H).

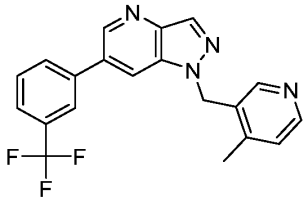
Example 167: 1-[(5-Methyl-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine.



The title compound was prepared in a manner analogous to Example 1, using 3-(chloromethyl)-5-methylpyridine hydrochloride instead of 2-(chloromethyl)pyrimidine hydrochloride. MS (ESI): mass calcd. for $C_{20}H_{15}F_3N_4$, 368.1; m/z found, 369.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ

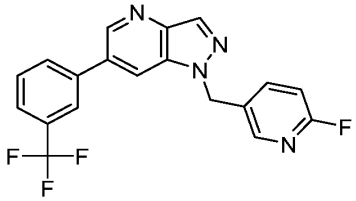
8.95 (d, *J* = 1.9 Hz, 1H), 8.76 – 8.74 (m, 1H), 8.43 – 8.39 (m, 2H), 8.34 – 8.32 (m, 1H), 8.20 – 8.15 (m, 2H), 7.85 – 7.77 (m, 2H), 7.53 – 7.50 (m, 1H), 5.77 (s, 2H), 2.26 – 2.22 (m, 3H).

Example 168: 1-[(4-Methyl-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine trifluoroacetate salt.



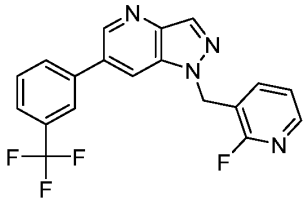
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((4-methylpyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 52) and (3-(trifluoromethyl)phenyl)boronic acid. MS (ESI): mass calcd. for $C_{20}H_{15}F_3N_4$, 368.1; m/z found, 369.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 9.00 (d, *J* = 1.9 Hz, 1H), 8.76 – 8.73 (m, 1H), 8.64 (d, *J* = 5.6 Hz, 1H), 8.47 – 8.45 (m, 1H), 8.38 (s, 1H), 8.21 – 8.15 (m, 2H), 7.87 – 7.77 (m, 2H), 7.73 (d, *J* = 5.6 Hz, 1H), 5.94 (s, 2H), 2.53 (s, 3H).

Example 169: 1-[(6-Fluoro-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine.



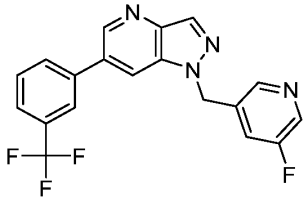
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((6-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 49) and (3-(trifluoromethyl)phenyl)boronic acid. MS (ESI): mass calcd. for $C_{19}H_{12}F_4N_4$, 372.1; m/z found, 373.0 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.96 (d, *J* = 1.9 Hz, 1H), 8.79 – 8.77 (m, 1H), 8.4 – 8.40 (m, 1H), 8.34 – 8.31 (m, 1H), 8.21 – 8.16 (m, 2H), 7.93 (td, *J* = 8.2, 2.6 Hz, 1H), 7.85 – 7.77 (m, 2H), 7.16 – 7.13 (m, 1H), 5.82 (s, 2H).

Example 170: 1-[(2-Fluoro-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine.



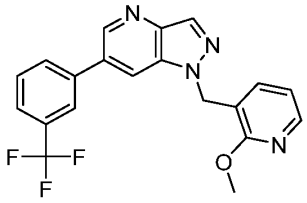
The title compound was prepared in a manner analogous to Example 1, using 3-(chloromethyl)-2-fluoropyridine instead of 2-(chloromethyl)pyrimidine hydrochloride. MS (ESI): mass calcd. for $C_{19}H_{12}F_4N_4$, 372.1; m/z found, 373.0 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.98 (d, J = 2.0 Hz, 1H), 8.76 – 8.72 (m, 1H), 8.44 – 8.41 (m, 1H), 8.21 – 8.15 (m, 3H), 7.86 – 7.76 (m, 2H), 7.69 – 7.62 (m, 1H), 7.34 – 7.29 (m, 1H), 5.85 (s, 2H).

Example 171: 1-[(5-Fluoro-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine.



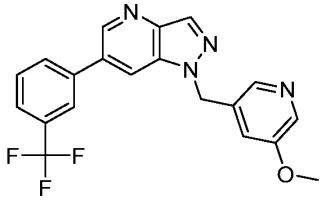
The title compound was prepared in a manner analogous to Example 1, using (5-fluoropyridin-3-yl)methyl methanesulfonate (Intermediate 7) instead of 2-(chloromethyl)pyrimidine hydrochloride. MS (ESI): mass calcd. for $C_{19}H_{12}F_4N_4$, 372.1; m/z found, 373.0 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.97 (d, J = 1.9 Hz, 1H), 8.78 – 8.75 (m, 1H), 8.52 (d, J = 2.8 Hz, 1H), 8.48 (t, J = 1.8 Hz, 1H), 8.44 – 8.43 (m, 1H), 8.21 – 8.16 (m, 2H), 7.85 – 7.77 (m, 2H), 7.69 – 7.64 (m, 1H), 5.87 (s, 2H).

Example 172: 1-[(2-Methoxy-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine trifluoroacetate salt.



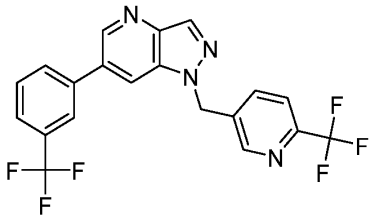
The title compound was prepared in a manner analogous to Example 1, using 3-(chloromethyl)-2-methoxypyridine instead of 2-(chloromethyl)pyrimidine hydrochloride. MS (ESI): mass calcd. for $C_{20}H_{15}F_3N_4O$, 384.1; m/z found, 385.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.97 (d, J = 1.9 Hz, 1H), 8.69 – 8.67 (m, 1H), 8.41 – 8.39 (m, 1H), 8.20 – 8.16 (m, 2H), 8.10 (dd, J = 5.0, 1.9 Hz, 1H), 7.84 – 7.76 (m, 2H), 7.19 – 7.15 (m, 1H), 6.92 (dd, J = 7.3, 5.0 Hz, 1H), 5.72 (s, 2H), 3.88 (s, 3H).

Example 173: 1-[(5-Methoxy-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine.



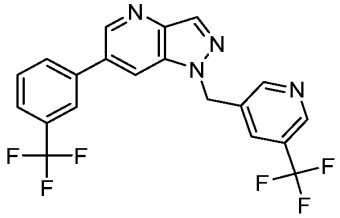
The title compound was prepared in a manner analogous to Example 1, using 3-(chloromethyl)-5-methoxypyridine hydrochloride instead of 2-(chloromethyl)pyrimidine hydrochloride. MS (ESI): mass calcd. for $C_{20}H_{15}F_3N_4O$, 384.1; m/z found, 385.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.96 (d, J = 1.9 Hz, 1H), 8.78 – 8.75 (m, 1H), 8.43 – 8.41 (m, 1H), 8.22 (d, J = 2.8 Hz, 1H), 8.20 – 8.16 (m, 3H), 7.85 – 7.77 (m, 2H), 7.35 – 7.33 (m, 1H), 5.80 (s, 2H), 3.78 (s, 3H).

Example 174: 6-[3-(Trifluoromethyl)phenyl]-1-[[6-(trifluoromethyl)-3-pyridyl]methyl]pyrazolo[4,3-b]pyridine.



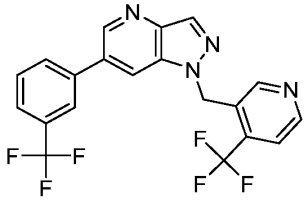
The title compound was prepared in a manner analogous to Example 1, using (6-(trifluoromethyl)pyridin-3-yl)methyl methanesulfonate (Intermediate 9) instead of 2-(chloromethyl)pyrimidine hydrochloride. MS (ESI): mass calcd. for $C_{20}H_{12}F_6N_4$, 422.1; m/z found, 423.0 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.98 (d, J = 1.9 Hz, 1H), 8.81 – 8.77 (m, 2H), 8.46 – 8.45 (m, 1H), 8.21 – 8.15 (m, 2H), 7.94 – 7.76 (m, 4H), 5.95 (s, 2H).

Example 175: 6-[3-(Trifluoromethyl)phenyl]-1-[[5-(trifluoromethyl)-3-pyridyl]methyl]pyrazolo[4,3-b]pyridine.



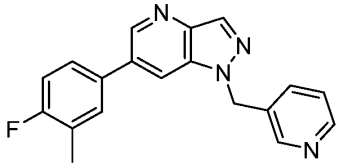
The title compound was prepared in a manner analogous to Example 1, using (5-(trifluoromethyl)pyridin-3-yl)methyl methanesulfonate (Intermediate 10) instead of 2-(chloromethyl)pyrimidine hydrochloride. MS (ESI): mass calcd. for $C_{20}H_{12}F_6N_4$, 422.1; m/z found, 423.0 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.97 (d, J = 1.9 Hz, 1H), 8.94 – 8.92 (m, 1H), 8.88 – 8.86 (m, 1H), 8.81 – 8.79 (m, 1H), 8.46 – 8.44 (m, 1H), 8.23 – 8.16 (m, 3H), 7.86 – 7.77 (m, 2H), 5.93 (s, 2H).

Example 176: 6-[3-(Trifluoromethyl)phenyl]-1-[[4-(trifluoromethyl)-3-pyridyl]methyl]pyrazolo[4,3-b]pyridine.



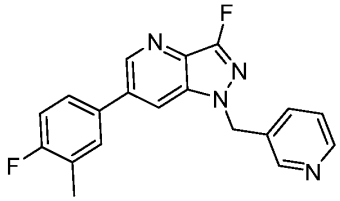
The title compound was prepared in a manner analogous to Example 1, using (4-(trifluoromethyl)pyridin-3-yl)methyl methanesulfonate instead (Intermediate 11) of 2-(chloromethyl)pyrimidine hydrochloride. MS (ESI): mass calcd. for $C_{20}H_{12}F_6N_4$, 422.1; m/z found, 423.0 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 9.00 (d, J = 1.9 Hz, 1H), 8.82 (d, J = 5.1 Hz, 1H), 8.76 – 8.74 (m, 1H), 8.46 – 8.43 (m, 1H), 8.32 (s, 1H), 8.22 – 8.16 (m, 2H), 7.87 – 7.77 (m, 3H), 6.01 (s, 2H).

Example 177: 6-(4-Fluoro-3-methyl-phenyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine.



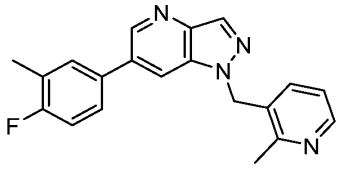
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-(pyridin-3-ylmethyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 50) and 4-fluoro-3-methylphenyl)boronic acid. MS (ESI): mass calcd. for $C_{19}H_{15}FN_4$, 318.1; m/z found, 319.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.86 (d, J = 2.0 Hz, 1H), 8.63 – 8.58 (m, 2H), 8.50 – 8.47 (m, 1H), 8.38 – 8.36 (m, 1H), 7.82 – 7.76 (m, 1H), 7.72 – 7.65 (m, 2H), 7.37 – 7.28 (m, 2H), 5.79 (s, 2H), 2.37 – 3.31 (m, 3H).

Example 178: 3-Fluoro-6-(4-fluoro-3-methyl-phenyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine.



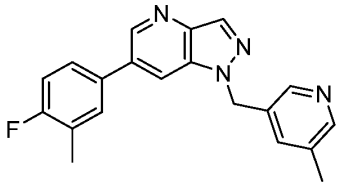
The title compound was made in an analogous manner to Intermediate 25 using 6-bromo-3-fluoro-1-(pyridin-3-ylmethyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 16) and (4-fluoro-3-methylphenyl)boronic acid. MS (ESI): mass calcd. for $C_{19}H_{14}F_2N_4$, 336.1; m/z found, 337.3 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.91 (d, J = 1.8 Hz, 1H), 8.69 – 8.63 (m, 1H), 8.64 – 8.58 (m, 1H), 8.51 (dd, J = 4.9, 1.7 Hz, 1H), 7.86 – 7.77 (m, 1H), 7.76 – 7.66 (m, 2H), 7.42 – 7.28 (m, 2H), 5.67 (s, 2H), 2.38 – 2.31 (m, 3H).

Example 179: 6-(4-Fluoro-3-methyl-phenyl)-1-[(2-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



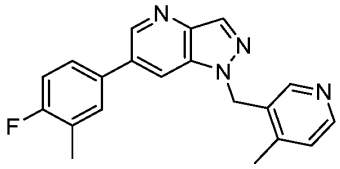
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((2-methylpyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 47) and (4-fluoro-3-methylphenyl)boronic acid. MS (ESI): mass calcd. for $C_{20}H_{17}FN_4$, 332.1; m/z found, 333.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.88 (d, J = 1.9 Hz, 1H), 8.52 – 8.49 (m, 1H), 8.40 – 8.39 (m, 1H), 8.36 – 8.34 (m, 1H), 7.78 – 7.75 (m, 1H), 7.69 – 7.65 (m, 1H), 7.33 – 7.27 (m, 1H), 7.15 – 7.07 (m, 2H), 5.80 (s, 2H), 2.55 (s, 3H), 2.35 – 2.32 (m, 3H).

Example 180: 6-(4-Fluoro-3-methyl-phenyl)-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine trifluoroacetate salt.



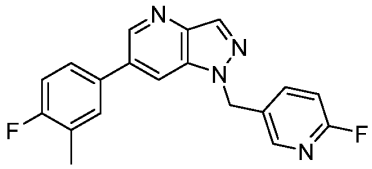
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((5-methylpyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 51) and (4-fluoro-3-methylphenyl)boronic acid. MS (ESI): mass calcd. for $C_{20}H_{17}FN_4$, 332.1; m/z found, 333.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.90 – 8.86 (m, 1H), 8.69 – 8.51 (m, 3H), 8.42 – 8.39 (m, 1H), 7.91 (s, 1H), 7.81 – 7.77 (m, 1H), 7.72 – 7.67 (m, 1H), 7.35 – 7.30 (m, 1H), 5.84 (s, 2H), 2.36 – 2.33 (m, 6H).

Example 181: 6-(4-Fluoro-3-methyl-phenyl)-1-[(4-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine trifluoroacetate salt.



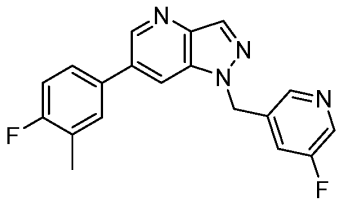
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((4-methylpyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 52) and (4-fluoro-3-methylphenyl)boronic acid. MS (ESI): mass calcd. for $C_{20}H_{17}FN_4$, 332.1; m/z found, 333.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-*d*$_6$) δ 8.90 (d, *J* = 1.9 Hz, 1H), 8.63 (d, *J* = 5.5 Hz, 1H), 8.60 – 8.58 (m, 1H), 8.42 – 8.41 (m, 1H), 8.36 (s, 1H), 7.81 – 7.77 (m, 1H), 7.74 – 7.67 (m, 2H), 7.35 – 7.30 (m, 1H), 5.91 (s, 2H), 2.53 (s, 3H), 2.36 – 2.33 (m, 3H).

Example 182: 6-(4-Fluoro-3-methyl-phenyl)-1-[(6-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



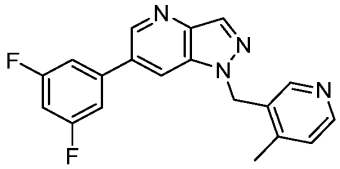
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((6-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 49) and (4-fluoro-3-methylphenyl)boronic acid. MS (ESI): mass calcd. for $C_{19}H_{14}F_2N_4$, 336.1; m/z found, 337.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-*d*$_6$) δ 8.87 (d, *J* = 1.9 Hz, 1H), 8.63 – 8.60 (m, 1H), 8.38 – 8.36 (m, 1H), 8.33 – 8.31 (m, 1H), 7.92 (td, *J* = 8.2, 2.6 Hz, 1H), 7.82 – 7.77 (m, 1H), 7.73 – 7.66 (m, 1H), 7.36 – 7.28 (m, 1H), 7.15 (dd, *J* = 8.5, 2.8 Hz, 1H), 5.79 (s, 2H), 2.36 – 2.33 (m, 3H).

Example 183: 6-(4-Fluoro-3-methyl-phenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



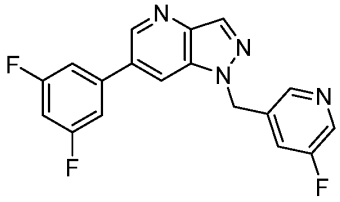
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((5-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 54) and (4-fluoro-3-methylphenyl)boronic acid. MS (ESI): mass calcd. for $C_{19}H_{14}F_2N_4$, 336.1; m/z found, 337.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.87 (d, J = 1.9 Hz, 1H), 8.62 – 8.60 (m, 1H), 8.52 (d, J = 2.7 Hz, 1H), 8.47 (t, J = 1.8 Hz, 1H), 8.40 (d, J = 1.0 Hz, 1H), 7.82 – 7.77 (m, 1H), 7.72 – 7.63 (m, 2H), 7.34 – 7.29 (m, 1H), 5.84 (s, 2H), 2.36 – 2.33 (m, 3H).

Example 184: 6-(3,5-Difluorophenyl)-1-[(4-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine trifluoroacetate salt.



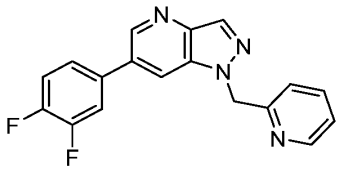
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((4-methylpyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 52) and (3,5-difluorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{19}H_{14}F_2N_4$, 336.1; m/z found, 337.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 9.00 (d, J = 1.9 Hz, 1H), 8.76 – 8.73 (m, 1H), 8.62 (d, J = 5.5 Hz, 1H), 8.47 – 8.44 (m, 1H), 8.38 (s, 1H), 7.73 – 7.65 (m, 3H), 7.36 (tt, J = 9.3, 2.3 Hz, 1H), 5.91 (s, 2H), 2.53 (s, 3H).

Example 185: 6-(3,5-Difluorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



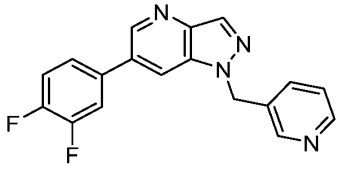
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((5-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 54) and (3,5-difluorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{18}H_{11}F_3N_4$, 340.1; m/z found, 341.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.97 (d, J = 1.9 Hz, 1H), 8.78 – 8.76 (m, 1H), 8.52 (d, J = 2.8 Hz, 1H), 8.50 – 8.48 (m, 1H), 8.44 – 8.42 (m, 1H), 7.73 – 7.64 (m, 3H), 7.35 (tt, J = 9.2, 2.3 Hz, 1H), 5.84 (s, 2H).

Example 186: 6-(3,4-Difluorophenyl)-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine trifluoroacetate salt.



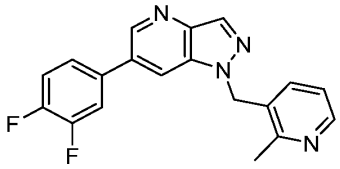
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-(pyridin-2-ylmethyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 53) and (3,4-difluorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{18}H_{12}F_2N_4$, 322.1; m/z found, 323.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.92 (d, J = 1.9 Hz, 1H), 8.61 – 8.59 (m, 1H), 8.53 – 8.50 (m, 1H), 8.40 – 8.38 (m, 1H), 7.99 (ddd, J = 12.2, 7.7, 2.3 Hz, 1H), 7.79 (td, J = 7.7, 1.8 Hz, 1H), 7.74 – 7.69 (m, 1H), 7.65 – 7.58 (m, 1H), 7.35 – 7.31 (m, 1H), 7.15 – 7.12 (m, 1H), 5.88 (s, 2H).

Example 187: 6-(3,4-Difluorophenyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine trifluoroacetate salt.



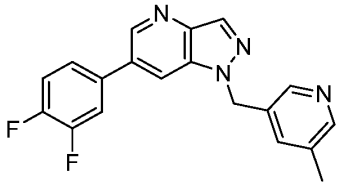
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-(pyridin-3-ylmethyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 50) and (3,4-difluorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{18}H_{12}F_2N_4$, 322.1; m/z found, 323.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.93 (d, J = 1.9 Hz, 1H), 8.77 – 8.74 (m, 1H), 8.71 – 8.69 (m, 1H), 8.65 – 8.61 (m, 1H), 8.44 – 8.41 (m, 1H), 8.04 – 7.96 (m, 2H), 7.77 – 7.71 (m, 1H), 7.68 – 7.58 (m, 2H), 5.86 (s, 2H).

Example 188: 6-(3,4-Difluorophenyl)-1-[(2-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



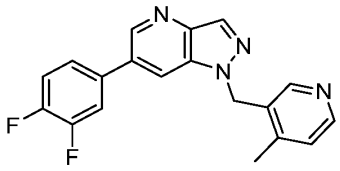
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((2-methylpyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 47) and (3,4-difluorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{19}H_{14}F_2N_4$, 336.1; m/z found, 337.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.93 (d, J = 2.0 Hz, 1H), 8.61 – 8.59 (m, 1H), 8.43 – 8.41 (m, 1H), 8.36 – 8.34 (m, 1H), 7.99 (ddd, J = 12.2, 7.7, 2.4 Hz, 1H), 7.74 – 7.69 (m, 1H), 7.66 – 7.58 (m, 1H), 7.16 – 7.09 (m, 2H), 5.79 (s, 2H), 2.56 (s, 3H).

Example 189: 6-(3,4-Difluorophenyl)-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



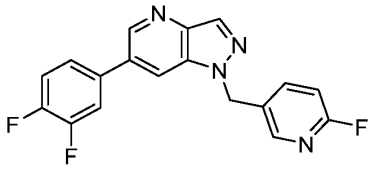
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((5-methylpyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 51) and (3,4-difluorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{19}H_{14}F_2N_4$, 336.1; m/z found, 337.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.91 (d, J = 1.9 Hz, 1H), 8.69 – 8.67 (m, 1H), 8.43 – 8.41 (m, 1H), 8.40 – 8.38 (m, 1H), 8.34 – 8.32 (m, 1H), 8.01 (ddd, J = 12.2, 7.7, 2.3 Hz, 1H), 7.76 – 7.71 (m, 1H), 7.66 – 7.60 (m, 1H), 7.53 – 7.50 (m, 1H), 5.74 (s, 2H), 2.24 (d, J = 0.8 Hz, 3H).

Example 190: 6-(3,4-Difluorophenyl)-1-[(4-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine trifluoroacetate salt.



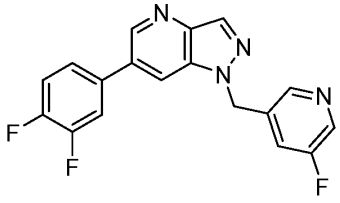
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((4-methylpyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 52) and (3,4-difluorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{19}H_{14}F_2N_4$, 336.1; m/z found, 337.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.95 (d, J = 1.9 Hz, 1H), 8.70 – 8.63 (m, 2H), 8.46 – 8.44 (m, 1H), 8.40 (s, 1H), 8.00 (ddd, J = 12.1, 7.8, 2.3 Hz, 1H), 7.79 – 7.71 (m, 2H), 7.68 – 7.60 (m, 1H), 5.92 (s, 2H), 2.55 (s, 3H).

Example 191: 6-(3,4-Difluorophenyl)-1-[(6-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((6-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 49) and (3,4-difluorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{18}H_{11}F_3N_4$, 340.1; m/z found, 341.0 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.91 (d, J = 1.9 Hz, 1H), 8.72 – 8.68 (m, 1H), 8.40 – 8.38 (d, J = 1.0 Hz, 1H), 8.34 – 8.32 (m, 1H), 8.01 (ddd, J = 12.2, 7.8, 2.3 Hz, 1H), 7.94 (td, J = 8.2, 2.5 Hz, 1H), 7.77 – 7.72 (m, 1H), 7.67 – 7.59 (m, 1H), 7.15 (dd, J = 8.5, 2.8 Hz, 1H), 5.79 (s, 2H).

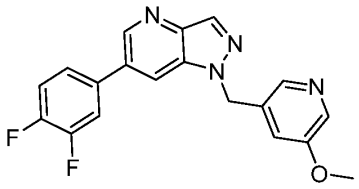
Example 192: 6-(3,4-Difluorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine trifluoroacetate salt.



The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((5-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 54) and (3,4-difluorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{18}H_{11}F_3N_4$, 340.1; m/z found, 341.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.93 (d, J = 1.9 Hz, 1H), 8.72 – 8.69 (m, 1H), 8.52

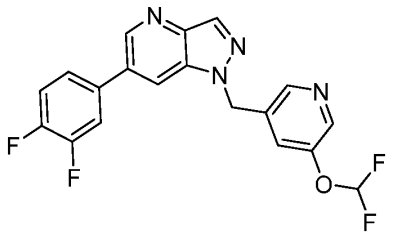
(d, J = 2.8 Hz, 1H), 8.49 – 8.48 (m, 1H), 8.43 – 8.41 (m, 1H), 8.01 (ddd, J = 12.2, 7.7, 2.3 Hz, 1H), 7.77 – 7.72 (m, 1H), 7.70 – 7.60 (m, 2H), 5.83 (s, 2H).

Example 193: 6-(3,4-Difluorophenyl)-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



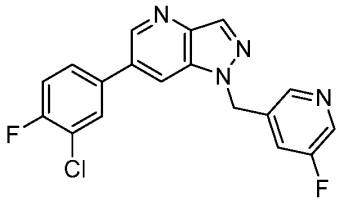
The title compound was made in an analogous manner to Intermediate 25 using 6-bromo-1-((5-methoxypyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 14) and (3,4-difluorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{19}H_{14}F_2N_4O$, 352.1; m/z found, 353.2 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.91 (d, J = 1.9 Hz, 1H), 8.73 – 8.64 (m, 1H), 8.42 – 8.36 (m, 1H), 8.22 (d, J = 2.8 Hz, 1H), 8.19 – 8.14 (m, 1H), 8.06 – 7.95 (m, 1H), 7.78 – 7.69 (m, 1H), 7.69 – 7.56 (m, 1H), 7.37 – 7.28 (m, 1H), 5.76 (s, 2H), 3.78 (s, 3H).

Example 194: 1-[[5-(Difluoromethoxy)-3-pyridyl]methyl]-6-(3,4-difluorophenyl)pyrazolo[4,3-b]pyridine.



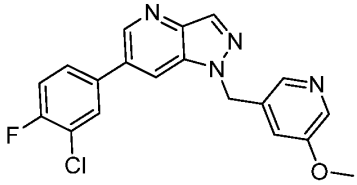
The title compound was made in an analogous manner to Intermediate 25 using 6-bromo-1-((5-(difluoromethoxy)pyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 17) and (3,4-difluorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{19}H_{12}F_4N_4O$, 388.1; m/z found, 389.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.92 (d, J = 1.9 Hz, 1H), 8.71 – 8.67 (m, 1H), 8.51 – 8.46 (m, 1H), 8.44 – 8.41 (m, 1H), 8.42 – 8.41 (m, 1H), 8.04 – 7.96 (m, 1H), 7.77 – 7.70 (m, 1H), 7.68 – 7.59 (m, 2H), 7.28 (t, J = 73.2 Hz, 1H), 5.83 (s, 2H).

Example 195: 6-(3-Chloro-4-fluoro-phenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



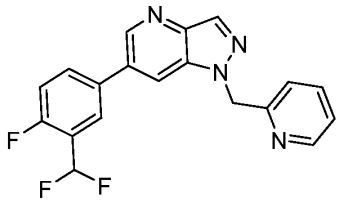
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((5-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 54) and (3-chloro-4-fluorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{18}H_{11}ClF_2N_4$, 356.1; m/z found, 357.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.92 (d, J = 1.9 Hz, 1H), 8.72 – 8.69 (m, 1H), 8.52 (d, J = 2.7 Hz, 1H), 8.49 – 8.47 (m, 1H), 8.43 – 8.40 (m, 1H), 8.13 (dd, J = 7.1, 2.4 Hz, 1H), 7.90 (ddd, J = 8.5, 4.6, 2.4 Hz, 1H), 7.69 – 7.64 (m, 1H), 7.63 – 7.58 (m, 1H), 5.83 (s, 2H).

Example 196: 6-(3-Chloro-4-fluoro-phenyl)-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



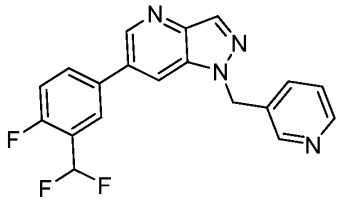
The title compound was made in an analogous manner to Intermediate 25 using 6-bromo-1-((5-methoxypyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 14) and (3-chloro-4-fluorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{19}H_{14}ClFN_4O$, 368.1; m/z found, 369.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.90 (d, J = 1.9 Hz, 1H), 8.71 – 8.69 (m, 1H), 8.40 (d, J = 0.9 Hz, 1H), 8.22 (d, J = 2.8 Hz, 1H), 8.19 – 8.16 (m, 1H), 8.12 (dd, J = 7.1, 2.3 Hz, 1H), 7.91 – 7.86 (m, 1H), 7.63 – 7.58 (m, 1H), 7.35 – 7.31 (m, 1H), 5.77 (s, 2H), 3.78 (s, 3H).

Example 197: 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine.



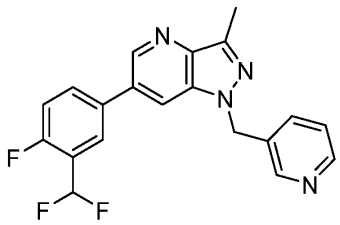
The title compound was made in an analogous manner to Example 8 using 2-(chloromethyl)pyridine instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{19}H_{13}F_3N_4$, 354.1; m/z found, 355.3 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.90 (d, J = 1.9 Hz, 1H), 8.61 – 8.58 (m, 1H), 8.51 – 8.47 (m, 1H), 8.39 (d, J = 1.0 Hz, 1H), 8.11 – 8.04 (m, 2H), 7.74 (td, J = 7.7, 1.8 Hz, 1H), 7.59 – 7.53 (m, 1H), 7.31 – 7.26 (m, 1H), 7.28 (t, J = 54.4 Hz, 1H), 7.11 – 7.06 (m, 1H), 5.88 (s, 2H).

Example 198: 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine.



The title compound was made in an analogous manner to Example 11, Step A, using 6-(3-(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 25) and 3-(chloromethyl)pyridine. MS (ESI): mass calcd. for $C_{19}H_{13}F_3N_4$, 354.1; m/z found, 355.2 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.90 (d, J = 1.9 Hz, 1H), 8.74 – 8.69 (m, 1H), 8.65 – 8.58 (m, 1H), 8.49 (dd, J = 4.8, 1.7 Hz, 1H), 8.43 – 8.38 (m, 1H), 8.14 – 8.04 (m, 2H), 7.72 – 7.65 (m, 1H), 7.63 – 7.53 (m, 1H), 7.39 – 7.32 (m, 1H), 7.30 (t, J = 54.2 Hz, 1H), 5.81 (s, 2H).

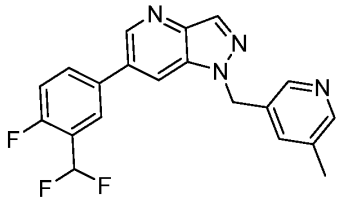
Example 199: 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-methyl-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine.



The title compound was prepared in a manner analogous to Example 11, Step A, using 6-(3-(difluoromethyl)-4-fluorophenyl)-3-methyl-1H-pyrazolo[4,3-*b*]pyridine (Intermediate 35) and 3-(chloromethyl)pyridine hydrochloride. MS (ESI): mass calcd. for $C_{20}H_{15}F_3N_4$, 368.1; m/z found, 369.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.73 (d, J = 1.9 Hz, 1H), 8.64 – 8.51 (m, 2H), 7.85

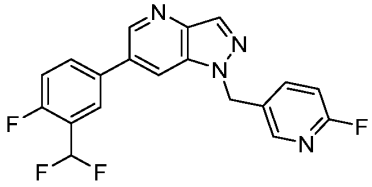
– 7.75 (m, 1H), 7.73 – 7.63 (m, 2H), 7.58 – 7.47 (m, 1H), 7.34 – 7.20 (m, 2H), 6.97 (t, J = 54.9 Hz, 1H), 5.59 (s, 2H), 2.72 (s, 3H).

Example 200: 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



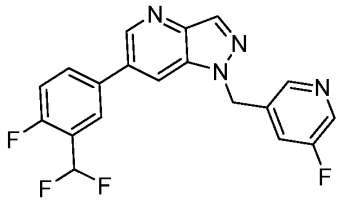
The title compound was made in an analogous manner to Example 8 using 3-(chloromethyl)-5-methylpyridine instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{20}H_{15}F_3N_4$, 368.1; m/z found, 369.1 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.89 (d, J = 1.9 Hz, 1H), 8.74 – 8.63 (m, 1H), 8.45 – 8.37 (m, 2H), 8.36 – 8.30 (m, 1H), 8.14 – 8.02 (m, 2H), 7.64 – 7.53 (m, 1H), 7.53 – 7.48 (m, 1H), 7.30 (t, J = 54.1 Hz, 1H), 5.76 (s, 2H), 2.24 (s, 3H).

Example 201: 6-(3-(Difluoromethyl)-4-fluorophenyl)-1-((6-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine.



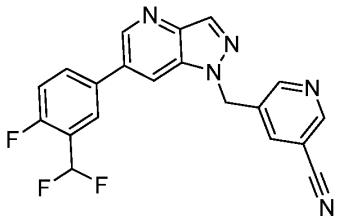
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((6-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 49) and 2-(3-(difluoromethyl)-4-fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd. for $C_{19}H_{12}F_4N_4$, 372.1; m/z found, 373.1 $[M+H]^+$.

Example 202: 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



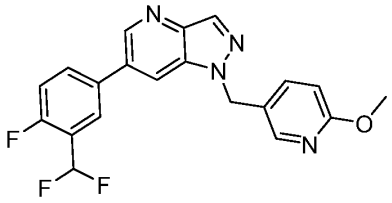
The title compound was made in an analogous manner to Example 8 using 3-(chloromethyl)-5-fluoropyridine instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{19}H_{12}F_4N_4$, 372.1; m/z found, 373.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.91 (d, J = 2.1 Hz, 1H), 8.75 – 8.66 (m, 1H), 8.52 (d, J = 2.7 Hz, 1H), 8.49 – 8.45 (m, 1H), 8.42 (s, 1H), 8.15 – 8.05 (m, 2H), 7.70 – 7.64 (m, 1H), 7.62 – 7.55 (m, 1H), 7.30 (t, J = 54.1 Hz, 1H), 5.85 (s, 2H).

Example 203: 5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile.



