SUBSTITUTED PYRAZOLO-PYRIDINE AMIDES AND THEIR USE AS GLUN2B RECEPTOR MODULATORS

Cross-Reference to Related Applications

This application claims the priority benefit of U.S. provisional application no. 62/861,656, filed June 14, 2019 and Argentinian application no. P 20 01 01623, filed June 9, 2020, the contents of each 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).

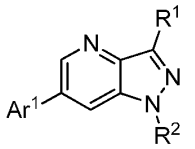
Compounds that modulate GluN2B-containing NMDA receptor function can be useful in treatment of many neurological and psychiatric disorders including but not limited to bipolar disorder (Martucci L et al., *Schizophrenia Res*, **2006**; 84(2-3):214-21), major depressive disorder (Miller OH et al., *eLife.* **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.* **2011**;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;

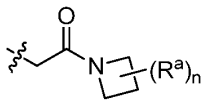
Ar^1 is selected from the group consisting of:

(a) phenyl substituted with one member selected from the group consisting of: halo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{1-6}perhaloalkyl, OC_{1-6}perhaloalkyl, CN, and C_{3-6}cycloalkyl;

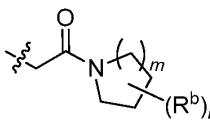
(b) phenyl substituted with two or three members each independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}perhaloalkyl, OC_{1-6}alkyl, OC_{1-6}perhaloalkyl, and $(C=O)CH_3$; and

(c) thienyl independently substituted with one or two members selected from: halo, C_{1-6}alkyl, and C_{1-6}perhaloalkyl; and pyridine substituted with CF_3;

R^2 is selected from the group consisting of:

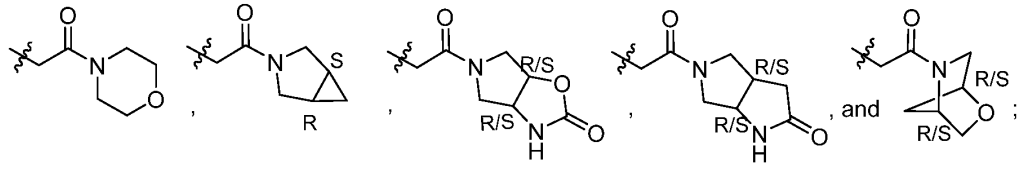
(d)  ; wherein

R^a is each independently selected from the group consisting of: H, halo, OH, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}haloalkenyl, C_{2-6}alkynyl, CH_2OH, $CH(OH)(CH_3)$, CH_2OCH_3, OC_{1-6}haloalkyl, OC_{1-6}alkyl, $NH(CH_3)$, $NHCO_2CH_3$, $NHC(=O)CH_3$, $NHC(=O)CF_3$, NHC(=O)cyclopropyl, $N(CH_3)C(=O)CH_3$, $C(=O)N(CH_3)_2$, $C(=O)CH_3$, CN, $NHSO_2CH_3$, SO_2CH_3, 1H-imidazol-2-yl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrimidin-4-yl, and pyrrolidine-2-one; or two R^a members combine to form a C_{3-6}cycloalkyl or heterocycloalkyl, wherein the cycloalkyl and heterocycloalkyl is optionally substituted one or two F members;

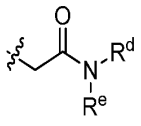
(e)  ; wherein

R^b is each independently selected from the group consisting of: H, OH, F, OCH_3, CH_2OCH_3, and $NHC(=O)CH_3$; or two R^b members come together to form =O;

(f)



and



(g) , wherein

R^d is selected from the group consisting of: C_{1-6}alkyl; C_{2-6}alkenyl C_{1-6}haloalkyl; $CH_2CH_2OCH_3$; CH_2CH_2OH; CH_2CN; NH_2; $NH\text{-}C(=O)CH_3$; C_{3-6}cycloalkyl; C_{3-6}cycloalkyl substituted with two F members; 1-methylazetidin-3-yl; and oxetan-3-yl;

R^e is H or CH_3;

n is 1 or 2; and

m is 1 or 2;

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.

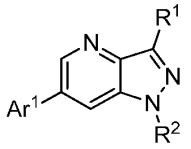
Additional embodiments of this invention include methods of making compounds of Formula (I), pharmaceutically acceptable salts of compounds of Formula (I), pharmaceutically acceptable prodrugs of compounds of Formula (I), and pharmaceutically active metabolites of Formula (I).

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



(I)

wherein

R^1 is H, halo, or CH_3;

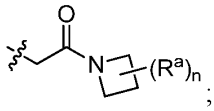
Ar^1 is selected from the group consisting of:

(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, $OC_{1\text{-}6}$perhaloalkyl, CN, and $C_{3\text{-}6}$cycloalkyl;

(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, $OC_{1\text{-}6}$alkyl, $OC_{1\text{-}6}$perhaloalkyl, and $(C{=}O)CH_3$; and

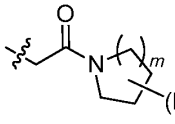
(c) thienyl independently substituted with one or two members selected from: halo, $C_{1\text{-}6}$alkyl, and $C_{1\text{-}6}$perhaloalkyl; and pyridine substituted with CF_3;

R^2 is selected from the group consisting of:

(d)  ; wherein

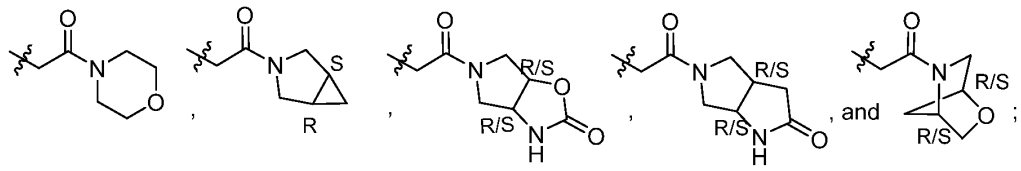
R^a is each independently selected from the group consisting of: H, halo, OH, $C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$haloalkyl, $C_{2\text{-}6}$alkenyl, $C_{2\text{-}6}$haloalkenyl, $C_{2\text{-}6}$alkynyl, CH_2OH, $CH(OH)(CH_3)$, CH_2OCH_3, $OC_{1\text{-}6}$haloalkyl, $OC_{1\text{-}6}$alkyl, $NH(CH_3)$, $NHCO_2CH_3$, $NHC(=O)CH_3$, $NHC(=O)CF_3$, NHC(=O)cyclopropyl,

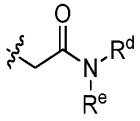
$N(CH_3)C(=O)CH_3$, $C(=O)N(CH_3)_2$, $C(=O)CH_3$, CN, $NHSO_2CH_3$, SO_2CH_3, 1H-imidazol-2-yl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrimidin-4-yl, and pyrrolidine-2-one; or two R^a members combine to form a C_{3-6}cycloalkyl or heterocycloalkyl, wherein the cycloalkyl and heterocycloalkyl is optionally substituted one or two F members;

(e)  ; wherein

R^b is each independently selected from the group consisting of: H, OH, F, OCH_3, CH_2OCH_3, and $NHC(=O)CH_3$; or two R^b members come together to form =O;

(f)

 and



(g) , wherein

R^d is selected from the group consisting of: C_{1-6}alkyl; C_{2-6}alkenyl C_{1-6}haloalkyl; $CH_2CH_2OCH_3$; CH_2CH_2OH; CH_2CN; NH_2; NH-C(=O)CH_3; C_{3-6}cycloalkyl; C_{3-6}cycloalkyl substituted with two F members; 1-methylazetidin-3-yl; and oxetan-3-yl;

R^e is H or CH_3;

n is 1 or 2; and

m is 1 or 2.

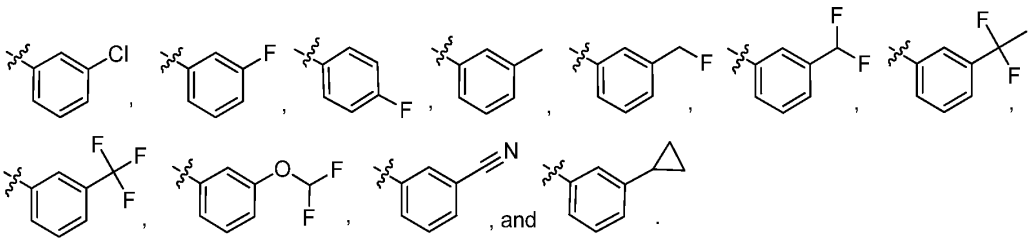
An additional embodiment of the invention is a compound of Formula (I) wherein R^1 is H.

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.

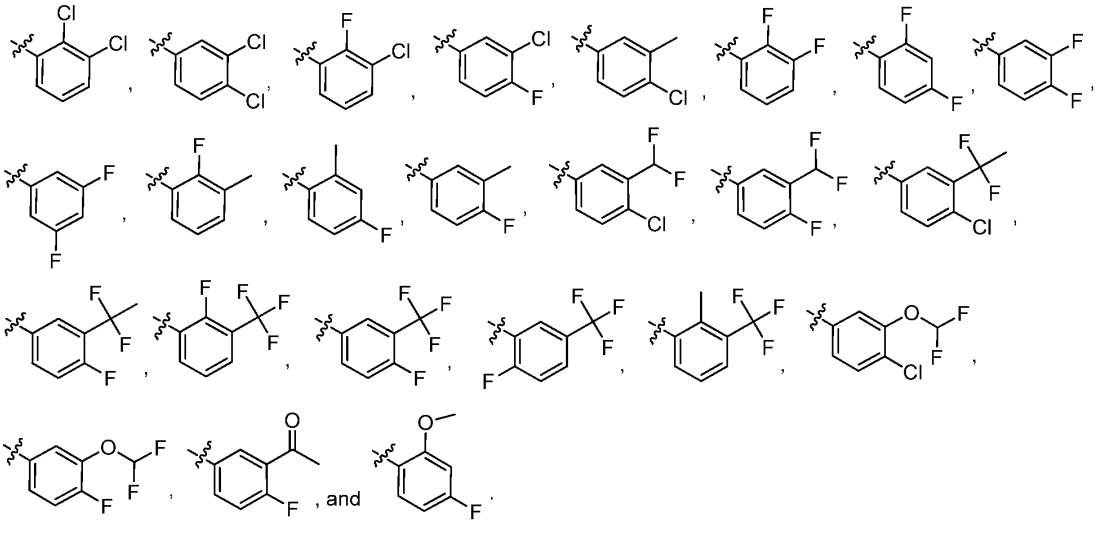
An additional embodiment of the invention is a compound of Formula (I) wherein Ar^1 is phenyl substituted with one member selected from the group consisting of: Cl, F, CH_3, OCH_3, CH_2F, CHF_2, CF_3, CHF_2CH_3, $OCHF_2$, CN, and cyclopropyl.

An additional embodiment of the invention is a compound of Formula (I) wherein Ar^1 is selected from the group consisting of:

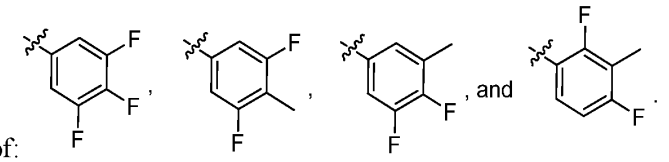


An additional embodiment of the invention is a compound of Formula (I) wherein Ar^1 is phenyl substituted with two members each independently selected from the group consisting of: Cl, F, CH_3, CHF_2, CF_3, CHF_2CH_3, OCH_3, $OCHF_2$, and $(C{=}O)CH_3$.

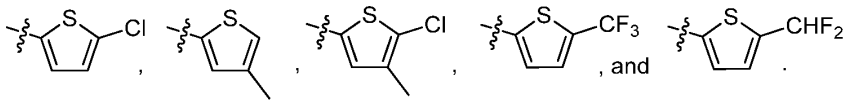
An additional embodiment of the invention is a compound of Formula (I) wherein Ar^1 is selected from the group consisting of:

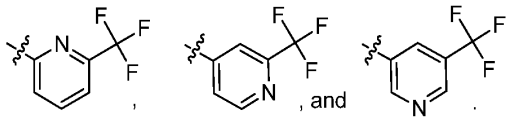


An additional embodiment of the invention is a compound of Formula (I) wherein Ar^1 is phenyl substituted with three members each independently selected from the group consisting of: halo, and CH_3.

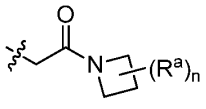
An additional embodiment of the invention is a compound of Formula (I) wherein Ar^1 is selected from the group consisting of: .

An additional embodiment of the invention is a compound of Formula (I) wherein Ar^1 is thienyl independently substituted with one or two members selected from: Cl, CH_3, CF_3 and CHF_2.

An additional embodiment of the invention is a compound of Formula (I) wherein Ar^1 is selected from the group consisting of: .

An additional embodiment of the invention is a compound of Formula (I) wherein Ar^1 is selected from the group consisting of: .