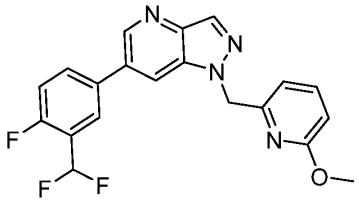
The title compound was made in an analogous manner to Intermediate 25 using 5-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)nicotinonitrile (Intermediate 21) and 2-(3-(difluoromethyl)-4-fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd. for $C_{20}H_{12}F_3N_5$, 379.1; m/z found, 380.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.96 (d, J = 2.0 Hz, 1H), 8.91 (d, J = 1.9 Hz, 1H), 8.86 (d, J = 2.2 Hz, 1H), 8.73 – 8.66 (m, 1H), 8.47 – 8.39 (m, 1H), 8.29 – 8.21 (m, 1H), 8.16 – 8.03 (m, 2H), 7.65 – 7.52 (m, 1H), 7.30 (t, J = 54.1 Hz, 1H), 5.87 (s, 2H).

Example 204: 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(6-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



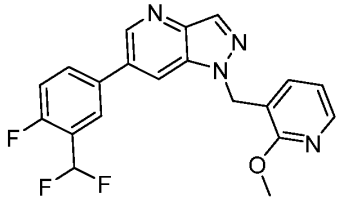
The title compound was made in an analogous manner to Example 8 using 5-(chloromethyl)-2-methoxypyridine instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{20}H_{15}F_3N_4O$, 384.1; m/z found, 385.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.88 (d, J = 1.9 Hz, 1H), 8.73 – 8.67 (m, 1H), 8.39 – 8.33 (m, 1H), 8.29 – 8.24 (m, 1H), 8.14 – 8.03 (m, 2H), 7.67 (dd, J = 8.6, 2.5 Hz, 1H), 7.63 – 7.53 (m, 1H), 7.30 (t, J = 54.1 Hz, 1H), 6.76 (d, J = 8.6 Hz, 1H), 5.70 (s, 2H), 3.80 (s, 3H).

Example 205: 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(6-methoxy-2-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



The title compound was made in an analogous manner to Example 8 using 2-(chloromethyl)-6-methoxypyridine instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{20}H_{15}F_3N_4O$, 384.1; m/z found, 385.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.91 (d, J = 2.0 Hz, 1H), 8.69 – 8.62 (m, 1H), 8.43 – 8.33 (m, 1H), 8.13 – 8.03 (m, 2H), 7.67 – 7.58 (m, 1H), 7.60 – 7.52 (m, 1H), 7.28 (t, J = 54.1 Hz, 1H), 6.69 (d, J = 8.3 Hz, 1H), 6.62 (d, J = 7.3 Hz, 1H), 5.79 (s, 2H), 3.63 (s, 3H).

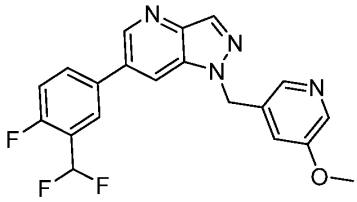
Example 206: 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(2-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



The title compound was made in an analogous manner to Example 8 using 3-(chloromethyl)-2-methoxypyridine instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{20}H_{15}F_3N_4O$, 384.1; m/z found, 385.2 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.91 (d, J = 1.9 Hz, 1H), 8.65 – 8.55 (m, 1H), 8.43 – 8.33 (m, 1H), 8.17 – 8.01 (m, 3H), 7.62 – 7.51 (m, 1H),

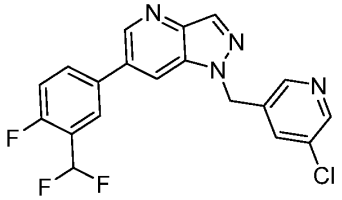
7.29 (t, *J* = 54.1 Hz, 1H), 7.16 (dd, *J* = 7.3, 1.9 Hz, 1H), 6.91 (dd, *J* = 7.3, 5.0 Hz, 1H), 5.70 (s, 2H), 3.88 (s, 3H).

Example 207: 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



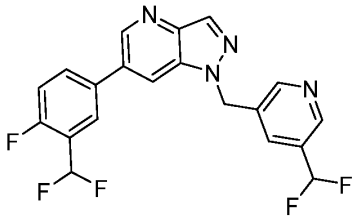
The title compound was made in an analogous manner to Example 8 using 5-(chloromethyl)-3-methoxypyridine instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{20}H_{15}F_3N_4O$, 384.1; m/z found, 385.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.90 (d, *J* = 2.0 Hz, 1H), 8.73 – 8.69 (m, 1H), 8.43 – 8.38 (m, 1H), 8.22 (d, *J* = 2.7 Hz, 1H), 8.19 – 8.14 (m, 1H), 8.13 – 8.06 (m, 2H), 7.62 – 7.54 (m, 1H), 7.35 – 7.32 (m, 1H), 7.30 (t, *J* = 54.1 Hz, 1H), 5.79 (s, 2H), 3.78 (s, 3H).

Example 208: 1-[(5-Chloro-3-pyridyl)methyl]-6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridine.



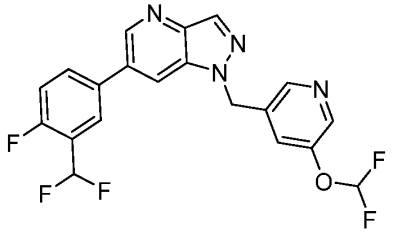
The title compound was made in an analogous manner to Example 8 using 3-chloro-5-(chloromethyl)pyridine instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{19}H_{12}ClF_3N_4$, 388.1; m/z found, 389.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.91 (d, *J* = 1.9 Hz, 1H), 8.76 – 8.67 (m, 1H), 8.59 – 8.56 (m, 1H), 8.55 (d, *J* = 1.9 Hz, 1H), 8.48 – 8.38 (m, 1H), 8.17 – 8.01 (m, 2H), 7.92 – 7.83 (m, 1H), 7.66 – 7.52 (m, 1H), 7.30 (t, *J* = 54.1 Hz, 1H), 5.83 (s, 2H).

Example 209: 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[[5-(difluoromethyl)-3-pyridyl]methyl]pyrazolo[4,3-b]pyridine.



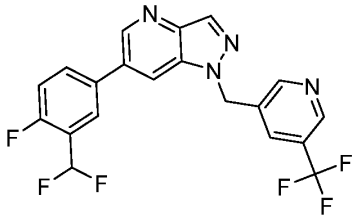
The title compound was made in an analogous manner to Example 8 using 3-(chloromethyl)-5-(difluoromethyl)pyridine (Intermediate 4) instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{20}H_{13}F_5N_4$, 404.1; m/z found, 405.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.91 (d, J = 2.0 Hz, 1H), 8.80 – 8.76 (m, 1H), 8.73 (dd, J = 2.0, 1.0 Hz, 1H), 8.73 – 8.69 (m, 1H), 8.43 (d, J = 1.0 Hz, 1H), 8.14 – 8.05 (m, 2H), 7.96 – 7.89 (m, 1H), 7.62 – 7.55 (m, 1H), 7.30 (t, J = 54.1 Hz, 1H), 7.13 (t, J = 55.2 Hz, 1H), 5.89 (s, 2H).

Example 210: 1-[[5-(Difluoromethoxy)-3-pyridyl]methyl]-6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridine.



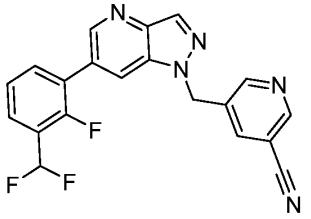
The title compound was prepared in a manner analogous to Example 12 using 3-(chloromethyl)-5-(difluoromethoxy)pyridine (Intermediate 3) instead of 3-(chloromethyl)pyridine. MS (ESI): mass calcd. for $C_{20}H_{13}F_5N_5O$, 420.1; m/z found, 421.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.91 (d, J = 1.9 Hz, 1H), 8.71 (dd, J = 2.0, 1.0 Hz, 1H), 8.49 – 8.47 (m, 1H), 8.44 – 8.41 (m, 2H), 8.11 – 8.06 (m, 2H), 7.64 – 7.61 (m, 1H), 7.61 – 7.55 (m, 1H), 7.30 (t, J = 54.1 Hz, 1H), 7.28 (t, J = 73.0 Hz, 1H), 5.85 (s, 2H).

Example 211: 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[[5-(trifluoromethyl)-3-pyridyl]methyl]pyrazolo[4,3-b]pyridine.



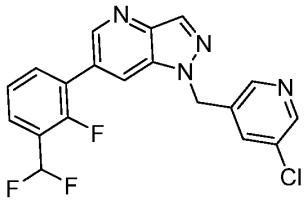
The title compound was made in an analogous manner to Example 8 using (5-(trifluoromethyl)pyridin-3-yl)methyl methanesulfonate (Intermediate 10) instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{20}H_{12}F_6N_4$, 422.1; m/z found, 423.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.94 – 8.90 (m, 2H), 8.88 – 8.84 (m, 1H), 8.75 – 8.71 (m, 1H), 8.45 – 8.42 (m, 1H), 8.22 – 8.18 (m, 1H), 8.12 – 8.07 (m, 2H), 7.62 – 7.55 (m, 1H), 7.30 (t, J = 54.1 Hz, 1H), 5.92 (s, 2H).

Example 212: 5-[[6-[3-(Difluoromethyl)-2-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile.



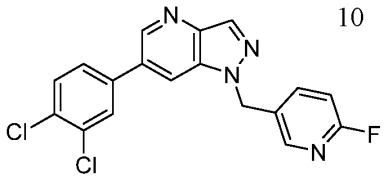
The title compound was made in an analogous manner Intermediate 25 using 5-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)nicotinonitrile (Intermediate 21) and (3-(difluoromethyl)-2-fluorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{20}H_{12}F_3N_5$, 379.1; m/z found, 380.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.96 (d, J = 2.0 Hz, 1H), 8.86 (d, J = 2.1 Hz, 1H), 8.79 – 8.69 (m, 1H), 8.66 – 8.58 (m, 1H), 8.46 (s, 1H), 8.31 – 8.22 (m, 1H), 7.96 – 7.86 (m, 1H), 7.80 – 7.71 (m, 1H), 7.54 (t, J = 7.8 Hz, 1H), 7.32 (t, J = 54.2 Hz, 1H), 5.86 (s, 2H).

Example 213: 1-[(5-Chloro-3-pyridyl)methyl]-6-[3-(difluoromethyl)-2-fluoro-phenyl]pyrazolo[4,3-b]pyridine.



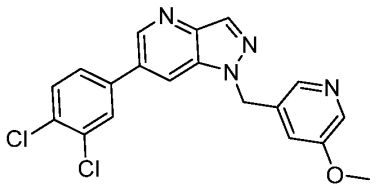
The title compound was made in an analogous manner to Intermediate 25 using 6-bromo-1-((5-chloropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 18) and (3-(difluoromethyl)-2-fluorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{19}H_{12}ClF_3N_4$, 388.1; m/z found, 389.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.76 – 8.69 (m, 1H), 8.67 – 8.60 (m, 1H), 8.57 (d, J = 2.4 Hz, 1H), 8.56 – 8.53 (m, 1H), 8.46 (s, 1H), 7.95 – 7.83 (m, 2H), 7.81 – 7.70 (m, 1H), 7.54 (t, J = 7.8 Hz, 1H), 7.32 (t, J = 54.2 Hz, 1H), 5.82 (s, 2H).

Example 214: 6-(3,4-Dichlorophenyl)-1-[(6-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((6-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 49) and (3,4-dichlorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{18}H_{11}Cl_2FN_4$, 372.0; m/z found, 373.0 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.93 (d, J = 1.9 Hz, 1H), 8.78 – 8.74 (m, 1H), 8.42 – 8.39 (m, 1H), 8.34 – 8.31 (m, 1H), 8.18 (d, J = 2.2 Hz, 1H), 7.93 (td, J = 8.2, 2.5 Hz, 1H), 7.90 – 7.87 (m, 1H), 7.83 – 7.80 (m, 1H), 7.15 (dd, J = 8.5, 2.7 Hz, 1H), 5.80 (s, 2H).

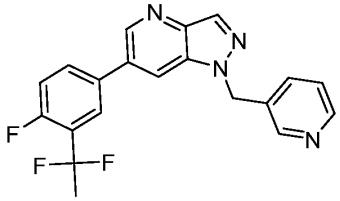
Example 215: 6-(3,4-Dichlorophenyl)-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



The title compound was made in an analogous manner to Intermediate 25 using 6-bromo-1-((5-methoxypyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 14) and (3,4-

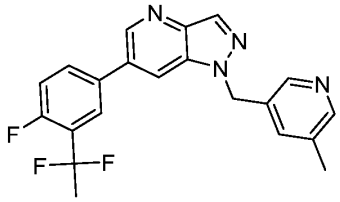
dichlorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{19}H_{14}Cl_2N_4O$, 384.0; m/z found, 385.0 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.93 (d, J = 1.9 Hz, 1H), 8.74 (dd, J = 2.0, 1.0 Hz, 1H), 8.41 (d, J = 1.0 Hz, 1H), 8.22 (d, J = 2.8 Hz, 1H), 8.19 – 8.15 (m, 2H), 7.88 (dd, J = 8.4, 2.2 Hz, 1H), 7.81 (d, J = 8.4 Hz, 1H), 7.35 – 7.32 (m, 1H), 5.78 (s, 2H), 3.78 (s, 3H).

Example 216: 6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine.



The title compound was made in an analogous manner to Example 11, Step A, using 6-(3-(1,1-difluoroethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 28) and 3-(chloromethyl)pyridine. MS (ESI): mass calcd. for $C_{20}H_{15}F_3N_4$, 368.1; m/z found, 369.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.90 (d, J = 1.9 Hz, 1H), 8.71 – 8.66 (m, 1H), 8.63 – 8.58 (m, 1H), 8.49 (dd, J = 4.8, 1.6 Hz, 1H), 8.40 (s, 1H), 8.07 – 7.99 (m, 1H), 8.00 – 7.93 (m, 1H), 7.71 – 7.64 (m, 1H), 7.56 (dd, J = 11.0, 8.6 Hz, 1H), 7.38 – 7.30 (m, 1H), 5.81 (s, 2H), 2.10 (t, J = 19.1 Hz, 3H).

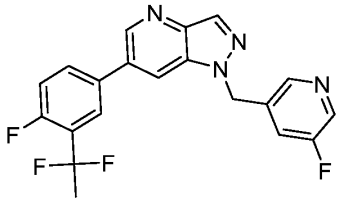
Example 217: 6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



The title compound was made in an analogous manner to Example 8 using 6-(3-(1,1-difluoroethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 28) and 3-(chloromethyl)-5-methylpyridine. MS (ESI): mass calcd. for $C_{21}H_{17}F_3N_4$, 382.1; m/z found, 383.2 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.90 (d, J = 1.9 Hz, 1H), 8.73 – 8.63 (m, 1H),

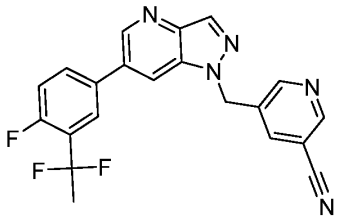
8.46 – 8.37 (m, 2H), 8.36 – 8.29 (m, 1H), 8.10 – 7.99 (m, 1H), 8.01 – 7.92 (m, 1H), 7.56 (dd, *J* = 11.2, 8.7 Hz, 1H), 7.54 – 7.46 (m, 1H), 5.77 (s, 2H), 2.24 (s, 3H), 2.10 (t, *J* = 19.2 Hz, 3H).

Example 218: 6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



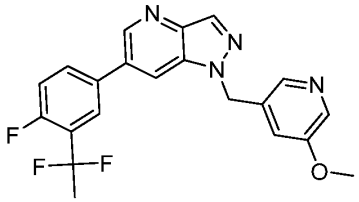
The title compound was made in an analogous manner to Example 8 using 6-(3-(1,1-difluoroethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 28) and 3-(chloromethyl)-5-fluoropyridine. MS (ESI): mass calcd. for $C_{20}H_{14}F_4N_4$, 386.1; m/z found, 387.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.91 (d, *J* = 1.9 Hz, 1H), 8.74 – 8.64 (m, 1H), 8.52 (d, *J* = 2.8 Hz, 1H), 8.49 – 8.43 (m, 1H), 8.42 (s, 1H), 8.10 – 7.99 (m, 1H), 8.00 – 7.93 (m, 1H), 7.70 – 7.62 (m, 1H), 7.56 (dd, *J* = 11.0, 8.6 Hz, 1H), 5.85 (s, 2H), 2.10 (t, *J* = 19.1 Hz, 3H).

Example 219: 5-[[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile.



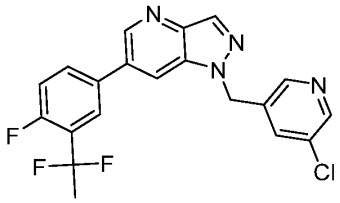
The title compound was made in an analogous manner to Intermediate 25 using 5-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)nicotinonitrile (Intermediate 21) and 2-(3-(1,1-difluoroethyl)-4-fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd. for $C_{21}H_{14}F_3N_5$, 393.1; m/z found, 394.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.99 – 8.94 (m, 1H), 8.94 – 8.89 (m, 1H), 8.88 – 8.83 (m, 1H), 8.71 – 8.66 (m, 1H), 8.43 (s, 1H), 8.28 – 8.23 (m, 1H), 8.08 – 8.01 (m, 1H), 8.00 – 7.95 (m, 1H), 7.61 – 7.52 (m, 1H), 5.87 (s, 2H), 2.10 (t, *J* = 19.1 Hz, 3H).

Example 220: 6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



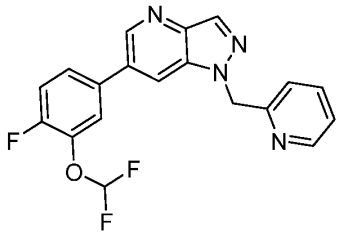
The title compound was made in an analogous manner to Example 11, Step A, using 6-(3-(1,1-difluoroethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 28) and 3-(chloromethyl)-5-methoxypyridine. MS (ESI): mass calcd. for $C_{21}H_{17}F_3N_4O$, 398.1; m/z found, 399.2 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.90 (d, J = 1.9 Hz, 1H), 8.72 – 8.65 (m, 1H), 8.41 (s, 1H), 8.22 (d, J = 2.8 Hz, 1H), 8.17 – 8.13 (m, 1H), 8.08 – 8.00 (m, 1H), 8.00 – 7.92 (m, 1H), 7.56 (dd, J = 11.0, 8.6 Hz, 1H), 7.37 – 7.30 (m, 1H), 5.79 (s, 2H), 3.78 (s, 3H), 2.10 (t, J = 19.1 Hz, 3H).

Example 221: 1-[(5-Chloro-3-pyridyl)methyl]-6-[3-(1,1-difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridine.



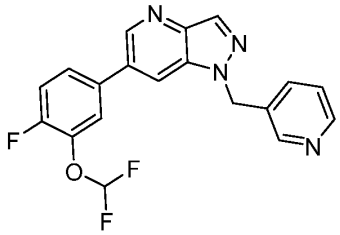
The title compound was made in an analogous manner to Example 8 using 6-(3-(1,1-difluoroethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 28) and 3-chloro-5-(chloromethyl)pyridine. MS (ESI): mass calcd. for $C_{20}H_{14}ClF_3N_4$, 402.1; m/z found, 403.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.91 (d, J = 2.2 Hz, 1H), 8.72 – 8.67 (m, 1H), 8.57 (d, J = 2.4 Hz, 1H), 8.55 – 8.52 (m, 1H), 8.42 (s, 1H), 8.07 – 8.01 (m, 1H), 8.01 – 7.95 (m, 1H), 7.90 – 7.83 (m, 1H), 7.61 – 7.52 (m, 1H), 5.83 (s, 2H), 2.10 (t, J = 19.1 Hz, 3H).

Example 222: 6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine.



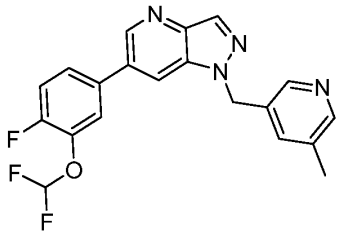
The title compound was made in an analogous manner to Example 8 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 2-(chloromethyl)pyridine. MS (ESI): mass calcd. for $C_{19}H_{13}F_3N_4O$, 370.1; m/z found, 371.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.90 (d, J = 1.9 Hz, 1H), 8.58 – 8.53 (m, 1H), 8.51 – 8.47 (m, 1H), 8.41 – 8.36 (m, 1H), 7.85 (dd, J = 7.6, 2.2 Hz, 1H), 7.80 – 7.71 (m, 2H), 7.58 (dd, J = 10.5, 8.6 Hz, 1H), 7.37 (t, J = 73.2 Hz, 1H), 7.32 – 7.26 (m, 1H), 7.12 – 7.07 (m, 1H), 5.87 (s, 2H).

Example 223: 6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine.



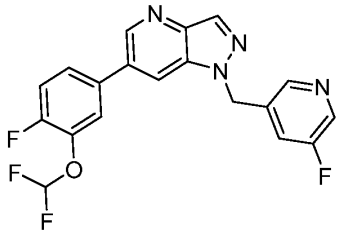
The title compound was made in an analogous manner to Example 11, Step A, using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 3-(chloromethyl)pyridine. MS (ESI): mass calcd. for $C_{19}H_{13}F_3N_4O$, 370.1; m/z found, 371.2 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.90 (d, J = 1.9 Hz, 1H), 8.69 – 8.65 (m, 1H), 8.64 – 8.58 (m, 1H), 8.49 (dd, J = 4.8, 1.6 Hz, 1H), 8.43 – 8.37 (m, 1H), 7.87 (dd, J = 7.6, 2.2 Hz, 1H), 7.83 – 7.76 (m, 1H), 7.71 – 7.65 (m, 1H), 7.60 (dd, J = 10.4, 8.8 Hz, 1H), 7.38 (t, J = 73.3 Hz, 1H), 7.37 – 7.30 (m, 1H), 5.80 (s, 2H).

Example 224: 6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



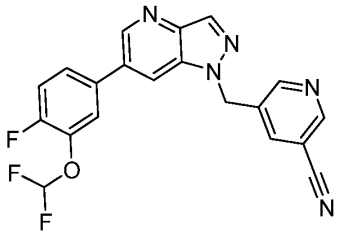
The title compound was made in an analogous manner to Example 8 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 3-(chloromethyl)-5-methylpyridine. MS (ESI): mass calcd. for $C_{20}H_{15}F_3N_4O$, 384.1; m/z found, 385.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.90 (d, J = 2.0 Hz, 1H), 8.66 – 8.63 (m, 1H), 8.42 – 8.40 (m, 1H), 8.40 – 8.38 (m, 1H), 8.35 – 8.31 (m, 1H), 7.86 (dd, J = 7.6, 2.3 Hz, 1H), 7.82 – 7.77 (m, 1H), 7.60 (dd, J = 10.5, 8.6 Hz, 1H), 7.53 – 7.50 (m, 1H), 7.37 (t, J = 73.2 Hz, 1H), 5.75 (s, 2H), 2.24 (s, 3H).

Example 225: 6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



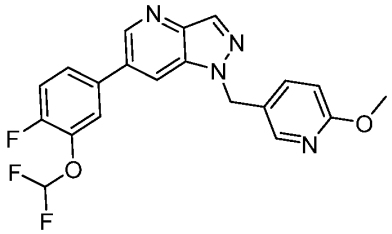
The title compound was made in an analogous manner to Example 8 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 3-(chloromethyl)-5-fluoropyridine. MS (ESI): mass calcd. for $C_{19}H_{12}F_4N_4O$, 388.1; m/z found, 389.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.91 (d, J = 2.0 Hz, 1H), 8.68 – 8.64 (m, 1H), 8.54 – 8.50 (m, 1H), 8.49 – 8.45 (m, 1H), 8.42 (d, J = 1.0 Hz, 1H), 7.87 (dd, J = 7.6, 2.3 Hz, 1H), 7.83 – 7.76 (m, 1H), 7.68 – 7.63 (m, 1H), 7.60 (dd, J = 10.5, 8.6 Hz, 1H), 7.37 (t, J = 73.2 Hz, 1H), 5.84 (s, 2H).

Example 226: 5-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile.



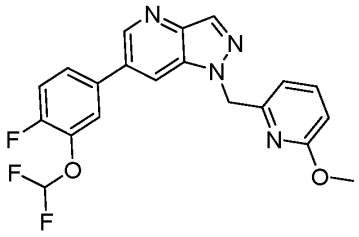
The title compound was prepared in a manner analogous to Example 8 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 5-(chloromethyl)pyridine-3-carbonitrile. MS (ESI): mass calcd. for $C_{20}H_{12}F_3N_5O$, 395.1; m/z found, 396.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.96 (d, J = 2.0 Hz, 1H), 8.91 (d, J = 1.9 Hz, 1H), 8.86 (d, J = 2.2 Hz, 1H), 8.69 – 8.64 (m, 1H), 8.43 (d, J = 1.0 Hz, 1H), 8.28 – 8.23 (m, 1H), 7.87 (dd, J = 7.6, 2.3 Hz, 1H), 7.83 – 7.77 (m, 1H), 7.61 (dd, J = 10.5, 8.6 Hz, 1H), 7.37 (t, J = 73.2 Hz, 1H), 5.86 (s, 2H).

Example 227: 6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(6-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



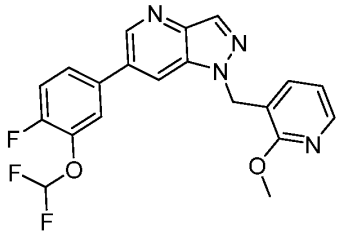
The title compound was made in an analogous manner to Example 8 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 5-(chloromethyl)-2-methoxypyridine. MS (ESI): mass calcd. for $C_{20}H_{15}F_3N_4O_2$, 400.1; m/z found, 401.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.89 (d, J = 1.9 Hz, 1H), 8.70 – 8.64 (m, 1H), 8.37 (s, 1H), 8.29 – 8.24 (m, 1H), 7.91 – 7.83 (m, 1H), 7.83 – 7.76 (m, 1H), 7.67 (dd, J = 8.6, 2.5 Hz, 1H), 7.60 (dd, J = 10.5, 8.8 Hz, 1H), 7.38 (t, J = 73.2 Hz, 1H), 6.76 (d, J = 8.5 Hz, 1H), 5.69 (s, 2H), 3.80 (s, 3H).

Example 228: 6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(6-methoxy-2-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



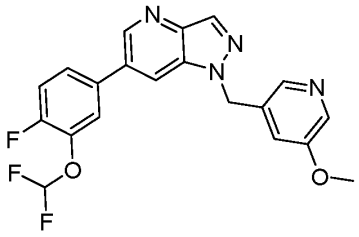
The title compound was made in an analogous manner to Example 8 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 2-(chloromethyl)-6-methoxypyridine. MS (ESI): mass calcd. for $C_{20}H_{15}F_3N_4O_2$, 400.1; m/z found, 401.2 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.91 (d, J = 1.9 Hz, 1H), 8.65 – 8.57 (m, 1H), 8.42 – 8.35 (m, 1H), 7.85 (dd, J = 7.7, 2.2 Hz, 1H), 7.81 – 7.74 (m, 1H), 7.67 – 7.59 (m, 1H), 7.57 (dd, J = 10.4, 8.6 Hz, 1H), 7.37 (t, J = 73.2 Hz, 1H), 6.69 (d, J = 8.3 Hz, 1H), 6.62 (d, J = 7.3 Hz, 1H), 5.78 (s, 2H), 3.63 (s, 3H).

Example 229: 6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(2-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



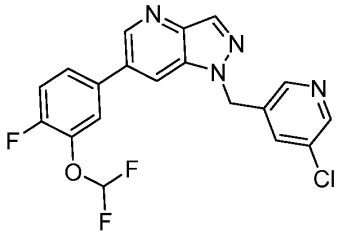
The title compound was made in an analogous manner to Example 8 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 3-(chloromethyl)-2-methoxypyridine. MS (ESI): mass calcd. for $C_{20}H_{15}F_3N_4O_2$, 400.1; m/z found, 401.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.90 (d, J = 2.0 Hz, 1H), 8.57 – 8.53 (m, 1H), 8.38 (d, J = 1.0 Hz, 1H), 8.10 (dd, J = 5.0, 1.8 Hz, 1H), 7.86 (dd, J = 7.6, 2.3 Hz, 1H), 7.81 – 7.76 (m, 1H), 7.59 (dd, J = 10.5, 8.6 Hz, 1H), 7.38 (t, J = 73.2 Hz, 1H), 7.19 – 7.15 (m, 1H), 6.91 (dd, J = 7.3, 5.0 Hz, 1H), 5.69 (s, 2H), 3.88 (s, 3H).

Example 230: 6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



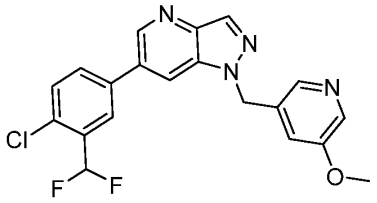
The title compound was made in an analogous manner to Example 8 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 3-(chloromethyl)-5-methoxypyridine. MS (ESI): mass calcd. for $C_{20}H_{15}F_3N_4O_2$, 400.1; m/z found, 401.2 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.90 (d, J = 1.9 Hz, 1H), 8.70 – 8.62 (m, 1H), 8.40 (s, 1H), 8.22 (d, J = 2.8 Hz, 1H), 8.18 – 8.14 (m, 1H), 7.90 – 7.83 (m, 1H), 7.83 – 7.75 (m, 1H), 7.61 (dd, J = 10.7, 8.6 Hz, 1H), 7.38 (t, J = 72.8 Hz, 1H), 7.36 – 7.29 (m, 1H), 5.78 (s, 2H), 3.78 (s, 3H).

Example 231: 1-[(5-Chloro-3-pyridyl)methyl]-6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridine.



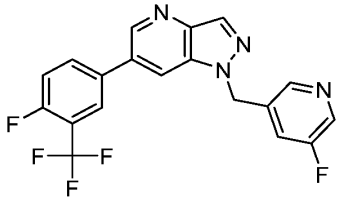
The title compound was made in an analogous manner to Example 8 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 3-chloro-5-(chloromethyl)pyridine. MS (ESI): mass calcd. for $C_{19}H_{12}ClF_3N_4O$, 404.1; m/z found, 405.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.96 – 8.87 (m, 1H), 8.72 – 8.65 (m, 1H), 8.62 – 8.50 (m, 2H), 8.47 – 8.38 (m, 1H), 7.93 – 7.83 (m, 2H), 7.84 – 7.74 (m, 1H), 7.67 – 7.55 (m, 1H), 7.38 (t, J = 73.0 Hz, 1H), 5.82 (s, 2H).

Example 232: 6-[4-chloro-3-(Difluoromethyl)phenyl]-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



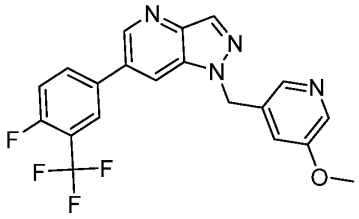
The title compound was made in an analogous manner to Intermediate 25 using 6-bromo-1-((5-methoxypyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 14) and 2-(4-chloro-3-(difluoromethyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd. for $C_{20}H_{15}ClF_2N_4O$, 400.1; m/z found, 401.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.92 (d, J = 1.9 Hz, 1H), 8.77 – 8.71 (m, 1H), 8.41 (s, 1H), 8.22 (d, J = 2.8 Hz, 1H), 8.18 – 8.15 (m, 1H), 8.15 – 8.12 (m, 1H), 8.08 – 8.03 (m, 1H), 7.79 (d, J = 8.4 Hz, 1H), 7.36 – 7.32 (m, 1H), 7.30 (t, J = 54.1 Hz, 1H), 5.80 (s, 2H), 3.78 (s, 3H).

Example 233: 1-[(5-Fluoro-3-pyridyl)methyl]-6-[4-fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine.



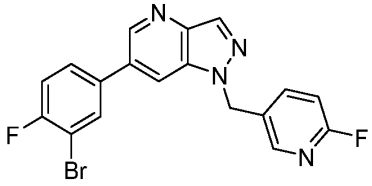
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((5-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 54) and (4-fluoro-3-(trifluoromethyl)phenyl)boronic acid. MS (ESI): mass calcd. for $C_{19}H_{11}F_5N_4$, 390.1; m/z found, 391.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.95 (d, J = 1.9 Hz, 1H), 8.76 – 8.74 (m, 1H), 8.52 (d, J = 2.8 Hz, 1H), 8.48 – 8.46 (t, J = 1.8 Hz, 1H), 8.44 – 8.42 (d, J = 1.1 Hz, 1H), 8.26 – 8.19 (m, 2H), 7.73 (dd, J = 10.6, 8.7 Hz, 1H), 7.69 – 7.65 (m, 1H), 5.85 (s, 2H).

Example 234: 6-[4-Fluoro-3-(trifluoromethyl)phenyl]-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



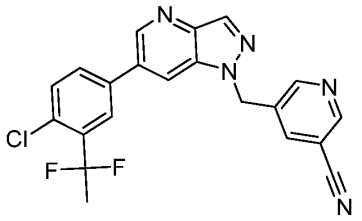
The title compound was made in an analogous manner to Intermediate 25 using 6-bromo-1-((5-methoxypyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 14) and (4-fluoro-3-(trifluoromethyl)phenyl)boronic acid. MS (ESI): mass calcd. for $C_{20}H_{14}F_4N_4O$, 402.1; m/z found, 403.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.93 (d, J = 2.0 Hz, 1H), 8.74 (dd, J = 2.0, 1.0 Hz, 1H), 8.41 (d, J = 1.0 Hz, 1H), 8.26 – 8.18 (m, 3H), 8.17 (d, J = 1.8 Hz, 1H), 7.72 (dd, J = 10.7, 8.7 Hz, 1H), 7.34 (dd, J = 2.8, 1.8 Hz, 1H), 5.78 (s, 2H), 3.78 (s, 3H).

Example 235: 6-(3-Bromo-4-fluorophenyl)-1-((6-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine.



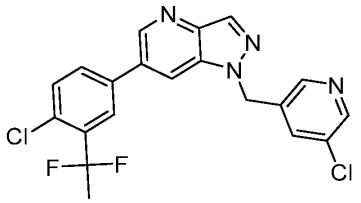
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((6-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 49) and (3-bromo-4-fluorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{18}H_{11}BrF_2N_4$, 401.2; m/z found, 403.1 MS $[M+H]^+$.

Example 236: 5-[[6-[4-Chloro-3-(1,1-difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile.



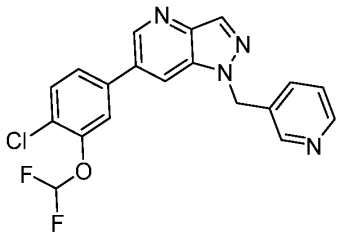
The title compound was made in an analogous manner to Intermediate 25 using 5-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)nicotinonitrile (Intermediate 21) and 2-(4-chloro-3-(1,1-difluoroethyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd. for $C_{21}H_{14}ClF_2N_5$, 409.1; m/z found, 410.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.96 (d, J = 2.0 Hz, 1H), 8.93 (d, J = 1.9 Hz, 1H), 8.86 (d, J = 2.2 Hz, 1H), 8.74 – 8.70 (m, 1H), 8.44 (d, J = 1.0 Hz, 1H), 8.28 – 8.23 (m, 1H), 8.04 (d, J = 2.2 Hz, 1H), 8.00 (dd, J = 8.3, 2.3 Hz, 1H), 7.78 (d, J = 8.3 Hz, 1H), 5.88 (s, 2H), 2.14 (t, J = 19.0 Hz, 3H).

Example 237: 6-[4-Chloro-3-(1,1-difluoroethyl)phenyl]-1-[(5-chloro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



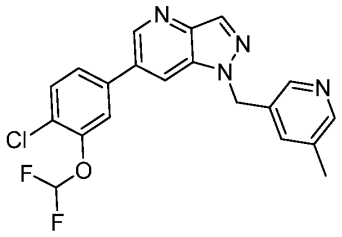
The title compound was made in an analogous manner to Intermediate 25 using 6-bromo-1-((5-chloropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 18) and 2-(4-chloro-3-(1,1-difluoroethyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd. for $C_{20}H_{14}Cl_2F_2N_4$, 418.1; m/z found, 419.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.93 (d, J = 1.9 Hz, 1H), 8.77 – 8.70 (m, 1H), 8.57 (d, J = 2.4 Hz, 1H), 8.54 (d, J = 1.9 Hz, 1H), 8.44 (s, 1H), 8.08 – 8.02 (m, 1H), 8.03 – 7.94 (m, 1H), 7.92 – 7.84 (m, 1H), 7.78 (d, J = 8.3 Hz, 1H), 5.84 (s, 2H), 2.14 (t, J = 19.0 Hz, 3H).

Example 238: 6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine.



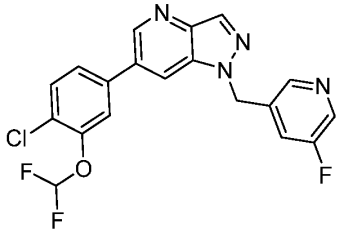
The title compound was made in an analogous manner to Example 11, Step A, using: 6-(4-chloro-3-(difluoromethoxy)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 27) and 3-(chloromethyl)pyridine. MS (ESI): mass calcd. for $C_{19}H_{13}ClF_2N_4O$, 386.1; m/z found, 387.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.93 (d, J = 1.9 Hz, 1H), 8.73 – 8.68 (m, 1H), 8.64 – 8.58 (m, 1H), 8.49 (dd, J = 4.9, 1.6 Hz, 1H), 8.42 (s, 1H), 7.89 – 7.81 (m, 1H), 7.81 – 7.75 (m, 2H), 7.72 – 7.64 (m, 1H), 7.44 (t, J = 73.3 Hz, 1H), 7.39 – 7.30 (m, 1H), 5.81 (s, 2H).

Example 239: 6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



The title compound was made in an analogous manner to Example 8 using 6-(4-chloro-3-(difluoromethoxy)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 27) and 3-(chloromethyl)-5-methylpyridine. MS (ESI): mass calcd. for $C_{20}H_{15}ClF_2N_4O$, 400.1; m/z found, 401.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.93 (d, J = 1.9 Hz, 1H), 8.72 – 8.66 (m, 1H), 8.44 – 8.37 (m, 2H), 8.36 – 8.30 (m, 1H), 7.87 – 7.82 (m, 1H), 7.82 – 7.75 (m, 2H), 7.55 – 7.49 (m, 1H), 7.44 (t, J = 73.2 Hz, 1H), 5.76 (s, 2H), 2.24 (s, 3H).

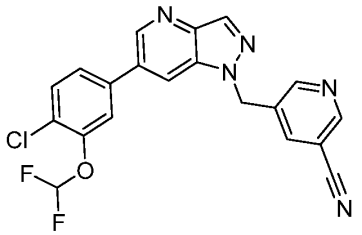
Example 240: 6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



The title compound was made in an analogous manner to Example 8 using 6-(4-chloro-3-(difluoromethoxy)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 27) and 3-(chloromethyl)-5-fluoropyridine. MS (ESI): mass calcd. for $C_{19}H_{12}ClF_3N_4O$, 404.1; m/z found, 405.1 $[M+H]^+$.

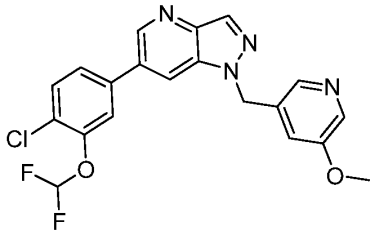
^{1}H NMR (500 MHz, DMSO-d_6) δ 8.94 (d, J = 1.9 Hz, 1H), 8.70 (dd, J = 2.0, 1.1 Hz, 1H), 8.52 (d, J = 2.8 Hz, 1H), 8.48 – 8.45 (m, 1H), 8.43 (d, J = 1.0 Hz, 1H), 7.87 – 7.82 (m, 1H), 7.81 – 7.75 (m, 2H), 7.69 – 7.62 (m, 1H), 7.43 (t, J = 73.2 Hz, 1H), 5.85 (s, 2H).

Example 241: 5-[[6-[4-Chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile.



The title compound was made in an analogous manner to Intermediate 25 using 5-((6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)nicotinonitrile (Intermediate 21) and 2-(4-chloro-3-(difluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd. for $C_{20}H_{12}ClF_2N_5O$, 411.1; m/z found, 412.1 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.97 (d, J = 2.0 Hz, 1H), 8.94 (d, J = 1.9 Hz, 1H), 8.86 (d, J = 2.1 Hz, 1H), 8.73 – 8.68 (m, 1H), 8.44 (s, 1H), 8.29 – 8.23 (m, 1H), 7.89 – 7.83 (m, 1H), 7.82 – 7.75 (m, 2H), 7.44 (t, J = 73.2 Hz, 1H), 5.87 (s, 2H).

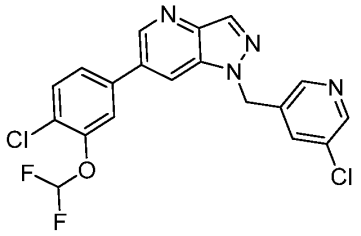
Example 242: 6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



The title compound was made in an analogous manner to Example 11, Step A, using 6-(4-chloro-3-(difluoromethoxy)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 27) and 3-(chloromethyl)-5-methoxypyridine. MS (ESI): mass calcd. for $C_{20}H_{15}ClF_2N_4O_2$, 416.1; m/z found, 417.1 $[M+H]^+$. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.94 – 8.91 (m, 1H), 8.71 – 8.68 (m,

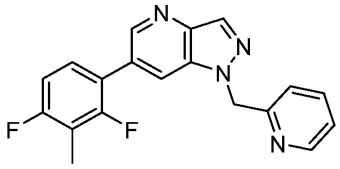
1H), 8.41 (s, 1H), 8.24 – 8.20 (m, 1H), 8.18 – 8.13 (m, 1H), 7.86 – 7.82 (m, 1H), 7.81 – 7.75 (m, 2H), 7.43 (t, J = 73.2 Hz, 1H), 7.35 – 7.31 (m, 1H), 5.78 (s, 2H), 3.78 (s, 3H).

Example 243: 6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-[(5-chloro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



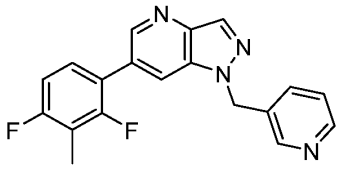
The title compound was made in an analogous manner to Example 8 using 6-(4-chloro-3-(difluoromethoxy)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 27) and 3-chloro-5-(chloromethyl)pyridine. MS (ESI): mass calcd. for $C_{19}H_{12}Cl_2F_2N_4O$, 420.0; m/z found, 421.0 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.94 (d, J = 1.9 Hz, 1H), 8.75 – 8.67 (m, 1H), 8.57 (d, J = 2.4 Hz, 1H), 8.54 (d, J = 1.8 Hz, 1H), 8.44 (s, 1H), 7.91 – 7.82 (m, 2H), 7.82 – 7.75 (m, 2H), 7.44 (t, J = 73.2 Hz, 1H), 5.83 (s, 2H).

Example 244: 6-(2,4-Difluoro-3-methyl-phenyl)-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine.



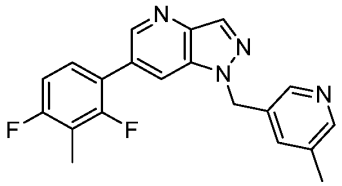
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-(pyridin-2-ylmethyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 53) and (2,4-difluoro-3-methylphenyl)boronic acid. MS (ESI): mass calcd. for $C_{19}H_{14}F_2N_4$, 336.1; m/z found, 337.0 $[M+H]^+$. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.68 (t, J = 1.9 Hz, 1H), 8.50 – 8.47 (m, 1H), 8.40 – 8.36 (m, 1H), 8.38 – 8.36 (m, 1H), 7.75 (td, J = 7.7, 1.8 Hz, 1H), 7.56 – 7.50 (m, 1H), 7.31 – 7.27 (m, 1H), 7.27 – 7.22 (m, 1H), 7.15 – 7.11 (m, 1H), 5.85 (s, 2H), 2.26 – 2.23 (m, 3H).

Example 245: 6-(2,4-Difluoro-3-methyl-phenyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine trifluoroacetate salt.



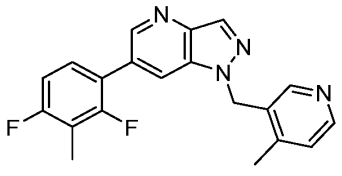
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-(pyridin-3-ylmethyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 50) and using (2,4-difluoro-3-methylphenyl)boronic acid. MS (ESI): mass calcd. for $C_{19}H_{14}F_2N_4$, 336.1; m/z found, 337.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.73 – 8.71 (m, 1H), 8.69 (t, J = 2.0 Hz, 1H), 8.62 – 8.59 (m, 1H), 8.53 – 8.51 (m, 1H), 8.44 – 8.42 (m, 1H), 7.95 – 7.90 (m, 1H), 7.60 – 7.51 (m, 2H), 7.30 – 7.23 (m, 1H), 5.85 (s, 2H), 2.28 – 2.23 (m, 3H).

Example 246: 6-(2,4-Difluoro-3-methyl-phenyl)-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



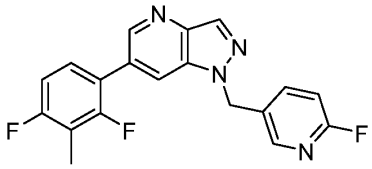
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((5-methylpyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 51) and (2,4-difluoro-3-methylphenyl)boronic acid. MS (ESI): mass calcd. for $C_{20}H_{16}F_2N_4$, 350.1; m/z found, 351.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.67 (t, J = 1.9 Hz, 1H), 8.51 – 8.49 (m, 1H), 8.42 – 8.39 (m, 2H), 8.34 – 8.32 (m, 1H), 7.60 – 7.50 (m, 2H), 7.29 – 7.23 (m, 1H), 5.74 (s, 2H), 2.28 – 2.22 (m, 6H).

Example 247: 6-(2,4-Difluoro-3-methyl-phenyl)-1-[(4-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine trifluoroacetate salt.



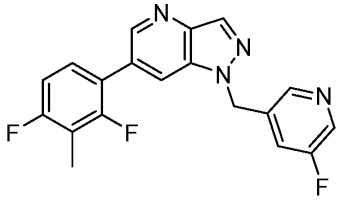
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((4-methylpyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 52) and (2,4-difluoro-3-methylphenyl)boronic acid. MS (ESI): mass calcd. for $C_{20}H_{16}F_2N_4$, 350.1; m/z found, 351.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.71 (t, J = 1.9 Hz, 1H), 8.60 (d, J = 5.5 Hz, 1H), 8.52 – 8.49 (m, 1H), 8.46 – 8.43 (m, 1H), 8.36 (s, 1H), 7.67 (d, J = 5.5 Hz, 1H), 7.60 – 7.52 (m, 1H), 7.30 – 7.24 (m, 1H), 5.90 (s, 2H), 2.27 – 2.24 (m, 3H).

Example 248: 6-(2,4-Difluoro-3-methyl-phenyl)-1-[(6-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine.



The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((6-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 49) and (2,4-difluoro-3-methylphenyl)boronic acid. MS (ESI): mass calcd. for $C_{19}H_{13}F_3N_4$, 354.1; m/z found, 355.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.68 (t, J = 1.9 Hz, 1H), 8.54 – 8.52 (m, 1H), 8.42 – 8.40 (m, 1H), 8.32 – 8.30 (m, 1H), 7.91 (td, J = 8.2, 2.5 Hz, 1H), 7.59 – 7.53 (m, 1H), 7.29 – 7.23 (m, 1H), 7.14 (dd, J = 8.5, 2.6 Hz, 1H), 5.79 (s, 2H), 2.27 – 2.24 (m, 3H).

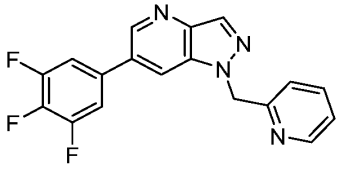
Example 249: 6-(2,4-Difluoro-3-methyl-phenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine trifluoroacetate salt.



The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((5-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 54) and (2,4-difluoro-3-methylphenyl)boronic acid. MS (ESI): mass calcd. for $C_{19}H_{13}F_3N_4$, 354.1; m/z found, 355.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.69 (t, J = 1.9 Hz, 1H), 8.55 – 8.51 (m, 2H), 8.48 –

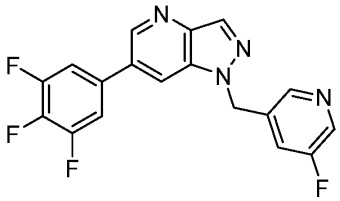
8.45 (m, 1H), 8.44 – 8.42 (m, 1H), 7.69 – 7.64 (m, 1H), 7.60 – 7.53 (m, 1H), 7.29 – 7.23 (m, 1H), 5.83 (s, 2H), 2.27 – 2.24 (m, 3H).

Example 250: 1-(2-Pyridylmethyl)-6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridine.



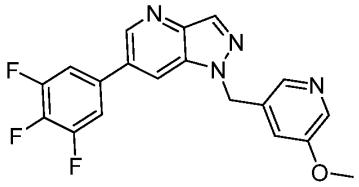
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-(pyridin-2-ylmethyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 53) and (3,4,5-trifluorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{18}H_{11}F_3N_4$, 340.1; m/z found, 341.0 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.95 (d, J = 2.0 Hz, 1H), 8.67 – 8.65 (m, 1H), 8.50 – 8.47 (m, 1H), 8.41 – 8.39 (m, 1H), 7.95 – 7.88 (m, 2H), 7.75 (td, J = 7.7, 1.8 Hz, 1H), 7.31 – 7.27 (m, 1H), 7.10 – 7.07 (m, 1H), 5.86 (s, 2H).

Example 251: 1-[(5-Fluoro-3-pyridyl)methyl]-6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridine.



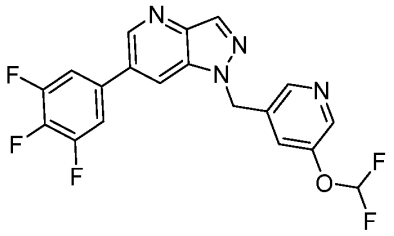
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-((5-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 54) and (3,4,5-trifluorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{18}H_{10}F_4N_4$, 358.1; m/z found, 359.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.96 (d, J = 1.9 Hz, 1H), 8.76 – 8.74 (dd, J = 2.0, 1.0 Hz, 1H), 8.52 (d, J = 2.8 Hz, 1H), 8.49 (t, J = 1.8 Hz, 1H), 8.43 (d, J = 0.9 Hz, 1H), 7.98 – 7.90 (m, 2H), 7.70 – 7.66 (m, 1H), 5.83 (s, 2H).

Example 252: 1-[(5-Methoxy-3-pyridyl)methyl]-6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridine.



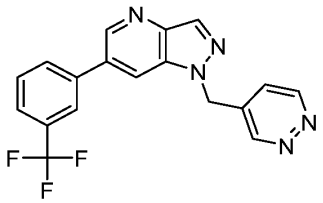
The title compound was made in an analogous manner to Intermediate 25 using 6-bromo-1-((5-methoxypyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 14) and (3,4,5-trifluorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{19}H_{13}F_3N_4O$, 370.1; m/z found, 371.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.94 (d, J = 2.0 Hz, 1H), 8.76 – 8.72 (m, 1H), 8.44 – 8.38 (m, 1H), 8.22 (d, J = 2.8 Hz, 1H), 8.18 (d, J = 1.7 Hz, 1H), 7.98 – 7.88 (m, 2H), 7.37 – 7.30 (m, 1H), 5.76 (s, 2H), 3.78 (s, 3H).

Example 253: 1-[[5-(Difluoromethoxy)-3-pyridyl]methyl]-6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridine.



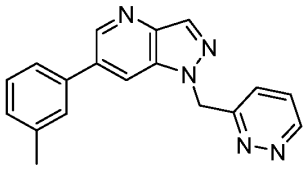
The title compound was made in an analogous manner to Intermediate 25 using 6-bromo-1-((5-(difluoromethoxy)pyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 17) and (3,4,5-trifluorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{19}H_{11}F_5N_4O$, 406.1; m/z found, 407.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.96 (d, J = 1.9 Hz, 1H), 8.80 – 8.71 (m, 1H), 8.52 – 8.46 (m, 1H), 8.46 – 8.38 (m, 2H), 8.01 – 7.86 (m, 2H), 7.69 – 7.61 (m, 1H), 7.29 (t, J = 73.2 Hz, 1H), 5.82 (s, 2H).

Example 254: 1-(Pyridazin-4-ylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine.



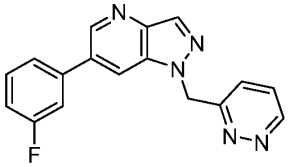
The title compound was prepared in a manner analogous to Example 1, using pyridazin-4-ylmethyl methanesulfonate (Intermediate 8) instead of 2-(chloromethyl)pyrimidine hydrochloride. MS (ESI): mass calcd. for $C_{18}H_{12}F_3N_5$, 355.1; m/z found, 356.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 9.19 – 9.17 (m, 1H), 9.16 – 9.13 (m, 1H), 8.99 (d, J = 1.9 Hz, 1H), 8.75 – 8.72 (m, 1H), 8.51 – 8.46 (m, 1H), 8.20 – 8.13 (m, 2H), 7.85 – 7.76 (m, 2H), 7.39 – 7.34 (m, 1H), 5.91 (s, 2H).

Example 255: 6-(m-Tolyl)-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine.



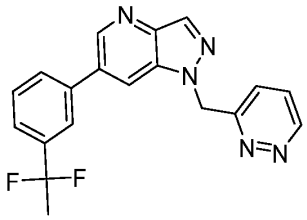
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-(pyridazin-3-ylmethyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 48) and *m*-tolylboronic acid. MS (ESI): mass calcd. for $C_{18}H_{15}N_5$, 301.1; m/z found, 302.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 9.16 (dd, J = 4.9, 1.6 Hz, 1H), 8.90 (d, J = 1.9 Hz, 1H), 8.57 – 8.54 (m, 1H), 8.41 – 8.38 (m, 1H), 7.68 – 7.64 (m, 2H), 7.64 – 7.59 (m, 1H), 7.46 – 7.40 (m, 2H), 7.30 – 7.25 (m, 1H), 6.10 (s, 2H), 2.42 (s, 3H).

Example 256: 6-(3-Fluorophenyl)-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine trifluoroacetate salt.



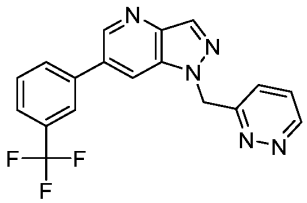
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-(pyridazin-3-ylmethyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 48) and (3-fluorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{17}H_{12}FN_5$, 305.1; m/z found, 306.0 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 9.17 (dd, J = 4.9, 1.6 Hz, 1H), 8.96 (d, J = 1.9 Hz, 1H), 8.68 – 8.66 (m, 1H), 8.43 – 8.41 (m, 1H), 7.76 – 7.69 (m, 2H), 7.67 (dd, J = 8.5, 4.9 Hz, 1H), 7.62 – 7.56 (m, 1H), 7.46 (dd, J = 8.5, 1.6 Hz, 1H), 7.32 – 7.27 (m, 1H), 6.10 (s, 2H).

Example 257: 6-[3-(1,1-Difluoroethyl)phenyl]-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine.



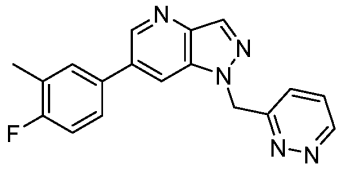
The title compound was made in an analogous manner to Example 8 using 6-(3-(1,1-difluoroethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 29) and 3-(chloromethyl)pyridazine. MS (ESI): mass calcd. for $C_{19}H_{15}F_2N_5$, 351.1; m/z found, 352.2 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 9.16 (dd, J = 4.9, 1.6 Hz, 1H), 8.96 (d, J = 1.9 Hz, 1H), 8.71 – 8.64 (m, 1H), 8.43 (s, 1H), 8.03 – 7.91 (m, 2H), 7.73 – 7.60 (m, 3H), 7.44 (dd, J = 8.5, 1.6 Hz, 1H), 6.12 (s, 2H), 2.06 (t, J = 18.9 Hz, 3H).

Example 258: 1-(Pyridazin-3-ylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine.



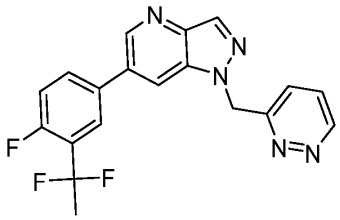
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-(pyridazin-3-ylmethyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 48) and (3-(trifluoromethyl)phenyl)boronic acid. MS (ESI): mass calcd. for $C_{18}H_{12}F_3N_5$, 355.1; m/z found, 356.0 $[M+H]^+$. ^1H NMR (600 MHz, DMSO-d_6) δ 9.16 (dd, J = 5.0, 1.6 Hz, 1H), 8.98 (d, J = 1.9 Hz, 1H), 8.75 – 8.73 (m, 1H), 8.44 – 8.43 (m, 1H), 8.20 – 8.15 (m, 2H), 7.84 – 7.76 (m, 2H), 7.66 (dd, J = 8.5, 4.9 Hz, 1H), 7.44 (dd, J = 8.5, 1.6 Hz, 1H), 6.12 (s, 2H).

Example 259: 6-(4-Fluoro-3-methyl-phenyl)-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine trifluoroacetate salt.



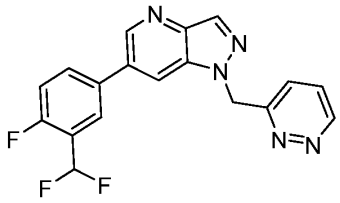
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-(pyridazin-3-ylmethyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 48) and (4-fluoro-3-methylphenyl)boronic acid. MS (ESI): mass calcd. for $C_{18}H_{14}FN_5$, 319.1; m/z found, 320.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 9.16 (dd, J = 5.0, 1.6 Hz, 1H), 8.89 (d, J = 1.9 Hz, 1H), 8.58 – 8.55 (m, 1H), 8.41 – 8.38 (m, 1H), 7.80 – 7.77 (m, 1H), 7.71 – 7.65 (m, 2H), 7.45 (dd, J = 8.5, 1.6 Hz, 1H), 7.33 – 7.28 (m, 1H), 6.09 (s, 2H), 2.35 – 2.32 (m, 3H).

Example 260: 6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine.



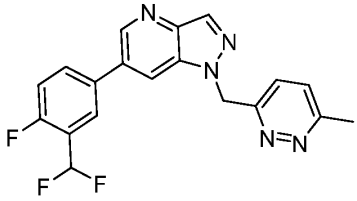
The title compound was made in an analogous manner to Example 8 using 6-(3-(1,1-difluoroethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 28) and 3-(chloromethyl)pyridazine. MS (ESI): mass calcd. for $C_{19}H_{14}F_3N_5$, 369.1; m/z found, 370.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 9.16 (dd, J = 4.9, 1.6 Hz, 1H), 8.93 (d, J = 1.9 Hz, 1H), 8.69 – 8.62 (m, 1H), 8.47 – 8.37 (m, 1H), 8.08 – 7.99 (m, 1H), 8.01 – 7.93 (m, 1H), 7.66 (dd, J = 8.5, 4.9 Hz, 1H), 7.55 (dd, J = 11.0, 8.6 Hz, 1H), 7.44 (dd, J = 8.6, 1.6 Hz, 1H), 6.11 (s, 2H), 2.09 (t, J = 19.1 Hz, 3H).

Example 261: 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine.



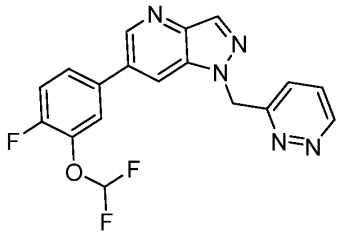
The title compound was made in an analogous manner to Example 8 using 3-(chloromethyl)pyridazine instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{18}H_{12}F_3N_5$, 355.1; m/z found, 356.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 9.20 – 9.13 (m, 1H), 8.93 (d, J = 1.9 Hz, 1H), 8.70 – 8.64 (m, 1H), 8.42 (s, 1H), 8.15 – 8.03 (m, 2H), 7.66 (dd, J = 8.5, 4.9 Hz, 1H), 7.62 – 7.51 (m, 1H), 7.44 (dd, J = 8.6, 1.6 Hz, 1H), 7.29 (t, J = 54.1 Hz, 1H), 6.10 (s, 2H).

Example 262: 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(6-methylpyridazin-3-yl)methyl]pyrazolo[4,3-b]pyridine.



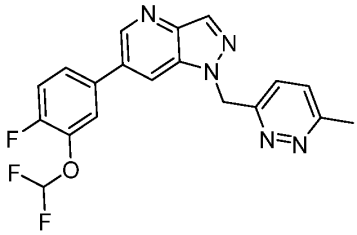
The title compound was made in an analogous manner to Example 8 using 3-(chloromethyl)-6-methylpyridazine (Intermediate 2) instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{19}H_{14}F_3N_5$, 369.1; m/z found, 370.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.91 (d, J = 2.0 Hz, 1H), 8.66 – 8.62 (m, 1H), 8.40 (d, J = 0.9 Hz, 1H), 8.11 – 8.04 (m, 2H), 7.60 – 7.54 (m, 1H), 7.51 (d, J = 8.6 Hz, 1H), 7.35 (d, J = 8.6 Hz, 1H), 7.29 (t, J = 54.2 Hz, 1H), 6.05 (s, 2H), 2.57 (s, 3H).

Example 263: 6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine.



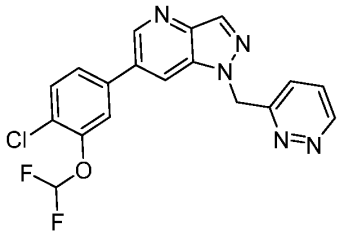
The title compound was prepared in a manner analogous to Example 12 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 3-(chloromethyl)pyridazine. MS (ESI): mass calcd. for $C_{18}H_{12}F_3N_5O$, 371.1; m/z found, 372.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 9.19 – 9.14 (m, 1H), 8.92 (d, J = 2.0 Hz, 1H), 8.65 – 8.60 (m, 1H), 8.44 – 8.40 (m, 1H), 7.86 (dd, J = 7.5, 2.2 Hz, 1H), 7.81 – 7.75 (m, 1H), 7.66 (dd, J = 8.5, 4.9 Hz, 1H), 7.59 (dd, J = 10.5, 8.6 Hz, 1H), 7.47 – 7.43 (m, 1H), 7.37 (t, J = 73.2 Hz, 1H), 6.09 (s, 2H).

Example 264: 6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(6-methylpyridazin-3-yl)methyl]pyrazolo[4,3-b]pyridine.



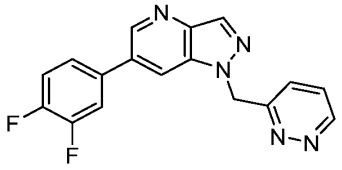
The title compound was made in an analogous manner to Example 8 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 3-(chloromethyl)-6-methylpyridazine (Intermediate 2). MS (ESI): mass calcd. for $C_{19}H_{14}F_3N_5O$, 385.1; m/z found, 386.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.92 (d, J = 1.9 Hz, 1H), 8.65 – 8.56 (m, 1H), 8.44 – 8.36 (m, 1H), 7.91 – 7.82 (m, 1H), 7.82 – 7.73 (m, 1H), 7.61 (dd, J = 8.7, 1.9 Hz, 1H), 7.52 (d, J = 8.6 Hz, 1H), 7.38 (t, J = 73.2 Hz, 1H), 7.35 (d, J = 8.6 Hz, 1H), 6.04 (s, 2H), 2.57 (s, 3H).

Example 265: 6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine.



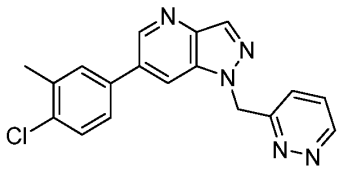
The title compound was made in an analogous manner to Example 8 using 6-(4-chloro-3-(difluoromethoxy)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 27) and 3-(chloromethyl)pyridazine. MS (ESI): mass calcd. for $C_{18}H_{12}ClF_2N_5O$, 387.1; m/z found, 388.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 9.19 – 9.12 (m, 1H), 8.95 (d, J = 2.0 Hz, 1H), 8.69 – 8.64 (m, 1H), 8.45 – 8.42 (m, 1H), 7.86 – 7.81 (m, 1H), 7.80 – 7.74 (m, 2H), 7.67 (dd, J = 8.5, 5.0 Hz, 1H), 7.47 – 7.45 (m, 1H), 7.44 (t, J = 73.8 Hz, 1H), 6.10 (s, 2H).

Example 266: 6-(3,4-Difluorophenyl)-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine.



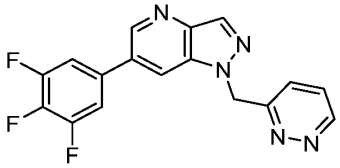
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-(pyridazin-3-ylmethyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 48) and (3,4-difluorophenyl)boronic acid. MS (ESI): mass calcd. for $C_{17}H_{11}F_2N_5$, 323.1; m/z found, 324.0 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 9.17 (dd, J = 4.9, 1.6 Hz, 1H), 8.94 (d, J = 1.9 Hz, 1H), 8.67 – 8.65 (m, 1H), 8.42 (d, J = 1.0 Hz, 1H), 8.00 (ddd, J = 12.2, 7.7, 2.3 Hz, 1H), 7.75 – 7.71 (m, 1H), 7.67 (dd, J = 8.5, 4.9 Hz, 1H), 7.65 – 7.59 (m, 1H), 7.46 (dd, J = 8.5, 1.6 Hz, 1H), 6.09 (s, 2H).

Example 267: 6-(4-Chloro-3-methyl-phenyl)-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine.



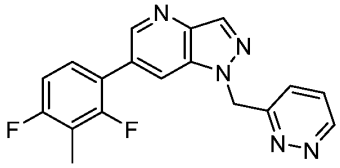
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-(pyridazin-3-ylmethyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 48) and (4-chloro-3-methylphenyl)boronic acid. MS (ESI): mass calcd. for $C_{18}H_{14}ClN_5$, 335.1; m/z found, 336.0 $[M+H]^+$. ^1H NMR (600 MHz, DMSO-d_6) δ 9.16 (dd, J = 4.9, 1.6 Hz, 1H), 8.91 (d, J = 1.9 Hz, 1H), 8.62 – 8.59 (m, 1H), 8.41 – 8.40 (m, 1H), 7.88 – 7.85 (m, 1H), 7.71 – 7.64 (m, 2H), 7.59 – 7.56 (m, 1H), 7.46 – 7.42 (m, 1H), 6.09 (s, 2H), 2.44 (s, 3H).

Example 268: 1-(Pyridazin-3-ylmethyl)-6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridine.



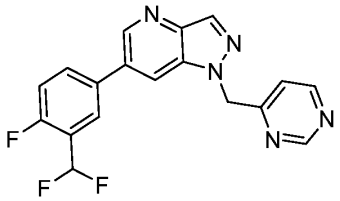
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-(pyridazin-3-ylmethyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 48) and (3,4,5-trifluorophenyl)boronic. MS (ESI): mass calcd. for $C_{17}H_{10}F_3N_5$, 341.1; m/z found, 342.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 9.17 (dd, J = 4.9, 1.6 Hz, 1H), 8.97 (d, J = 1.9 Hz, 1H), 8.73 – 8.70 (m, 1H), 8.43 (d, J = 1.0 Hz, 1H), 7.96 – 7.88 (m, 2H), 7.67 (dd, J = 8.5, 4.9 Hz, 1H), 7.45 (dd, J = 8.6, 1.6 Hz, 1H), 6.08 (s, 2H).

Example 269: 6-(2,4-Difluoro-3-methyl-phenyl)-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine trifluoroacetate salt.



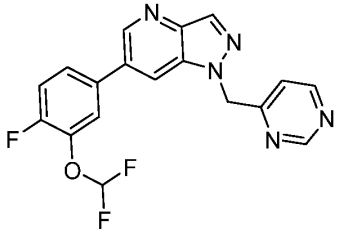
The title compound was prepared in a manner analogous to Example 4 using 6-bromo-1-(pyridazin-3-ylmethyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 48) and (2,4-difluoro-3-methylphenyl)boronic acid. MS (ESI): mass calcd. for $C_{18}H_{13}F_2N_5$, 337.1; m/z found, 338.0 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 9.17 (dd, J = 4.9, 1.6 Hz, 1H), 8.71 (t, J = 1.9 Hz, 1H), 8.46 – 8.44 (m, 1H), 8.44 – 8.42 (m, 1H), 7.67 (dd, J = 8.5, 4.9 Hz, 1H), 7.58 – 7.52 (m, 1H), 7.48 (dd, J = 8.5, 1.6 Hz, 1H), 7.28 – 7.22 (m, 1H), 6.08 (s, 2H), 2.26 – 2.24 (m, 3H).

Example 270: 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(pyrimidin-4-ylmethyl)pyrazolo[4,3-b]pyridine.