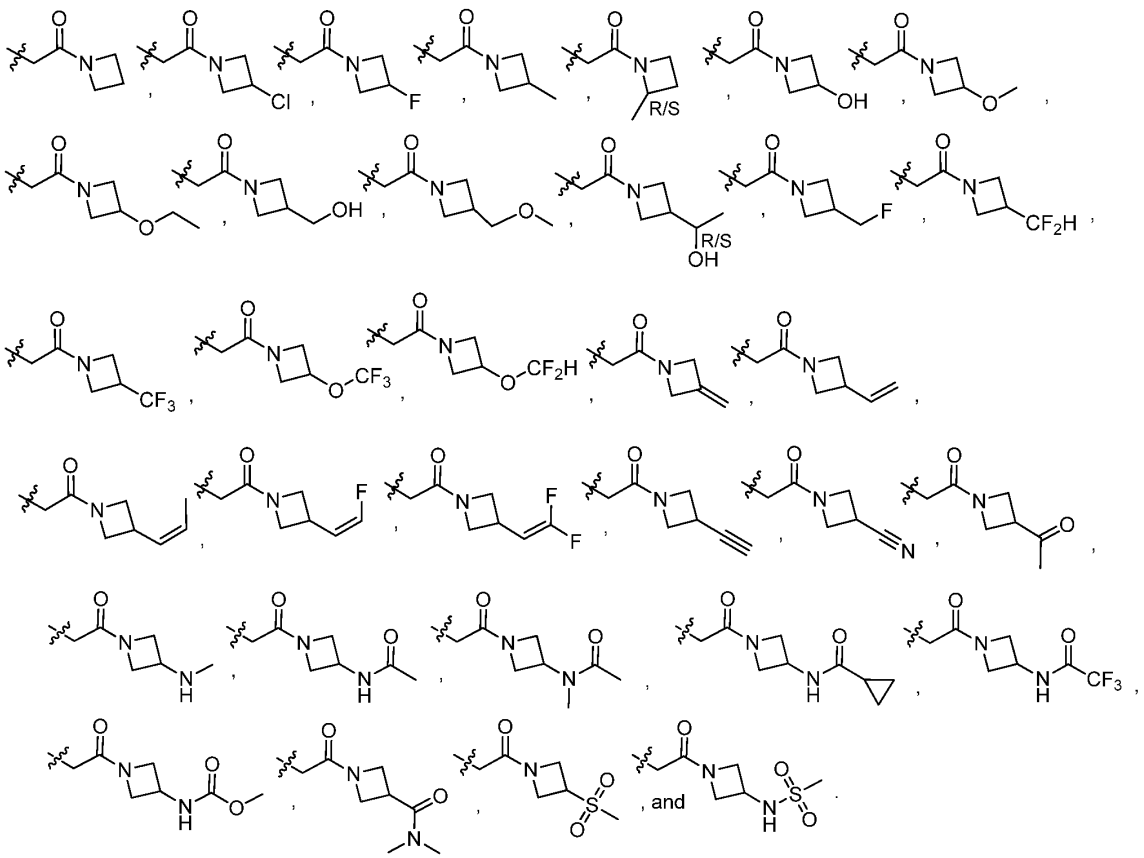
An additional embodiment of the invention is a compound of Formula (I) wherein

R^2 is ; wherein

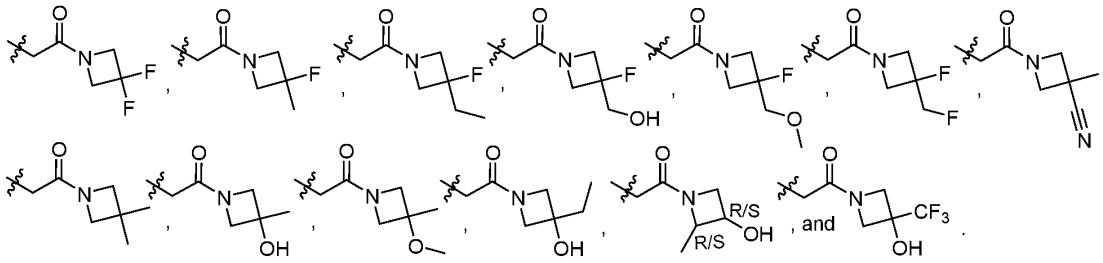
R^a is each independently selected from the group consisting of: H, Cl, F, OH, CH_3, CH_2CH_3, CH_2F, CHF_2, CF_3, $=CH_2$, $CH=CH_2$, $CH=CH(CH_3)$, $CH=CH(F)$, $CH=CF(F)$, $C^{\equiv}CH$, CH_2OH, $CH(OH)(CH_3)$, CH_2OCH_3, $OCHF_2$, OCF_3, OCH_3, OCH_2CH_3, $NH(CH_3)$, $NHCO_2CH_3$, $NHC(=O)CH_3$, $NHC(=O)CF_3$, NHC(=O)cyclopropyl, $N(CH_3)C(=O)CH_3$, $C(=O)N(CH_3)_2$, $C(=O)CH_3$, CN, $NHSO_2CH_3$, SO_2CH_3, 1H-imidazol-2-yl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrimidin-4-yl, and pyrrolidine-2-one; or two R^a members combine to form a cyclopropyl, cyclobutyl, or oxetanyl; wherein the cyclopropyl is optionally substituted one or two F members;

and n is 1 or 2.

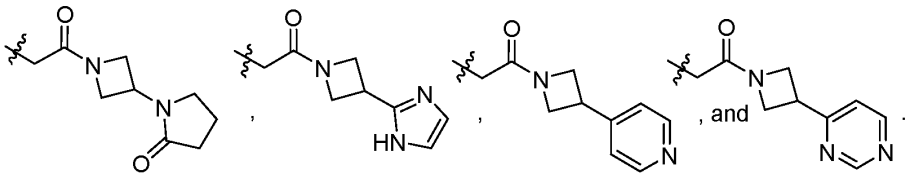
An additional embodiment of the invention is a compound of Formula (I) wherein R^2 is selected from the group consisting of:



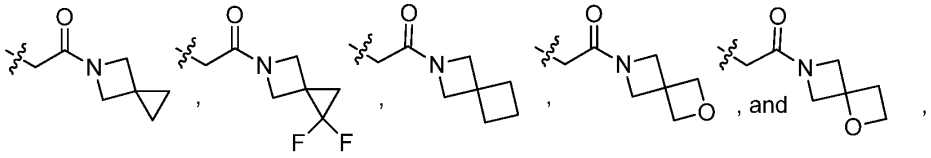
An additional embodiment of the invention is a compound of Formula (I) wherein R^2 is selected from the group consisting of:



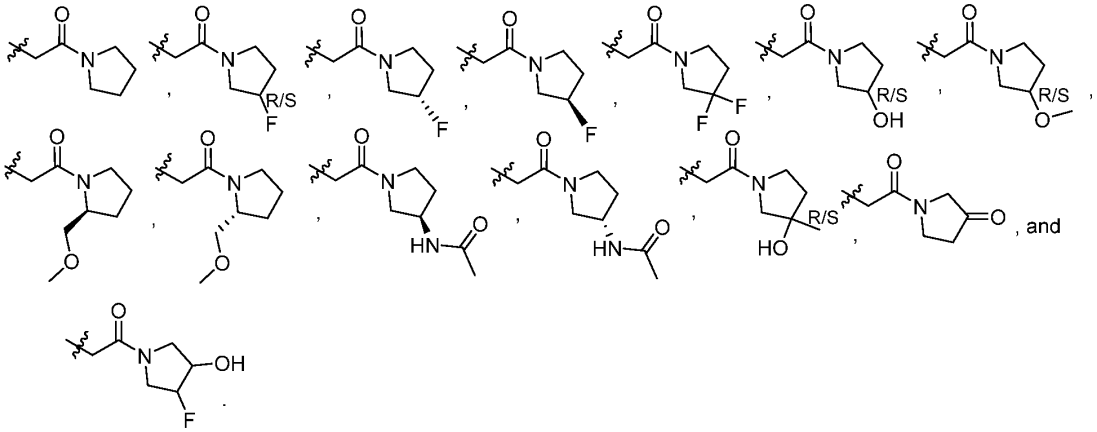
An additional embodiment of the invention is a compound of Formula (I) wherein R^2 is selected from the group consisting of:



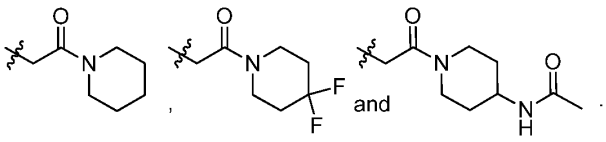
An additional embodiment of the invention is a compound of Formula (I) wherein R^2 is selected from the group consisting of:



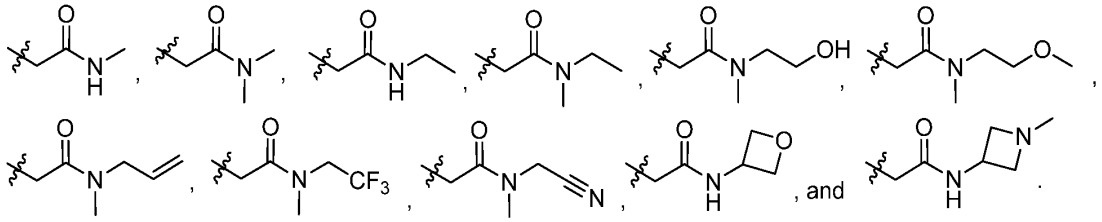
An additional embodiment of the invention is a compound of Formula (I) wherein R^2 is selected from the group consisting of:



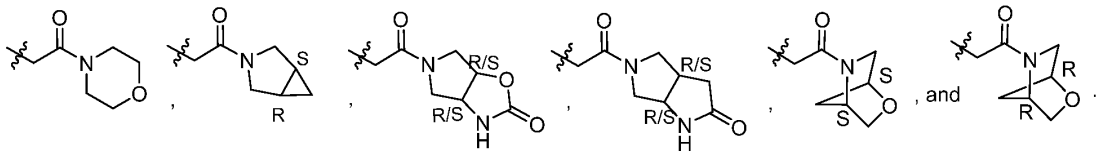
An additional embodiment of the invention is a compound of Formula (I) wherein R^2 is selected from the group consisting of:



An additional embodiment of the invention is a compound of Formula (I) wherein R^2 is selected from the group consisting of:



An additional embodiment of the invention is a compound of Formula (I) wherein R^2 is selected from the group consisting of:



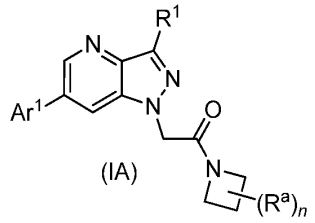
An additional embodiment of the invention is a compound of Formula (I) wherein n is 1.

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

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

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

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



(IA)

wherein

R^1 is H, F, 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, OC_{1-6}perhaloalkyl, CN, and C_{3-6}cycloalkyl;

(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}alkyl, OC_{1-6}perhaloalkyl, and $(C=O)CH_3$; and

(c) thienyl independently substituted with one or two members selected from: halo, C_{1-6}alkyl, and C_{1-6}perhaloalkyl; and pyridine substituted with CF_3;

R^a is each independently selected from the group consisting of: H, halo, OH, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}haloalkenyl, C_{2-6}alkynyl, CH_2OH, $CH(OH)(CH_3)$, CH_2OCH_3, OC_{1-6}haloalkyl, OC_{1-6}alkyl, $NH(CH_3)$, $NHCO_2CH_3$, $NHC(=O)CH_3$, $NHC(=O)CF_3$, NHC(=O)cyclopropyl, $N(CH_3)C(=O)CH_3$, $C(=O)N(CH_3)_2$, $C(=O)CH_3$, CN, $NHSO_2CH_3$, SO_2CH_3, 1H-imidazol-2-yl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrimidin-4-yl, and pyrrolidine-2-one; or two R^a members combine to form a C_{3-6}cycloalkyl or heterocycloalkyl, wherein the C_{3-6}cycloalkyl and heterocycloalkyl is optionally substituted one or two F members; and

n is 1 or 2.

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

R^1 is H, F, or CH_3;

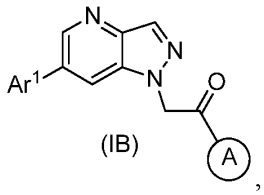
Ar^1 is phenyl substituted with two or three members each independently selected from the group consisting of: halo, C_{1-4}alkyl, C_{1-4}perhaloalkyl, OC_{1-4}alkyl, and OC_{1-4}perhaloalkyl;

R^a is each independently selected from the group consisting of: H, Cl, F, OH, CH_3, CH_2CH_3, CH_2F, CHF_2, CF_3, $=CH_2$, $CH=CH_2$, $CH=CH(CH_3)$, CH=CH(F), CH=CF(F), $C^{=}CH$, CH_2OH, $CH(OH)(CH_3)$, CH_2OCH_3, $OCHF_2$, OCF_3, OCH_3, OCH_2CH_3, $NH(CH_3)$, $NHCO_2CH_3$, $NHC(=O)CH_3$, $NHC(=O)CF_3$, NHC(=O)cyclopropyl, $N(CH_3)C(=O)CH_3$, $C(=O)CH_3$, CN, $NHSO_2CH_3$, 1H-imidazol-2-yl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrimidin-4-yl, and pyrrolidine-2-one; or two R^a members combine to form a cyclopropyl, cyclobutyl, or oxetanyl; wherein the cyclopropyl is optionally substituted one or two F members;

and n is 1 or 2.

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

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



,

wherein

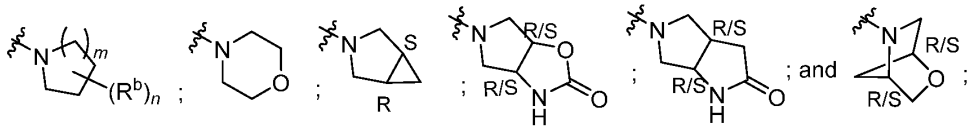
Ar^1 is selected from the group consisting of:

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

(c) thienyl independently substituted with one or two members selected from: halo, $C_{1\text{-}6}$alkyl, and $C_{1\text{-}6}$perhaloalkyl; and pyridine substituted with CF_3;

Ring (A) is selected from the group consisting of:

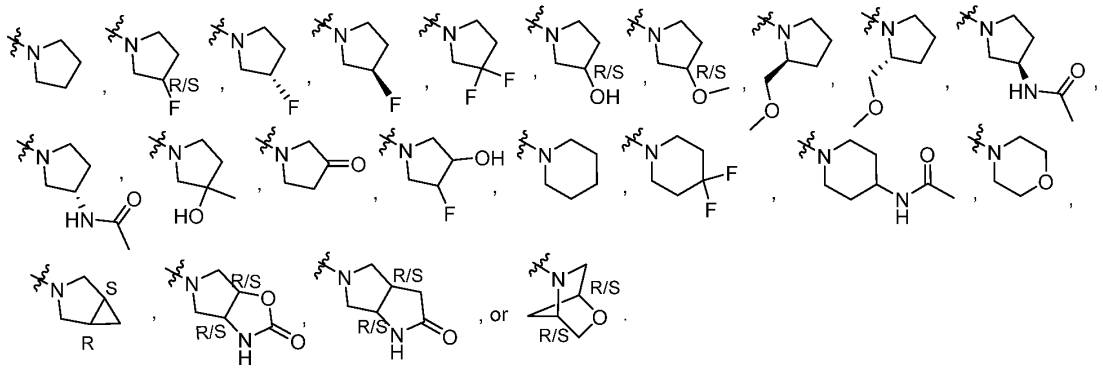


R^b is each independently selected from the group consisting of: H, OH, F, OCH_3, CH_2OCH_3, and $NHC(=O)CH_3$; or two R^b members come together to form =O;

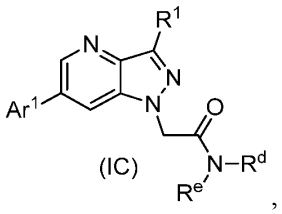
n is 1 or 2; and

m is 1 or 2.