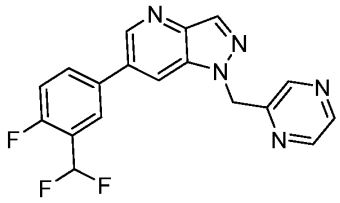
The title compound was made in an analogous manner to Example 8 using 4-(chloromethyl)pyrimidine instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{18}H_{12}F_3N_5$, 355.1; m/z found, 356.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 9.12 – 9.07 (m, 1H), 8.93 (d, J = 2.0 Hz, 1H), 8.76 – 8.71 (m, 1H), 8.65 – 8.60 (m, 1H), 8.47 – 8.42 (m, 1H), 8.11 – 8.04 (m, 2H), 7.61 – 7.52 (m, 1H), 7.28 (t, J = 54.1 Hz, 1H), 7.14 – 7.10 (m, 1H), 5.94 (s, 2H).

Example 271: 6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(pyrimidin-4-ylmethyl)pyrazolo[4,3-b]pyridine.



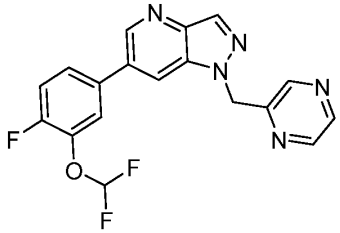
The title compound was made in an analogous manner to Example 8 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 4-(chloromethyl)pyrimidine. MS (ESI): mass calcd. for $C_{18}H_{12}F_3N_5O$, 371.1; m/z found, 372.2 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 9.14 – 9.06 (m, 1H), 8.96 – 8.90 (m, 1H), 8.73 (dd, J = 5.2, 1.7 Hz, 1H), 8.61 – 8.55 (m, 1H), 8.48 – 8.41 (m, 1H), 7.89 – 7.81 (m, 1H), 7.81 – 7.73 (m, 1H), 7.63 – 7.52 (m, 1H), 7.37 (t, J = 73.3 Hz, 1H), 7.17 – 7.08 (m, 1H), 5.93 (s, 2H).

Example 272: 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(pyrazin-2-ylmethyl)pyrazolo[4,3-b]pyridine.



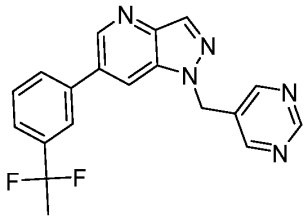
The title compound was made in an analogous manner to Example 8 using 2-(chloromethyl)pyrazine instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{18}H_{12}F_3N_5$, 355.1; m/z found, 356.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.91 (d, J = 1.9 Hz, 1H), 8.66 – 8.63 (m, 1H), 8.59 (d, J = 1.5 Hz, 1H), 8.59 – 8.56 (m, 1H), 8.56 – 8.54 (m, 1H), 8.39 (d, J = 1.0 Hz, 1H), 8.11 – 8.05 (m, 2H), 7.61 – 7.54 (m, 1H), 7.29 (t, J = 54.1 Hz, 1H), 5.97 (s, 2H).

Example 273: 6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(pyrazin-2-ylmethyl)pyrazolo[4,3-b]pyridine.



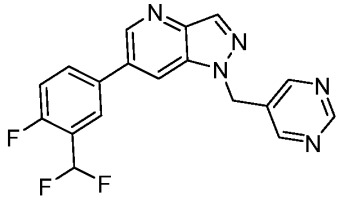
The title compound was made in an analogous manner to Example 8 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 2-(chloromethyl)pyrazine. MS (ESI): mass calcd. for $C_{18}H_{12}F_3N_5O$, 371.1; m/z found, 372.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.97 – 8.86 (m, 1H), 8.65 – 8.58 (m, 2H), 8.60 – 8.51 (m, 2H), 8.44 – 8.36 (m, 1H), 7.91 – 7.82 (m, 1H), 7.83 – 7.74 (m, 1H), 7.66 – 7.56 (m, 1H), 7.38 (t, J = 73.2 Hz, 1H), 5.96 (s, 2H).

Example 274: 6-[3-(1,1-Difluoroethyl)phenyl]-1-(pyrimidin-5-ylmethyl)pyrazolo[4,3-b]pyridine.



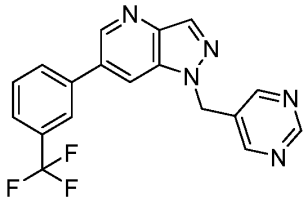
The title compound was prepared in a manner analogous to Example 12 using 6-(3-(1,1-difluoroethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 29) and 5-(chloromethyl)pyrimidine. MS (ESI): mass calcd. for $C_{19}H_{15}F_2N_5$, 351.1; m/z found, 352.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 9.13 (s, 1H), 8.98 – 8.91 (m, 1H), 8.82 (s, 2H), 8.77 – 8.70 (m, 1H), 8.46 – 8.40 (m, 1H), 8.05 – 7.93 (m, 2H), 7.74 – 7.62 (m, 2H), 5.85 (s, 2H), 2.07 (t, J = 18.9 Hz, 3H).

Example 275: 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(pyrimidin-5-ylmethyl)pyrazolo[4,3-b]pyridine.



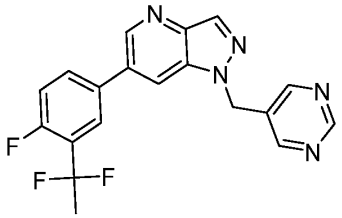
The title compound was made in an analogous manner to Example 8 using 5-(chloromethyl)pyrimidine instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{18}H_{12}F_3N_5$, 355.1; m/z found, 356.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 9.13 (s, 1H), 8.91 (d, J = 1.9 Hz, 1H), 8.82 (s, 2H), 8.76 – 8.70 (m, 1H), 8.43 (s, 1H), 8.15 – 8.05 (m, 2H), 7.64 – 7.54 (m, 1H), 7.31 (t, J = 54.1 Hz, 1H), 5.84 (s, 2H).

Example 276: 1-(Pyrimidin-5-ylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine hydrochloride salt.



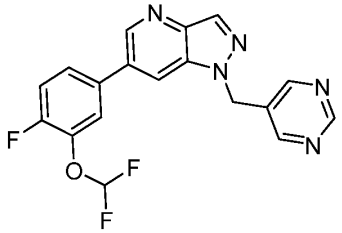
The title compound was prepared in a manner analogous to Example 6, using 5-pyrimidinemethanol instead of 4-(hydroxymethyl)pyrimidine. ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.14 (s, 1 H), 9.00 (d, J=1.73 Hz, 1 H), 8.92 – 8.79 (m, 3 H), 8.46 (s, 1 H), 8.28 – 8.15 (m, 2 H), 7.74 - 7.90 – 7.74 (m, 2 H), 5.87 (s, 2 H).

Example 277: 6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-(pyrimidin-5-ylmethyl)pyrazolo[4,3-b]pyridine.



The title compound was prepared in a manner analogous to Example 12 using 6-(3-(1,1-difluoroethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 28) and 5-(chloromethyl)pyrimidine. MS (ESI): mass calcd. for $C_{19}H_{14}F_3N_5$, 369.1; m/z found, 370.1 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.13 (s, 1H), 8.91 (d, J = 1.9 Hz, 1H), 8.82 (s, 2H), 8.75 – 8.68 (m, 1H), 8.45 – 8.39 (m, 1H), 8.09 – 8.01 (m, 1H), 8.02 – 7.95 (m, 1H), 7.57 (dd, J = 11.0, 8.6 Hz, 1H), 5.84 (s, 2H), 2.10 (t, J = 19.1 Hz, 3H).

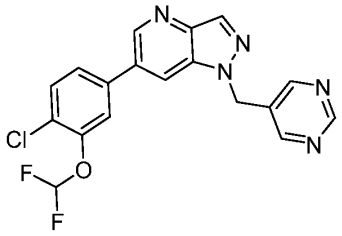
Example 278: 6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(pyrimidin-5-ylmethyl)pyrazolo[4,3-b]pyridine.



The title compound was prepared in a manner analogous to Example 12 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 5-(chloromethyl)pyrimidine. MS (ESI): mass calcd. for $C_{18}H_{12}F_3N_5O$, 371.1; m/z found, 372.1 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.13 (s, 1H), 8.91 (d, J = 1.9 Hz, 1H), 8.82 (s, 2H),

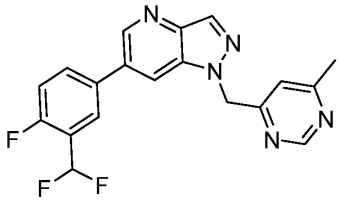
8.72 – 8.66 (m, 1H), 8.44 – 8.39 (m, 1H), 7.92 – 7.85 (m, 1H), 7.84 – 7.75 (m, 1H), 7.58 (dd, *J* = 10.4, 8.7 Hz, 1H), 7.38 (t, *J* = 73.2 Hz, 1H), 5.83 (s, 2H).

Example 279: 6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-(pyrimidin-5-ylmethyl)pyrazolo[4,3-b]pyridine.



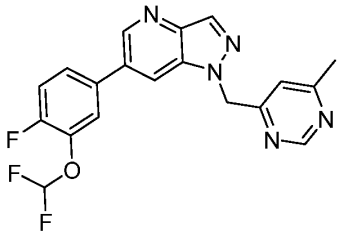
The title compound was prepared in a manner analogous to Example 12 using 6-(4-chloro-3-(difluoromethoxy)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 27) and 5-(chloromethyl)pyrimidine. MS (ESI): mass calcd. for $C_{18}H_{12}ClF_2N_5O$, 387.1; m/z found, 388.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-*d*$_6$) δ 9.13 (s, 1H), 8.94 (d, *J* = 1.9 Hz, 1H), 8.82 (s, 2H), 8.77 – 8.69 (m, 1H), 8.47 – 8.40 (m, 1H), 7.89 – 7.83 (m, 1H), 7.82 – 7.76 (m, 2H), 7.44 (t, *J* = 73.2 Hz, 1H), 5.84 (s, 2H).

Example 280: 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(6-methylpyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine.



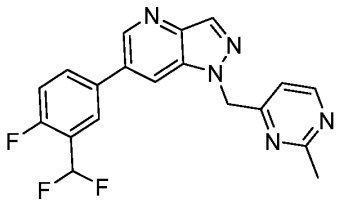
The title compound was made in an analogous manner to Example 8 using 4-(chloromethyl)-6-methylpyrimidine instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{19}H_{14}F_3N_5$, 369.1; m/z found, 370.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-*d*$_6$) δ 8.99 – 8.88 (m, 2H), 8.64 – 8.58 (m, 1H), 8.47 – 8.40 (m, 1H), 8.13 – 8.03 (m, 2H), 7.62 – 7.52 (m, 1H), 7.29 (t, *J* = 54.1 Hz, 1H), 7.04 – 6.98 (m, 1H), 5.87 (s, 2H), 2.39 (s, 3H).

Example 281: 6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(6-methylpyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine.



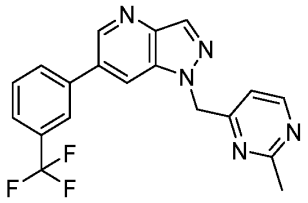
The title compound was made in an analogous manner to Example 8 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 4-(chloromethyl)-6-methylpyrimidine. MS (ESI): mass calcd. for $C_{19}H_{14}F_3N_5O$, 385.1; m/z found, 386.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.95 – 8.93 (m, 1H), 8.93 – 8.92 (m, 1H), 8.59 – 8.55 (m, 1H), 8.43 (d, J = 1.0 Hz, 1H), 7.85 (dd, J = 7.6, 2.3 Hz, 1H), 7.81 – 7.75 (m, 1H), 7.58 (dd, J = 10.5, 8.6 Hz, 1H), 7.36 (t, J = 73.2 Hz, 1H), 7.05 – 6.99 (m, 1H), 5.86 (s, 2H), 2.40 (s, 3H).

Example 282: 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(2-methylpyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine.



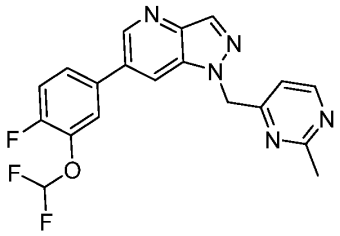
The title compound was made in an analogous manner to Example 8 using 4-(chloromethyl)-2-methylpyrimidine instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{19}H_{14}F_3N_5$, 369.1; m/z found, 370.2 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.94 (d, J = 1.9 Hz, 1H), 8.65 – 8.61 (m, 1H), 8.58 (d, J = 5.2 Hz, 1H), 8.48 – 8.43 (m, 1H), 8.13 – 8.03 (m, 2H), 7.62 – 7.51 (m, 1H), 7.28 (t, J = 54.1 Hz, 1H), 6.71 (d, J = 5.2 Hz, 1H), 5.87 (s, 2H), 2.58 (s, 3H).

Example 283: 1-[(2-Methylpyrimidin-4-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine.



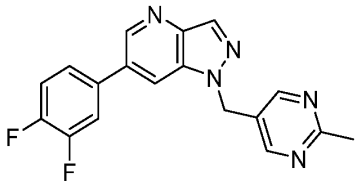
The title compound was prepared in a manner analogous to Example 6, using (2-methylpyrimidin-4-yl)methanol instead of 4-(hydroxymethyl)pyrimidine. MS (ESI): mass calcd. for $C_{19}H_{14}F_3N_5$, 369.1; m/z found, 370.1 $[M+H]^+$.

Example 284: 6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(2-methylpyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine.



The title compound was made in an analogous manner to Example 8 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 4-(chloromethyl)-2-methylpyrimidine. MS (ESI): mass calcd. for $C_{19}H_{14}F_3N_5O$, 385.1; m/z found, 386.1 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.94 (d, J = 1.9 Hz, 1H), 8.63 – 8.53 (m, 2H), 8.50 – 8.39 (m, 1H), 7.89 – 7.82 (m, 1H), 7.82 – 7.74 (m, 1H), 7.58 (dd, J = 10.1, 9.0 Hz, 1H), 7.36 (t, J = 73.2 Hz, 1H), 6.71 (d, J = 5.2 Hz, 1H), 5.86 (s, 2H), 2.58 (s, 3H).

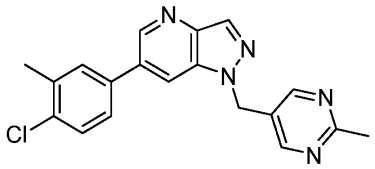
Example 285: 6-(3,4-Difluorophenyl)-1-[(2-methylpyrimidin-5-yl)methyl]pyrazolo[4,3-b]pyridine trifluoroacetate salt.



The title compound was prepared in a manner analogous to Example 4 using (3,4-difluorophenyl)boronic acid instead of (3-(trifluoromethyl)phenyl)boronic acid. MS (ESI): mass

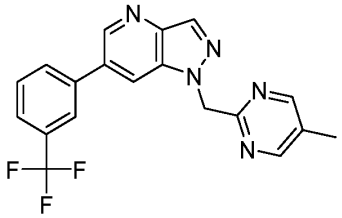
calcd. for $C_{18}H_{13}F_2N_5$, 337.1; m/z found, 338.0 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.92 (d, J = 1.9 Hz, 1H), 8.75 – 8.69 (m, 3H), 8.42 – 8.38 (m, 1H), 8.05 – 7.99 (m, 1H), 7.78 – 7.72 (m, 1H), 7.68 – 7.60 (m, 1H), 5.76 (s, 2H), 2.58 (s, 3H).

Example 286: 6-(4-Chloro-3-methyl-phenyl)-1-[(2-methylpyrimidin-5-yl)methyl]pyrazolo[4,3-b]pyridine.



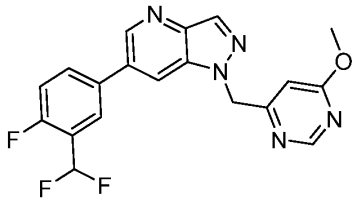
The title compound was prepared in a manner analogous to Example 4 using (4-chloro-3-methylphenyl)boronic acid instead of (3-(trifluoromethyl)phenyl)boronic acid. MS (ESI): mass calcd. for $C_{19}H_{16}ClN_5$, 349.1; m/z found, 350.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.89 (d, J = 1.9 Hz, 1H), 8.72 (s, 2H), 8.68 – 8.66 (m, 1H), 8.39 – 8.38 (m, 1H), 7.89 – 7.86 (m, 1H), 7.73 – 7.69 (dd, J = 8.4, 2.3 Hz, 1H), 7.61 - 7.56 (m, 1H), 5.77 (s, 2H), 2.57 (s, 3H), 2.45 (s, 3H).

Example 287: 1-[(5-Methylpyrimidin-2-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine.



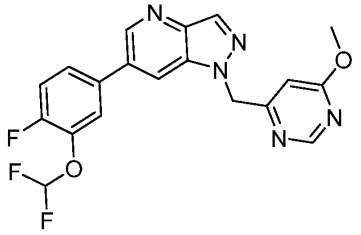
The title compound was prepared in a manner analogous to Example 1, using 2-(chloromethyl)-5-methylpyrimidine instead of 2-(chloromethyl)pyrimidine hydrochloride. MS (ESI): mass calcd. for $C_{19}H_{14}F_3N_5$, 369.1; m/z found, 370.2 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.96 (d, J = 1.9 Hz, 1H), 8.64 – 8.62 (m, 1H), 8.58 – 8.55 (m, 2H), 8.38 – 8.35 (m, 1H), 8.18 – 8.13 (m, 2H), 7.84 – 7.74 (m, 2H), 5.97 (s, 2H), 2.22 (s, 3H).

Example 288: 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(6-methoxypyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine.



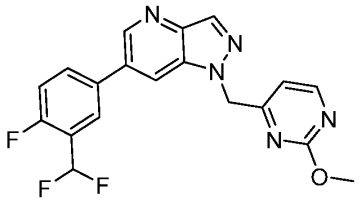
The title compound was made in an analogous manner to Example 8 using 4-(chloromethyl)-6-methoxypyrimidine instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{19}H_{14}F_3N_5O$, 385.1; m/z found, 386.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.92 (d, J = 1.9 Hz, 1H), 8.70 (d, J = 1.1 Hz, 1H), 8.63 – 8.59 (m, 1H), 8.42 (d, J = 1.0 Hz, 1H), 8.12 – 8.04 (m, 2H), 7.60 – 7.53 (m, 1H), 7.28 (t, J = 54.1 Hz, 1H), 6.51 – 6.49 (m, 1H), 5.83 (s, 2H), 3.88 (s, 3H).

Example 289: 6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(6-methoxypyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine.



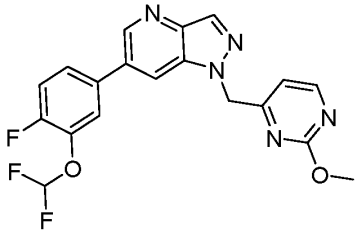
The title compound was made in an analogous manner to Example 8 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 4-(chloromethyl)-6-methoxypyrimidine. MS (ESI): mass calcd. for $C_{19}H_{14}F_3N_5O_2$, 401.1; m/z found, 402.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.92 (d, J = 2.0 Hz, 1H), 8.70 (d, J = 1.1 Hz, 1H), 8.59 – 8.54 (m, 1H), 8.42 (d, J = 1.0 Hz, 1H), 7.85 (dd, J = 7.6, 2.3 Hz, 1H), 7.80 – 7.75 (m, 1H), 7.58 (dd, J = 10.5, 8.6 Hz, 1H), 7.37 (t, J = 73.2 Hz, 1H), 6.52 – 6.49 (m, 1H), 5.82 (s, 2H), 3.88 (s, 3H).

Example 290: 6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(2-methoxypyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine.



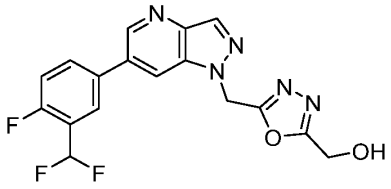
The title compound was made in an analogous manner to Example 8 using 4-(chloromethyl)-2-methoxypyrimidine instead of 2-(chloromethyl)-5-methyl-1,3-oxazole. MS (ESI): mass calcd. for $C_{19}H_{14}F_3N_5O$, 385.1; m/z found, 386.2 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.93 (d, J = 1.9 Hz, 1H), 8.65 – 8.59 (m, 1H), 8.51 (d, J = 5.0 Hz, 1H), 8.47 – 8.40 (m, 1H), 8.12 – 8.03 (m, 2H), 7.61 – 7.51 (m, 1H), 7.28 (t, J = 54.1 Hz, 1H), 6.66 (d, J = 5.0 Hz, 1H), 5.86 (s, 2H), 3.79 (s, 3H).

Example 291: 6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(2-methoxypyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine.



The title compound was made in an analogous manner to Example 8 using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 26) and 4-(chloromethyl)-2-methoxypyrimidine. MS (ESI): mass calcd. for $C_{19}H_{14}F_3N_5O_2$, 401.1; m/z found, 402.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.93 (d, J = 1.9 Hz, 1H), 8.61 – 8.55 (m, 1H), 8.51 (d, J = 5.0 Hz, 1H), 8.46 – 8.42 (m, 1H), 7.88 – 7.81 (m, 1H), 7.81 – 7.74 (m, 1H), 7.59 (dd, J = 10.2, 8.7 Hz, 1H), 7.36 (t, J = 73.2 Hz, 1H), 6.66 (d, J = 5.0 Hz, 1H), 5.85 (s, 2H), 3.79 (s, 3H).

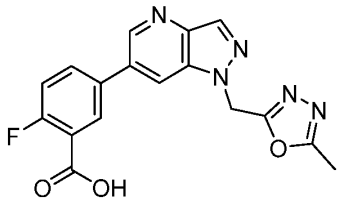
Example 292: (5-((6-(3-(Difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-1,3,4-oxadiazol-2-yl)methanol.



Step A. 2-(((*tert*-Butyldimethylsilyl)oxy)methyl)-5-((6-(3-(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-1,3,4-oxadiazole: 6-(3-(Difluoromethyl)-4-fluorophenyl)-1*H*-pyrazolo[4,3-*b*]pyridine (Intermediate 65, 187 mg, 0.709 mmol), 2-(((*tert*-butyldimethylsilyl)oxy)methyl)-5-(chloromethyl)-1,3,4-oxadiazole (205 mg, 0.780 mmol), and cesium carbonate (347 mg, 1.06 mmol) were taken up in DMF (3 mL) and stirred at r.t. for one hour. The reaction mixture was partitioned between water and ethyl acetate, the organic layer was washed 2x with water, dried ($MgSO_4$) and concentrated. Purification (FCC, SiO_2, 0-100% ethyl acetate/hexanes) afforded 310 mg (0.633 mmol, 89% yield) of the titled product. MS (ESI): mass calcd. for $C_{23}H_{26}F_3N_5O_2Si$, 489.2; m/z found, 490.2 $[M+H]^+$.

Step B. (5-((6-(3-(Difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-1,3,4-oxadiazol-2-yl)methanol: 2-(((*tert*-Butyldimethylsilyl)oxy)methyl)-5-((6-(3-(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-1,3,4-oxadiazole (263 mg, 0.537 mmol) and cesium fluoride (816 mg, 5.37 mmol) were taken up in MeCN (10 mL) and stirred overnight at r.t. The reaction mixture was diluted with methanol, concentrated onto Celite®, and purified on silica gel (50-100% ethyl acetate/hexanes) followed by reverse phase HPLC (METHOD F) to obtain 66.7 mg (0.178 mmol, 33% yield) of the desired product. MS (ESI): mass calcd. for $C_{17}H_{12}F_3N_5O_2$, 375.1; m/z found, 376.1 $[M+H]^+$. ^1H NMR (400 MHz, MeOH-d_4) δ 8.86 (d, J = 1.9 Hz, 1H), 8.48 (dd, J = 1.9, 1.0 Hz, 1H), 8.31 (d, J = 1.0 Hz, 1H), 8.06 – 7.92 (m, 2H), 7.50 – 7.39 (m, 1H), 7.08 (t, J = 54.6 Hz, 1H), 6.07 (s, 2H), 4.69 (s, 2H).

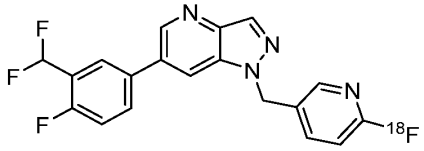
Example 293: 2-Fluoro-5-(1-((5-methyl-1,3,4-oxadiazol-2-yl)methyl)-1H-pyrazolo[4,3-b]pyridin-6-yl)benzoic acid.



Step A. Ethyl 2-fluoro-5-(1-((5-methyl-1,3,4-oxadiazol-2-yl)methyl)-1H-pyrazolo[4,3-b]pyridin-6-yl)benzoate: To a solution of 2-((6-bromo-1*H*-pyrazolo[4,3-*b*]pyridin-1-yl)methyl)-5-methyl-1,3,4-oxadiazole (Intermediate 19, 120 mg, 0.408 mmol) in dioxane (5 mL) were added 3-ethoxycarbonyl-4-fluorophenylboronic acid (115 mg, 0.530 mmol), RuPhos Pd G3 (17 mg, 0.020 mmol), and cesium carbonate (399 mg, 1.22 mmol). The reaction mixture was stirred at 100 °C overnight, allowed to cool to r.t., and partitioned between water and DCM. The aqueous layer was extracted 2x with DCM and the combined organic layers were concentrated and purified on silica gel (0-100% ethyl acetate/hexanes) to obtain 70 mg (0.184 mmol, 45% yield) of the desired product. MS (ESI): mass calcd. for $C_{19}H_{16}FN_5O_3$, 381.1; m/z found, 382.2 $[M+H]^+$.

Step B. 2-Fluoro-5-(1-((5-methyl-1,3,4-oxadiazol-2-yl)methyl)-1H-pyrazolo[4,3-b]pyridin-6-yl)benzoic acid: Ethyl 2-fluoro-5-(1-((5-methyl-1,3,4-oxadiazol-2-yl)methyl)-1H-pyrazolo[4,3-b]pyridin-6-yl)benzoate (70 mg, 0.184 mmol) was dissolved in MeOH (1 mL) and 1N aq. NaOH solution (1 mL) was added. The mixture was stirred at room temperature for one hour, acidified carefully with 1N aq. HCl, and extracted 5x with DCM. The combined organics were concentrated and purified by reverse phase HPLC (METHOD G) to obtain 2.5 mg (0.0071 mmol, 4% yield) of the title compound. MS (ESI): mass calcd. for $C_{17}H_{12}FN_5O_3$, 353.1; m/z found, 354.1 $[M+H]^+$. ^{1}H NMR (400 MHz, chloroform-*d*) δ 8.80 (d, J = 1.9 Hz, 1H), 8.31 (d, J = 1.0 Hz, 1H), 8.24 (dd, J = 6.7, 2.6 Hz, 1H), 8.02 (s, 1H), 7.82 – 7.75 (m, 1H), 7.31 – 7.23 (m, 1H), 5.80 (s, 2H), 2.44 (s, 3H). Carboxylic acid proton not observed.

Example 294: 6-(3-(Difluoromethyl)-4-fluorophenyl)-1-((6-(fluoro-18F)pyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine.

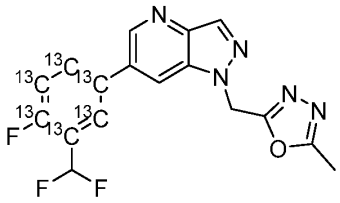


[^{18}F]fluoride in a shipping vial (obtained from the cyclotron facility) was transferred onto and trapped on an ion exchange cartridge. It was then eluted into the reaction vessel (RV1) of a Synthra RNPlus ® module with a solution of potassium bicarbonate (1.09 mg, 0.011 mmol) and Kryptofix 222 (7.2 mg, 0.019 mmol) in 0.8 mL of acetonitrile/water (6/2,

v/v). The solvent was evaporated under a stream of Nitrogen at 85 °C and under vacuum. Anhydrous CH_3CN (0.5 mL) was added and the above process was repeated with the temperature increased to 110 °C for 3.5 min. The reaction vial was then cooled to 70°C before a solution of (3.0 mg, 0.0069 mmol) of 1-((6-bromopyridin-3-yl)methyl)-6-(3-(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 68) in anhydrous NMP (0.7 mL) was added to reaction vessel. The reaction mixture was heated at 120 °C for 10 min. The reactor was then cooled to 40 °C and diluted with water (4.3 mL) and the contents was transferred into the HPLC injector loop for purification.

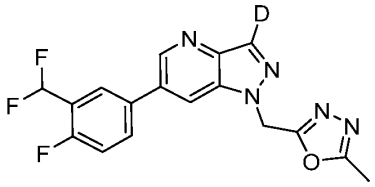
Purification was performed by HPLC using a semi-preparative Eclipse XDB-C18 column (5 µm, 9.4 mm x 250 mm) with a mixture of 10 mM NH4OAc and MeCN (53:47 v/v) at a flow rate of 4 mL/min with UV detection at 254 nm. The purified radiotracer solution was diluted with 30 mL of water and passed through a SepPak Light C-18 cartridge. The C-18 cartridge was further washed with10 mL of water before 0.5 mL EtOH was used to elute the tracer. The tracer solution was further diluted with 4.5 mL of saline. The final formulation contains an ethanol concentration of 10%, suitable for intravenous injection (IV).

Example 295: 2-((6-(3-(Difluoromethyl)-4-fluorophenyl-1,2,3,4,5,6-$^{13}C_6$)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-5-methyl-1,3,4-oxadiazole.



The title compound was prepared in a manner analogous to Example 10 using 2-(3-(difluoromethyl)-4-fluorophenyl-1,2,3,4,5,6-$^{13}C_6$)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Intermediate 67) and Intermediate 19: 2-((6-Bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-5-methyl-1,3,4-oxadiazole. MS (ESI): mass calcd. for $C_{11}{}^{13}C_6H_{12}F_3N_5O$, 365.12; m/z found, 3668.1 $[M+H]^+$.

Example 296: 2-[[3-Deuterio-6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole.



Step A. 2-((3-Bromo-6-(3-(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-5-methyl-1,3,4-oxadiazole. The title compound was prepared in a manner analogous to Example 8 using 3-bromo-6-(3-(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 66) and 2-(chloromethyl)-5-methyl-1,3,4-oxadiazole. MS (ESI): mass calcd. for $C_{17}H_{11}BrF_3N_5O$, 437.0; m/z found, 438.1 $[M+H]^+$. ^1H NMR (500 MHz, Chloroform-*d*) δ 8.85 (d, *J* = 1.9 Hz, 1H), 8.00 (d, *J* = 1.8 Hz, 1H), 7.85 – 7.82 (m, 1H), 7.75 – 7.70 (m, 1H), 7.34 – 7.28 (m, 1H), 6.98 (t, *J* = 54.8 Hz, 1H), 5.80 (s, 2H), 2.51 (s, 3H).

Step B. 2-[[3-Deuterio-6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole. Pd/C (10%, 36 mg, 0.03 mmol) was added to a mixture of 2-((3-bromo-6-(3-(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-5-methyl-1,3,4-oxadiazole (15 mg, 0.03 mmol) and DIPEA (59 µL. 0.3 mmol) in DMF (1 mL) at room temperature. Upon addition of Pd/C, the reaction mixture was purged with D_2 gas (99.96 atom% D). After 10 minutes, the reaction mixture was purged with nitrogen and filtered. The filtrate was concentrated under reduced pressure and purification (FCC, SiO_2, 0-99% EtOAc in hexanes) afforded the title compound (6 mg, 47%, H:D 0.09:1.00). MS (ESI): mass calcd. for $C_{17}H_{11}DF_3N_5O$, 360.1; m/z found, 361.1 $[M+H]^+$. ^1H NMR (500 MHz, Chloroform-*d*) δ 8.82 (d, *J* = 1.9 Hz, 1H), 7.99 (d, *J* = 1.9 Hz, 1H), 7.87 – 7.83 (m, 1H), 7.76 – 7.71 (m, 1H), 7.33 – 7.27 (m, 1H), 6.98 (t, *J* = 54.8 Hz, 1H), 5.83 (s, 2H), 2.50 (s, 3H).

BIOLOGICAL ASSAYS

Effects of Test Articles on Cloned Human NR1/GluN2B Ion Channels Expressed in Mammalian Cells

NMDA receptors are ion channels that are highly permeable to Ca^{2+} ions, rendering it possible to monitor NMDA receptor function using cell-based calcium flux assay. In this assay, co-agonists

glutamate and glycine are added to cells heterologously expressing human GluN1/ GluN2B NMDA receptors to initiate cellular Ca^{2+} influx. The time course of the changes in intracellular calcium is measured using a fluorescent dye and a FLIPR (Fluorometric Imaging Plate Reader) device.

Twenty-four hours before measurements, the expression of the NMDA receptors in the stable cell line is induced with Tet-On inducible system in the presence of a non-selective NMDA receptor blocker. On the day of the experiment, cell culture media is carefully washed, and the cells are loaded with Calcium 5 Dye Kit (Molecular Devices) in dye loading buffer containing 137 mM NaCl, 4 mM KCl, 2 mM $CaCl_2$, 0.5 mM $MgCl_2$ (standard assay) or 1.5 mM $MgCl_2$ (HTS assay), 10 mM HEPES and 5 mM D-glucose; pH 7.4. After 1h incubation at the room temperature, the dye is washed away with the assay buffer (137 mM NaCl (standard assay) or 150 mM (HTS assay), 4 mM KCl (standard assay) or 3 mM (HTS assay), 2 mM $CaCl_2$, 0.01 mM EDTA, 10 mM HEPES and 5 mM D-glucose; pH 7.4) In the FLIPR TETRA reader, various concentrations of the test compounds are added to the cells for 5 min while fluorescence is monitored to detect potential agonist activity. Next, co-agonists, glutamate and glycine are added for another 5 minutes. The concentration of glutamate corresponding to ~EC_{40} (standard assay) or EC_{40} (HTS assay) is used to maximize the assay's signal window and ability to detect NMDA receptor antagonists and negative allosteric modulators. A saturating concentration (10 μM) of glycine is also present in the assay. A non-selective NMDA receptor antagonist, (+)MK-801 is used as a positive control for antagonist activity. The fluorescent signal in the presence of test compounds is quantified and normalized to the signal defined by the appropriate control wells. Table 3.

Ex #	Compound Name	GluN2B IC50 (μM)
1	1-(Pyrimidin-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	0.800
2	1-[(5-Bromo-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	0.329
3	5-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;	0.483
4	1-[(2-Methylpyrimidin-5-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	4.670

Ex #	Compound Name	GluN2B IC50 (μM)
5	1-(Pyrazin-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	0.237
6	1-(Pyrimidin-4-ylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	0.819
7	2-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole;	0.748
8	2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-oxazole;	0.028
9	2-[[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-oxazole;	0.078
10	2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;	0.019
11	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(1H-pyrazol-4-ylmethyl)pyrazolo[4,3-b]pyridine;	0.486
12	6-[3-(1,1-Difluoroethyl)phenyl]-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;	0.026
13	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-methyl-4H-1,2,4-triazol-3-yl)methyl]pyrazolo[4,3-b]pyridine;	1.960
14	1-[(3-Methyl-1H-pyrazol-5-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	4.740
15	5-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-N-methyl-1,3,4-thiadiazol-2-amine;	>2.99
16	5-[[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazol-2-amine;	1.050
17	5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazol-2-ol;	0.064
18	5-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazol-2-amine;	3.550
19	N-(5-((6-(3-(Difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-1,3,4-thiadiazol-2-yl)acetamide;	>2.99
20	3-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,2,4-oxadiazole;	0.751

Ex #	Compound Name	GluN2B IC50 (μM)
21	1-Benzyl-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	3.280
22	1-[(3-Fluorophenyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	1.820
23	3-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]benzonitrile;	0.400
24	1-[(4-Methoxyphenyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	7.930
25	6-[3-(Trifluoromethyl)phenyl]-1-[[4-(trifluoromethyl)phenyl]methyl]pyrazolo[4,3-b]pyridine;	>10
26	3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]benzonitrile;	0.062
27	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(3,5-difluorophenyl)methyl]pyrazolo[4,3-b]pyridine;	0.394
28	3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-fluoro-benzonitrile;	0.125
29	3-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]benzonitrile;	0.065
30	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(3,5-difluorophenyl)methyl]pyrazolo[4,3-b]pyridine;	0.536
31	3-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-fluoro-benzonitrile;	0.389
32	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-methyl-2-thienyl)methyl]pyrazolo[4,3-b]pyridine;	>2.99
33	6-(3-(Difluoromethyl)-4-fluorophenyl)-1-((5-fluorothiophen-2-yl)methyl)-1H-pyrazolo[4,3-b]pyridine;	1.030
34	5-((6-(3-(Difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)thiophene-2-carbonitrile;	0.353
35	6-[3-(1,1-Difluoroethyl)phenyl]-1-(1H-pyrazol-4-ylmethyl)pyrazolo[4,3-b]pyridine;	0.648
36	1-[(1-Methylimidazol-4-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	0.668

Ex #	Compound Name	GluN2B IC50 (μM)
37	1-[(2,5-Dimethylpyrazol-3-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	3.950
38	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(1H-pyrazol-4-ylmethyl)pyrazolo[4,3-b]pyridine;	0.226
39	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(1-methylpyrazol-3-yl)methyl]pyrazolo[4,3-b]pyridine;	0.271
40	6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-(1H-pyrazol-4-ylmethyl)pyrazolo[4,3-b]pyridine;	0.825
41	6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-(1H-pyrazol-4-ylmethyl)pyrazolo[4,3-b]pyridine;	0.423
42	5-[[6-(4-Fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-isoxazole;	0.475
43	3-[[6-(4-Fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-isoxazole;	0.139
44	3-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]isoxazole;	0.165
45	3-[[6-[3-(1,1-Difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-isoxazole;	0.044
46	4-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]oxazole;	0.538
47	5-Methyl-3-[[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]isoxazole;	0.148
48	5-[[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-2-methyl-oxazole;	0.113
49	2-[[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-oxazole;	0.053
50	5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]isoxazole;	0.031
51	3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]isoxazole;	0.023
52	5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-isoxazole;	0.022

Ex #	Compound Name	GluN2B IC50 (μM)
53	3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-isoxazole;	0.018
54	5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-2-methyl-oxazole;	0.133
55	4-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-2-methyl-oxazole;	0.285
56	3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-4-methyl-isoxazole;	0.056
57	4-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3,5-dimethyl-isoxazole;	0.082
58	3-[[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-isoxazole;	0.158
59	3-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-isoxazole;	0.061
60	5-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-2-methyl-oxazole;	0.559
61	2-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-oxazole;	0.160
62	3-[[6-[4-Chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-isoxazole;	0.159
63	5-[[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-2-methyl-oxazole;	0.268
64	5-Methyl-3-[[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]isothiazole;	2.240
65	2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-thiazole;	0.084
66	2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-4-methyl-thiazole;	0.410
67	4-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-2-methyl-thiazole;	0.466
68	2-[[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-thiazole;	0.265

Ex #	Compound Name	GluN2B IC50 (μM)
69	2-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-thiazole;	0.104
70	2-[[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-thiazole;	0.350
71	1-[(1-Methyl-1,2,4-triazol-3-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	0.891
72	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(1-methyltriazol-4-yl)methyl]pyrazolo[4,3-b]pyridine;	0.827
73	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(1-methyl-1,2,4-triazol-3-yl)methyl]pyrazolo[4,3-b]pyridine;	0.383
74	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(4-methyl-1,2,4-triazol-3-yl)methyl]pyrazolo[4,3-b]pyridine;	0.111
75	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(4,5-dimethyl-1,2,4-triazol-3-yl)methyl]pyrazolo[4,3-b]pyridine;	0.139
76	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-ethyl-4-methyl-1,2,4-triazol-3-yl)methyl]pyrazolo[4,3-b]pyridine;	3.830
77	2-[[6-(5-Chloro-2-thienyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;	0.089
78	2-Methyl-5-[[6-[5-(trifluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole;	0.143
79	2-[[6-[5-(Difluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;	0.153
80	5-[[6-(4-Fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;	0.957
81	5-[[6-(3-Methoxyphenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;	2.310
82	2-[[6-[3-(1,1-Difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;	0.160
83	2-[[6-[3-(1,1-Difluoroethyl)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;	0.126
84	3-Methyl-5-[[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,2,4-oxadiazole;	0.293

Ex #	Compound Name	GluN2B IC50 (μM)
85	2-Methyl-5-[[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole;	0.143
86	5-Methyl-3-[[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,2,4-oxadiazole;	0.202
87	5-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,2,4-oxadiazole;	0.383
88	2-Methyl-5-[[6-[2-(trifluoromethyl)-4-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole;	0.467
89	2-[[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;	0.037
90	2-[[3-Fluoro-6-(4-fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;	0.033
91	2-[[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-(trifluoromethyl)-1,3,4-oxadiazole;	0.145
92	2-[[6-(3-Chloro-4-fluoro-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;	0.090
93	2-[[6-(3-Chloro-4-fluoro-phenyl)-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;	0.087
94	2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole;	0.058
95	5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;	0.040
96	2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;	0.038
97	3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,2,4-oxadiazole;	0.041
98	3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-4-methyl-1,2,5-oxadiazole;	0.034
99	2-Cyclopropyl-5-[[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole;	0.070
100	2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-isopropyl-1,3,4-oxadiazole;	0.550

Ex #	Compound Name	GluN2B IC50 (μM)
101	5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-N,N-dimethyl-1,3,4-oxadiazol-2-amine;	>2.99
102	2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-(trifluoromethyl)-1,3,4-oxadiazole;	0.049
103	2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-phenyl-1,3,4-oxadiazole;	>2.99
104	2-[[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;	0.244
105	2-[[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;	0.367
106	2-[[6-[4-Chloro-3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;	0.115
107	2-[[6-[4-Chloro-3-(difluoromethyl)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;	0.347
108	5-[[6-[3-Fluoro-5-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;	0.815
109	5-[[6-[2-Fluoro-5-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;	3.260
110	5-[[6-[4-Fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;	0.400
111	5-[[6-[2-Fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;	0.183
112	5-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;	0.289
113	2-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;	0.104
114	3-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,2,4-oxadiazole;	0.279
115	2-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-(trifluoromethyl)-1,3,4-oxadiazole;	0.414
116	2-[[6-[4-Chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;	0.283

Ex #	Compound Name	GluN2B IC50 (μM)
117	2-[[6-[4-Chloro-3-(difluoromethoxy)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;	0.655
118	2-[[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;	0.035
119	2-[[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-(trifluoromethyl)-1,3,4-oxadiazole;	0.245
120	4-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]thiadiazole;	0.895
121	2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazole;	0.025
122	2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;	0.018
123	2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;	0.042
124	2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-methyl-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;	0.066
125	2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-ethyl-1,3,4-thiadiazole;	0.138
126	5-((6-(3-(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-N-methyl-1,3,4-thiadiazol-2-amine;	1.620
127	2-[[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methoxy-1,3,4-thiadiazole;	0.850
128	N-(5-((6-(3-(Difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-1,3,4-thiadiazol-2-yl)acetamide;	>2.99
129	2-(Difluoromethyl)-5-[[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazole;	0.017
130	2-Cyclopropyl-5-[[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazole;	0.123
131	2-[[6-[4-Chloro-3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;	0.057
132	2-[[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;	0.033

Ex #	Compound Name	GluN2B IC50 (μM)
133	2-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;	0.072
134	2-[[6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methoxy-1,3,4-thiadiazole;	1.320
135	2-[[6-[4-Chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;	0.133
136	2-[[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;	0.017
137	6-(4-Methyl-2-thienyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;	0.116
138	1-[(5-Methyl-3-pyridyl)methyl]-6-(4-methyl-2-thienyl)pyrazolo[4,3-b]pyridine;	0.159
139	6-(5-Methyl-2-thienyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;	0.089
140	5-[[6-(5-Chloro-2-thienyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;	0.170
141	6-(3-Chloro-2-thienyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;	0.061
142	5-[[6-[5-(Difluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;	0.219
143	1-((6-Fluoropyridin-3-yl)methyl)-6-(5-(trifluoromethyl)thiophen-2-yl)-1H-pyrazolo[4,3-b]pyridine;	0.132
144	5-[[6-[5-(Trifluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;	0.582
145	1-[(6-Fluoro-3-pyridyl)methyl]-6-(m-tolyl)pyrazolo[4,3-b]pyridine;	0.036
146	1-[(5-Fluoro-3-pyridyl)methyl]-6-(m-tolyl)pyrazolo[4,3-b]pyridine;	0.009
147	3-Fluoro-1-[(5-fluoro-3-pyridyl)methyl]-6-(m-tolyl)pyrazolo[4,3-b]pyridine;	0.048
148	6-(4-Chlorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.634

Ex #	Compound Name	GluN2B IC50 (μM)
149	6-(4-Fluorophenyl)-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;	3.460
150	6-(4-Fluorophenyl)-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.410
151	1-[[5-(Difluoromethoxy)-3-pyridyl]methyl]-6-(4-fluorophenyl)pyrazolo[4,3-b]pyridine;	1.150
152	6-(3-Fluorophenyl)-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;	2.180
153	6-(2-Fluorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.720
154	6-(3-Methoxyphenyl)-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;	7.371
155	1-[(6-Fluoro-3-pyridyl)methyl]-6-(3-methoxyphenyl)pyrazolo[4,3-b]pyridine;	1.650
156	6-[3-(Difluoromethyl)phenyl]-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;	0.740
157	5-[[6-[3-(Difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;	0.064
158	1-[(5-Chloro-3-pyridyl)methyl]-6-[3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	0.014
159	6-[3-(Difluoromethoxy)phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.249
160	6-[3-(1,1-Difluoroethyl)phenyl]-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.112
161	6-[3-(1,1-Difluoroethyl)phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.040
162	1-(2-Pyridylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	0.930
163	1-(3-Pyridylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	0.090
164	1-(4-Pyridylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	0.798

Ex #	Compound Name	GluN2B IC50 (μM)
165	1-[(6-Methyl-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	2.170
166	1-[(2-Methyl-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	0.870
167	1-[(5-Methyl-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	0.250
168	1-[(4-Methyl-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	0.161
169	1-[(6-Fluoro-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	0.234
170	1-[(2-Fluoro-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	1.040
171	1-[(5-Fluoro-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	0.212
172	1-[(2-Methoxy-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	7.780
173	1-[(5-Methoxy-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	0.210
174	6-[3-(Trifluoromethyl)phenyl]-1-[[6-(trifluoromethyl)-3-pyridyl]methyl]pyrazolo[4,3-b]pyridine;	11.899
175	6-[3-(Trifluoromethyl)phenyl]-1-[[5-(trifluoromethyl)-3-pyridyl]methyl]pyrazolo[4,3-b]pyridine;	2.300
176	6-[3-(Trifluoromethyl)phenyl]-1-[[4-(trifluoromethyl)-3-pyridyl]methyl]pyrazolo[4,3-b]pyridine;	1.300
177	6-(4-Fluoro-3-methyl-phenyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;	0.023
178	3-Fluoro-6-(4-fluoro-3-methyl-phenyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;	0.026
179	6-(4-Fluoro-3-methyl-phenyl)-1-[(2-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.507
180	6-(4-Fluoro-3-methyl-phenyl)-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.062

Ex #	Compound Name	GluN2B IC50 (μM)
181	6-(4-Fluoro-3-methyl-phenyl)-1-[(4-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.113
182	6-(4-Fluoro-3-methyl-phenyl)-1-[(6-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.064
183	6-(4-Fluoro-3-methyl-phenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.021
184	6-(3,5-Difluorophenyl)-1-[(4-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.068
185	6-(3,5-Difluorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.045
186	6-(3,4-Difluorophenyl)-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;	2.520
187	6-(3,4-Difluorophenyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;	0.218
188	6-(3,4-Difluorophenyl)-1-[(2-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	3.620
189	6-(3,4-Difluorophenyl)-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.070
190	6-(3,4-Difluorophenyl)-1-[(4-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.158
191	6-(3,4-Difluorophenyl)-1-[(6-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.176
192	6-(3,4-Difluorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.048
193	6-(3,4-Difluorophenyl)-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.277
194	1-[[5-(Difluoromethoxy)-3-pyridyl]methyl]-6-(3,4-difluorophenyl)pyrazolo[4,3-b]pyridine;	0.850
195	6-(3-Chloro-4-fluoro-phenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.025
196	6-(3-Chloro-4-fluoro-phenyl)-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.152

Ex #	Compound Name	GluN2B IC50 (μM)
197	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;	0.130
198	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;	0.008
199	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-methyl-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;	0.034
200	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.012
201	6-(3-(difluoromethyl)-4-fluorophenyl)-1-((6-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine;	0.016
202	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.014
203	5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;	0.031
204	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(6-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	1.620
205	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(6-methoxy-2-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.177
206	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(2-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.307
207	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.028
208	1-[(5-Chloro-3-pyridyl)methyl]-6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridine;	0.026
209	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[[5-(difluoromethyl)-3-pyridyl]methyl]pyrazolo[4,3-b]pyridine;	0.020
210	1-[[5-(Difluoromethoxy)-3-pyridyl]methyl]-6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridine;	0.110
211	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[[5-(trifluoromethyl)-3-pyridyl]methyl]pyrazolo[4,3-b]pyridine;	0.047
212	5-[[6-[3-(Difluoromethyl)-2-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;	0.067

Ex #	Compound Name	GluN2B IC50 (μM)
213	1-[(5-Chloro-3-pyridyl)methyl]-6-[3-(difluoromethyl)-2-fluoro-phenyl]pyrazolo[4,3-b]pyridine;	0.068
214	6-(3,4-Dichlorophenyl)-1-[(6-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	1.910
215	6-(3,4-Dichlorophenyl)-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.217
216	6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;	0.109
217	6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.189
218	6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.107
219	5-[[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;	0.158
220	6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.089
221	1-[(5-Chloro-3-pyridyl)methyl]-6-[3-(1,1-difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridine;	0.064
222	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;	0.502
223	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;	0.038
224	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.056
225	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.039
226	5-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;	0.068
227	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(6-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	1.620
228	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(6-methoxy-2-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.383

Ex #	Compound Name	GluN2B IC50 (μM)
229	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(2-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.716
230	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.048
231	1-[(5-Chloro-3-pyridyl)methyl]-6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridine;	0.039
232	6-[4-Chloro-3-(Difluoromethyl)phenyl]-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.040
233	1-[(5-Fluoro-3-pyridyl)methyl]-6-[4-fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	0.075
234	6-[4-Fluoro-3-(trifluoromethyl)phenyl]-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.092
235	6-(3-Bromo-4-fluorophenyl)-1-((6-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine;	0.253
236	5-[[6-[4-Chloro-3-(1,1-difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;	0.494
237	6-[4-Chloro-3-(1,1-difluoroethyl)phenyl]-1-[(5-chloro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.200
238	6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;	0.117
239	6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.120
240	6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.166
241	5-[[6-[4-Chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;	0.151
242	6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.500
243	6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-[(5-chloro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.146
244	6-(2,4-Difluoro-3-methyl-phenyl)-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;	0.310

Ex #	Compound Name	GluN2B IC50 (μM)
245	6-(2,4-Difluoro-3-methyl-phenyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;	0.033
246	6-(2,4-Difluoro-3-methyl-phenyl)-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.052
247	6-(2,4-Difluoro-3-methyl-phenyl)-1-[(4-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.128
248	6-(2,4-Difluoro-3-methyl-phenyl)-1-[(6-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.062
249	6-(2,4-Difluoro-3-methyl-phenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;	0.040
250	1-(2-Pyridylmethyl)-6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridine;	2.630
251	1-[(5-Fluoro-3-pyridyl)methyl]-6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridine;	0.025
252	1-[(5-Methoxy-3-pyridyl)methyl]-6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridine;	0.382
253	1-[[5-(Difluoromethoxy)-3-pyridyl]methyl]-6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridine;	0.980
254	1-(Pyridazin-4-ylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	0.548
255	6-(m-Tolyl)-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;	0.329
256	6-(3-Fluorophenyl)-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;	1.410
257	6-[3-(1,1-Difluoroethyl)phenyl]-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;	0.110
258	1-(Pyridazin-3-ylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	0.240
259	6-(4-Fluoro-3-methyl-phenyl)-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;	0.030
260	6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;	0.162

Ex #	Compound Name	GluN2B IC50 (μM)
261	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;	0.023
262	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(6-methylpyridazin-3-yl)methyl]pyrazolo[4,3-b]pyridine;	0.273
263	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;	0.112
264	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(6-methylpyridazin-3-yl)methyl]pyrazolo[4,3-b]pyridine;	0.626
265	6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;	0.115
266	6-(3,4-Difluorophenyl)-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;	0.670
267	6-(4-Chloro-3-methyl-phenyl)-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;	0.404
268	1-(Pyridazin-3-ylmethyl)-6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridine;	0.673
269	6-(2,4-Difluoro-3-methyl-phenyl)-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;	0.108
270	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(pyrimidin-4-ylmethyl)pyrazolo[4,3-b]pyridine;	0.176
271	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(pyrimidin-4-ylmethyl)pyrazolo[4,3-b]pyridine;	0.401
272	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(pyrazin-2-ylmethyl)pyrazolo[4,3-b]pyridine;	0.037
273	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(pyrazin-2-ylmethyl)pyrazolo[4,3-b]pyridine;	0.320
274	6-[3-(1,1-Difluoroethyl)phenyl]-1-(pyrimidin-5-ylmethyl)pyrazolo[4,3-b]pyridine;	0.051
275	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(pyrimidin-5-ylmethyl)pyrazolo[4,3-b]pyridine;	0.012
276	1-(Pyrimidin-5-ylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	0.145

Ex #	Compound Name	GluN2B IC50 (μM)
277	6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-(pyrimidin-5-ylmethyl)pyrazolo[4,3-b]pyridine;	0.065
278	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(pyrimidin-5-ylmethyl)pyrazolo[4,3-b]pyridine;	0.052
279	6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-(pyrimidin-5-ylmethyl)pyrazolo[4,3-b]pyridine;	0.090
280	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(6-methylpyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;	0.226
281	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(6-methylpyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;	0.984
282	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(2-methylpyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;	0.387
283	1-[(2-Methylpyrimidin-4-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	3.250
284	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(2-methylpyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;	0.942
285	6-(3,4-Difluorophenyl)-1-[(2-methylpyrimidin-5-yl)methyl]pyrazolo[4,3-b]pyridine;	>10
286	6-(4-Chloro-3-methyl-phenyl)-1-[(2-methylpyrimidin-5-yl)methyl]pyrazolo[4,3-b]pyridine;	3.016
287	1-[(5-Methylpyrimidin-2-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;	3.243
288	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(6-methoxypyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;	0.182
289	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(6-methoxypyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;	0.350
290	6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(2-methoxypyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;	0.320
291	6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(2-methoxypyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;	0.938
292	(5-((6-(3-(Difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-1,3,4-oxadiazol-2-yl)methanol;	0.170

Ex #	Compound Name	GluN2B IC50 (μM)
293	2-Fluoro-5-(1-((5-methyl-1,3,4-oxadiazol-2-yl)methyl)-1H-pyrazolo[4,3-b]pyridin-6-yl)benzoic acid;	>10
294	6-(3-(Difluoromethyl)-4-fluorophenyl)-1-((6-(fluoro-18F)pyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine;	NT
295	2-[[3-Bromo-6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;	NT
296	2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole; and	NT
297	2-[[3-Deuterio-6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole.	0.024

NT means not tested.

Protocol for Liver Microsomal Stability (Extraction Ratio)

Liver Microsomal Stability. Microsomal stability studies (Chrovian et al, "1H-Pyrrolo[3,2-b]pyridine GluN2B-Selective Negative Allosteric Modulators". ACS Med Chem Lett. 2019 Jan 10;10(3):261-266) were conducted on a Biomek® FX Robotic Liquid Handling Workstation (Beckman Coulter, Brea, CA), which consists of a 96-channel pipette head, a 12- postion workstation deck, and a plate incubator. Test compounds (1 μM) were spiked in a reaction mix consisting of 100 mM potassium phosphate buffer (pH 7.4), 3 mM $MgCl_2$, and 0.5 mg/mL liver microsomes from mouse, rat, and human (BD Gentest). The reaction was brought to 37 °C and initiated by adding NADPH to a final concentration of 1 mM. After mixing on the platedeck, 50 μL aliquots were excised from the reaction plate at 0, 5, 10, 20, 40, and 60 min and quenched with four volumes of acetonitrile spiked with 500 μg/nL of the internal standard phenytoin. Quenched plates were centrifuged at 5700 rpm for 10 min at 4 °C, and supernatant was diluted 1:3 in water before LC/MS/MS analysis. The compound half-lives were derived from plots of the ln of percent remaining compound over time to determine the intrinsic clearance. The predicted hepatic clearance was derived from the intrinsic clearance value using equations from the well-stirred model (Current Drug Metabolism, 2008, 9, 940-951), where no correction was made plasma protein binding and the blood to plasma concentration ratio was assumed to be one. The

extraction ratio (ER) was calculated by dividing the predicted hepatic clearance by species blood flow (Q), where Q is 90, 55, and 21.7 mL/min/kg for mouse, rat and human, respectively.

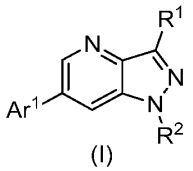
Results of the assay performed on the compounds of Examples are shown in Table 4.

Example #	Extraction Ratio @ 1 μM
8	0.68
10	0.31
52	0.69
96	<0.298
97	0.42
122	0.60
198	0.65
202	0.57
261	<0.298
275	0.36

Specific Embodiments

The present disclosure is exemplified by specific embodiments 1-54 below.

1. A compound having the structure of Formula (I):



(I)

wherein

R^1 is H, halo, or CH_3;

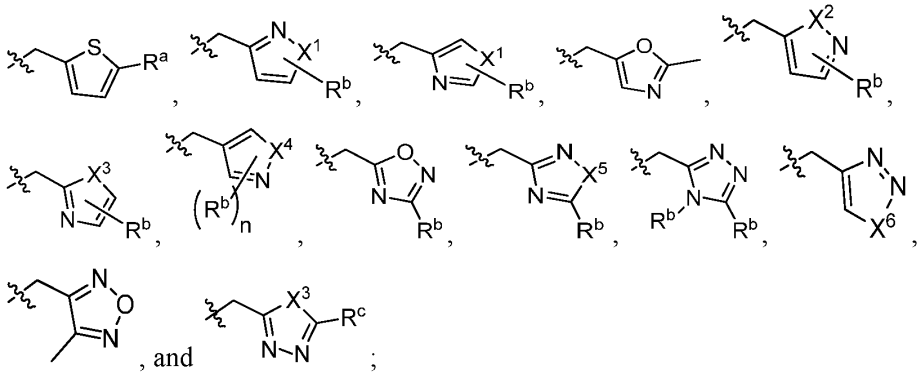
Ar^1 is selected from the group consisting of:

(a) phenyl substituted with one member selected from the group consisting of: halo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{1-6}perhaloalkyl, and OC_{1-6}perhaloalkyl;

(b) phenyl substituted with two or three members each independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}perhaloalkyl, OC_{1-6}perhaloalkyl, and CO_2H; and

(c) thienyl substituted with a member selected from the group consisting of: halo, C_{1-6}alkyl, and C_{1-6}perhaloalkyl; and pyridine substituted with CF_3; and

R^2 is selected from the group consisting of:

(d) 

wherein

R^a is halo, C_{1-6}alkyl or CN;

R^b is H or C_{1-2}alkyl;

R^c is selected from the group consisting of: H, C_{1-6}alkyl, C_{1-6}perhaloalkyl, CH_2OH, OC_{1-6}alkyl, OH, NH_2, $NH(CH_3)$, $N(CH_3)_2$, $NH(C{=}O)CH_3$, cyclopropyl, and phenyl;

X^1 is NCH_3, S or O;

X^2 is O, NH or NCH_3;

X^3 is O or S;

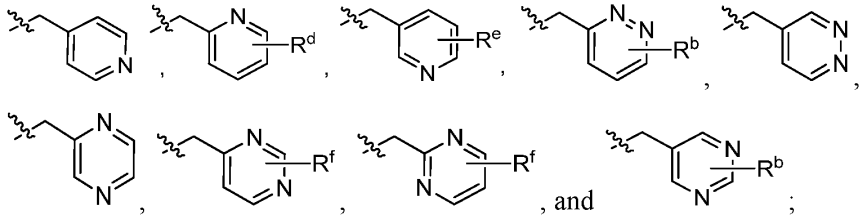
X^4 is NH or O;

X^5 is NCH_3 or O;

X^6 is NCH_3 or S;

and n is 2;

(e) phenyl; phenyl substituted with one or two members independently selected from the group consisting of: halo, OC_{1-6}alkyl, C_{1-6}perhaloalkyl, and CN; and

(f) 

wherein

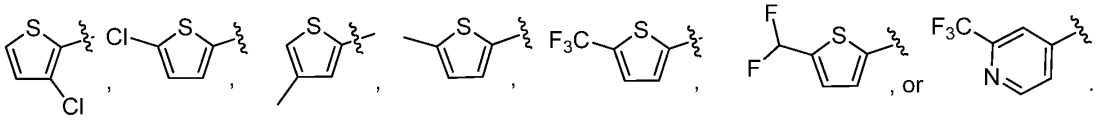
R^d is H or OC_{1-6}alkyl;

R^e is a member selected from the group consisting of: H, halo, C_{1-6}alkyl, C_{1-6}perhaloalkyl, OC_{1-6}alkyl, OC_{1-6}perhaloalkyl, and CN; and

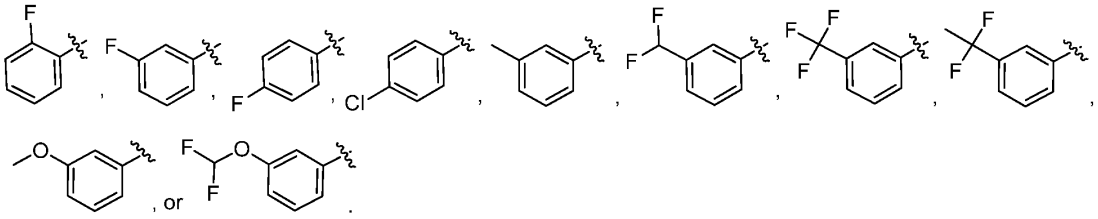
R^f is H, C_{1-6}alkyl or OC_{1-6}alkyl;

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

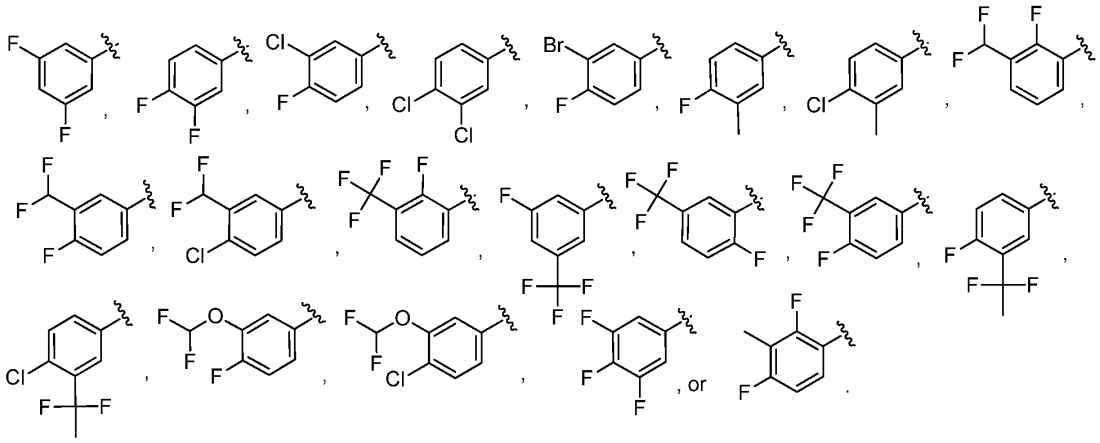
2. The compound of embodiment 1, wherein R^1 is H.
3. The compound of embodiment 1, wherein R^1 is F.
4. The compound of embodiment 1, wherein R^1 is CH_3.
5. The compound of embodiment 1, wherein Ar^1 is



6. The compound of embodiment 1, wherein Ar^1 is phenyl substituted with F, Cl, CH_3, OCH_3, CF_2H, CF_3, CF_2CH_3, or $OCHF_2$.
7. The compound of embodiment 1, wherein Ar^1 is



8. The compound of embodiment 1, wherein Ar^1 is phenyl substituted with two or three members independently selected from the group consisting of: F, Cl, Br, CH_3, CF_2H, CF_3, CF_2CH_3, or $OCHF_2$.
9. The compound of embodiment 1, wherein Ar^1 is



10. The compound of embodiment 1, wherein R^a is F, CH_3 or CN.

11. The compound of embodiment 1, wherein R^b is H, CH_3 or CH_2CH_3.

12. The compound of embodiment 1, wherein R^b is H or CH_3.

13. The compound of embodiment 1, wherein R^c is H, CH_3, CH_2CH_3, CF_3, OCH_3, OH, NH_2, $NH(CH_3)$, $N(CH_3)_2$, $NH(C{=}O)CH_3$, cyclopropyl, or phenyl.

14. The compound of embodiment 1, wherein R^d is H.

15. The compound of embodiment 1, wherein R^d is OCH_3.

16. The compound of embodiment 1, wherein R^e is H, Br, Cl, F, CH_3, CF_2H, CF_3, OCH_3, OCF_2H, or CN.

17. The compound of embodiment 1, wherein R^f is H, CH_3, or OCH_3.

18. The compound of embodiment 1, wherein X^1 is NCH_3.

19. The compound of embodiment 1, wherein X^1 is O.

20. The compound of embodiment 1, wherein X^1 is S.

21. The compound of embodiment 1, wherein X^2 is O.

22. The compound of embodiment 1, wherein X^2 is NH.

23. The compound of embodiment 1, wherein X^2 is NCH_3.

24. The compound of embodiment 1, wherein X^3 is O.

25. The compound of embodiment 1, wherein X^3 is S.

26. The compound of embodiment 1, wherein X^4 is NH.

27. The compound of embodiment 1, wherein X^4 is O.

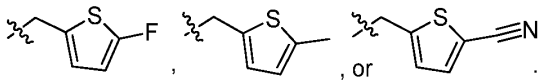
28. The compound of embodiment 1, wherein X^5 is NCH_3.

29. The compound of embodiment 1, wherein X^5 is O.

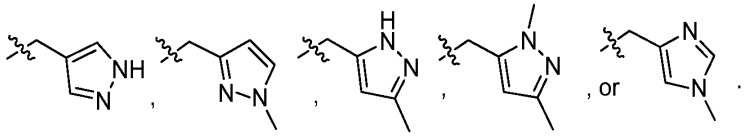
30. The compound of embodiment 1, wherein X^6 is NCH_3.