An additional embodiment of the invention is a compound of Formula (IB), wherein Ring A is



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



wherein

R^1 is H, F, 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, and C_{1-6}perhaloalkyl;

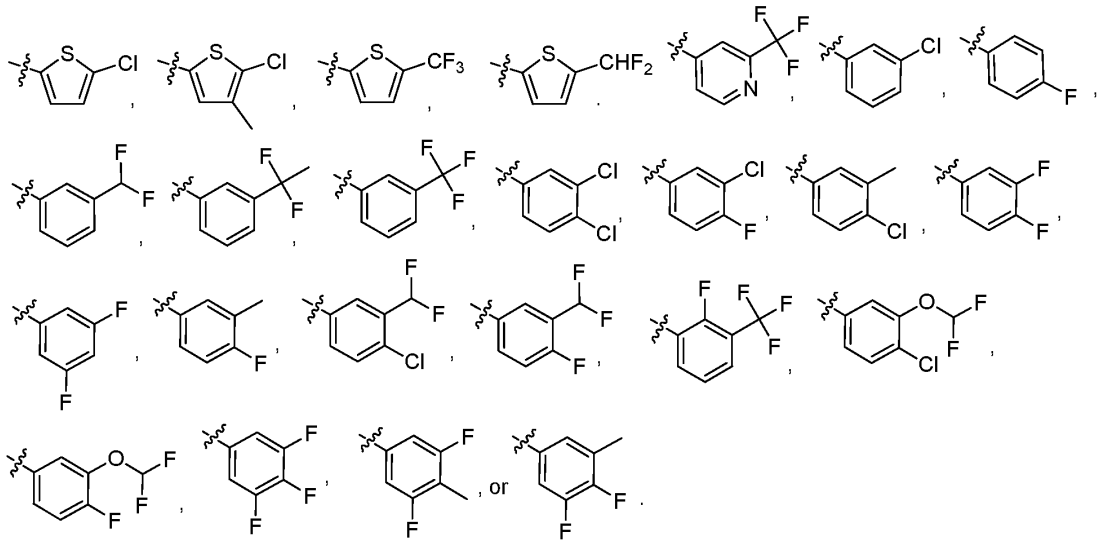
(b) phenyl substituted with two or three members each independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}perhaloalkyl, OC_{1-6}perhaloalkyl; and

(c) thienyl independently substituted with one or two members selected from: halo, C_{1-6}alkyl, and C_{1-6}perhaloalkyl; and pyridine substituted with CF_3;

R^d is selected from the group consisting of: C_{1-6}alkyl; $CH_2CH{=}CH_2$; C_{1-6}haloalkyl; $CH_2CH_2OCH_3$; CH_2CH_2OH; CH_2CN; NH_2; NH-C(=O)CH_3; cyclopropyl; cyclobutyl; 3-bicyclo[1.1.1]pentanyl; 3,3-difluorocyclobutyl; 1-methylazetidin-3-yl; and oxetan-3-yl; and

R^e is H or CH_3.

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



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

Example#	Compound Name
1	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-hydroxy-3-(trifluoromethyl)azetidin-1-yl]ethanone;
2	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methyleneazetidin-1-yl)ethanone;
3	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-(methylamino)azetidin-1-yl]ethanone;
4	N-[1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]azetidin-3-yl]-N-methyl-acetamide;
5	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

Example#	Compound Name
6	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
7	2-[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
8	N,N-Dimethyl-2-[6-[6-(trifluoromethyl)-2-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;
9	2-[6-[4-Chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;
10	2-[6-[4-Chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
11	N,N-Dimethyl-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;
12	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-morpholino-ethanone;
13	1-Morpholino-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
14	N-Cyclopropyl-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;
15	N-(1-Methylazetidin-3-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;
16	1-(3-Fluoroazetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
17	1-(3,3-Difluoroazetidin-1-yl)-2-[6-(2,4-difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
18	1-(Azetidin-1-yl)-2-[6-(5-chloro-2-thienyl)-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]ethanone;
19	1-(Azetidin-1-yl)-2-[6-[5-(difluoromethyl)-2-thienyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]ethanone;

Example#	Compound Name
20	1-(Azetidin-1-yl)-2-[3-fluoro-6-[5-(trifluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
21	1-(Azetidin-1-yl)-2-[6-(4-fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
22	1-(Azetidin-1-yl)-2-[6-(3-chlorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
23	1-(Azetidin-1-yl)-2-[6-[3-(fluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
24	1-(Azetidin-1-yl)-2-[6-[3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
25	1-(Azetidin-1-yl)-2-[6-[3-(1,1-difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
26	1-(Azetidin-1-yl)-2-[6-[3-(1,1-difluoroethyl)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]ethanone;
27	1-(Azetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
28	1-(Azetidin-1-yl)-2-[3-methyl-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
29	1-(Azetidin-1-yl)-2-[6-(3,4-dichlorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
30	1-(Azetidin-1-yl)-2-[6-(2,3-dichlorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
31	1-(Azetidin-1-yl)-2-[6-(3-chloro-2-fluoro-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
32	1-(Azetidin-1-yl)-2-[6-(3,4-difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
33	1-(Azetidin-1-yl)-2-[6-[2-fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

Example#	Compound Name
34	1-(Azetidin-1-yl)-2-[6-[3-(1,1-difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
35	1-(Azetidin-1-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
36	1-(Azetidin-1-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]ethanone;
37	1-(Azetidin-1-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]-3-methyl-pyrazolo[4,3-b]pyridin-1-yl]ethanone;
38	1-(Azetidin-1-yl)-2-[6-(4-chloro-3-methylphenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
39	1-(Azetidin-1-yl)-2-[6-(4-chloro-3-methylphenyl)-3-methyl-pyrazolo[4,3-b]pyridin-1-yl]ethanone;
40	1-(Azetidin-1-yl)-2-[6-(2-fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
41	1-(Azetidin-1-yl)-2-[6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
42	1-(Azetidin-1-yl)-2-[6-[3-(difluoromethoxy)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]ethanone;
43	1-(Azetidin-1-yl)-2-[6-[4-chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
44	1-(Azetidin-1-yl)-2-[6-[4-chloro-3-(difluoromethoxy)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]ethanone;
45	1-(Azetidin-1-yl)-2-[6-(4-fluoro-2-methoxy-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
46	2-[6-(3-Acetyl-4-fluoro-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(azetidin-1-yl)ethanone;
47	1-(Azetidin-1-yl)-2-[6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;

Example#	Compound Name
48	1-(Azetidin-1-yl)-2-[6-[2-(trifluoromethyl)-4-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
49	2-[6-(5-Chloro-2-thienyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;
50	2-[6-(5-Chloro-2-thienyl)-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;
51	2-[6-[5-(Difluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;
52	2-[6-[5-(Difluoromethyl)-2-thienyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;
53	1-(3-Fluoroazetidin-1-yl)-2-[6-[5-(trifluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
54	1-(3-Fluoroazetidin-1-yl)-2-[3-fluoro-6-[5-(trifluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
55	1-(3-Fluoroazetidin-1-yl)-2-[6-(3-fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
56	1-(3-Fluoroazetidin-1-yl)-2-[6-(4-fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
57	2-[6-(3-Chlorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;
58	1-(3-Fluoroazetidin-1-yl)-2-[6-(m-tolyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
59	1-(3-Fluoroazetidin-1-yl)-2-[6-[3-(fluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
60	2-[6-[3-(Difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;
61	2-[6-[3-(1,1-Difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

Example#	Compound Name
62	2-[6-[3-(Difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;
63	2-[6-(2,3-Difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;
64	2-[6-(2,4-Difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;
65	2-[6-(3,4-Difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;
66	2-[6-(3,5-Difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;
67	2-[6-(3-Chloro-2-fluoro-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;
68	2-[6-(3-Chloro-4-fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;
69	1-(3-Chloroazetidin-1-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
70	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;
71	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-methyl-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;
72	2-[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;
73	2-[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;
74	2-[6-[4-Chloro-3-(1,1-difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;
75	2-[6-[4-Chloro-3-(1,1-difluoroethyl)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

Example#	Compound Name
76	2-[6-[4-Chloro-3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;
77	2-[6-(4-Chloro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;
78	1-(3-Fluoroazetidin-1-yl)-2-[6-(4-fluoro-2-methoxy-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
79	2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;
80	2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;
81	2-[6-[4-Chloro-3-(difluoromethoxy)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;
82	2-[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;
83	2-[6-(3,4-Difluoro-5-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;
84	1-(3-Fluoroazetidin-1-yl)-2-[6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
85	1-(3-Fluoroazetidin-1-yl)-2-[6-[2-(trifluoromethyl)-4-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
86	1-(3-Methylazetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
87	(Racemic) 1-(2-Methylazetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
88	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methylazetidin-1-yl)ethanone;
89	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methylazetidin-1-yl)ethanone;

Example#	Compound Name
90	(Racemic) 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(2-methylazetidin-1-yl)ethanone;
91	2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methylazetidin-1-yl)ethanone;
92	2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methylazetidin-1-yl)ethanone;
93	2-[6-[4-Chloro-3-(difluoromethoxy)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methylazetidin-1-yl)ethanone;
94	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-ethynylazetidin-1-yl)ethanone;
95	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-vinylazetidin-1-yl)ethanone;
96	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-[(Z)-prop-1-enyl]azetidin-1-yl]ethanone;
97	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-(fluoromethyl)azetidin-1-yl]ethanone;
98	1-[3-(Difluoromethyl)azetidin-1-yl]-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
99	1-[3-(Trifluoromethyl)azetidin-1-yl]-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
100	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-(trifluoromethyl)azetidin-1-yl]ethanone;
101	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-[(Z)-2-fluorovinyl]azetidin-1-yl]ethanone;
102	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-(2,2-difluorovinyl)azetidin-1-yl]ethanone;
103	1-(3-Methoxyazetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

Example#	Compound Name
104	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methoxyazetidin-1-yl)ethanone;
105	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-ethoxyazetidin-1-yl)ethanone;
106	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-(methoxymethyl)azetidin-1-yl]ethanone;
107	1-[3-(Methoxymethyl)azetidin-1-yl]-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
108	(Racemic) 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-(1-hydroxyethyl)azetidin-1-yl]ethanone;
109	1-[3-(Difluoromethoxy)azetidin-1-yl]-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
110	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-(trifluoromethoxy)azetidin-1-yl]ethanone;
111	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-hydroxyazetidin-1-yl)ethanone;
112	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-hydroxyazetidin-1-yl)ethanone;
113	1-(3-Hydroxyazetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
114	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-(hydroxymethyl)azetidin-1-yl]ethanone;
115	1-(3,3-Difluoroazetidin-1-yl)-2-[6-(4-methyl-2-thienyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
116	1-(3,3-Difluoroazetidin-1-yl)-2-[6-(4-fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
117	2-[6-(3-Chlorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3,3-difluoroazetidin-1-yl)ethanone;

Example#	Compound Name
118	1-(3,3-Difluoroazetidin-1-yl)-2-[6-(m-tolyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
119	1-(3,3-Difluoroazetidin-1-yl)-2-[6-[3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
120	1-(3,3-Difluoroazetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
121	3-[1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]pyrazolo[4,3-b]pyridin-6-yl]benzonitrile;
122	1-(3,3-Difluoroazetidin-1-yl)-2-[6-[6-(trifluoromethyl)-2-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
123	1-(3,3-Difluoroazetidin-1-yl)-2-[6-[2-(trifluoromethyl)-4-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
124	1-(3,3-Difluoroazetidin-1-yl)-2-[6-[5-(trifluoromethyl)-3-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
125	1-(3,3-Difluoroazetidin-1-yl)-2-[6-(3,4-difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
126	1-(3,3-Difluoroazetidin-1-yl)-2-[6-(3,5-difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
127	2-[6-(3-Chloro-4-fluoro-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3,3-difluoroazetidin-1-yl)ethanone;
128	2-[6-(3-Chloro-2-fluoro-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3,3-difluoroazetidin-1-yl)ethanone;
129	1-(3,3-Difluoroazetidin-1-yl)-2-[6-(4-fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
130	1-(3,3-Difluoroazetidin-1-yl)-2-[6-(4-fluoro-2-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
131	1-(3,3-Difluoroazetidin-1-yl)-2-[6-(2-fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;

Example#	Compound Name
132	1-(3,3-Difluoroazetidin-1-yl)-2-[6-[2-fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
133	1-(3,3-Difluoroazetidin-1-yl)-2-[6-[4-fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
134	1-(3,3-Difluoroazetidin-1-yl)-2-[6-[2-fluoro-5-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
135	1-(3,3-Difluoroazetidin-1-yl)-2-[6-[2-methyl-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
136	1-(3,3-Difluoroazetidin-1-yl)-2-[6-(4-fluoro-2-methoxy-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
137	1-(3,3-Difluoroazetidin-1-yl)-2-[6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
138	1-(3,3-Dimethylazetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
139	1-(3-Fluoro-3-methyl-azetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
140	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3,3-dimethylazetidin-1-yl)ethanone;
141	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoro-3-methyl-azetidin-1-yl)ethanone;
142	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-ethyl-3-fluoro-azetidin-1-yl)ethanone;
143	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-fluoro-3-(fluoromethyl)azetidin-1-yl]ethanone;
144	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methoxy-3-methyl-azetidin-1-yl)ethanone;
145	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-ethyl-3-hydroxy-azetidin-1-yl)ethanone;

Example#	Compound Name
146	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-hydroxy-3-methyl-azetidin-1-yl)ethanone;
147	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-fluoro-3-(hydroxymethyl)azetidin-1-yl]ethanone;
148	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-fluoro-3-(methoxymethyl)azetidin-1-yl]ethanone;
149	[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-hydroxy-2-methyl-azetidin-1-yl)ethanone;
150	1-[2-[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]azetidine-3-carbonitrile;
151	1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]azetidine-3-carbonitrile;
152	1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]-3-methyl-azetidine-3-carbonitrile;
153	1-(3-Acetylazetidin-1-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
154	N-[1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]azetidin-3-yl]acetamide;
155	1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]-N,N-dimethyl-azetidine-3-carboxamide;
156	MethylN-[1-[2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]azetidin-3-yl]carbamate;
157	N-[1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]azetidin-3-yl]-2,2,2-trifluoro-acetamide;
158	N-[1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]azetidin-3-yl]cyclopropanecarboxamide;
159	N-[1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]azetidin-3-yl]methanesulfonamide;