31. The compound of embodiment 1, wherein X^6 is S.

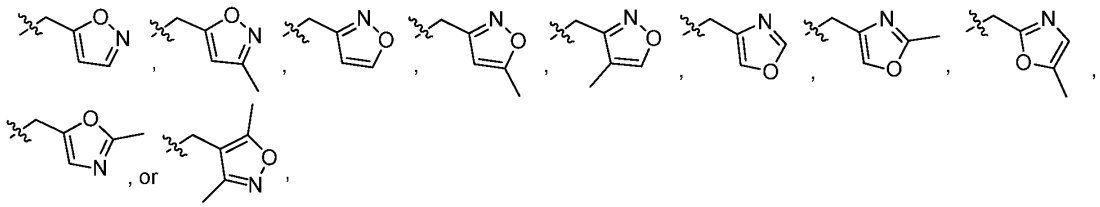
32. The compound of embodiment 1, wherein R^2 is



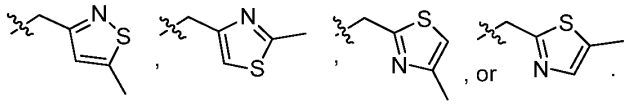
33. The compound of embodiment 1, wherein R^2 is



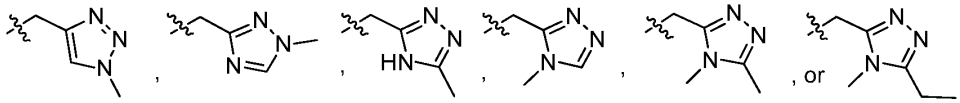
34. The compound of embodiment 1, wherein R^2 is



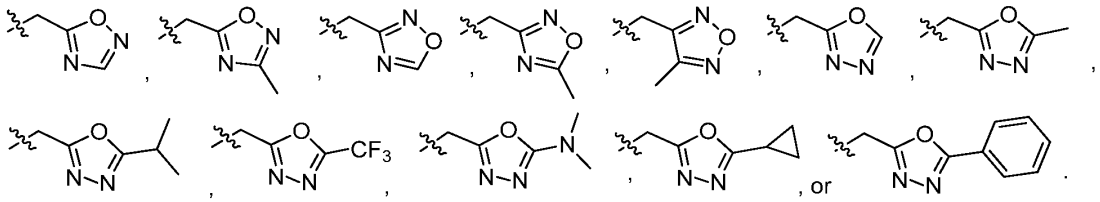
35. The compound of embodiment 1, wherein R^2 is



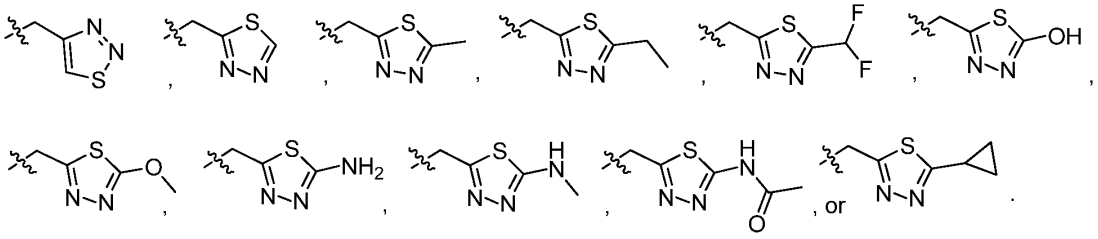
36. The compound of embodiment 1, wherein R^2 is



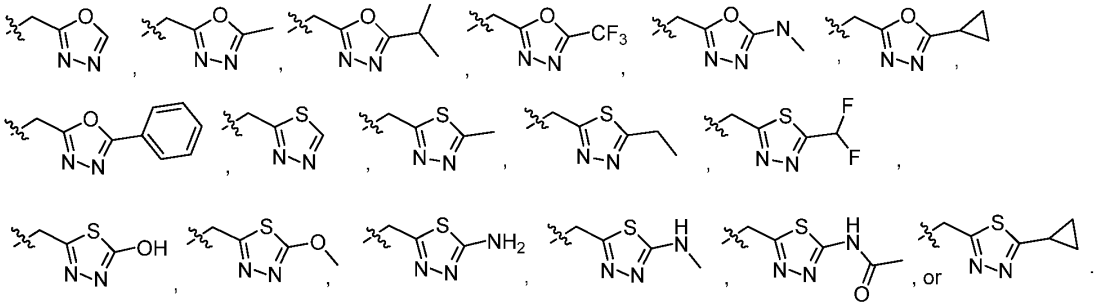
37. The compound of embodiment 1, wherein R^2 is



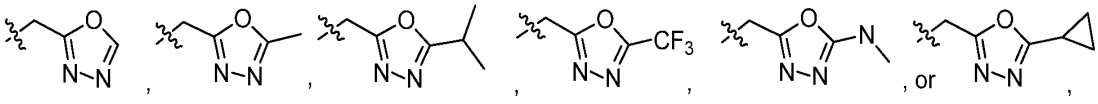
38. The compound of embodiment 1, wherein R^2 is



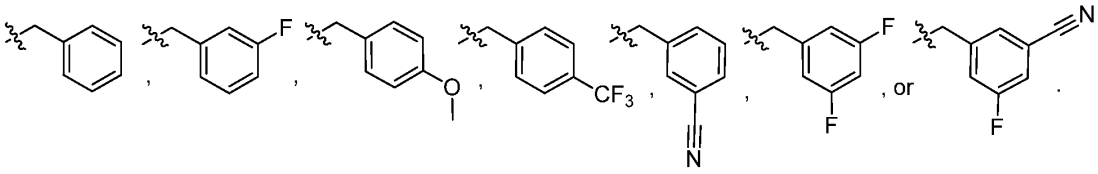
39. The compound of embodiment 1, wherein R^2 is



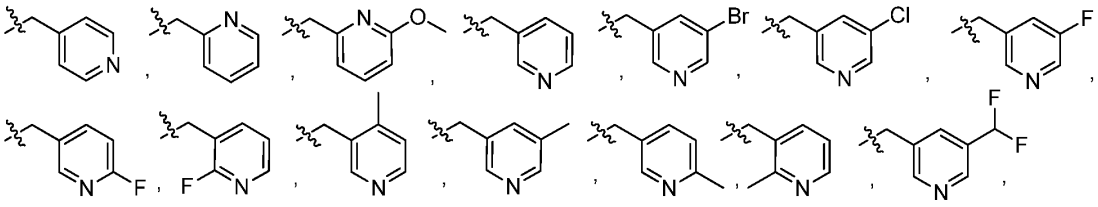
40. The compound of embodiment 1, wherein R^2 is

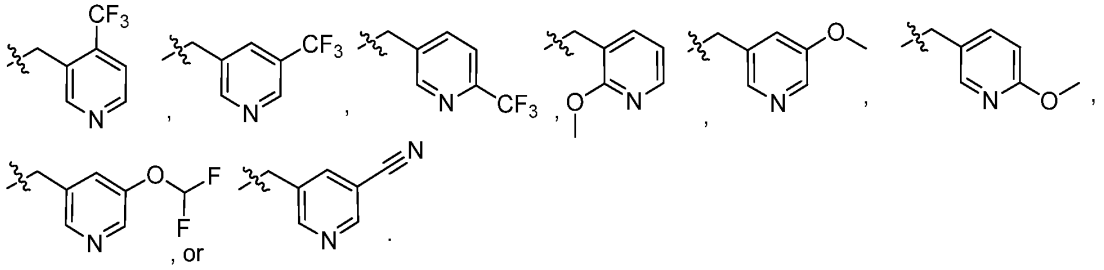


41. The compound of embodiment 1, wherein R^2 is

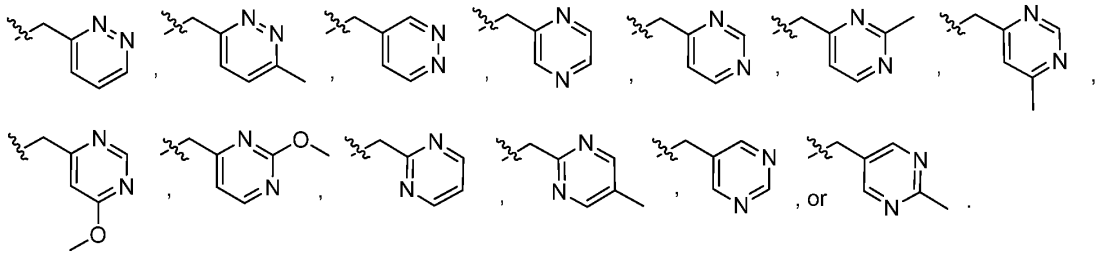


42. The compound of embodiment 1, wherein R^2 is

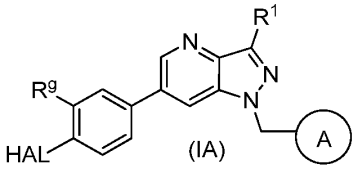




43. The compound of embodiment 1, wherein R^2 is



44. The compound of embodiment 1, and pharmaceutically acceptable salts, solvates, or N-oxides thereof, having the structure of Formula (1A):



(IA)

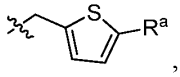
wherein

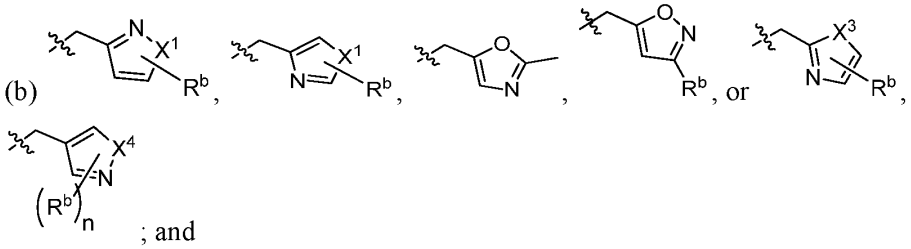
R^1 is H, F, or CH_3;

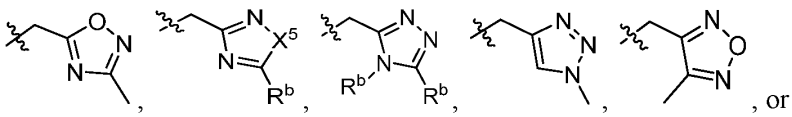
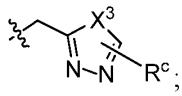
HAL is F or Cl;

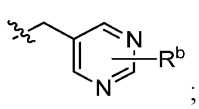
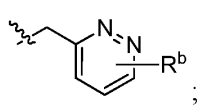
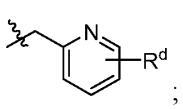
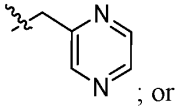
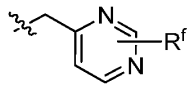
R^g is selected from the group consisting of: H, Cl, CH_3, CF_2H, CF_2CH_3, CF_3, and OCF_2H; and

Ring A is selected from the group consisting of:

(a) , wherein R^a is F, CH_3 or CN;

(b) ; and

(c) , or ;

(d) ; ; ; ; or ;

X^1 is O, NCH_3 or S;

X^3 is O or S;

X^4 is NH or O;

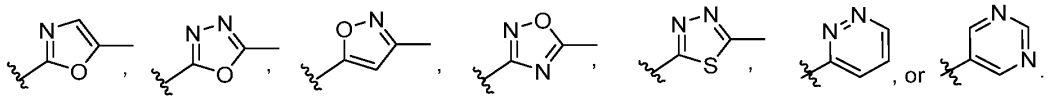
X^5 is NCH_3 or O;

R^b is H, CH_3, or CH_2CH_3;

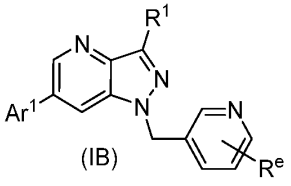
R^c is selected from the group consisting of: H, CH_3, CH_2CH_3, $CH(CH_3)_2$, CF_3, CHF_2, OCH_3, OH, NH_2, $NH(CH_3)$, $N(CH_3)_2$, $NH(C{=}O)CH_3$, cyclopropyl, and phenyl;

R^d is H or OCH_3; and

R^f is H, CH_3 or OCH_3.

45. The compound of embodiment 44, wherein ring A is .

46. The compound of embodiment 1, and pharmaceutically acceptable salts, solvates, or N-oxides thereof, having the structure of Formula (1B):


(IB)

wherein

R^1 is H, F, or CH_3;

R^e is a member selected from the group consisting of: H, Br, Cl, F, C_{1-4}alkyl, C_{1-4}perhaloalkyl, OC_{1-4}alkyl, OC_{1-4}perhaloalkyl, and CN; and

Ar^1 is selected from the group consisting of:

(a) phenyl substituted with one member selected from the group consisting of: Cl, F, C_{1-4}alkyl, OC_{1-4}alkyl, C_{1-4}perhaloalkyl, and OC_{1-4}perhaloalkyl;

(b) phenyl substituted with two or three members each independently selected from the group consisting of: Br, Cl, F, C_{1-4}alkyl, C_{1-4}perhaloalkyl, and OC_{1-4}perhaloalkyl; and

(c) thienyl substituted with a member selected from the group consisting of: Cl, CH_3, and CHF_2, CF_3.

47. The compound of embodiment 46, wherein R^1 is H, and R^e is H or F.

48. A compound selected from the group consisting of:

1-(Pyrimidin-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

1-[(5-Bromo-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

5-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;

1-[(2-Methylpyrimidin-5-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

1-(Pyrazin-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

1-(Pyrimidin-4-ylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

2-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-oxazole;

2-[[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-oxazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(1H-pyrazol-4-ylmethyl)pyrazolo[4,3-b]pyridine;

6-[3-(1,1-Difluoroethyl)phenyl]-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-methyl-4H-1,2,4-triazol-3-yl)methyl]pyrazolo[4,3-b]pyridine;

1-[(3-Methyl-1H-pyrazol-5-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

5-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-N-methyl-1,3,4-thiadiazol-2-amine;

5-[[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazol-2-amine;

5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazol-2-ol;

5-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazol-2-amine;

N-(5-((6-(3-(Difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-1,3,4-thiadiazol-2-yl)acetamide;

3-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,2,4-oxadiazole;

1-Benzyl-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

1-[(3-Fluorophenyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

3-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]benzonitrile;

1-[(4-Methoxyphenyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

6-[3-(Trifluoromethyl)phenyl]-1-[[4-(trifluoromethyl)phenyl]methyl]pyrazolo[4,3-b]pyridine;

3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]benzonitrile;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(3,5-difluorophenyl)methyl]pyrazolo[4,3-b]pyridine;

3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-fluoro-benzonitrile;

3-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]benzonitrile;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(3,5-difluorophenyl)methyl]pyrazolo[4,3-b]pyridine;

3-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-fluoro-benzonitrile;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-methyl-2-thienyl)methyl]pyrazolo[4,3-b]pyridine;

6-(3-(Difluoromethyl)-4-fluorophenyl)-1-((5-fluorothiophen-2-yl)methyl)-1H-pyrazolo[4,3-b]pyridine;

5-((6-(3-(Difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)thiophene-2-carbonitrile;

6-[3-(1,1-Difluoroethyl)phenyl]-1-(1H-pyrazol-4-ylmethyl)pyrazolo[4,3-b]pyridine;

1-[(1-Methylimidazol-4-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

1-[(2,5-Dimethylpyrazol-3-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(1H-pyrazol-4-ylmethyl)pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(1-methylpyrazol-3-yl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-(1H-pyrazol-4-ylmethyl)pyrazolo[4,3-b]pyridine;

6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-(1H-pyrazol-4-ylmethyl)pyrazolo[4,3-b]pyridine;

5-[[6-(4-Fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-isoxazole;

3-[[6-(4-Fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-isoxazole;

3-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]isoxazole;

3-[[6-[3-(1,1-Difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-isoxazole;

4-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]oxazole;

5-Methyl-3-[[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]isoxazole;

5-[[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-2-methyl-oxazole;

2-[[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-oxazole;

5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]isoxazole;

3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]isoxazole;

5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-isoxazole;

3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-isoxazole;

5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-2-methyl-oxazole;

4-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-2-methyl-oxazole;

3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-4-methyl-isoxazole;

4-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3,5-dimethyl-isoxazole;

3-[[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-isoxazole;

3-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-isoxazole;

5-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-2-methyl-oxazole;

2-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-oxazole;

3-[[6-[4-Chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-isoxazole;

5-[[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-2-methyl-oxazole;

5-Methyl-3-[[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]isothiazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-thiazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-4-methyl-thiazole;

4-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-2-methyl-thiazole;

2-[[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-thiazole;

2-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-thiazole;

2-[[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-thiazole;

1-[(1-Methyl-1,2,4-triazol-3-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(1-methyltriazol-4-yl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(1-methyl-1,2,4-triazol-3-yl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(4-methyl-1,2,4-triazol-3-yl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(4,5-dimethyl-1,2,4-triazol-3-yl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-ethyl-4-methyl-1,2,4-triazol-3-yl)methyl]pyrazolo[4,3-b]pyridine;

2-[[6-(5-Chloro-2-thienyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

2-Methyl-5-[[6-[5-(trifluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole;

2-[[6-[5-(Difluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

5-[[6-(4-Fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;

5-[[6-(3-Methoxyphenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;

2-[[6-[3-(1,1-Difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

2-[[6-[3-(1,1-Difluoroethyl)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

3-Methyl-5-[[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,2,4-oxadiazole;

2-Methyl-5-[[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole;

5-Methyl-3-[[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,2,4-oxadiazole;

5-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,2,4-oxadiazole;

2-Methyl-5-[[6-[2-(trifluoromethyl)-4-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole;

2-[[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

2-[[3-Fluoro-6-(4-fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

2-[[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-(trifluoromethyl)-1,3,4-oxadiazole;

2-[[6-(3-Chloro-4-fluoro-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

2-[[6-(3-Chloro-4-fluoro-phenyl)-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole;

5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,2,4-oxadiazole;

3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-4-methyl-1,2,5-oxadiazole;

2-Cyclopropyl-5-[[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-isopropyl-1,3,4-oxadiazole;

5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-N,N-dimethyl-1,3,4-oxadiazol-2-amine;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-(trifluoromethyl)-1,3,4-oxadiazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-phenyl-1,3,4-oxadiazole;

2-[[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

2-[[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

2-[[6-[4-Chloro-3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

2-[[6-[4-Chloro-3-(difluoromethyl)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

5-[[6-[3-Fluoro-5-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;

5-[[6-[2-Fluoro-5-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;

5-[[6-[4-Fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;

5-[[6-[2-Fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;

5-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;

2-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

3-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,2,4-oxadiazole;

2-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-(trifluoromethyl)-1,3,4-oxadiazole;

2-[[6-[4-Chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

2-[[6-[4-Chloro-3-(difluoromethoxy)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

2-[[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

2-[[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-(trifluoromethyl)-1,3,4-oxadiazole;

4-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]thiadiazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-methyl-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-ethyl-1,3,4-thiadiazole;

5-((6-(3-(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-N-methyl-1,3,4-thiadiazol-2-amine;

2-[[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methoxy-1,3,4-thiadiazole;

N-(5-((6-(3-(Difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-1,3,4-thiadiazol-2-yl)acetamide;

2-(Difluoromethyl)-5-[[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazole;

2-Cyclopropyl-5-[[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazole;

2-[[6-[4-Chloro-3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;

2-[[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;

2-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;

2-[[6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methoxy-1,3,4-thiadiazole;

2-[[6-[4-Chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;

2-[[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;

6-(4-Methyl-2-thienyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;

1-[(5-Methyl-3-pyridyl)methyl]-6-(4-methyl-2-thienyl)pyrazolo[4,3-b]pyridine;

6-(5-Methyl-2-thienyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;

5-[[6-(5-Chloro-2-thienyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;

6-(3-Chloro-2-thienyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;

5-[[6-[5-(Difluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;

1-((6-Fluoropyridin-3-yl)methyl)-6-(5-(trifluoromethyl)thiophen-2-yl)-1H-pyrazolo[4,3-b]pyridine;

5-[[6-[5-(Trifluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;

1-[(6-Fluoro-3-pyridyl)methyl]-6-(m-tolyl)pyrazolo[4,3-b]pyridine;

1-[(5-Fluoro-3-pyridyl)methyl]-6-(m-tolyl)pyrazolo[4,3-b]pyridine;

3-Fluoro-1-[(5-fluoro-3-pyridyl)methyl]-6-(m-tolyl)pyrazolo[4,3-b]pyridine;

6-(4-Chlorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-(4-Fluorophenyl)-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;

6-(4-Fluorophenyl)-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

1-[[5-(Difluoromethoxy)-3-pyridyl]methyl]-6-(4-fluorophenyl)pyrazolo[4,3-b]pyridine;

6-(3-Fluorophenyl)-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;

6-(2-Fluorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
6-(3-Methoxyphenyl)-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;
1-[(6-Fluoro-3-pyridyl)methyl]-6-(3-methoxyphenyl)pyrazolo[4,3-b]pyridine;
6-[3-(Difluoromethyl)phenyl]-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;
5-[[6-[3-(Difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;
1-[(5-Chloro-3-pyridyl)methyl]-6-[3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
6-[3-(Difluoromethoxy)phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
6-[3-(1,1-Difluoroethyl)phenyl]-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
6-[3-(1,1-Difluoroethyl)phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
1-(2-Pyridylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
1-(3-Pyridylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
1-(4-Pyridylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
1-[(6-Methyl-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
1-[(2-Methyl-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
1-[(5-Methyl-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
1-[(4-Methyl-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
1-[(6-Fluoro-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
1-[(2-Fluoro-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
1-[(5-Fluoro-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
1-[(2-Methoxy-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
1-[(5-Methoxy-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
6-[3-(Trifluoromethyl)phenyl]-1-[[6-(trifluoromethyl)-3-pyridyl]methyl]pyrazolo[4,3-b]pyridine;
6-[3-(Trifluoromethyl)phenyl]-1-[[5-(trifluoromethyl)-3-pyridyl]methyl]pyrazolo[4,3-b]pyridine;
6-[3-(Trifluoromethyl)phenyl]-1-[[4-(trifluoromethyl)-3-pyridyl]methyl]pyrazolo[4,3-b]pyridine;
6-(4-Fluoro-3-methyl-phenyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;
3-Fluoro-6-(4-fluoro-3-methyl-phenyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;
6-(4-Fluoro-3-methyl-phenyl)-1-[(2-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-(4-Fluoro-3-methyl-phenyl)-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
6-(4-Fluoro-3-methyl-phenyl)-1-[(4-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
6-(4-Fluoro-3-methyl-phenyl)-1-[(6-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
6-(4-Fluoro-3-methyl-phenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
6-(3,5-Difluorophenyl)-1-[(4-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
6-(3,5-Difluorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
6-(3,4-Difluorophenyl)-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;
6-(3,4-Difluorophenyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;
6-(3,4-Difluorophenyl)-1-[(2-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
6-(3,4-Difluorophenyl)-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
6-(3,4-Difluorophenyl)-1-[(4-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
6-(3,4-Difluorophenyl)-1-[(6-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
6-(3,4-Difluorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
6-(3,4-Difluorophenyl)-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
1-[[5-(Difluoromethoxy)-3-pyridyl]methyl]-6-(3,4-difluorophenyl)pyrazolo[4,3-b]pyridine;
6-(3-Chloro-4-fluoro-phenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
6-(3-Chloro-4-fluoro-phenyl)-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;
6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;
6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-methyl-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;
6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
6-(3-(Difluoromethyl)-4-fluorophenyl)-1-((6-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine;
6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(6-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(6-methoxy-2-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(2-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

1-[(5-Chloro-3-pyridyl)methyl]-6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[[5-(difluoromethyl)-3-pyridyl]methyl]pyrazolo[4,3-b]pyridine;

1-[[5-(Difluoromethoxy)-3-pyridyl]methyl]-6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[[5-(trifluoromethyl)-3-pyridyl]methyl]pyrazolo[4,3-b]pyridine;

5-[[6-[3-(Difluoromethyl)-2-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;

1-[(5-Chloro-3-pyridyl)methyl]-6-[3-(difluoromethyl)-2-fluoro-phenyl]pyrazolo[4,3-b]pyridine;

6-(3,4-Dichlorophenyl)-1-[(6-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-(3,4-Dichlorophenyl)-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;

6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

5-[[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;

6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

1-[(5-Chloro-3-pyridyl)methyl]-6-[3-(1,1-difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

5-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(6-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(6-methoxy-2-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(2-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

1-[(5-Chloro-3-pyridyl)methyl]-6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridine;

6-[4-Chloro-3-(Difluoromethyl)phenyl]-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

1-[(5-Fluoro-3-pyridyl)methyl]-6-[4-fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

6-[4-Fluoro-3-(trifluoromethyl)phenyl]-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-(3-Bromo-4-fluorophenyl)-1-((6-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine;

5-[[6-[4-Chloro-3-(1,1-difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;

6-[4-Chloro-3-(1,1-difluoroethyl)phenyl]-1-[(5-chloro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;
6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
5-[[6-[4-Chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;
6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-[(5-chloro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
6-(2,4-Difluoro-3-methyl-phenyl)-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;
6-(2,4-Difluoro-3-methyl-phenyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;
6-(2,4-Difluoro-3-methyl-phenyl)-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
6-(2,4-Difluoro-3-methyl-phenyl)-1-[(4-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
6-(2,4-Difluoro-3-methyl-phenyl)-1-[(6-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
6-(2,4-Difluoro-3-methyl-phenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
1-(2-Pyridylmethyl)-6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridine;
1-[(5-Fluoro-3-pyridyl)methyl]-6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridine;
1-[(5-Methoxy-3-pyridyl)methyl]-6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridine;
1-[[5-(Difluoromethoxy)-3-pyridyl]methyl]-6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridine;
1-(Pyridazin-4-ylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
6-(m-Tolyl)-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
6-(3-Fluorophenyl)-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
6-[3-(1,1-Difluoroethyl)phenyl]-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
1-(Pyridazin-3-ylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

6-(4-Fluoro-3-methyl-phenyl)-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(6-methylpyridazin-3-yl)methyl]pyrazolo[4,3-b]pyridine;
6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(6-methylpyridazin-3-yl)methyl]pyrazolo[4,3-b]pyridine;
6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
6-(3,4-Difluorophenyl)-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
6-(4-Chloro-3-methyl-phenyl)-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
1-(Pyridazin-3-ylmethyl)-6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridine;
6-(2,4-Difluoro-3-methyl-phenyl)-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(pyrimidin-4-ylmethyl)pyrazolo[4,3-b]pyridine;
6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(pyrimidin-4-ylmethyl)pyrazolo[4,3-b]pyridine;
6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(pyrazin-2-ylmethyl)pyrazolo[4,3-b]pyridine;
6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(pyrazin-2-ylmethyl)pyrazolo[4,3-b]pyridine;
6-[3-(1,1-Difluoroethyl)phenyl]-1-(pyrimidin-5-ylmethyl)pyrazolo[4,3-b]pyridine;
6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(pyrimidin-5-ylmethyl)pyrazolo[4,3-b]pyridine;
1-(Pyrimidin-5-ylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-(pyrimidin-5-ylmethyl)pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(pyrimidin-5-ylmethyl)pyrazolo[4,3-b]pyridine;

6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-(pyrimidin-5-ylmethyl)pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(6-methylpyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(6-methylpyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(2-methylpyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;

1-[(2-Methylpyrimidin-4-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(2-methylpyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;

6-(3,4-Difluorophenyl)-1-[(2-methylpyrimidin-5-yl)methyl]pyrazolo[4,3-b]pyridine;

6-(4-Chloro-3-methyl-phenyl)-1-[(2-methylpyrimidin-5-yl)methyl]pyrazolo[4,3-b]pyridine;

1-[(5-Methylpyrimidin-2-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(6-methoxypyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(6-methoxypyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(2-methoxypyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(2-methoxypyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;

(5-((6-(3-(Difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-1,3,4-oxadiazol-2-yl)methanol;

2-Fluoro-5-(1-((5-methyl-1,3,4-oxadiazol-2-yl)methyl)-1H-pyrazolo[4,3-b]pyridin-6-yl)benzoic acid;

6-(3-(Difluoromethyl)-4-fluorophenyl)-1-((6-(fluoro-18F)pyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine;

2-[[3-Bromo-6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole; and

2-[[3-Deuterio-6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

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

49. A compound selected from the group consisting of:

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-oxazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-isoxazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,2,4-oxadiazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

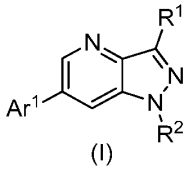
6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine; and

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(pyrimidin-5-ylmethyl)pyrazolo[4,3-b]pyridine;

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

50. A pharmaceutical composition comprising:

(A) an effective amount of at least one compound of Formula (I):



(I)

wherein

R^1 is H, halo, or CH_3;

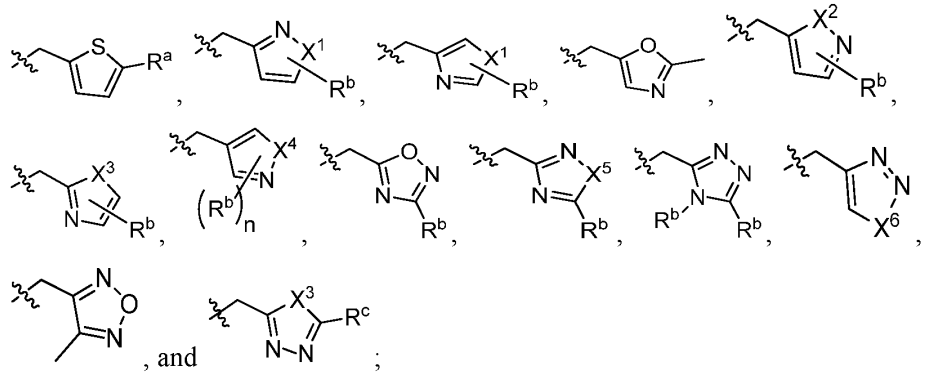
Ar^1 is selected from the group consisting of:

(a) phenyl substituted with one member selected from the group consisting of: halo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{1-6}perhaloalkyl, and OC_{1-6}perhaloalkyl;

(b) phenyl substituted with two or three members each independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}perhaloalkyl, OC_{1-6}perhaloalkyl, and CO_2H; and

(c) thienyl substituted with a member selected from the group consisting of: halo, C_{1-6}alkyl, and C_{1-6}perhaloalkyl; and pyridine substituted with CF_3; and

R^2 is selected from the group consisting of:

(d) 

wherein

R^a is halo, C_{1-6}alkyl or CN;

R^b is H or C_{1-2}alkyl;

R^c is selected from the group consisting of: H, C_{1-6}alkyl, C_{1-6}perhaloalkyl, CH_2OH, OC_{1-6}alkyl, OH, NH_2, $NH(CH_3)$, $N(CH_3)_2$, $NH(C{=}O)CH_3$, cyclopropyl, and phenyl;

X^1 is NCH_3, S or O;

X^2 is O, NH or NCH_3;

X^3 is O or S;

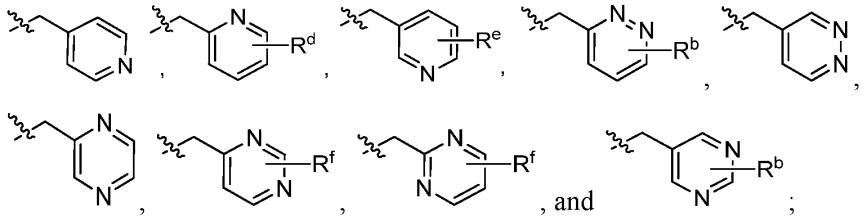
X^4 is NH or O;

X^5 is NCH_3 or O;

X^6 is NCH_3 or S;

and n is 2;

(e) phenyl; phenyl substituted with one or two members independently selected from the group consisting of: halo, OC_{1-6}alkyl, C_{1-6}perhaloalkyl, and CN; and

(f) 

wherein

R^d is H or OC_{1-6}alkyl;

R^e is a member selected from the group consisting of: H, halo, C_{1-6}alkyl, C_{1-6}perhaloalkyl, OC_{1-6}alkyl, OC_{1-6}perhaloalkyl, and CN; and

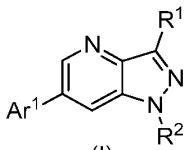
R^f is H, C_{1-6}alkyl or OC_{1-6}alkyl;

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

(B) at least one pharmaceutically acceptable excipient.

51. A pharmaceutical composition comprising an effective amount of at least one compound of embodiment 50 and at least one pharmaceutically acceptable excipient.

52. A method of treating a subject suffering from or diagnosed with a disease, disorder, or medical condition mediated by GluN2B 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):



(I)

wherein

R^1 is H, halo, or CH_3;

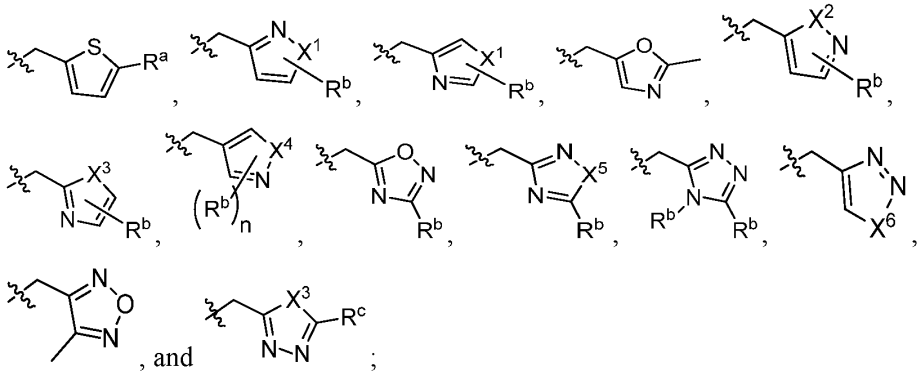
Ar^1 is selected from the group consisting of:

(a) phenyl substituted with one member selected from the group consisting of: halo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{1-6}perhaloalkyl, and OC_{1-6}perhaloalkyl;

(b) phenyl substituted with two or three members each independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}perhaloalkyl, OC_{1-6}perhaloalkyl, and CO_2H; and

(c) thienyl substituted with a member selected from the group consisting of: halo, C_{1-6}alkyl, and C_{1-6}perhaloalkyl; and pyridine substituted with CF_3; and

R^2 is selected from the group consisting of:

(d) 

wherein

R^a is halo, C_{1-6}alkyl or CN;

R^b is H or C_{1-2}alkyl;

R^c is selected from the group consisting of: H, C_{1-6}alkyl, C_{1-6}perhaloalkyl, CH_2OH, OC_{1-6}alkyl, OH, NH_2, $NH(CH_3)$, $N(CH_3)_2$, $NH(C=O)CH_3$, cyclopropyl, and phenyl;

X^1 is NCH_3, S or O;

X^2 is O, NH or NCH_3;

X^3 is O or S;

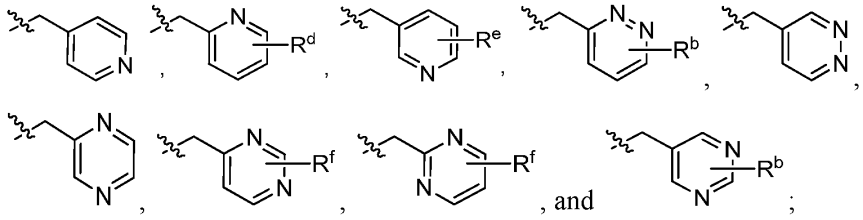
X^4 is NH or O;

X^5 is NCH_3 or O;

X^6 is NCH_3 or S;

and n is 2;

(e) phenyl; phenyl substituted with one or two members independently selected from the group consisting of: halo, OC_{1-6}alkyl, C_{1-6}perhaloalkyl, and CN; and

(f) 

wherein

R^d is H or OC_{1-6}alkyl;

R^e is a member selected from the group consisting of: H, halo, C_{1-6}alkyl, C_{1-6}perhaloalkyl, OC_{1-6}alkyl, OC_{1-6}perhaloalkyl, and CN; and

R^f is H, C_{1-6}alkyl or OC_{1-6}alkyl;

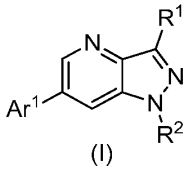
and pharmaceutically acceptable salts, stereoisomers, isotopic variants, N-oxides, or solvates of compounds of Formula (I).

53. The method of embodiment 52, wherein the disorder, disease or condition mediated by the GluN2B 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.

54. The method of embodiment 52 wherein the disorder, disease or condition is selected from the group consisting of treatment-resistant depression, major depressive disorder and bipolar disorder.

The present disclosure is further exemplified by specific embodiments 1-72 below.