Example#	Compound Name
160	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methylsulfonylazetidin-1-yl)ethanone;
161	1-[1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]azetidin-3-yl]pyrrolidin-2-one;
162	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-(1H-imidazol-2-yl)azetidin-1-yl]ethanone;
163	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-(4-pyridyl)azetidin-1-yl]ethanone;
164	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-pyrimidin-4-ylazetidin-1-yl)ethanone;
165	1-(5-Azaspiro[2.3]hexan-5-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
166	1-(2,2-Difluoro-5-azaspiro[2.3]hexan-5-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
167	1-(6-Azaspiro[3.3]heptan-6-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
168	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-oxa-6-azaspiro[3.3]heptan-6-yl)ethanone;
169	1-(6-Oxa-2-azaspiro[3.3]heptan-2-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
170	2-[6-(4-Fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-pyrrolidin-1-yl-ethanone;
171	1-Pyrrolidin-1-yl-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
172	2-[6-(3-Cyclopropylphenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-pyrrolidin-1-yl-ethanone;
173	2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-pyrrolidin-1-yl-ethanone;

Example#	Compound Name
174	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-pyrrolidin-1-yl-ethanone;
175	2-[6-(3,5-Difluoro-4-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-pyrrolidin-1-yl-ethanone;
176	1-[(3R)-3-Fluoropyrrolidin-1-yl]-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
177	1-[(3S)-3-Fluoropyrrolidin-1-yl]-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
178	(Racemic) (R,S)-2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoropyrrolidin-1-yl)ethanone;
179	(Racemic) (R,S)-2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoropyrrolidin-1-yl)ethanone;
180	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[(3R)-3-fluoropyrrolidin-1-yl]ethanone;
181	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[(3S)-3-fluoropyrrolidin-1-yl]ethanone;
182	(Racemic) (R,S)-2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-hydroxypyrrolidin-1-yl)ethanone;
183	(Racemic) (R,S)-2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-hydroxypyrrolidin-1-yl)ethanone;
184	(Racemic) 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methoxypyrrolidin-1-yl)ethanone;
185	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[(2R)-2-(methoxymethyl)pyrrolidin-1-yl]ethanone;
186	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[(2S)-2-(methoxymethyl)pyrrolidin-1-yl]ethanone;
187	N-[(3S)-1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]pyrrolidin-3-yl]acetamide;

Example#	Compound Name
188	N-[(3R)-1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]pyrrolidin-3-yl]acetamide;
189	1-(3,3-Difluoropyrrolidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
190	2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3,3-difluoropyrrolidin-1-yl)ethanone;
191	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3,3-difluoropyrrolidin-1-yl)ethanone;
192	(Racemic) 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-hydroxy-3-methyl-pyrrolidin-1-yl)ethanone;
193	(Racemic) Trans-2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoro-4-hydroxy-pyrrolidin-1-yl)ethanone;
194	1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]pyrrolidin-3-one;
195	1-[2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]pyrrolidin-3-one;
196	1-(1-Piperidyl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
197	1-(4,4-Difluoro-1-piperidyl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
198	N-[1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]-4-piperidyl]acetamide;
199	2-[6-(4-Fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-morpholino-ethanone;
200	1-[(1R,5S)-3-Azabicyclo[3.1.0]hexan-3-yl]-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
201	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[(1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl]ethanone;

Example#	Compound Name
202	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[(1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl]ethanone;
203	(Racemic) Cis-5-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]-3a,4,6,6a-tetrahydro-3H-pyrrolo[3,4-d]oxazol-2-one;
204	(Racemic) Cis-5-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]-1,3,3a,4,6,6a-hexahydropyrrolo[2,3-c]pyrrol-2-one;
205	2-[6-[5-(Difluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
206	N,N-Dimethyl-2-[6-[5-(trifluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;
207	2-[6-(5-Chloro-2-thienyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
208	2-[6-(5-Chloro-4-methyl-2-thienyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
209	2-[6-[3-(Difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
210	2-[6-[3-(Difluoromethyl)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
211	2-[3-Fluoro-6-(4-fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
212	2-[3-Fluoro-6-(3-fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
213	2-[6-(3-Chlorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
214	N,N-Dimethyl-2-[6-[2-(trifluoromethyl)-4-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;
215	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N-methyl-acetamide;

Example#	Compound Name
216	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N-ethyl-acetamide;
217	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N-ethyl-N-methyl-acetamide;
218	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
219	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-methyl-pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
220	2-[6-[4-Chloro-3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
221	2-[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
222	2-[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-N-methyl-acetamide;
223	2-[3-Fluoro-6-(4-fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
224	2-[6-(4-Chloro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
225	2-[6-(3-Chloro-4-fluoro-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
226	2-[6-(3,4-Dichlorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
227	2-[6-(3,5-Difluorophenyl)-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
228	2-[6-(3,4-Difluorophenyl)-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
229	2-[6-[3-(1,1-Difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

Example#	Compound Name
230	2-[6-[3-(1,1-Difluoroethyl)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
231	2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
232	2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
233	2-[6-[2-Fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
234	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N-(2-methoxyethyl)-N-methyl-acetamide;
235	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N-(2-hydroxyethyl)-N-methyl-acetamide;
236	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;
237	N-(Cyanomethyl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N-methyl-acetamide;
238	N-Allyl-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N-methyl-acetamide;
239	N,N-Dimethyl-2-[6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]acetamide;
240	2-[6-(3,4-Difluoro-5-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
241	2-[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
242	N-Cyclopropyl-N-methyl-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;
243	N-Cyclopropyl-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;

Example#	Compound Name
244	N-Cyclopropyl-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N-methyl-acetamide;
245	N-Cyclopropyl-2-[3-methyl-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;
246	N-Cyclopropyl-2-[6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;
247	N-Cyclobutyl-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;
248	N-Cyclobutyl-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N-methyl-acetamide;
249	N-Cyclobutyl-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;
250	N-(3,3-Difluorocyclobutyl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;
251	N-(3,3-Difluorocyclobutyl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;
252	N-(3-Bicyclo[1.1.1]pentanyl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N-methyl-acetamide;
253	N-(Oxetan-3-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;
254	2-(6-(3-(Difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-(pyridin-3-yl)azetidin-1-yl)ethan-1-one;
255	2-(6-(3-(Difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-(pyridin-2-yl)azetidin-1-yl)ethan-1-one;
256	Methyl (1-(2-(6-(3-(Difluoromethyl)-4-fluorophenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)acetyl)azetidin-3-yl)carbamate;
257	(*S*)-*N*-(1-(2-(6-(3-(Difluoromethyl)-4-fluorophenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)acetyl)pyrrolidin-3-yl)acetamide;

Example#	Compound Name
258	(*R*)-*N*-(1-(2-(6-(3-(Difluoromethyl)-4-fluorophenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)acetyl)pyrrolidin-3-yl)acetamide; and
259	1-(3-(Fluoro-18F)azetidin-1-yl)-2-(6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)ethan-1-one;

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]-1-(3-fluoroazetidin-1-yl)ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

2-[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

2-[6-[4-Chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

1-(Azetidin-1-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(Azetidin-1-yl)-2-[6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

2-[6-[4-Chloro-3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

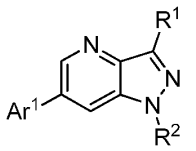
2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone; and

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

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

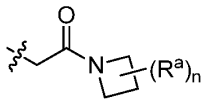
Ar^1 is selected from the group consisting of:

(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, OC_{1-6}perhaloalkyl, CN, and C_{3-6}cycloalkyl;

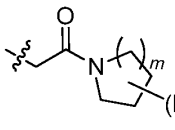
(b) phenyl substituted with two or three members each independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}perhaloalkyl, OC_{1-6}alkyl, OC_{1-6}perhaloalkyl, and $(C=O)CH_3$; and

(c) thienyl independently substituted with one or two members selected from: halo, C_{1-6}alkyl, and C_{1-6}perhaloalkyl; and pyridine substituted with CF_3;

R^2 is selected from the group consisting of:

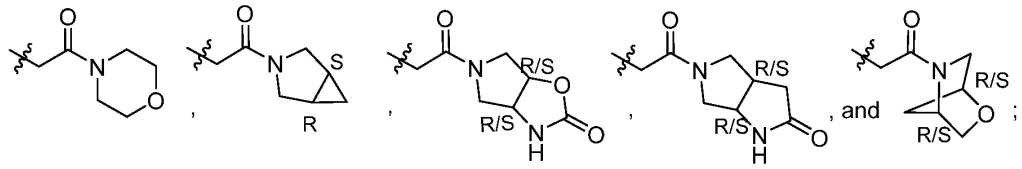
(d) ; wherein

R^a is each independently selected from the group consisting of: H, halo, OH, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}haloalkenyl, C_{2-6}alkynyl, CH_2OH, $CH(OH)(CH_3)$, CH_2OCH_3, OC_{1-6}haloalkyl, OC_{1-6}alkyl, $NH(CH_3)$, $NHCO_2CH_3$, $NHC(=O)CH_3$, $NHC(=O)CF_3$, NHC(=O)cyclopropyl, $N(CH_3)C(=O)CH_3$, $C(=O)N(CH_3)_2$, $C(=O)CH_3$, CN, $NHSO_2CH_3$, SO_2CH_3, 1H-imidazol-2-yl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrimidin-4-yl, and pyrrolidine-2-one; or two R^a members combine to form a C_{3-6}cycloalkyl or heterocycloalkyl, wherein the cycloalkyl and heterocycloalkyl is optionally substituted one or two F members;

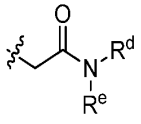
(e)  ; wherein

R^b is each independently selected from the group consisting of: H, OH, F, OCH_3, CH_2OCH_3, and $NHC(=O)CH_3$; or two R^b members come together to form =O;

(f)

 , and ;

and

(g)  , wherein

R^d is selected from the group consisting of: $C_{1\text{-}6}$alkyl; $C_{2\text{-}6}$alkenyl $C_{1\text{-}6}$haloalkyl; $CH_2CH_2OCH_3$; CH_2CH_2OH; CH_2CN; NH_2; $NH\text{-}C(=O)CH_3$; $C_{3\text{-}6}$cycloalkyl; $C_{3\text{-}6}$cycloalkyl substituted with two F members; 1-methylazetidin-3-yl; and oxetan-3-yl;

R^e is H or CH_3;

n is 1 or 2; and

m is 1 or 2;

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.

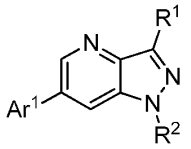
An additional embodiment of the invention is a pharmaceutical composition comprising and effective amount of at least one compound of Formula (IC), as well as pharmaceutically acceptable salts, N-oxides or solvates of compounds of Formula (IC), pharmaceutically acceptable prodrugs of compounds of Formula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

An additional embodiment of the invention is a pharmaceutical composition comprising 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), (IB), and (IC)). Also within the scope of the invention are the pharmaceutically acceptable salts, N-oxides or solvates of the compounds of Formula (I) (as well as Formulas (IA), (IB), and (IC)). Also within the scope of the invention are the pharmaceutically acceptable prodrugs of compounds of Formula (I) (as well as Formulas (IA), (IB), and (IC)), and pharmaceutically active metabolites of the compounds of Formula (I) (as well as Formulas (IA), (IB), and (IC)).

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

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;

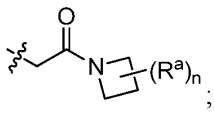
Ar^1 is selected from the group consisting of:

(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, OC_{1-6}perhaloalkyl, CN, and C_{3-6}cycloalkyl;

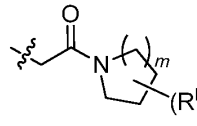
(b) phenyl substituted with two or three members each independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}perhaloalkyl, OC_{1-6}alkyl, OC_{1-6}perhaloalkyl, and $(C=O)CH_3$; and

(c) thienyl independently substituted with one or two members selected from: halo, C_{1-6}alkyl, and C_{1-6}perhaloalkyl; and pyridine substituted with CF_3;

R^2 is selected from the group consisting of:

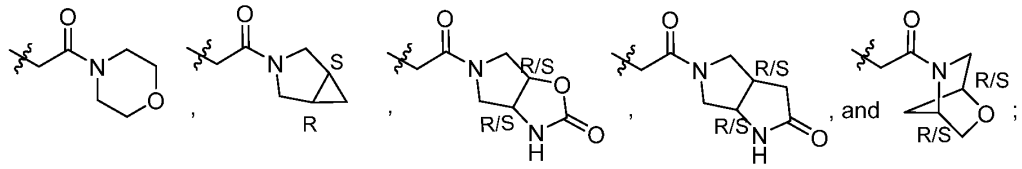
(d)  ; wherein

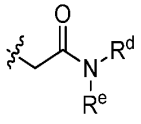
R^a is each independently selected from the group consisting of: H, halo, OH, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}haloalkenyl, C_{2-6}alkynyl, CH_2OH, $CH(OH)(CH_3)$, CH_2OCH_3, OC_{1-6}haloalkyl, OC_{1-6}alkyl, $NH(CH_3)$, $NHCO_2CH_3$, $NHC(=O)CH_3$, $NHC(=O)CF_3$, NHC(=O)cyclopropyl, $N(CH_3)C(=O)CH_3$, $C(=O)N(CH_3)_2$, $C(=O)CH_3$, CN, $NHSO_2CH_3$, SO_2CH_3, 1H-imidazol-2-yl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrimidin-4-yl, and pyrrolidine-2-one; or two R^a members combine to form a C_{3-6}cycloalkyl or heterocycloalkyl, wherein the cycloalkyl and heterocycloalkyl is optionally substituted one or two F members;

(e)  ; wherein

R^b is each independently selected from the group consisting of: H, OH, F, OCH_3, CH_2OCH_3, and $NHC(=O)CH_3$; or two R^b members come together to form =O;

(f)

 and

(g)  , wherein

R^d is selected from the group consisting of: C_{1-6}alkyl; C_{2-6}alkenyl C_{1-6}haloalkyl; $CH_2CH_2OCH_3$; CH_2CH_2OH; CH_2CN; NH_2; $NH\text{-}C(=O)CH_3$; C_{3-6}cycloalkyl; C_{3-6}cycloalkyl substituted with two F members; 1-methylazetidin-3-yl; and oxetan-3-yl;

R^e is H or CH_3;

n is 1 or 2; and

m is 1 or 2;

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), (IB), and (IC)), 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 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);

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_{1-6}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 "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_{1-3}perhaloalkyl" as used here refers to a straight- or branched-chain alkyl group having from 1 to 3 carbon atoms in the chain, optionally substituting hydrogens with halogens. The term "C_{1-6}perhaloalkyl" 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 ($CF(CF_3)_2$), chloropropyl ($CH_2CH_2CH_2Cl$), 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 "alkoxy" includes a straight chain or branched alkyl group with a terminal oxygen linking the alkyl group to the rest of the molecule. Alkoxy includes methoxy, ethoxy, propoxy, isopropoxy, butoxy, t-butoxy, pentoxy and so on.