1. A compound having the structure of Formula (I):



(I)

or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof,

wherein

R^1 is H, halo, or CH_3;

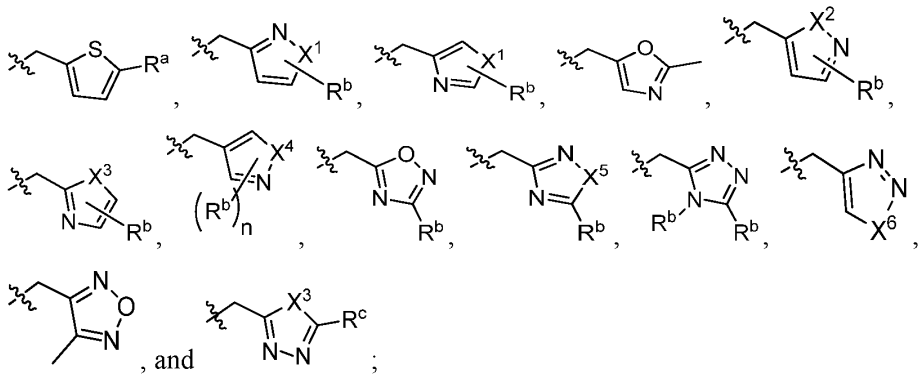
Ar^1 is selected from the group consisting of:

(a) phenyl substituted with one member selected from the group consisting of: halo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{1-6}perhaloalkyl, and OC_{1-6}perhaloalkyl;

(b) phenyl substituted with two or three members each independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}perhaloalkyl, OC_{1-6}perhaloalkyl, and CO_2H; and

(c) thienyl substituted with a member selected from the group consisting of: halo, C_{1-6}alkyl, and C_{1-6}perhaloalkyl; and pyridine substituted with CF_3; and

R^2 is selected from the group consisting of:

(d) 

wherein

R^a is halo, C_{1-6}alkyl or CN;

R^b is H or C_{1-2}alkyl;

R^c is selected from the group consisting of: H, C_{1-6}alkyl, C_{1-6}perhaloalkyl, CH_2OH, OC_{1-6}alkyl, OH, NH_2, $NH(CH_3)$, $N(CH_3)_2$, $NH(C=O)CH_3$, cyclopropyl, and phenyl;

X^1 is NCH_3, S or O;

X^2 is O, NH or NCH_3;

X^3 is O or S;

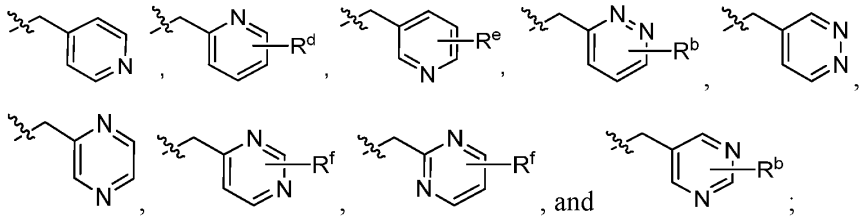
X^4 is NH or O;

X^5 is NCH_3 or O;

X^6 is NCH_3 or S;

and n is 2;

(e) phenyl; phenyl substituted with one or two members independently selected from the group consisting of: halo, OC_{1-6}alkyl, C_{1-6}perhaloalkyl, and CN; and

(f) 

wherein

R^d is H or OC_{1-6}alkyl;

R^e is a member selected from the group consisting of: H, halo, C_{1-6}alkyl, C_{1-6}perhaloalkyl, OC_{1-6}alkyl, OC_{1-6}perhaloalkyl, and CN; and

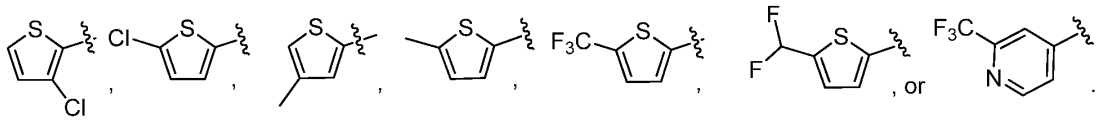
R^f is H, C_{1-6}alkyl or OC_{1-6}alkyl.

2. The compound of embodiment 1 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^1 is H.

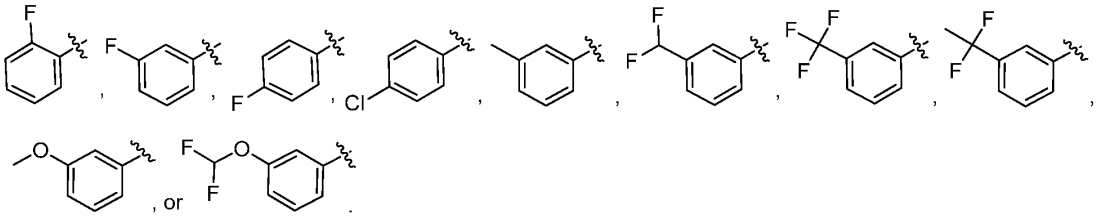
3. The compound of embodiment 1 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^1 is F.

4. The compound of embodiment 1 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^1 is CH_3.

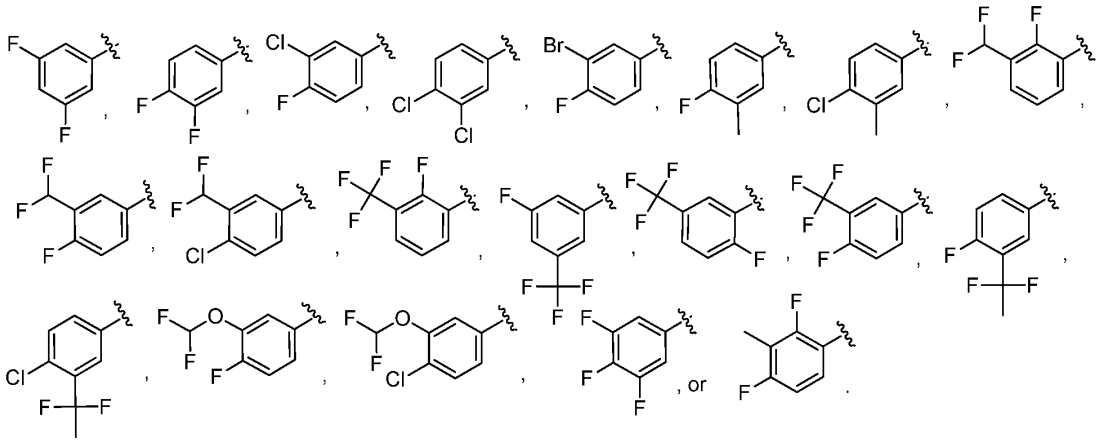
5. The compound of any one of embodiments 1 to 4, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein Ar^1 is



6. The compound of any one of embodiments 1 to 4, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein Ar^1 is phenyl substituted with F, Cl, CH_3, OCH_3, CF_2H, CF_3, CF_2CH_3, or $OCHF_2$.
7. The compound of any one of embodiments 1 to 4, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein Ar^1 is



8. The compound of any one of embodiments 1 to 4, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein Ar^1 is phenyl substituted with two or three members independently selected from the group consisting of: F, Cl, Br, CH_3, CF_2H, CF_3, CF_2CH_3, and $OCHF_2$.
9. The compound of any one of embodiments 1 to 4, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein Ar^1 is



10. The compound of any one of embodiments 1 to 9, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^a is F, CH_3 or CN.
11. The compound of any one of embodiments 1 to 10, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^b is H, CH_3 or CH_2CH_3.
12. The compound of any one of embodiments 1 to 11, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^b is H or CH_3.

13. The compound of any one of embodiments 1 to 12, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^c is H, CH_3, CH_2CH_3, CF_3, OCH_3, OH, NH_2, $NH(CH_3)$, $N(CH_3)_2$, $NH(C{=}O)CH_3$, cyclopropyl, or phenyl.
14. The compound of any one of embodiments 1 to 13, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^d is H.
15. The compound of any one of embodiments 1 to 13, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^d is OCH_3.
16. The compound of any one of embodiments 1 to 15, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^e is H, Br, Cl, F, CH_3, CF_2H, CF_3, OCH_3, OCF_2H, or CN.
17. The compound of any one of embodiments 1 to 16, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^f is H, CH_3, or OCH_3.
18. The compound of any one of embodiments 1 to 18, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein X^1 is NCH_3.
19. The compound of any one of embodiments 1 to 18, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein X^1 is O.
20. The compound of any one of embodiments 1 to 18, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein X^1 is S.
21. The compound of any one of embodiments 1 to 20, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein X^2 is O.
22. The compound of any one of embodiments 1 to 20, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein X^2 is NH.
23. The compound of any one of embodiments 1 to 20, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein X^2 is NCH_3.
24. The compound of any one of embodiments 1 to 23, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein X^3 is O.
25. The compound of any one of embodiments 1 to 23, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein X^3 is S.
26. The compound of any one of embodiments 1 to 25, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein X^4 is NH.

27. The compound of any one of embodiments 1 to 25, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein X^4 is O.

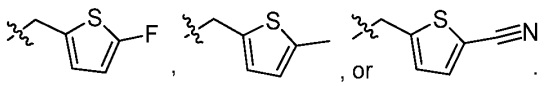
28. The compound of any one of embodiments 1 to 27, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein X^5 is NCH_3.

29. The compound of any one of embodiments 1 to 27, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein X^5 is O.

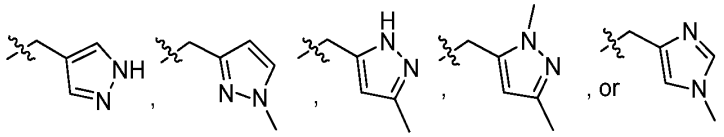
30. The compound of any one of embodiments 1 to 29, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein X^6 is NCH_3.

31. The compound of any one of embodiments 1 to 29, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein X^6 is S.

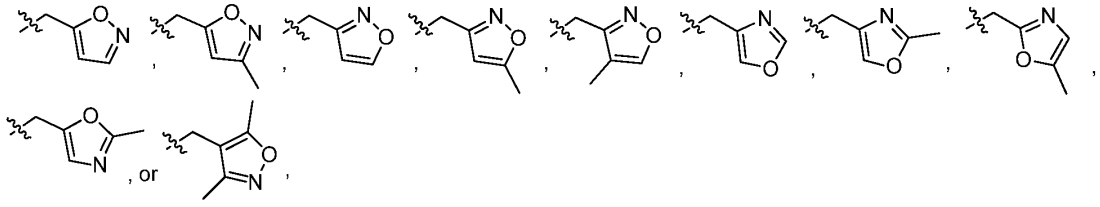
32. The compound of any one of embodiments 1 to 31, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^2 is



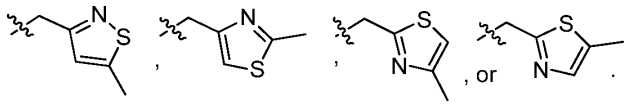
33. The compound of any one of embodiments 1 to 32, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^2 is



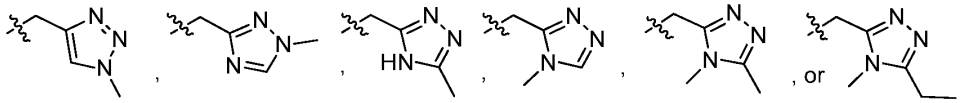
34. The compound of any one of embodiments 1 to 32, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^2 is



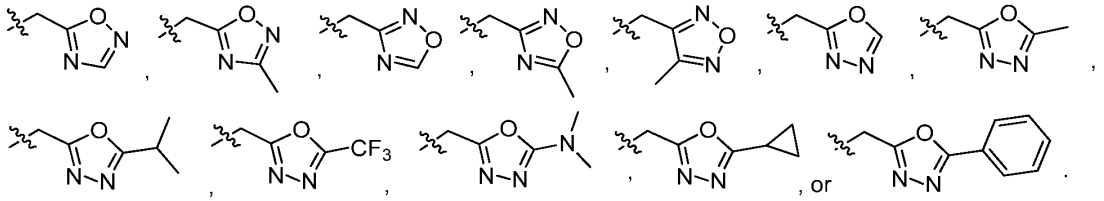
35. The compound of any one of embodiments 1 to 32, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^2 is



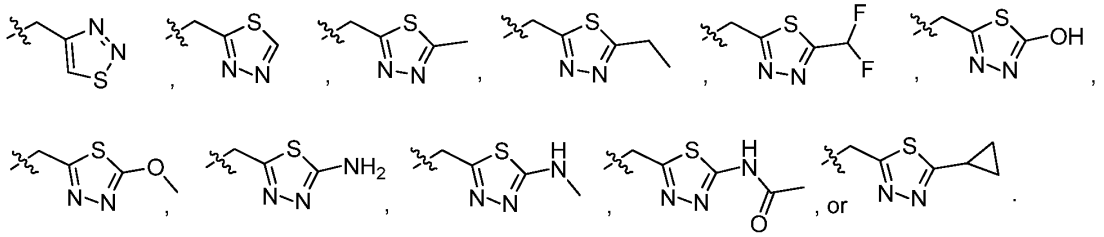
36. The compound of any one of embodiments 1 to 32, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^2 is



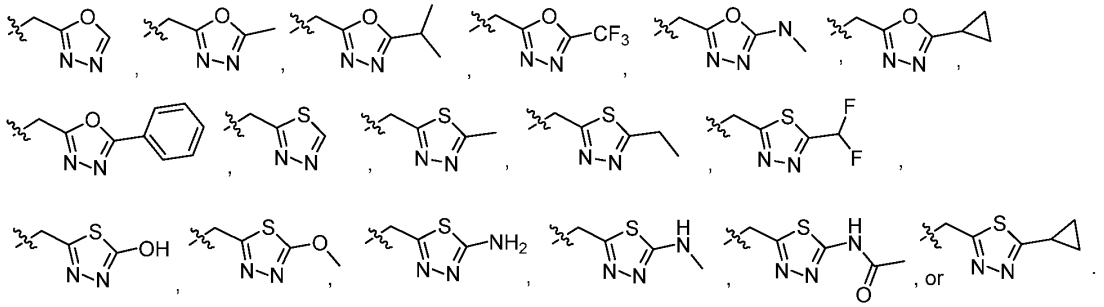
37. The compound of any one of embodiments 1 to 32, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^2 is



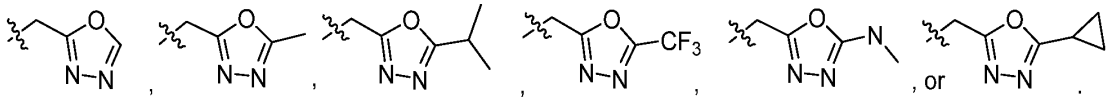
38. The compound of any one of embodiments 1 to 32, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^2 is



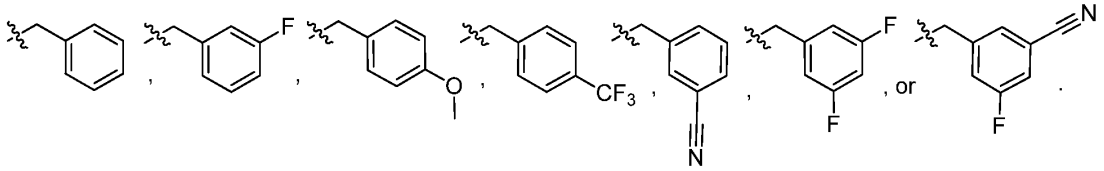
39. The compound of any one of embodiments 1 to 32, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^2 is



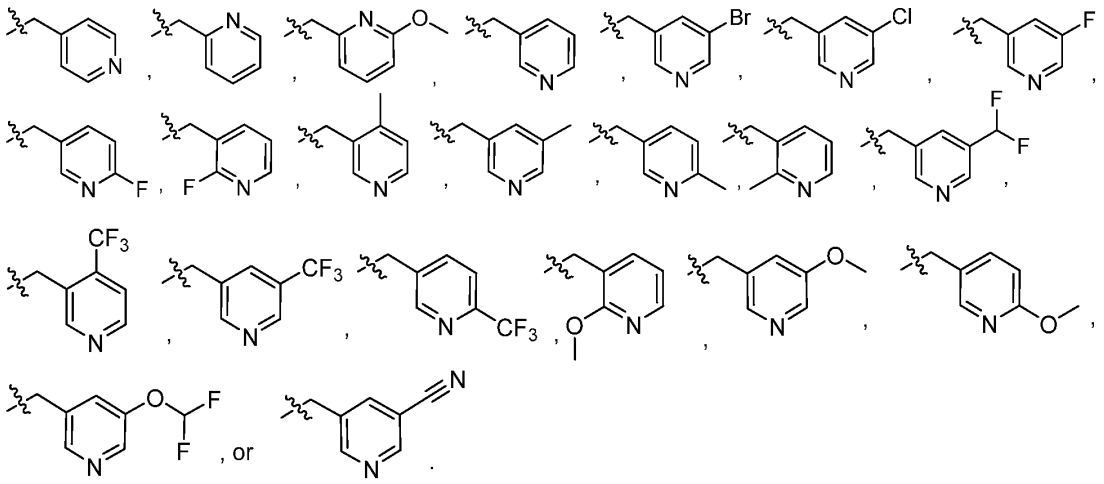
40. The compound of any one of embodiments 1 to 32, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^2 is



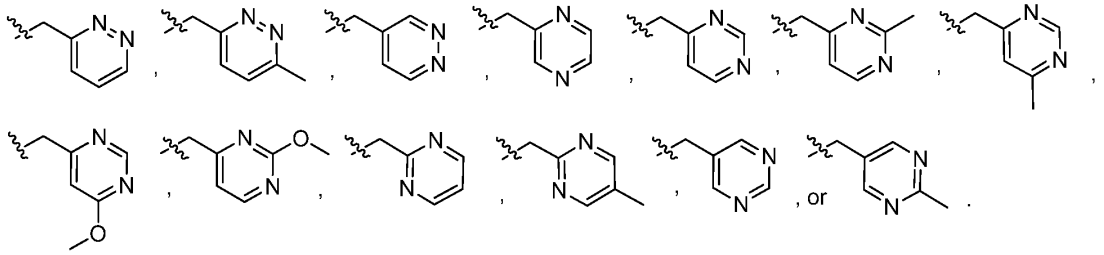
41. The compound of any one of embodiments 1 to 32, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^2 is



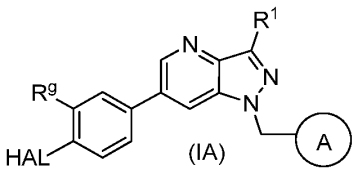
42. The compound of any one of embodiments 1 to 32, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^2 is



43. The compound of any one of embodiments 1 to 32, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^2 is



44. The compound of embodiment 1 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, having the structure of Formula (1A):



wherein

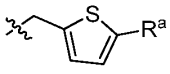
R^1 is H, F, or CH_3;

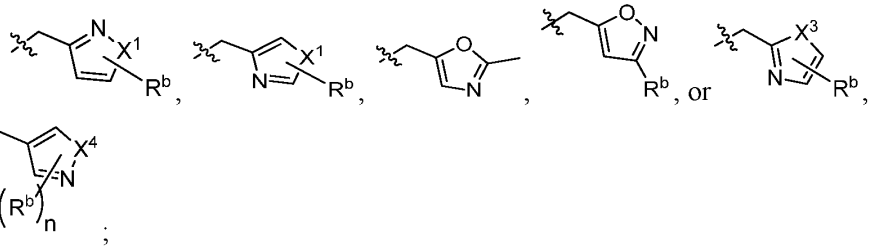
HAL is F or Cl;

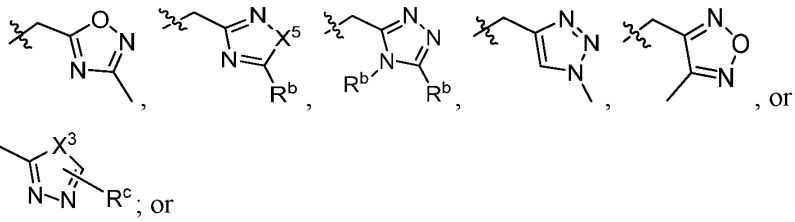
R^g is selected from the group consisting of: H, Cl, CH_3, CF_2H, CF_2CH_3, CF_3, and OCF_2H;

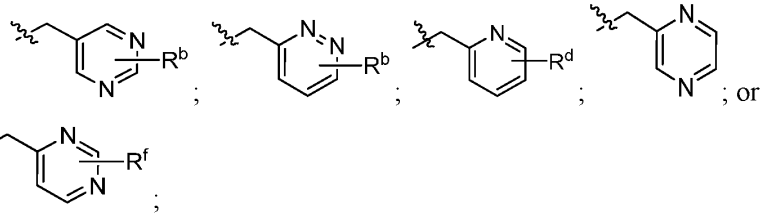
and

Ring A is:

(a) , wherein R^a is F, CH_3 or CN;

(b) ;

(c) ; or

(d) ;

X^1 is O, NCH_3 or S;

X^3 is O or S;

X^4 is NH or O;

X^5 is NCH_3 or O;

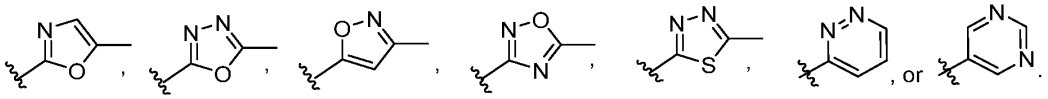
R^b is H, CH_3, or CH_2CH_3;

R^c is selected from the group consisting of: H, CH_3, CH_2CH_3, $CH(CH_3)_2$, CF_3, CHF_2, OCH_3, OH, NH_2, $NH(CH_3)$, $N(CH_3)_2$, $NH(C=O)CH_3$, cyclopropyl, and phenyl;

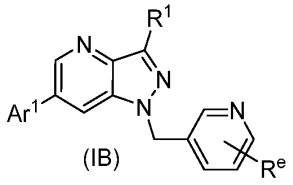
R^d is H or OCH_3; and

R^f is H, CH_3 or OCH_3.

45. The compound of embodiment 44 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein ring A is



46. The compound of embodiment 1 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, having the structure of Formula (1B):



(IB)

wherein

R^1 is H, F, or CH_3;

R^e is a member selected from the group consisting of: H, Br, Cl, F, C_{1-4}alkyl, C_{1-4}perhaloalkyl, OC_{1-4}alkyl, OC_{1-4}perhaloalkyl, and CN; and

Ar^1 is selected from the group consisting of:

(a) phenyl substituted with one member selected from the group consisting of: Cl, F, C_{1-4}alkyl, OC_{1-4}alkyl, C_{1-4}perhaloalkyl, and OC_{1-4}perhaloalkyl;

(b) phenyl substituted with two or three members each independently selected from the group consisting of: Br, Cl, F, C_{1-4}alkyl, C_{1-4}perhaloalkyl, and OC_{1-4}perhaloalkyl; and

(c) thienyl substituted with a member selected from the group consisting of: Cl, CH_3, and CHF_2, CF_3.

47. The compound of embodiment 46 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^1 is H, and R^e is H or F.

48. A compound selected from the compounds in Table 1 and pharmaceutically acceptable salts, solvates, stereoisomers, isotopic variants, and N-oxides thereof.

49. The compound of any one of embodiments 1 to 48, or a pharmaceutically acceptable salt or solvate thereof.

50. The compound of any one of embodiments 1 to 48, or a pharmaceutically acceptable salt or N-oxide thereof.
51. The compound of any one of embodiments 1 to 48, or a pharmaceutically acceptable salt thereof.
52. The compound of any one of embodiments 1 to 48.
53. A pharmaceutically acceptable salt of the compound of any one of embodiments 1 to 48.
54. A pharmaceutical composition comprising the compound of any one of embodiments 1 to 48, or a pharmaceutically acceptable salt, solvate, isotopic variant, or N-oxide thereof, and a pharmaceutically acceptable excipient.
55. A pharmaceutical composition comprising the compound of any one of embodiments 1 to 48, or a pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable excipient.
56. A pharmaceutical composition comprising the compound of any one of embodiments 1 to 48, or a pharmaceutically acceptable salt or N-oxide thereof, and a pharmaceutically acceptable excipient.
57. A pharmaceutical composition comprising the compound of any one of embodiments 1 to 48, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.
58. A pharmaceutical composition comprising the compound of any one of embodiments 1 to 48 and a pharmaceutically acceptable excipient.
59. A pharmaceutical composition comprising a pharmaceutically acceptable salt of the compound of any one of embodiments 1 to 48, and a pharmaceutically acceptable excipient.
60. A unit dosage form comprising a therapeutically effective amount of the pharmaceutical composition of any one of embodiments 54 to 59.
61. A method of treating a subject suffering from or diagnosed with a disease, disorder, or medical condition mediated by GluN2B receptor activity, comprising administering to the subject a therapeutically effective amount of the compound of any one of embodiments 1 to 48, or a pharmaceutically acceptable salt, solvate, isotopic variant, or N-oxide thereof.
62. A method of treating a subject suffering from or diagnosed with a disease, disorder, or medical condition mediated by GluN2B receptor activity, comprising administering to the subject a therapeutically effective amount of the compound of any one of embodiments 1 to 48, or a pharmaceutically acceptable salt, or solvate thereof.

63. A method of treating a subject suffering from or diagnosed with a disease, disorder, or medical condition mediated by GluN2B receptor activity, comprising administering to the subject a therapeutically effective amount of the compound of any one of embodiments 1 to 48, or a pharmaceutically acceptable salt or N-oxide thereof.

64. A method of treating a subject suffering from or diagnosed with a disease, disorder, or medical condition mediated by GluN2B receptor activity, comprising administering to the subject a therapeutically effective amount of the compound of any one of embodiments 1 to 48, or a pharmaceutically acceptable salt thereof.

65. A method of treating a subject suffering from or diagnosed with a disease, disorder, or medical condition mediated by GluN2B receptor activity, comprising administering to the subject a therapeutically effective amount of the pharmaceutical composition of any one of embodiments 54 to 59 or the unit dosage form of embodiment 60.

66. The method of any one of embodiments 61 to 65, wherein the disease, disorder or medical condition mediated by GluN2B receptor activity comprises bipolar disorder, major depressive disorder, treatment-resistant depression, a mood disorder, 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 a bacterial or chronic infection, pain, diabetic neuropathy, migraine, cerebral ischemia, schizophrenia, encephalitis, autism or an autism spectrum disorder, a memory disorder, a learning disorder, obsessive compulsive disorder, attention deficit hyperactivity disorder (ADHD) or an addictive illness.

67. The method of embodiment 66, wherein the disease, disorder or medical condition mediated by GluN2B receptor activity comprises bipolar disorder, a mood disorder, treatment resistant depression, major depressive disorder, or epilepsy.

68. The method of embodiment 66, wherein the disease, disorder or medical condition mediated by GluN2B receptor activity comprises bipolar disorder.

69. The method of embodiment 66, wherein the disease, disorder or medical condition mediated by GluN2B receptor activity comprises a mood disorder.

70. The method of embodiment 66, wherein the disease, disorder or medical condition mediated by GluN2B receptor activity comprises treatment resistant depression.

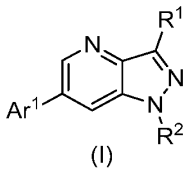
71. The method of embodiment 66, wherein the disease, disorder or medical condition mediated by GluN2B receptor activity comprises major depressive disorder.
72. The method of embodiment 66, wherein the disease, disorder or medical condition mediated by GluN2B receptor activity comprises epilepsy.

5

CLAIMS

What is claimed:

1. A compound having the structure of Formula (I):



(I)

or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof,

wherein

R^1 is H, halo, or CH_3;

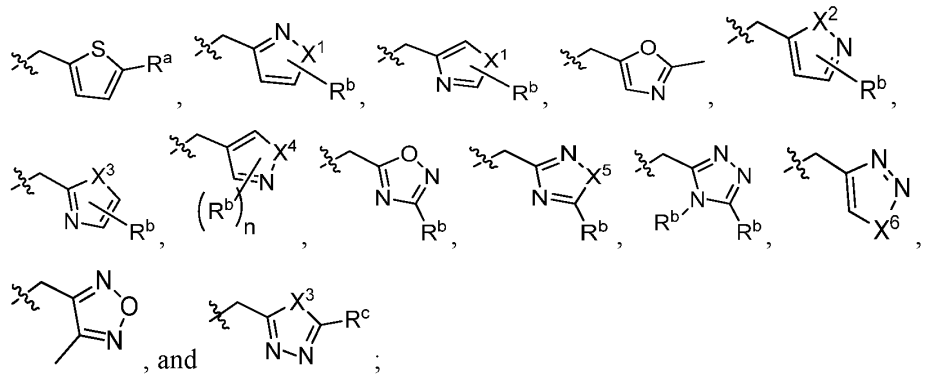
Ar^1 is selected from the group consisting of:

(a) phenyl substituted with one member selected from the group consisting of: halo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{1-6}perhaloalkyl, and OC_{1-6}perhaloalkyl;

(b) phenyl substituted with two or three members each independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}perhaloalkyl, OC_{1-6}perhaloalkyl, and CO_2H; and

(c) thienyl substituted with a member selected from the group consisting of: halo, C_{1-6}alkyl, and C_{1-6}perhaloalkyl; and pyridine substituted with CF_3; and

R^2 is selected from the group consisting of:

(d) 

wherein

R^a is halo, C_{1-6}alkyl or CN;

R^b is H or C_{1-2}alkyl;

R^c is selected from the group consisting of: H, C_{1-6}alkyl, C_{1-6}perhaloalkyl, CH_2OH, OC_{1-6}alkyl, OH, NH_2, $NH(CH_3)$, $N(CH_3)_2$, $NH(C{=}O)CH_3$, cyclopropyl, and phenyl;

X^1 is NCH_3, S or O;

X^2 is O, NH or NCH_3;

X^3 is O or S;

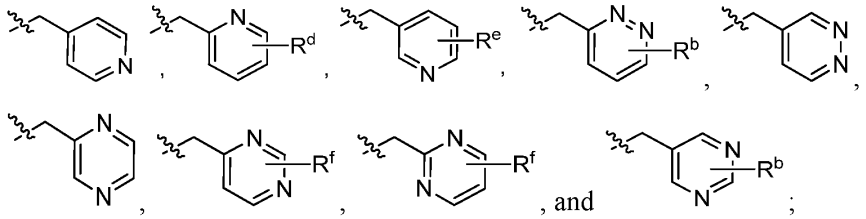
X^4 is NH or O;

X^5 is NCH_3 or O;

X^6 is NCH_3 or S;

and n is 2;

(e) phenyl; phenyl substituted with one or two members independently selected from the group consisting of: halo, OC_{1-6}alkyl, C_{1-6}perhaloalkyl, and CN; and

(f) 

wherein

R^d is H or OC_{1-6}alkyl;

R^e is a member selected from the group consisting of: H, halo, C_{1-6}alkyl, C_{1-6}perhaloalkyl, OC_{1-6}alkyl, OC_{1-6}perhaloalkyl, and CN; and

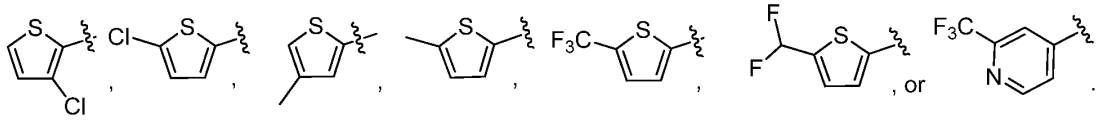
R^f is H, C_{1-6}alkyl or OC_{1-6}alkyl.

2. The compound of claim 1 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^1 is H.

3. The compound of claim 1 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^1 is F.

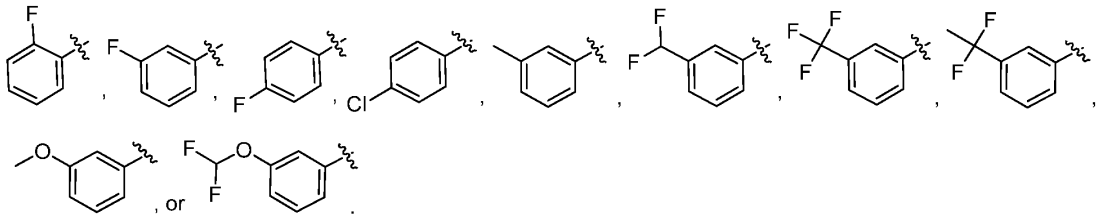
4. The compound of claim 1 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^1 is CH_3.

5. The compound of claim 1 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein Ar^1 is



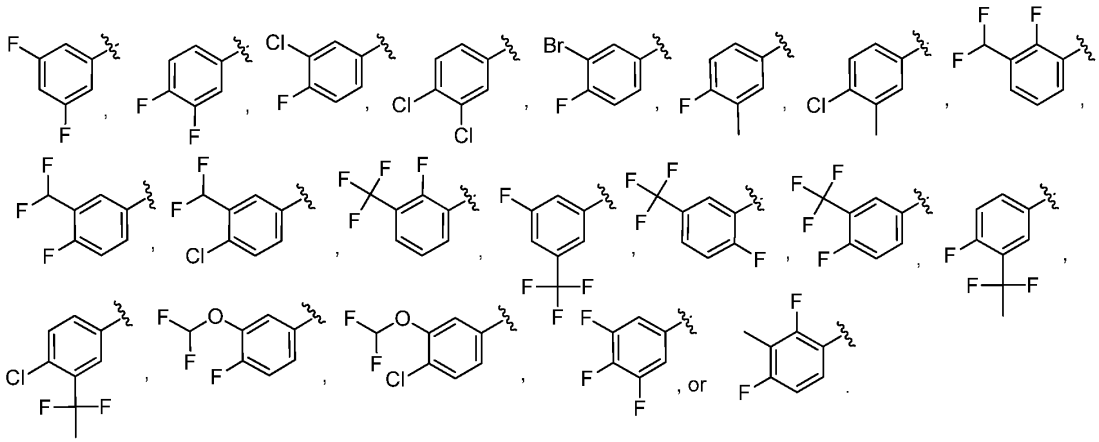
6. The compound of claim 1 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein Ar^1 is phenyl substituted with F, Cl, CH_3, OCH_3, CF_2H, CF_3, CF_2CH_3, or $OCHF_2$.

7. The compound of claim 1 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein Ar^1 is

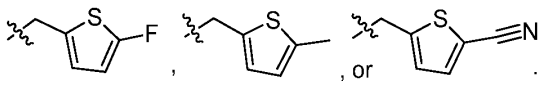


8. The compound of claim 1 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein Ar^1 is phenyl substituted with two or three members independently selected from the group consisting of: F, Cl, Br, CH_3, CF_2H, CF_3, CF_2CH_3, and $OCHF_2$.