The term "cyano" refers to the group -CN.

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.)

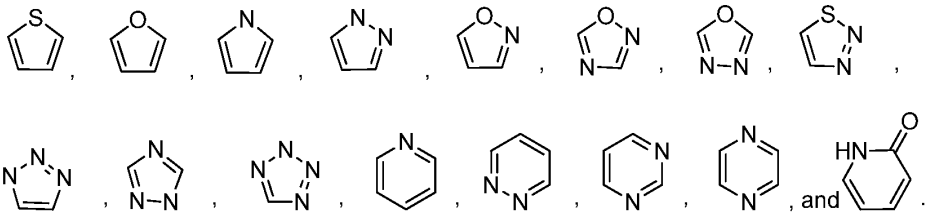
The term "phenyl" represents the following moiety:



The term "thienyl" represents the following moiety:

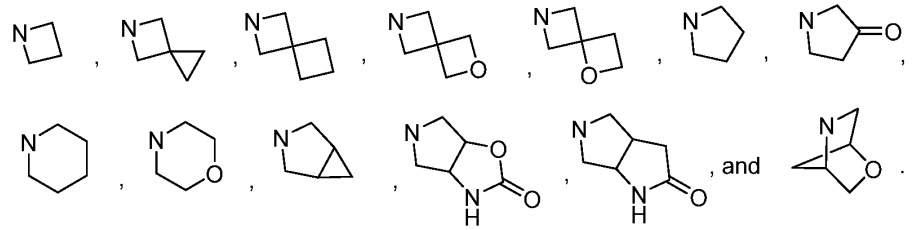


The term "heteroaryl" refers to a monocyclic or fused bicyclic heterocycle (ring structure having ring atoms selected from carbon atoms and up to four heteroatoms selected from nitrogen, oxygen, and sulfur) having from 3 to 9 ring atoms per heterocycle. Illustrative examples of heteroaryl groups include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

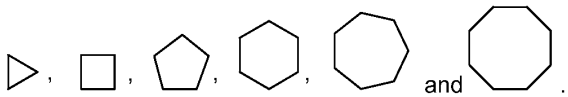


Those skilled in the art will recognize that the species of heteroaryl, cycloalkyl, aryl and heterocycloalkyl groups listed or illustrated above are not exhaustive, and that additional species within the scope of these defined terms may also be selected.

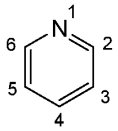
A "heterocycloalkyl" refers to a monocyclic, bicyclic (fused or spirocyclic) ring structure that is saturated or partially saturated and has from 4 to 7 ring atoms per ring structure selected from carbon atoms and up to two heteroatoms selected from nitrogen, oxygen, and sulfur. The ring structure may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



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:

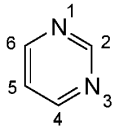


The term "pyridinyl" or "pyridyl" represents the following moiety:



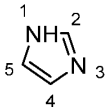
The pyridinyl or pyridyl moiety can be attached through any one of the 2-, 3-, 4-, 5-, or 6-position carbon atoms.

The term "pyrimidinyl" represents the following moiety:



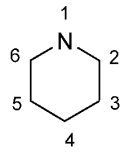
The pyrimidinyl moiety can be attached through any one of the 2-, 4-, 5-, or 6-position carbon atoms.

The term "imidazolyl" represents the following moiety:



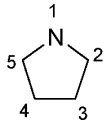
The imidazolyl moiety can be attached through any one of the 1-, 2-, 3-, 4-, or 5-position carbon atoms.

The term "piperidinyl" represents the following moiety:



When the piperidinyl moiety is a substituent, it can be attached through any one of the 1-, 2-, 3-, 4-, 5-, or 6-position atoms, as permitted.

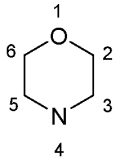
The term “pyrrolidinyl” represents the following moiety:



When the piperidinyl moiety is a substituent, it can be attached through any one of the 1-, 2-, 3-, 4-, or 5- position atoms, as permitted.

The term “azetidinyl” represents a 4-membered heterocycloalkyl moiety having one ring nitrogen. When the azetidinyl moiety is a substituent, it can be attached through any carbon atom or through the nitrogen atom, as permitted.

The term “morpholinyl” represents the following moiety:

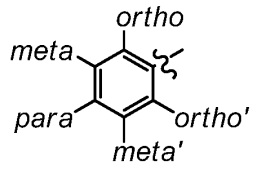


When the morpholinyl moiety is a substituent, it can be attached through any one of the 2-, 3-, 4-, 5-, or 6-position atoms, as permitted.

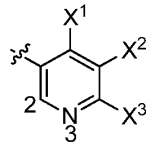
The term “substituted” means that the specified group or moiety bears one or more substituents. The term "unsubstituted" means that the specified group bears no substituents. The term “optionally substituted” means that the specified group is unsubstituted or substituted by one or more substituents. 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."

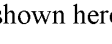
"Tautomers" refer to compounds that are interchangeable forms of a particular compound structure, and that vary in the displacement of hydrogen atoms and electrons. Thus, two structures may be in equilibrium through the movement of π electrons and an atom (usually H). For example, enols and ketones are 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), (IB), and (IC)), or pharmaceutically acceptable salts of compounds of Formula (I) (as well as Formulas (IA), (IB), and (IC)) may be obtained as solvates. Solvates include those formed from the interaction or complexation of compounds of the invention with one or more solvents, either in solution or as a solid or crystalline form. In some embodiments, the solvent is water and the solvates are hydrates. In addition, certain crystalline forms of compounds of Formula (I) (as well as Formulas (IA), (IB), and (IC)) or pharmaceutically acceptable salts of compounds of Formula (I) (as well as Formulas (IA), (IB), and (IC)) 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, $R\text{-}COOH_{(s)}$, $R\text{-}COOH_{(sol)}$, and $R\text{-}COO^{-}{}_{(sol)}$. In this example, $R\text{-}COOH_{(s)}$ refers to the solid compound, as it could be for example in a tablet or some other solid pharmaceutical composition or preparation; $R\text{-}COOH_{(sol)}$ refers to the undissociated form of the compound in a solvent; and $R\text{-}COO^{-}{}_{(sol)}$ 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 using 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^1, R^2, R^a, R^b, R^d, R^e Ar^1, n, m, X, 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^1, R^2, R^a, R^b, R^d, R^e Ar^1, n, m, X, 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_{1-6} 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), (IB), and (IC)), 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. Pharmacopeia or other generally recognized pharmacopoeia for use in animals, and more particularly, in humans.

A "pharmaceutically acceptable salt" is intended to mean a salt of a free acid or base of compounds represented by Formula (I) (as well as Formulas (IA), (IB), and (IC)) that are non-toxic, biologically tolerable, or otherwise biologically suitable for administration to the subject. It should possess the desired pharmacological activity of the parent compound. See, generally, G.S. Paulekuhn, et al., "Trends in Active Pharmaceutical Ingredient Salt Selection based on Analysis of the Orange Book Database", *J. Med. Chem.*, **2007**, 50:6665–72, S.M. Berge, et al., "Pharmaceutical Salts", *J Pharm Sci.*, **1977**, 66:1-19, and *Handbook of Pharmaceutical Salts, Properties, Selection, and Use,* Stahl and Wermuth, Eds., Wiley-VCH and VHCA, Zurich, **2002**. Examples of pharmaceutically acceptable salts are those that are pharmacologically effective and suitable for contact with the tissues of patients without undue toxicity, irritation, or allergic response. A compound of Formula (I) (as well as Formulas (IA), (IB), and (IC)) 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), (IB), and (IC)) contain a basic nitrogen, the desired pharmaceutically acceptable salt may be prepared by any suitable method available in the art. For example, treatment of the free base with an inorganic acid, such as hydrochloric acid, hydrobromic acid, sulfuric acid, sulfamic acid, nitric acid, boric acid, phosphoric acid, and the like, or with an organic acid, such as acetic acid, phenylacetic acid, propionic acid, stearic acid, lactic acid, ascorbic acid, maleic acid, hydroxymaleic acid, isethionic acid, succinic acid, valeric acid, fumaric acid, malonic acid, pyruvic acid, oxalic acid, glycolic acid, salicylic acid, oleic acid, palmitic acid, lauric acid, a pyranosidyl acid, such as glucuronic

acid or galacturonic acid, an alpha-hydroxy acid, such as mandelic acid, citric acid, or tartaric acid, an amino acid, such as aspartic acid, glutaric acid or glutamic acid, an aromatic acid, such as benzoic acid, 2-acetoxybenzoic acid, naphthoic acid, or cinnamic acid, a sulfonic acid, such as laurylsulfonic acid, *p*-toluenesulfonic acid, methanesulfonic acid, ethanesulfonic acid, any compatible mixture of acids such as those given as examples herein, and any other acid and mixture thereof that are regarded as equivalents or acceptable substitutes in light of the ordinary level of skill in this technology.

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

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

Exemplary prodrugs include compounds having an amino acid residue, or a polypeptide chain of two or more (e.g., two, three or four) amino acid residues, covalently joined through an

amide or ester bond to a free amino, hydroxyl, or carboxylic acid group of a compound of Formula (I) (as well as Formulas (IA), (IB), and (IC)). 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), (IB), and (IC)) 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), (IB), and (IC)), 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), (IB), and (IC) 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), (IB), and (IC)) 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

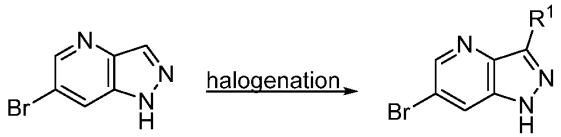
Term	Acronym
Millimoles	mmol
Mass spectrometry	MS
Normal	N
Nuclear magnetic resonance	NMR
Parts per million	ppm
Precipitate	ppt
Polytetrafluoroethylene	PTFE
Retention time	R_t
Room temperature	rt
Saturated	sat
Supercritical Fluid Chromatography	SFC
Temperature	T
Thin layer chromatography	TLC
Volume in 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

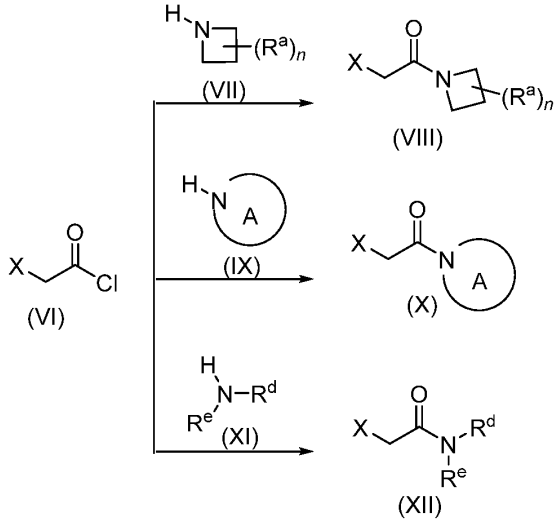


(V)

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), where R^1 is halo. 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®),

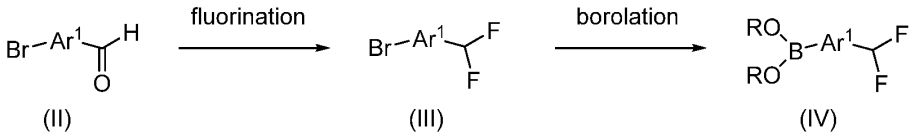
preferably Selectflor®; in a suitable solvent such as acetonitrile (ACN), and the like; at temperatures ranging from 0 to 100 °C; to provide a compound of formula (V), where R^1 is F.

SCHEME 2



According to SCHEME 2, a 2-haloacetyl chloride of formula (VI), where X is Cl or Br, such as 2-chloroacetyl chloride, 2-bromoacetyl chloride, and the like; is reacted with a commercially available or synthetically accessible suitably substituted azetidine of formula (VII), where R^a is H, halo, or C_{1-6}alkyl, and *n* is 1 or 2; or a suitably substituted heterocycloalkylamine of formula (IX), where ring A is as described in Formula (IB); or a suitably substituted amine of formula (XI), where R^d is C_{3-6}cycloalkyl or C_{3-6}cycloalkyl substituted with two F members, and R^e is H or CH_3; in the presence of a suitable base such as triethylamine (TEA) or sodium bicarbonate; in a solvent such as acetonitrile (ACN) or dichloromethane (DCM); at temperatures ranging from 0 °C to rt; to provide a compound of formula (VIII), formula (X), and formula (XII).

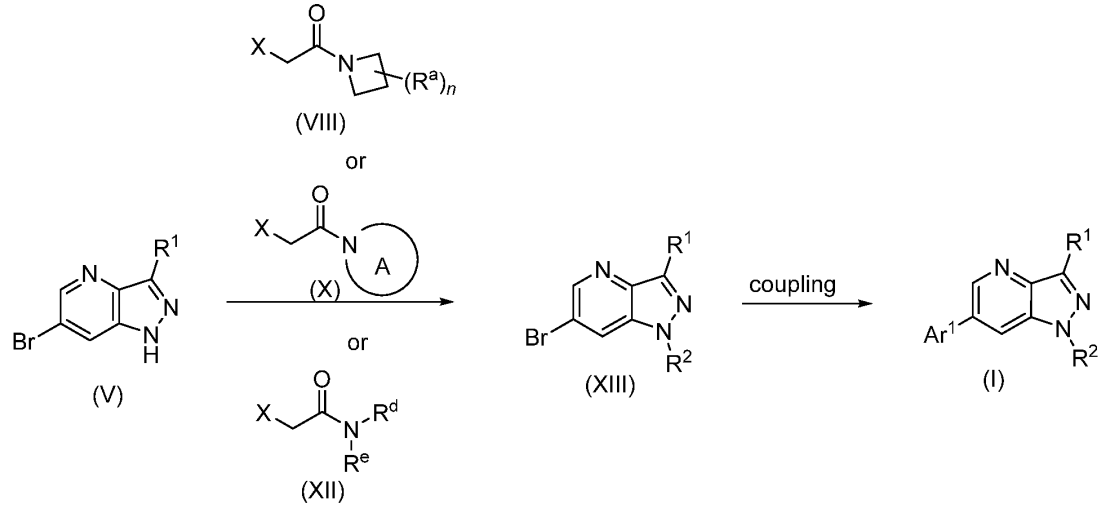
SCHEME 3



According to SCHEME 3, difluorination of bromoaryl carbaldehyde (II) is achieved employing diethylaminosulfur trifluoride (DAST), and the like; in a suitable solvent such as DCM; to provide bromo (difluoromethyl)aryl (III). Bromo (difluoromethyl)aryl (III), is borylated by methods known to those skilled in the art, for example, bromo (difluoromethyl)aryl (III) may be treated with a transition metal catalyst, 1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II) ($Pd(dppf)Cl_2$) for example, in a solvent like dimethylsulfoxide (DMSO) or 1,4-dioxane, and a base like KOAc with bis(pinacolato)diboron to give a compound of formula (IV).

Alternatively, a compound of formula (III), 2-bromo-5-(difluoromethyl)thiophene for example, is borylated via a metal halogen exchange of the bromide with organolithium or magnesium reagents, with or without the presence of lithium chloride at a temperature of about -78 °C in a solvent like ether or tetrahydrofuran (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 (IV), 2-(5-(difluoromethyl)thiophen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane for example.

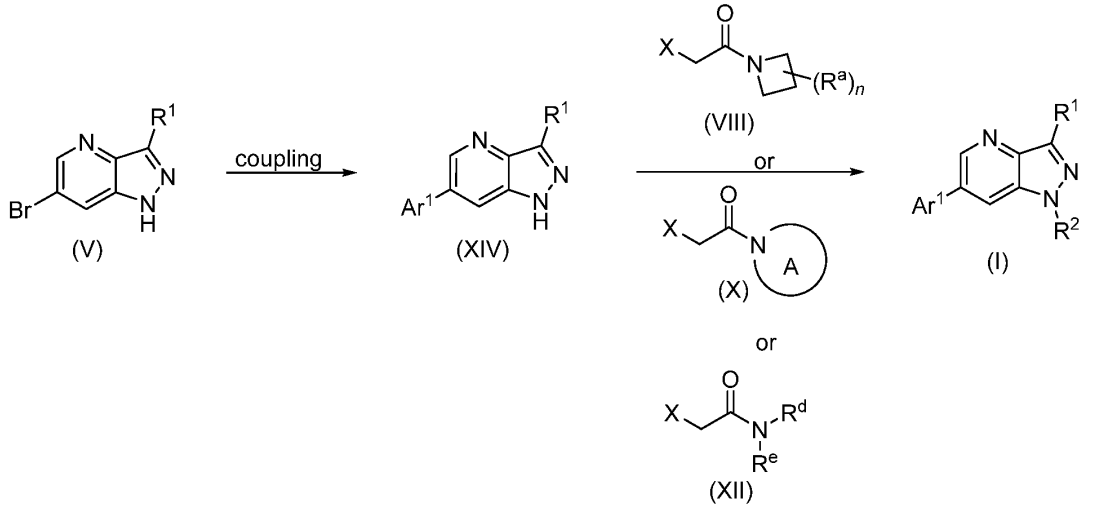
SCHEME 4



According to SCHEME 4, a compound of formula (V), where R^1 is H, CH_3, or F, is alkylated with a compound of formula (VIII), (X), or (XII), where X is Cl or Br, employing a base such as Cs_2CO_3, NaH, and the like; in a suitable solvent such as dimethylformamide (DMF), and the like; at temperatures ranging from 0 °C to rt; to afford a compound of formula

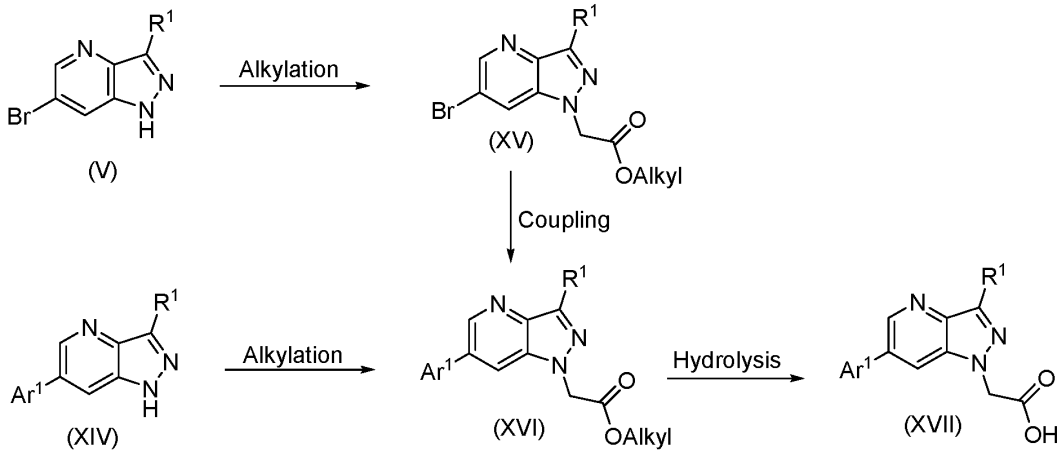
(XIII), where R^2 is as defined in claim 1. A compound of formula (XIII) is reacted in a metal mediated cross coupling reaction to provide a compound of Formula (I), where Ar^1 is as defined in claim 1. For example, a compound of formula (XIII), where H, CH_3, or F, is reacted with a suitably substituted aryl or heteroaryl boronic acid, boronate ester, and the like; in the presence of a palladium catalyst such as $PdCl_2$(dtbpf), $Pd(PPh_3)_4$, *bis*(triphenylphosphine)palladium(II)chloride ($PdCl_2(PPh_3)_2$), bis(diphenylphosphino)ferrocene]dichloropalladium(II) complex with dichloromethane, (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) ($Pd(dppf)Cl_2$), and the like; a base such as KF, K_3PO_4, aq. Na_2CO_3, Cs_2CO_3, and the like; in a suitable solvent such as 1,4-dioxane, DMF, acetonitrile (ACN), water, or a mixture thereof; at a temperature ranging from 60 to 120 °C; for a period of about 16 to 48 hours; to provide a compound of Formula (I).

SCHEME 5



According to SCHEME 5, a compound of formula (V), where R^1 is H, CH_3, or F, is reacted in a metal-mediated cross-coupling reaction with a suitably substituted aryl or heteroaryl boronic acid, boronate ester as previously described, to provide a compound of formula (XIV), where Ar^1 is a group as defined in Formula (I). Subsequent alkylation with a compound of formula (VIII), or formula (X), or formula (XII), employing conditions previously described provides a compound of Formula (I).

SCHEME 6

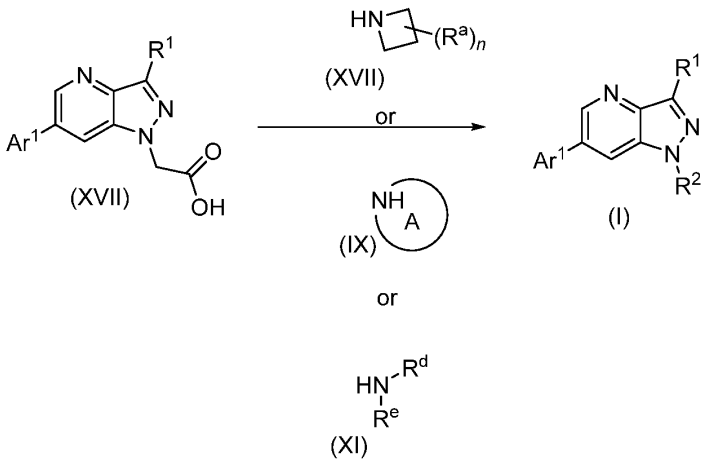


According to SCHEME 6, a compound of formula (V) or a compound of formula (XV) where R^1 is H, CH_3, or F and Ar^1 is as described in Formula (I), is alkylated with an electrophile such as ethyl 2-bromoacetate, tert-butyl 2-bromoacetate, and the like; a base such as NaH, Cs_2CO_3, and the like; in a suitable solvent such as DMF, and the like; at temperatures ranging from 0 °C to rt. A compound of formula (XIV) is coupled in a metal-mediated cross coupling reaction as previously described, with a suitably substituted phenyl or thienyl boronic acid or ester, employing conditions previously described, to provide a compound of formula (XVI).

A compound of formula (XVI), where Ar^1 is phenyl substituted with CH_2OH, is fluorinated with a fluorinating agent such as bis(2-methoxyethyl)aminosulfur trifluoride (Deoxo-Fluor®), in a suitable solvent such as DCM, and the like; at 0 °C; for a period of 1 to 4 hours, provides a compound of formula (XVI), where Ar^1 is phenyl substituted with CH_2F.

Saponification of an ester of formula (XVI) under basic conditions such as NaOH, LiOH, KOH, and the like; in a suitable solvent such as methanol (MeOH), ethanol (EtOH), THF, ACN, H_2O, or a mixture thereof; affords a compound of formula (XVII). Alternatively, acidic hydrolysis of an ester of formula (XVI) is accomplished using an acidic solvent such as 6 N aqueous HCl and the like; at temperatures ranging from room temperature (rt) to 80 °C; to afford a compound of formula (XVII). It will be understood that in certain instances, *in situ* ester hydrolysis, without the isolation of a discrete ester (XVI) may occur to provide a compound of formula (XVII).

SCHEME 7



According to SCHEME 7, a compound of Formula (I), where R^1 is H, CH_3, or F, Ar^1 is a suitably substituted phenyl or thienyl, and R^2 is as defined in claim 1, is prepared by conventional amide bond-forming techniques such as coupling reactions which are well known to those skilled in the art (such as HATU (1-[bis(dimethylamino)methylene]-1*H*-1,2,3-triazolo[4,5-*b*]pyridinium 3-oxid hexafluorophosphate), BOP (benzotriazol- 1-yloxy-tris(dimethylamino)phosphonium hexafluorophosphate), or conversion of the acid to an acid chloride). For example, reaction of a suitably substituted heterocycloalkyl amine of formula (IX), or a suitably substituted azetidine of formula (XVIII), or an amine of formula (XI) where R^d is as defined in claim 1 and R^e is H or CH_3, with an acid compound of formula (XVII), 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. 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 (I).

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% ACN:10 mM $(NH_4)HCO_3$ (9:1) in 10 mM aqueous $(NH_4)HCO_3$ with 0.1% NH_4OH over 16 min or 18 min, with a flow rate of 30 mL/min.

METHOD F. A Gilson HPLC with C18 XBridge column (30 x 100 mm 5 um), mobile phase: Gradient from 60% 0.1% NH_4CO_3H/NH_4OH pH 9 solution in Water, 40% CH_3CN to 43% 0.1% NH_4CO_3H/NH_4OH pH 9 solution in Water, 57% CH_3CN, at a flow rate of 80 mL/min.

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

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

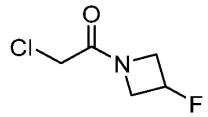
Nuclear magnetic resonance (NMR) spectra were obtained on Bruker model DRX spectrometers. Definitions for multiplicity are as follows: s = singlet, d = doublet, t= triplet, q = quartet, m = multiplet, br = broad. It will be understood that for compounds comprising an exchangeable proton, said proton may or may not be visible on an NMR spectrum depending on the choice of solvent used for running the NMR spectrum and the concentration of the compound in the solution.

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.

EXAMPLES

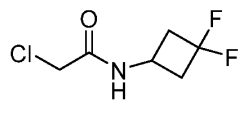
Intermediate 1: 2-Chloro-1-(3-fluoroazetidin-1-yl)ethanone.



Method A. To a mixture of chloroacetyl chloride (1.57 mL, 19.7 mmol, 1.42 g/mL) and sodium bicarbonate ($NaHCO_3$) (4.52 g, 53.8 mmol) in dichloromethane (DCM) (40 mL) was added 3-fluoroazetidine hydrochloride (2.0 g, 17.9 mmol) in portions at 0 °C under argon and the reaction was stirred at 0 °C for 2 h. The reaction mixture was allowed to reach room temperature and stirred for 1 h. The mixture was filtered, and the precipitate was washed with DCM (3 x 4 mL). The combined filtrates were evaporated to give the title compound (2.70 g, 17.8 mmol, 99%) as a colorless liquid. MS (ESI): mass calcd. for C_5H_7ClFNO, 151.0; m/z found, 152.1 $[M+H]^+$.

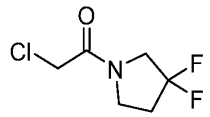
Method B. Potassium carbonate (K_2CO_3) (46 g, 330 mmol) and 3-fluoroazetidine (16.7 g, 150 mmol) were stirred in 100 mL distilled water until all solids had dissolved completely. To this solution was added 100 mL DCM, and the biphasic reaction was cooled to 0 °C and stirred vigorously while chloroacetyl chloride (14.3 mL, 180 mmol,) was added dropwise. Upon completion of addition, the reaction mixture was stirred at rt for 2 hours, diluted with water until all solids dissolved. The layers were separated, and the aqueous layer was extracted 4x with DCM. The combined organics were concentrated to afford the title compound as a pale-yellow liquid, which was sufficiently pure for use directly in subsequent steps (15.9 g, 105 mmol, 70%). ^1H NMR (400 MHz, $CDCl_3$) δ 5.54 – 5.15 (m, 1H), 4.68 – 4.50 (m, 1H), 4.48 – 4.26 (m, 2H), 4.28 – 4.11 (m, 1H), 3.92 (s, 2H).

Intermediate 2: 2-Chloro-*N*-(3,3-difluorocyclobutyl)acetamide.



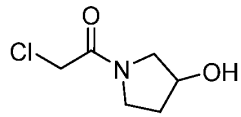
The title compound was made in a manner analogous to Method A of Intermediate 1 using 3,3-difluorocyclobutan-1-amine in place of 3-fluoroazetidine. MS (ESI): mass calcd. for $C_6H_8ClF_2NO$; 183.0 m/z found, 182.1 $[M-H]^-$.

Intermediate 3: 2-Chloro-1-(3,3-difluoropyrrolidin-1-yl)ethan-1-one.



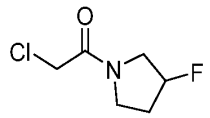
The title compound was made in a manner analogous to Method A of Intermediate 1 using 3,3-difluoropyrrolidine in place of 3-fluoroazetidine. MS (ESI): mass calcd. for $C_6H_8ClF_2NO$; 183.0 m/z found, 184.1 $[M+H]^+$.