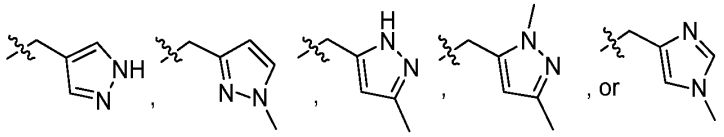
9. The compound of claim 1 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein Ar^1 is



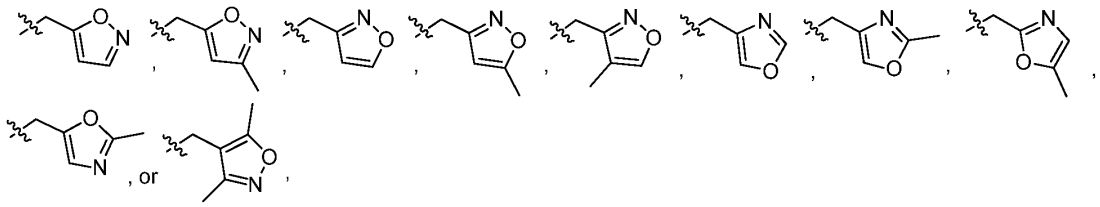
10. The compound of claim 1 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^2 is



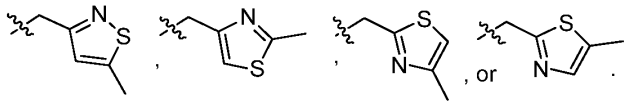
11. The compound of claim 1 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^2 is



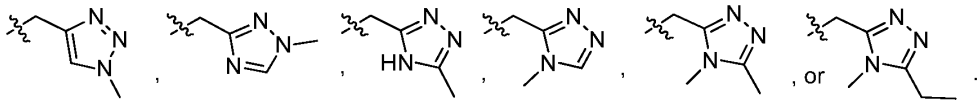
12. The compound of claim 1 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^2 is



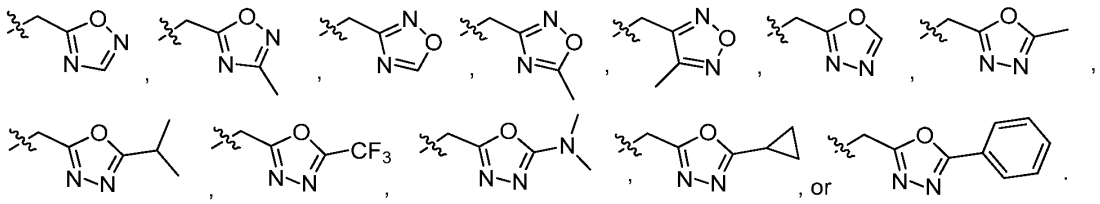
13. The compound of claim 1 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^2 is



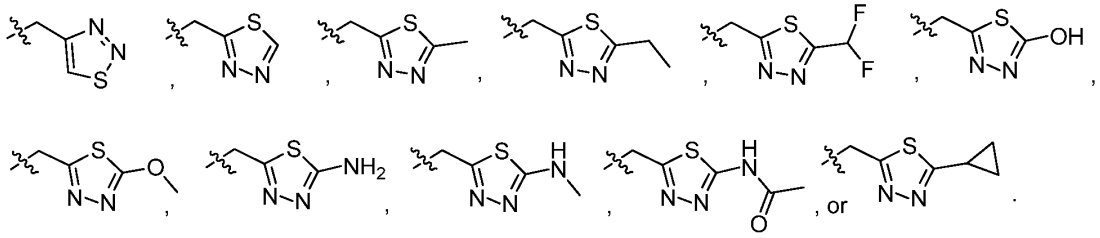
14. The compound of claim 1 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^2 is



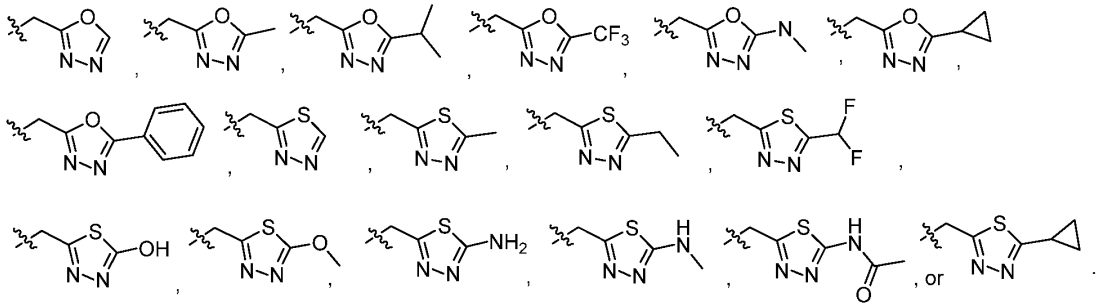
15. The compound of claim 1 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^2 is



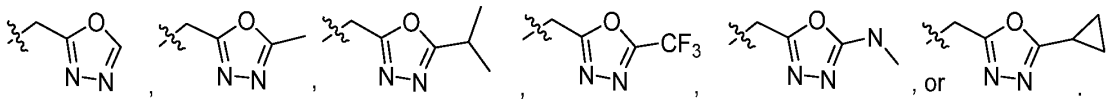
16. The compound of claim 1 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^2 is



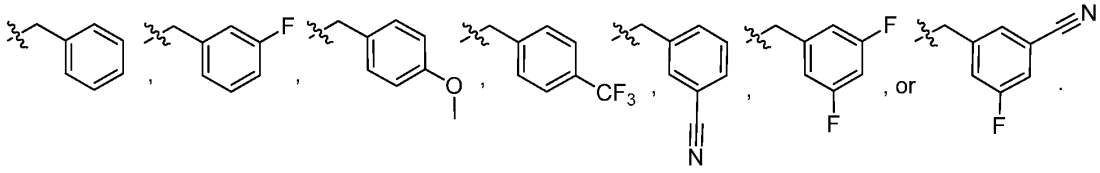
17. The compound of claim 1 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^2 is



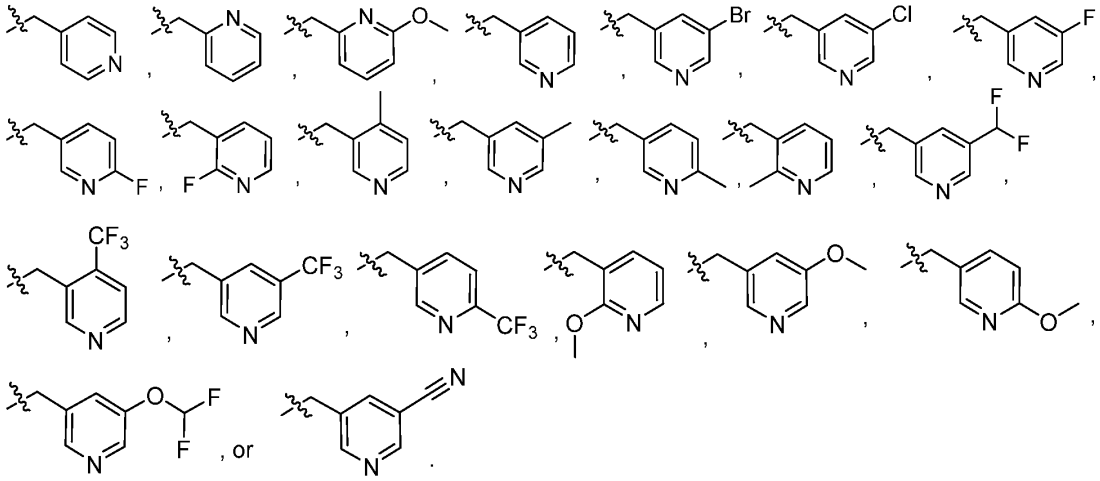
18. The compound of claim 1 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^2 is



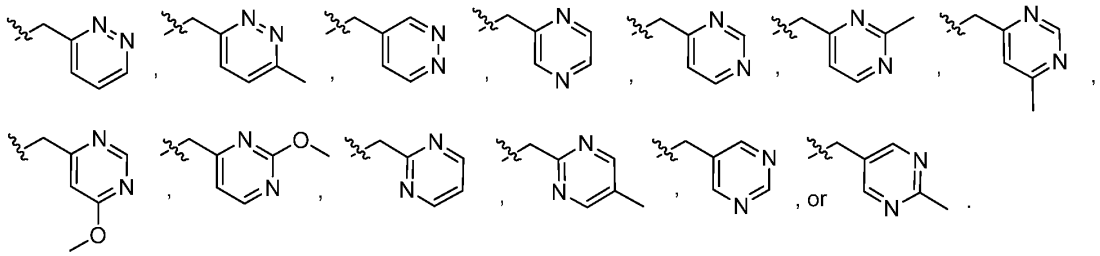
19. The compound of claim 1 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^2 is



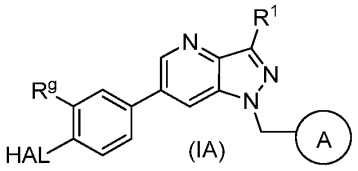
20. The compound of claim 1 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^2 is



21. The compound of claim 1 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^2 is



22. The compound of claim 1 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, having the structure of Formula (1A):



(IA)

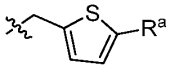
wherein

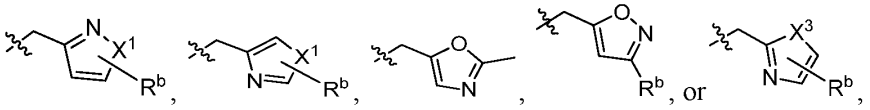
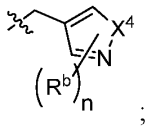
R^1 is H, F, or CH_3;

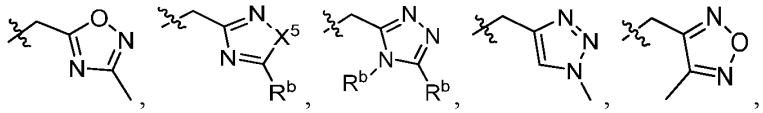
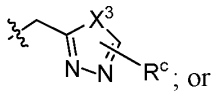
HAL is F or Cl;

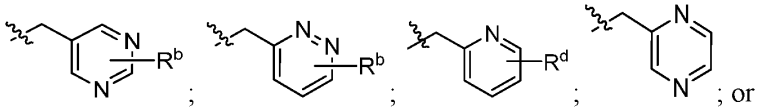
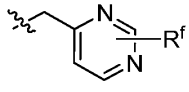
R^g is selected from the group consisting of: H, Cl, CH_3, CF_2H, CF_2CH_3, CF_3, and OCF_2H; and

Ring A is:

(a) , wherein R^a is F, CH_3 or CN;

(b) 

;

(c) 

; or

(d) 

;

X^1 is O, NCH_3 or S;

X^3 is O or S;

X^4 is NH or O;

X^5 is NCH_3 or O;

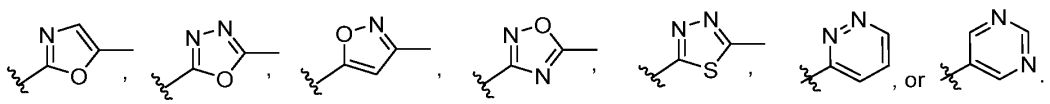
R^b is H, CH_3, or CH_2CH_3;

R^c is selected from the group consisting of: H, CH_3, CH_2CH_3, $CH(CH_3)_2$, CF_3, CHF_2, OCH_3, OH, NH_2, $NH(CH_3)$, $N(CH_3)_2$, $NH(C{=}O)CH_3$, cyclopropyl, and phenyl;

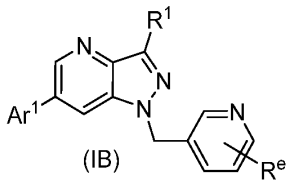
R^d is H or OCH_3; and

R^f is H, CH_3 or OCH_3.

23. The compound of claim 22 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein ring A is



24. The compound of claim 1 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, having the structure of Formula (1B):



(IB)

wherein

R^1 is H, F, or CH_3;

R^e is a member selected from the group consisting of: H, Br, Cl, F, C_{1-4}alkyl, C_{1-4}perhaloalkyl, OC_{1-4}alkyl, OC_{1-4}perhaloalkyl, and CN; and

Ar^1 is selected from the group consisting of:

(d) phenyl substituted with one member selected from the group consisting of: Cl, F, C_{1-4}alkyl, OC_{1-4}alkyl, C_{1-4}perhaloalkyl, and OC_{1-4}perhaloalkyl;

(e) phenyl substituted with two or three members each independently selected from the group consisting of: Br, Cl, F, C_{1-4}alkyl, C_{1-4}perhaloalkyl, and OC_{1-4}perhaloalkyl; and

(f) thienyl substituted with a member selected from the group consisting of: Cl, CH_3, and CHF_2, CF_3.

25. The compound of claim 24 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^1 is H, and R^e is H or F.

26. A compound selected from the group consisting of:

1-(Pyrimidin-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

1-[(5-Bromo-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

5-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;

1-[(2-Methylpyrimidin-5-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

1-(Pyrazin-2-ylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

1-(Pyrimidin-4-ylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

2-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-oxazole;

2-[[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-oxazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(1H-pyrazol-4-ylmethyl)pyrazolo[4,3-b]pyridine;

6-[3-(1,1-Difluoroethyl)phenyl]-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-methyl-4H-1,2,4-triazol-3-yl)methyl]pyrazolo[4,3-b]pyridine;

1-[(3-Methyl-1H-pyrazol-5-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

5-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-N-methyl-1,3,4-thiadiazol-2-amine;

5-[[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazol-2-amine;

5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazol-2-ol;

5-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazol-2-amine;

N-(5-((6-(3-(Difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-1,3,4-thiadiazol-2-yl)acetamide;

3-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,2,4-oxadiazole;

1-Benzyl-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

1-[(3-Fluorophenyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

3-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]benzonitrile;

1-[(4-Methoxyphenyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

6-[3-(Trifluoromethyl)phenyl]-1-[[4-(trifluoromethyl)phenyl]methyl]pyrazolo[4,3-b]pyridine;

3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]benzonitrile;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(3,5-difluorophenyl)methyl]pyrazolo[4,3-b]pyridine;

3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-fluoro-benzonitrile;

3-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]benzonitrile;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(3,5-difluorophenyl)methyl]pyrazolo[4,3-b]pyridine;

3-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-fluoro-benzonitrile;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-methyl-2-thienyl)methyl]pyrazolo[4,3-b]pyridine;

6-(3-(Difluoromethyl)-4-fluorophenyl)-1-((5-fluorothiophen-2-yl)methyl)-1H-pyrazolo[4,3-b]pyridine;

5-((6-(3-(Difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)thiophene-2-carbonitrile;

6-[3-(1,1-Difluoroethyl)phenyl]-1-(1H-pyrazol-4-ylmethyl)pyrazolo[4,3-b]pyridine;

1-[(1-Methylimidazol-4-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

1-[(2,5-Dimethylpyrazol-3-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(1H-pyrazol-4-ylmethyl)pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(1-methylpyrazol-3-yl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-(1H-pyrazol-4-ylmethyl)pyrazolo[4,3-b]pyridine;

6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-(1H-pyrazol-4-ylmethyl)pyrazolo[4,3-b]pyridine;

5-[[6-(4-Fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-isoxazole;

3-[[6-(4-Fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-isoxazole;

3-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]isoxazole;

3-[[6-[3-(1,1-Difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-isoxazole;

4-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]oxazole;

5-Methyl-3-[[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]isoxazole;

5-[[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-2-methyl-oxazole;

2-[[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-oxazole;

5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]isoxazole;

3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]isoxazole;

5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-isoxazole;

3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-isoxazole;

5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-2-methyl-oxazole;

4-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-2-methyl-oxazole;

3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-4-methyl-isoxazole;

4-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3,5-dimethyl-isoxazole;

3-[[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-isoxazole;

3-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-isoxazole;

5-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-2-methyl-oxazole;

2-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-oxazole;

3-[[6-[4-Chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-isoxazole;

5-[[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-2-methyl-oxazole;

5-Methyl-3-[[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]isothiazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-thiazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-4-methyl-thiazole;

4-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-2-methyl-thiazole;

2-[[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-thiazole;

2-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-thiazole;

2-[[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-thiazole;

1-[(1-Methyl-1,2,4-triazol-3-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(1-methyltriazol-4-yl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(1-methyl-1,2,4-triazol-3-yl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(4-methyl-1,2,4-triazol-3-yl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(4,5-dimethyl-1,2,4-triazol-3-yl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-ethyl-4-methyl-1,2,4-triazol-3-yl)methyl]pyrazolo[4,3-b]pyridine;

2-[[6-(5-Chloro-2-thienyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

2-Methyl-5-[[6-[5-(trifluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole;

2-[[6-[5-(Difluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

5-[[6-(4-Fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;

5-[[6-(3-Methoxyphenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;

2-[[6-[3-(1,1-Difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

2-[[6-[3-(1,1-Difluoroethyl)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

3-Methyl-5-[[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,2,4-oxadiazole;

2-Methyl-5-[[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole;

5-Methyl-3-[[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,2,4-oxadiazole;

5-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,2,4-oxadiazole;

2-Methyl-5-[[6-[2-(trifluoromethyl)-4-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole;

2-[[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

2-[[3-Fluoro-6-(4-fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

2-[[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-(trifluoromethyl)-1,3,4-oxadiazole;

2-[[6-(3-Chloro-4-fluoro-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

2-[[6-(3-Chloro-4-fluoro-phenyl)-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole;

5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,2,4-oxadiazole;

3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-4-methyl-1,2,5-oxadiazole;

2-Cyclopropyl-5-[[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-oxadiazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-isopropyl-1,3,4-oxadiazole;

5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-N,N-dimethyl-1,3,4-oxadiazol-2-amine;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-(trifluoromethyl)-1,3,4-oxadiazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-phenyl-1,3,4-oxadiazole;

2-[[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

2-[[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

2-[[6-[4-Chloro-3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

2-[[6-[4-Chloro-3-(difluoromethyl)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

5-[[6-[3-Fluoro-5-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;

5-[[6-[2-Fluoro-5-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;

5-[[6-[4-Fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;

5-[[6-[2-Fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;

5-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-1,2,4-oxadiazole;

2-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

3-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,2,4-oxadiazole;

2-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-(trifluoromethyl)-1,3,4-oxadiazole;

2-[[6-[4-Chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

2-[[6-[4-Chloro-3-(difluoromethoxy)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

2-[[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;

2-[[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-(trifluoromethyl)-1,3,4-oxadiazole;

4-[[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]thiadiazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-methyl-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-ethyl-1,3,4-thiadiazole;

5-((6-(3-(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-N-methyl-1,3,4-thiadiazol-2-amine;

2-[[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methoxy-1,3,4-thiadiazole;

N-(5-((6-(3-(Difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-1,3,4-thiadiazol-2-yl)acetamide;

2-(Difluoromethyl)-5-[[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazole;

2-Cyclopropyl-5-[[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-1,3,4-thiadiazole;

2-[[6-[4-Chloro-3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;

2-[[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;

2-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;

2-[[6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methoxy-1,3,4-thiadiazole;

2-[[6-[4-Chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;

2-[[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;

6-(4-Methyl-2-thienyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;

1-[(5-Methyl-3-pyridyl)methyl]-6-(4-methyl-2-thienyl)pyrazolo[4,3-b]pyridine;

6-(5-Methyl-2-thienyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;

5-[[6-(5-Chloro-2-thienyl)pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;

6-(3-Chloro-2-thienyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;

5-[[6-[5-(Difluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;

1-((6-Fluoropyridin-3-yl)methyl)-6-(5-(trifluoromethyl)thiophen-2-yl)-1H-pyrazolo[4,3-b]pyridine;

5-[[6-[5-(Trifluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;

1-[(6-Fluoro-3-pyridyl)methyl]-6-(m-tolyl)pyrazolo[4,3-b]pyridine;
1-[(5-Fluoro-3-pyridyl)methyl]-6-(m-tolyl)pyrazolo[4,3-b]pyridine;
3-Fluoro-1-[(5-fluoro-3-pyridyl)methyl]-6-(m-tolyl)pyrazolo[4,3-b]pyridine;
6-(4-Chlorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
6-(4-Fluorophenyl)-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;
6-(4-Fluorophenyl)-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
1-[[5-(Difluoromethoxy)-3-pyridyl]methyl]-6-(4-fluorophenyl)pyrazolo[4,3-b]pyridine;
6-(3-Fluorophenyl)-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;
6-(2-Fluorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
6-(3-Methoxyphenyl)-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;
1-[(6-Fluoro-3-pyridyl)methyl]-6-(3-methoxyphenyl)pyrazolo[4,3-b]pyridine;
6-[3-(Difluoromethyl)phenyl]-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;
5-[[6-[3-(Difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;
1-[(5-Chloro-3-pyridyl)methyl]-6-[3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
6-[3-(Difluoromethoxy)phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
6-[3-(1,1-Difluoroethyl)phenyl]-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
6-[3-(1,1-Difluoroethyl)phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;
1-(2-Pyridylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
1-(3-Pyridylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
1-(4-Pyridylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
1-[(6-Methyl-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
1-[(2-Methyl-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
1-[(5-Methyl-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
1-[(4-Methyl-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
1-[(6-Fluoro-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
1-[(2-Fluoro-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
1-[(5-Fluoro-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
1-[(2-Methoxy-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
1-[(5-Methoxy-3-pyridyl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

6-[3-(Trifluoromethyl)phenyl]-1-[[6-(trifluoromethyl)-3-pyridyl]methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Trifluoromethyl)phenyl]-1-[[5-(trifluoromethyl)-3-pyridyl]methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Trifluoromethyl)phenyl]-1-[[4-(trifluoromethyl)-3-pyridyl]methyl]pyrazolo[4,3-b]pyridine;

6-(4-Fluoro-3-methyl-phenyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;

3-Fluoro-6-(4-fluoro-3-methyl-phenyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;

6-(4-Fluoro-3-methyl-phenyl)-1-[(2-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-(4-Fluoro-3-methyl-phenyl)-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-(4-Fluoro-3-methyl-phenyl)-1-[(4-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-(4-Fluoro-3-methyl-phenyl)-1-[(6-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-(4-Fluoro-3-methyl-phenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-(3,5-Difluorophenyl)-1-[(4-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-(3,5-Difluorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-(3,4-Difluorophenyl)-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;

6-(3,4-Difluorophenyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;

6-(3,4-Difluorophenyl)-1-[(2-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-(3,4-Difluorophenyl)-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-(3,4-Difluorophenyl)-1-[(4-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-(3,4-Difluorophenyl)-1-[(6-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-(3,4-Difluorophenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-(3,4-Difluorophenyl)-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

1-[[5-(Difluoromethoxy)-3-pyridyl]methyl]-6-(3,4-difluorophenyl)pyrazolo[4,3-b]pyridine;

6-(3-Chloro-4-fluoro-phenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-(3-Chloro-4-fluoro-phenyl)-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-methyl-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-(3-(Difluoromethyl)-4-fluorophenyl)-1-((6-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(6-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(6-methoxy-2-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(2-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

1-[(5-Chloro-3-pyridyl)methyl]-6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[[5-(difluoromethyl)-3-pyridyl]methyl]pyrazolo[4,3-b]pyridine;

1-[[5-(Difluoromethoxy)-3-pyridyl]methyl]-6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[[5-(trifluoromethyl)-3-pyridyl]methyl]pyrazolo[4,3-b]pyridine;

5-[[6-[3-(Difluoromethyl)-2-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;

1-[(5-Chloro-3-pyridyl)methyl]-6-[3-(difluoromethyl)-2-fluoro-phenyl]pyrazolo[4,3-b]pyridine;

6-(3,4-Dichlorophenyl)-1-[(6-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-(3,4-Dichlorophenyl)-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;

6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

5-[[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;

6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

1-[(5-Chloro-3-pyridyl)methyl]-6-[3-(1,1-difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

5-[[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(6-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(6-methoxy-2-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(2-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

1-[(5-Chloro-3-pyridyl)methyl]-6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridine;

6-[4-Chloro-3-(Difluoromethyl)phenyl]-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

1-[(5-Fluoro-3-pyridyl)methyl]-6-[4-fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

6-[4-Fluoro-3-(trifluoromethyl)phenyl]-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-(3-Bromo-4-fluorophenyl)-1-((6-fluoropyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine;

5-[[6-[4-Chloro-3-(1,1-difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;

6-[4-Chloro-3-(1,1-difluoroethyl)phenyl]-1-[(5-chloro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;

6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

5-[[6-[4-Chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]pyridine-3-carbonitrile;

6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-[(5-methoxy-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-[(5-chloro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-(2,4-Difluoro-3-methyl-phenyl)-1-(2-pyridylmethyl)pyrazolo[4,3-b]pyridine;

6-(2,4-Difluoro-3-methyl-phenyl)-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;

6-(2,4-Difluoro-3-methyl-phenyl)-1-[(5-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-(2,4-Difluoro-3-methyl-phenyl)-1-[(4-methyl-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-(2,4-Difluoro-3-methyl-phenyl)-1-[(6-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

6-(2,4-Difluoro-3-methyl-phenyl)-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

1-(2-Pyridylmethyl)-6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridine;

1-[(5-Fluoro-3-pyridyl)methyl]-6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridine;

1-[(5-Methoxy-3-pyridyl)methyl]-6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridine;
1-[[5-(Difluoromethoxy)-3-pyridyl]methyl]-6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridine;
1-(Pyridazin-4-ylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
6-(m-Tolyl)-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
6-(3-Fluorophenyl)-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
6-[3-(1,1-Difluoroethyl)phenyl]-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
1-(Pyridazin-3-ylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;
6-(4-Fluoro-3-methyl-phenyl)-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(6-methylpyridazin-3-yl)methyl]pyrazolo[4,3-b]pyridine;
6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(6-methylpyridazin-3-yl)methyl]pyrazolo[4,3-b]pyridine;
6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
6-(3,4-Difluorophenyl)-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
6-(4-Chloro-3-methyl-phenyl)-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
1-(Pyridazin-3-ylmethyl)-6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridine;
6-(2,4-Difluoro-3-methyl-phenyl)-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;
6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(pyrimidin-4-ylmethyl)pyrazolo[4,3-b]pyridine;
6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(pyrimidin-4-ylmethyl)pyrazolo[4,3-b]pyridine;
6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(pyrazin-2-ylmethyl)pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(pyrazin-2-ylmethyl)pyrazolo[4,3-b]pyridine;

6-[3-(1,1-Difluoroethyl)phenyl]-1-(pyrimidin-5-ylmethyl)pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(pyrimidin-5-ylmethyl)pyrazolo[4,3-b]pyridine;

1-(Pyrimidin-5-ylmethyl)-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-1-(pyrimidin-5-ylmethyl)pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-(pyrimidin-5-ylmethyl)pyrazolo[4,3-b]pyridine;

6-[4-Chloro-3-(difluoromethoxy)phenyl]-1-(pyrimidin-5-ylmethyl)pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(6-methylpyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(6-methylpyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(2-methylpyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;

1-[(2-Methylpyrimidin-4-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(2-methylpyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;

6-(3,4-Difluorophenyl)-1-[(2-methylpyrimidin-5-yl)methyl]pyrazolo[4,3-b]pyridine;

6-(4-Chloro-3-methyl-phenyl)-1-[(2-methylpyrimidin-5-yl)methyl]pyrazolo[4,3-b]pyridine;

1-[(5-Methylpyrimidin-2-yl)methyl]-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(6-methoxypyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(6-methoxypyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(2-methoxypyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;
6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-1-[(2-methoxypyrimidin-4-yl)methyl]pyrazolo[4,3-b]pyridine;
(5-((6-(3-(Difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)methyl)-1,3,4-oxadiazol-2-yl)methanol;
2-Fluoro-5-(1-((5-methyl-1,3,4-oxadiazol-2-yl)methyl)-1H-pyrazolo[4,3-b]pyridin-6-yl)benzoic acid;
6-(3-(Difluoromethyl)-4-fluorophenyl)-1-((6-(fluoro-18F)pyridin-3-yl)methyl)-1H-pyrazolo[4,3-b]pyridine;
2-[[3-Bromo-6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;
2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;
2-[[3-Deuterio-6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;
and pharmaceutically acceptable salts, solvates, stereoisomers, isotopic variants, and N-oxides thereof.

27. A compound selected from the group consisting of:
2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-oxazole;
2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;
5-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-3-methyl-isoxazole;
2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-oxadiazole;
3-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,2,4-oxadiazole;

2-[[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]methyl]-5-methyl-1,3,4-thiadiazole;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(3-pyridylmethyl)pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-[(5-fluoro-3-pyridyl)methyl]pyrazolo[4,3-b]pyridine;

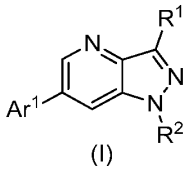
6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(pyridazin-3-ylmethyl)pyrazolo[4,3-b]pyridine;

6-[3-(Difluoromethyl)-4-fluoro-phenyl]-1-(pyrimidin-5-ylmethyl)pyrazolo[4,3-b]pyridine;

and pharmaceutically acceptable salts, solvates, stereoisomers, isotopic variants, and N-oxides thereof.

28. A pharmaceutical composition comprising:

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



(I)

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

wherein

R^1 is H, halo, or CH_3;

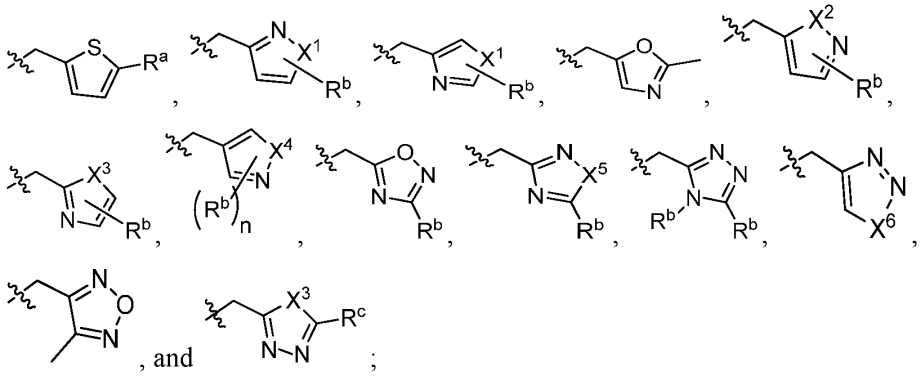
Ar^1 is selected from the group consisting of:

(a) phenyl substituted with one member selected from the group consisting of: halo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{1-6}perhaloalkyl, and OC_{1-6}perhaloalkyl;

(b) phenyl substituted with two or three members each independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}perhaloalkyl, OC_{1-6}perhaloalkyl, and CO_2H; and

(c) thienyl substituted with a member selected from the group consisting of: halo, C_{1-6}alkyl, and C_{1-6}perhaloalkyl; and pyridine substituted with CF_3; and

R^2 is selected from the group consisting of:

(d) 

wherein

R^a is halo, $C_{1\text{-}6}$alkyl or CN;

R^b is H or $C_{1\text{-}2}$alkyl;

R^c is selected from the group consisting of: H, $C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$perhaloalkyl, CH_2OH, $OC_{1\text{-}6}$alkyl, OH, NH_2, $NH(CH_3)$, $N(CH_3)_2$, $NH(C{=}O)CH_3$, cyclopropyl, and phenyl;

X^1 is NCH_3, S or O;

X^2 is O, NH or NCH_3;

X^3 is O or S;

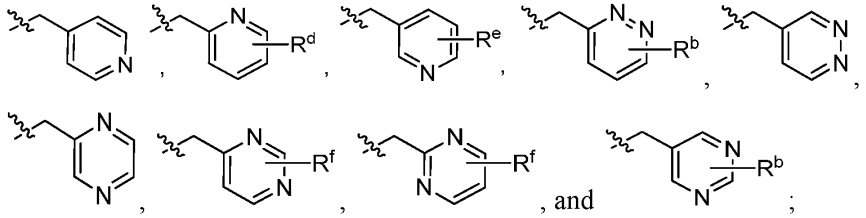
X^4 is NH or O;

X^5 is NCH_3 or O;

X^6 is NCH_3 or S;

and n is 2;

(e) phenyl; phenyl substituted with one or two members independently selected from the group consisting of: halo, $OC_{1\text{-}6}$alkyl, $C_{1\text{-}6}$perhaloalkyl, and CN; and

(f) 

wherein

R^d is H or $OC_{1\text{-}6}$alkyl;

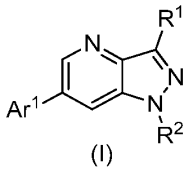
R^e is a member selected from the group consisting of: H, halo, C_{1-6}alkyl, C_{1-6}perhaloalkyl, OC_{1-6}alkyl, OC_{1-6}perhaloalkyl, and CN; and

R^f is H, C_{1-6}alkyl or OC_{1-6}alkyl;

and

(B) at least one pharmaceutically acceptable excipient.

29. A method of treating a subject suffering from or diagnosed with a disease, disorder, or medical condition mediated by GluN2B 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):



(I)

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

wherein

R^1 is H, halo, or CH_3;

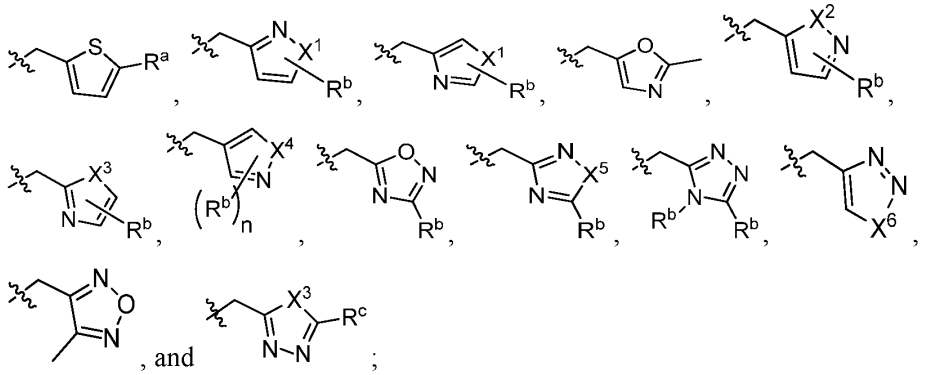
Ar^1 is selected from the group consisting of:

(a) phenyl substituted with one member selected from the group consisting of: halo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{1-6}perhaloalkyl, and OC_{1-6}perhaloalkyl;

(b) phenyl substituted with two or three members each independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}perhaloalkyl, OC_{1-6}perhaloalkyl, and CO_2H; and

(c) thienyl substituted with a member selected from the group consisting of: halo, C_{1-6}alkyl, and C_{1-6}perhaloalkyl; and pyridine substituted with CF_3; and

R^2 is selected from the group consisting of:

(d) 

wherein

R^a is halo, C_{1-6}alkyl or CN;

R^b is H or C_{1-2}alkyl;

R^c is selected from the group consisting of: H, C_{1-6}alkyl, C_{1-6}perhaloalkyl, CH_2OH, OC_{1-6}alkyl, OH, NH_2, $NH(CH_3)$, $N(CH_3)_2$, $NH(C{=}O)CH_3$, cyclopropyl, and phenyl;

X^1 is NCH_3, S or O;

X^2 is O, NH or NCH_3;

X^3 is O or S;

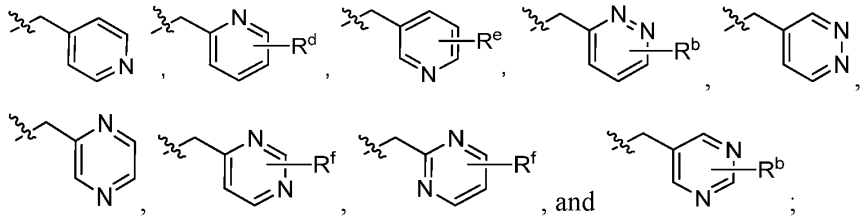
X^4 is NH or O;

X^5 is NCH_3 or O;

X^6 is NCH_3 or S;

and n is 2;

(e) phenyl; phenyl substituted with one or two members independently selected from the group consisting of: halo, OC_{1-6}alkyl, C_{1-6}perhaloalkyl, and CN; and

(f) 

wherein

R^d is H or OC_{1-6}alkyl;

R^e is a member selected from the group consisting of: H, halo, C_{1-6}alkyl, C_{1-6}perhaloalkyl, OC_{1-6}alkyl, OC_{1-6}perhaloalkyl, and CN; and
R^f is H, C_{1-6}alkyl or OC_{1-6}alkyl.

30. The method of claim 29, wherein the disorder, disease or condition mediated by the GluN2B 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.

31. The method of claim 29, wherein the disorder, disease or condition is selected from the group consisting of treatment-resistant depression, major depressive disorder and bipolar disorder.