Intermediate 4: (racemic) 2-Chloro-1-(3-hydroxypyrrolidin-1-yl)ethan-1-one.



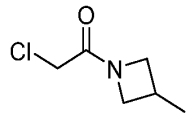
The title compound was made in a manner analogous to Method A of Intermediate 1 using 3-hydroxypyrrolidine in place of 3-fluoroazetidine. MS (ESI): mass calcd. for $C_6H_{10}ClNO_2$; 163.0 m/z found, 164.1 $[M+H]^+$.

Intermediate 5: (racemic) 2-Chloro-1-(3-fluoropyrrolidin-1-yl)ethan-1-one.



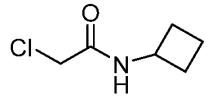
The title compound was made in a manner analogous to Method A of Intermediate 1 using 3-fluoropyrrolidine in place of 3-fluoroazetidine. MS (ESI): mass calcd. for C_6H_9ClFNO; 165.0 m/z found, 166.1 $[M+H]^+$.

Intermediate 6: 2-Chloro-1-(3-methylazetidin-1-yl)ethan-1-one.



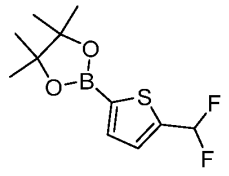
To a solution of 3-methylazetidine hydrochloride (500 mg, 4.65 mmol) in DCM (7.75 mL) was added K_2CO_3 (1.93 g, 14.0 mmol) at 0 °C and the reaction was stirred for 10 min. To the reaction mixture was added chloroacetyl chloride (407 µL, 5.11 mmol, 1.42 g/mL) dropwise at 0 °C. The reaction mixture was allowed to reach room temperature and stirred for 17 h. The suspension was filtered, and the precipitate was washed with DCM (2 x 10 mL). The combined filtrates were concentrated under reduced pressure. Purification (FCC, SiO_2, 0 to 100% DCM/MeOH) afforded the title compound (580 mg, 3.93 mmol, 85%) as a yellow oil. MS (ESI): mass calcd. for $C_6H_{10}ClNO$; 147.1 m/z found, 148.1 $[M+H]^+$.

Intermediate 7: 2-Chloro-*N*-cyclobutylacetamide.



To a solution of cyclobutylamine (1.0 g, 14.1 mmol) in freshly distilled tetrahydrofuran (THF) (60 mL) was added triethylamine (Et_3N) (2.16 mL, 15.5 mmol, 0.726 g/mL) dropwise at room temperature. The mixture was cooled to 0 °C. Chloroacetyl chloride (1.23 mL, 15.5 mmol, 1.42 g/mL) at 0 °C was then added and the reaction stirred for 1 h. The reaction mixture was allowed to reach room temperature and stirred for 17 h. The reaction mixture was concentrated, and the residue was taken up in water (70 mL) and extracted with ethyl acetate (EtOAc) (1 x 70 mL). The organic layer was washed with 1 M hydrochloric acid (HCl) (1 x 35 mL), saturated $NaHCO_3$ (1 x 35 mL), and saturated ammonium chloride (NH_4Cl) (1 x 35 mL), dried over sodium sulfate (Na_2SO_4), filtered and concentrated. Purification (FCC, SiO_2, 10 to 100% n-heptane/EtOAc) afforded a residue that was triturated with n-heptane (10 mL) to give the title compound (1.37 g, 9.28 mmol, 66%) as a white crystalline solid. MS (ESI): mass calcd. for $C_6H_{10}ClNO$;147.1 m/z found, 148.1 $[M+H]^+$.

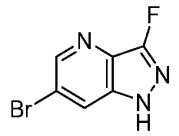
Intermediate 8: 2-(5-(Difluoromethyl)thiophen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.



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 under reduced pressure. 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 (*n*-BuLi)(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 NH_4Cl (30 mL) and 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. The corresponding boronic acid MS (ESI): mass calcd. for $C_5H_5BF_2O_2S$; 178.0 m/z found, 177.1 $[M-H]^-$.

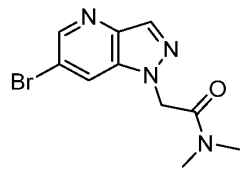
Intermediate 9: 6-Bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridine.



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 *N*-fluoro-*N'*-(chloromethyl)triethylenediamine bis(tetrafluoroborate) (6.7 g, 18.9 mmol). The reaction mixture was stirred at 90 °C for 22 h. The reaction mixture was 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 under reduced pressure. 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 $[M+H]^+$.

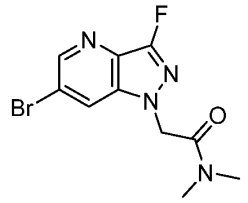
Intermediate 10: 2-(6-Bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-*N*,*N*-dimethylacetamide.



Method A. To a solution of 6-bromo-1H-pyrazolo[4,3-b]pyridine (2.00 g, 10.1 mmol) in dry DMF (40 mL) was added NaH (60% in mineral oil, 444 mg, 11.1 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 0.5 h. To the reaction mixture was added 2-chloro-*N*,*N*-dimethylacetamide (1.14 mL, 11.1 mmol, 1.18 g/mL) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 18 h. The reaction mixture was poured into water (50 mL) and the mixture was extracted with ethyl acetate (EA, EtOAc) (3 x 40 mL). The combined organic layers were evaporated. Purification (FCC, SiO_2, 25 to 100% hexanes/EtOAc) afforded a solid that was triturated with Et_2O (4 mL) to afford the title compound (1.83 g, 6.47 mmol, 64%) as an off-white powder. MS (ESI): mass calcd for $C_{10}H_{11}BrN_4O$, 282.0; m/z found, 283.0 $[M+H]^+$

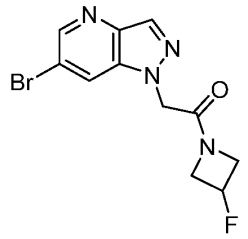
Method B. A solution of 6-bromo-1H-pyrazolo[4,3-*b*]pyridine (15.0 g, 75.7 mmol) in DMF (250 mL) was treated with 2-chloro-*N*,*N*-dimethylacetamide (8.6 mL, 83 mmol) and K_2CO_3 (12.6 g, 90.9 mmol) and the reaction mixture was stirred at r.t. overnight. DMF was removed under reduced pressure until approximately 50 mL total volume, then diluted with water (300 mL) and let stand overnight. The resulting precipitate was collected by filtration to afford the title compound (14.0 g, 49.5 mmol, 65%). MS (ESI): mass calcd for $C_{10}H_{11}BrN_4O$, 282.0; m/z found, 283.0 $[M+H]^+$. ^1H NMR (400 MHz, CHCl3-*d*) δ 8.60 (d, *J* = 1.9 Hz, 1H), 8.22 (d, *J* = 1.0 Hz, 1H), 8.00 (dd, *J* = 1.9, 1.0 Hz, 1H), 5.20 (s, 2H), 3.15 (s, 3H), 2.99 (s, 3H).

Intermediate 11: 2-(6-Bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)-*N*,*N*-dimethylacetamide.



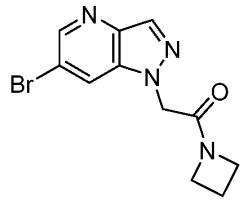
The title compound was made in a manner analogous to Method A of Intermediate 10 using 6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridine (Intermediate 9). MS (ESI): mass calcd for $C_{10}H_{10}BrFN_4O$, 300.0; m/z found, 301.0 $[M+H]^+$.

Intermediate 12: 2-(6-Bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one.



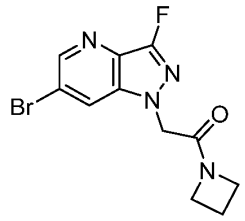
A solution of 6-bromo-1H-pyrazolo[4,3-*b*]pyridine (10.0 g, 50.5 mmol) in DMF (100 mL) was treated with 2-chloro-1-(3-fluoroazetidin-1-yl)ethan-1-one (8.42 g, 55.5 mmol) and K_2CO_3 (8.4 g, 61 mmol). The reaction mixture was stirred at r.t. for 48 hours. The reaction mixture was partitioned between DCM and water, the aqueous layer was extracted DCM (2x). The combined organics were concentrated. The residual DMF was removed under azeotropic conditions with heptanes. Purification (FCC, SiO_2, 0 to 10% DCM/MeOH) afforded a solid that was then recrystallized from EtOAc. Isolated 8.33 g (26.6 mmol, 53%) of the title compound. MS (ESI): mass calcd for $C_{11}H_{10}BrFN_4O$, 312.0; m/z found, 313.0 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.61 (d, J = 2.0 Hz, 1H), 8.51 (dd, J = 2.0, 1.0 Hz, 1H), 8.36 (d, J = 1.0 Hz, 1H), 5.57 – 5.37 (m, 1H), 5.28 (d, J = 4.1 Hz, 2H), 4.65 – 4.45 (m, 1H), 4.42 – 4.16 (m, 2H), 4.06 – 3.92 (m, 1H).

Intermediate 13: 1-(Azetidin-1-yl)-2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)ethan-1-one.



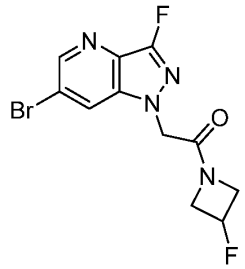
The title compound was made in a manner analogous to Method A of Intermediate 10 using 1-(azetidin-1-yl)-2-chloroethan-1-one in place of 2-chloro-*N*,*N*-dimethylacetamide. MS (ESI): mass calcd for $C_{11}H_{11}BrN_4O$, 294.0; m/z found, 295.0 $[M+H]^+$.

Intermediate 14: 1-(Azetidin-1-yl)-2-(6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)ethan-1-one.



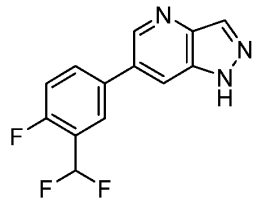
The title compound was made in a manner analogous to Method A of Intermediate 10 using 1-(azetidin-1-yl)-2-chloroethan-1-one in place of 2-chloro-*N*,*N*-dimethylacetamide and 6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridine (Intermediate 9) in place of 6-bromo-1H-pyrazolo[4,3-b]pyridine. MS (ESI): mass calcd for $C_{11}H_{10}BrFN_4O$, 312.0; m/z found, 313.0 $[M+H]^+$.

Intermediate 15: 2-(6-Bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one.



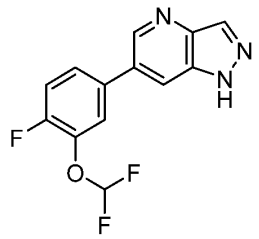
The title compound was made in a manner analogous to Intermediate 12 using 6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridine (Intermediate 9) in place of 6-bromo-1H-pyrazolo[4,3-b]pyridine. MS (ESI): mass calcd for $C_{11}H_9BrF_2N_4O$, 329.9; m/z found, 331.0 $[M+H]^+$.

Intermediate 16: 6-(3-(Difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine.



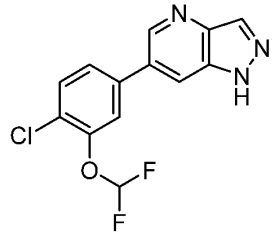
A mixture of 6-bromo-1H-pyrazolo[4,3-b]pyridine (1.40 g, 7.07 mmol), 2-[3-(difluoromethyl)-4-fluoro-phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.31 g, 8.49 mmol), [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (0.673 g, 0.92 mmol) and Na_2CO_3 (2.25 g, 21.2 mmol) in degassed acetonitrile (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 under reduced pressure. 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 17: 6-(3-(Difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine.



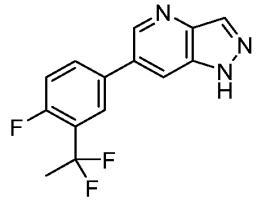
The title compound was made in a manner analogous to Intermediate 16 using 2-(3-(difluoromethoxy)-4-fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in place of 2-[3-(difluoromethyl)-4-fluoro-phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd for $C_{13}H_8F_3N_3O$, 279.0; m/z found, 280.2 $[M+H]^+$.

Intermediate 18: 6-(4-Chloro-3-(difluoromethoxy)phenyl)-1H-pyrazolo[4,3-b]pyridine.



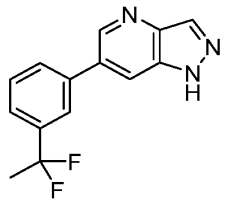
The title compound was made in a manner analogous to Intermediate 16 using 2-(3-(difluoromethoxy)-4-chlorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in place of 2-[3-(difluoromethyl)-4-fluoro-phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd for $C_{13}H_8ClF_2N_3O$, 295.0; m/z found, 296.0 $[M+H]^+$.

Intermediate 19: 6-(3-(1,1-Difluoroethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine.



The title compound was made in a manner analogous to Intermediate 16 using 2-(3-(1,1-difluoroethyl)-4-fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in place 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 $[M+H]^+$.

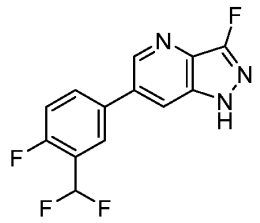
Intermediate 20: 6-(3-(1,1-Difluoroethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine.



The title compound was made in a manner analogous to Intermediate 16 using 2-(3-(1,1-difluoroethyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in place of 2-[3-(difluoromethyl)-

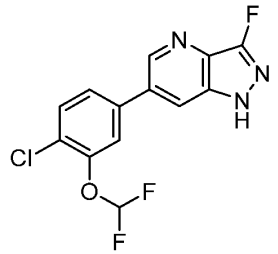
4-fluoro-phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd for $C_{14}H_{11}F_2N_3$, 259.1; m/z found, 260.1 $[M+H]^+$.

Intermediate 21: 6-(3-(Difluoromethyl)-4-fluorophenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridine.



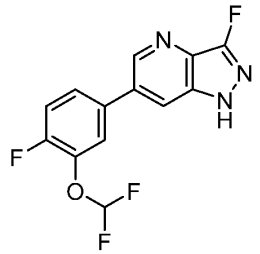
The title compound was made in a manner analogous to Intermediate 16 using 6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridine (Intermediate 9) in place of 6-bromo-1H-pyrazolo[4,3-b]pyridine. MS (ESI): mass calcd for $C_{13}H_7F_4N_3$, 281.1; m/z found, 282.1 $[M+H]^+$.

Intermediate 22: 6-(4-Chloro-3-(difluoromethoxy)phenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridine.



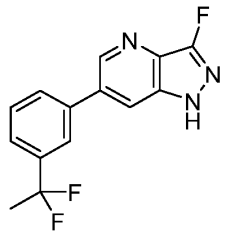
The title compound was made in a manner analogous to Intermediate 16 using 6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridine (Intermediate 9) in place of 6-bromo-1H-pyrazolo[4,3-b]pyridine and 2-(3-(difluoromethoxy)-4-chlorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in place of 2-[3-(difluoromethyl)-4-fluoro-phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd for $C_{13}H_7ClF_3N_3O$, 313.0; m/z found, 314.1 $[M+H]^+$.

Intermediate 23: 6-(3-(Difluoromethoxy)-4-fluorophenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridine.



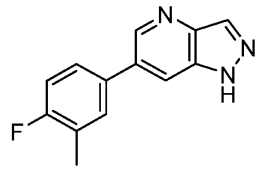
The title compound was made in a manner analogous to Intermediate 16 using 6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridine (Intermediate 9) in place of 6-bromo-1H-pyrazolo[4,3-b]pyridine and using 2-(3-(difluoromethoxy)-4-fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in place of 2-[3-(difluoromethyl)-4-fluoro-phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd for $C_{13}H_7F_4N_3O$, 297.1; m/z found, 298.0 $[M+H]^+$.

Intermediate 24: 6-(3-(1,1-Difluoroethyl)phenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridine.



The title compound was made in a manner analogous to Intermediate 16 using 6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridine (Intermediate 9) in place 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 in place 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 $[M+H]^+$.

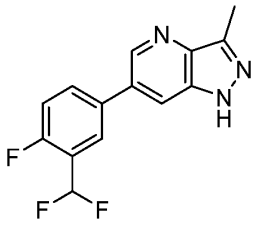
Intermediate 25: 6-(4-Fluoro-3-methylphenyl)-1H-pyrazolo[4,3-b]pyridine.



The title compound was made in a manner analogous to Intermediate 16 using 2-(4-fluoro-3-methylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in place of 2-[3-(difluoromethyl)-4-

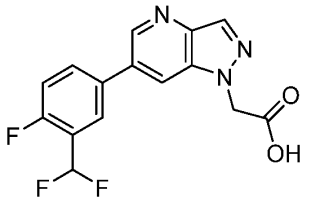
fluoro-phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd for $C_{13}H_{10}FN_3$, 227.1; m/z found, 228.1 $[M+H]^+$.

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



The title compound was made in a manner analogous to Intermediate 16, using 6-bromo-3-methyl-1H-pyrazolo[4,3-b]pyridine in place 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 $[M+H]^+$.

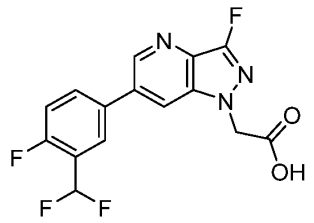
Intermediate 27: 2-(6-(3-(Difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid.



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 16, 2.00 g, 7.6 mmol) in DMF (30 mL) was added Cs_2CO_3 (2.72 g, 8.35 mmol) at 0 °C. 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 under reduced pressure. Purification (FCC, SiO_2, 0 to 75% n-heptane/EtOAc) afforded the title compound (1.60 g, 4.58 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 $[M+H]^+$.

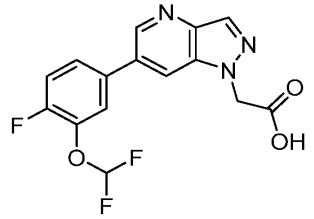
Step B. 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetic acid. To a solution of ethyl 2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetate (1.60 g, 4.58 mmol) in 1,4-dioxane (14 mL) and water (9 mL) was added lithium hydroxide monohydrate (385 mg, 9.17 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, 5.416 mmol, 118%) 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 28: 2-(6-(3-(Difluoromethyl)-4-fluorophenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid.



The title compound was made in a manner analogous to Intermediate 27, using 6-(3-(difluoromethyl)-4-fluorophenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridine (Intermediate 21) in place 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 $[M+H]^+$.

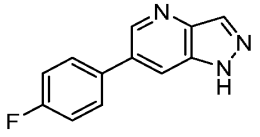
Intermediate 29: 2-(6-(3-(Difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid.



The title compound was made in a manner analogous to Intermediate 27, using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 17) in place of 6-

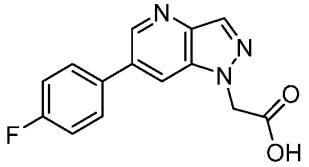
[3-(difluoromethyl)-4-fluorophenyl]-1H-pyrazolo[4,3-b]pyridine. MS (ESI): mass calcd for $C_{15}H_{10}F_3N_3O_3$, 337.1; m/z found, 338.1 $[M+H]^+$.

Intermediate 30: 6-(4-Fluorophenyl)-1H-pyrazolo[4,3-b]pyridine



6-Bromo-1H-pyrazolo[4,3-b]pyridine (845 mg, 4.27 mmol), 4-fluorophenylboronic acid (896 mg, 6.40 mmol) and sodium carbonate (1.36 g, 12.8 mmol) were taken up in dioxane (15 mL) and water (5 mL). A stream of nitrogen gas was bubbled through the reaction mixture for 10 minutes, then tetrakis(triphenylphosphine)palladium (247 mg, 0.21 mmol) was added, and the reaction mixture was stirred at 90 °C for 24 hours. The reaction mixture was cooled to room temperature, diluted with water and DCM, and the aqueous layer was extracted using DCM (2x). The combined organic layers were dried ($MgSO_4$), concentrated, and adsorbed onto silica gel. Purification (FCC, SiO_2, 0-100% hexanes/EtOAc then 3-8% MeOH/DCM) afforded the title compound (530 mg, 58%). MS (ESI): mass calcd. for $C_{12}H_8FN_3$, 213.1; m/z found, 214.1 $[M+H]^+$.

Intermediate 31: 2-(6-(4-Fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid.

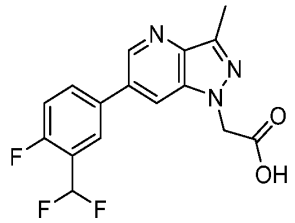


Step A. Ethyl 2-(6-(4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetate. 6-(4-Fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 30, 470 mg, 2.20 mmol) was taken up in DMF (7 mL) and heated to 50 °C. To this solution was added sodium hydride (60% dispersion in mineral oil, 106 mg, 2.65 mmol) and the reaction mixture was stirred for 15 minutes at 50 °C. The mixture was allowed to cool to room temperature and ethyl bromoacetate (515 mg, 3.09 mmol) was added. The reaction mixture was stirred at room temperature for 3 hours, poured onto ice, and extracted EtOAc (2x). The combined organic layers were dried ($MgSO_4$) and concentrated.

Purification (FCC, SiO_2, 0 to 100% hexanes/EtOAc) afforded 422 mg (1.41 mmol, 64%). MS (ESI): mass calcd. for $C_{16}H_{14}FN_3O_2$, 299.1; m/z found, 300.1 $[M+H]^+$.

Step B. 2-(6-(4-Fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid. Ethyl 2-(6-(4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetate (400 mg, 1.34 mmol) and sodium hydroxide (80 mg, 2.01 mmol) were dissolved in a 1:1 mixture of water and acetonitrile (10 mL). The reaction was stirred overnight at 50 °C. The pH of the mixture was adjusted to pH 1 with aqueous HCl and then extracted with DCM (4x). The combined organic layers were dried ($MgSO_4$) and concentrated to afford the title compound (400 mg, 1.475 mmol, 110%). The title compound was carried on crude the next steps. MS (ESI): mass calcd. for $C_{14}H_{10}FN_3O_2$, 271.1; m/z found, 272.1 $[M+H]^+$.

Intermediate 32: 2-(6-(3-(Difluoromethyl)-4-fluorophenyl)-3-methyl-1H-pyrazolo[4,3-*b*]pyridin-1-yl)acetic acid.

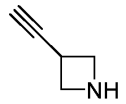


Step A. Ethyl 2-(6-(3-(difluoromethyl)-4-fluorophenyl)-3-methyl-1H-pyrazolo[4,3-b]pyridin-1-yl)acetate. To a stirred solution of 6-(3-(difluoromethyl)-4-fluorophenyl)-3-methyl-1H-pyrazolo[4,3-*b*]pyridine (Intermediate 26, 300 mg, 1.08 mmol) in DMF (6 mL) was added Cs_2CO_3 (1.06 g, 3.25 mmol), followed by ethyl bromoacetate (240 mg, 1.41 mmol). The reaction mixture was stirred at room temperature for 2 hours. The reaction mixture was diluted with water and Et_2O, and the aqueous layer was extracted with Et_2O (2x). The combined organics were washed with water, brine, dried ($MgSO_4$) and concentrated. Purification (FCC, SiO_2, 0 to 100% hexanes/EtOAc) afforded the title compound (313 mg, 0.861 mmol, 80%). MS (ESI): mass calcd. for $C_{18}H_{16}F_3N_3O_2$, 363.1; m/z found, 364.1 $[M+H]^+$.

Step B. 2-(6-(3-(Difluoromethyl)-4-fluorophenyl)-3-methyl-1H-pyrazolo[4,3-*b*]pyridin-1-yl)acetic acid. To a solution of ethyl 2-(6-(3-(difluoromethyl)-4-fluorophenyl)-3-methyl-1H-pyrazolo[4,3-*b*]pyridin-1-yl)acetate (313 mg, 0.861 mmol) in THF (15 mL) was added 4 N aqueous lithium hydroxide (5 mL). The biphasic mixture was stirred vigorously overnight. The

reaction mixture was partitioned between water and Et_2O and the layers separated. The organic layer was extracted with water (2x). The combined aqueous layers were acidified to pH 1 with 1N HCl. The resulting precipitate was collected by filtration, washed with water and dried to afford the title compound (293 mg, 100%) as a white solid. The compound was sufficiently pure to be carried on to subsequent steps without further purification. MS (ESI): mass calcd. for $C_{16}H_{12}F_3N_3O_2$, 335.1; m/z found, 336.1 $[M+H]^+$.

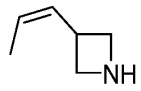
Intermediate 33: 3-Ethynylazetidine•HCl salt.



Step A. *tert*-Butyl 3-ethynylazetidine-1-carboxylate. *tert*-Butyl 3-formylazetidine-1-carboxylate (500 mg, 2.70 mmol), dimethyl (1-diazo-2-oxopropyl)phosphonate (10% wt., 9.2 mL, 4.05 mmol), and potassium carbonate (1120 mg, 8.10 mmol) were taken up in methanol (10 mL). The reaction mixture was stirred at room temperature for 3 hours, concentrated, diluted with diethyl ether and water. The organic layer was separated and was washed with water followed by sat. aqueous sodium carbonate, dried ($MgSO_4$), and concentrated. Purification (FCC, SiO_2, 0-25% ethyl acetate/hexanes gradient) afforded the title compound (356 mg, 1.96 mmol, 73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.14 (t, J = 8.5 Hz, 2H), 3.94 (dd, J = 8.2, 6.3 Hz, 2H), 3.36 – 3.25 (m, 1H), 2.28 (d, J = 2.4 Hz, 1H), 1.44 (s, 9H).

Step B. 3-Ethynylazetidine•HCl salt. *tert*-Butyl 3-ethynylazetidine-1-carboxylate (50 mg, 0.28 mmol) was dissolved in 4 N HCl in dioxane (1 mL) and the reaction mixture was stirred for 2 hours at room temperature. The mixture was concentrated, and the hydrochloride salt of the title compound was used directly in the next step without further purification.

Intermediate 34: (*Z*)-3-(Prop-1-en-1-yl)azetidine•HCl salt.

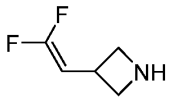


Step A. *tert*-Butyl (Z)-3-(prop-1-en-1-yl)azetidine-1-carboxylate. Ethyl(triphenyl)phosphonium bromide (1.21 g, 3.24 mmol) was suspended in dry THF (15 mL). The suspension was cooled to 0 °C. *n*-BuLi (2.5M in hexanes, 1.3 mL, 3.24 mmol) was added dropwise to the reaction mixture with stirring, and the reaction mixture was stirred for 1 hour at 0 °C. *tert*-Butyl 3-

formylazetidine-1-carboxylate (500 mg, 2.70 mmol) was added slowly to the reaction mixture at 0 °C and the reaction mixture was allowed to warm to rt and stirred overnight. The reaction mixture was concentrated, partitioned between DCM and water, the aqueous layer was extracted using DCM (2x), and the combined organics were concentrated. The crude material was purified on silica gel (FCC, SiO_2, 0-50% ethyl acetate/hexanes gradient) to afford the title compound as a 7:1 mixture of Z/E isomers (318 mg, 1.61 mmol, 60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.69 – 5.56 (m, 1H), 5.56 – 5.45 (m, 1H), 4.12 (t, *J* = 8.4 Hz, 2H), 3.67 (dd, *J* = 8.4, 6.0 Hz, 2H), 3.50 – 3.47 (m, 1H), 1.58 (dd, *J* = 6.8, 1.6 Hz, 3H), 1.44 (d, *J* = 1.5 Hz, 9H).

Step B. (*Z*)-3-(Prop-1-en-1-yl)azetidine•HCl salt. *tert*-Butyl (*Z*)-3-(prop-1-en-1-yl)azetidine-1-carboxylate (50 mg, 0.28 mmol) was dissolved in 4 N HCl in dioxane (1 mL) and the reaction mixture was stirred for 2 hours at room temperature. The mixture was concentrated, and the hydrochloride salt of the title compound was used directly in the next step.

Intermediate 35: 3-(2,2-Difluorovinyl)azetidine•HCl salt.

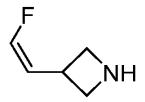


Step A. *tert*-Butyl 3-(2,2-difluorovinyl)azetidine-1-carboxylate. *tert*-Butyl 3-formylazetidine-1-carboxylate (1000 mg, 5.40 mmol) and triphenylphosphine (2.8 g, 10.8 mmol) were taken up in dry DMF (10 mL) and heated to 100 °C with stirring. Sodium chlorodifluoroacetate (1.7 g, 10.8 mmol) was added portion-wise over 30 minutes, and the reaction mixture was stirred at 100 °C for another 15 minutes after complete addition. The reaction mixture was cooled to room temperature, concentrated under reduced pressure to remove DMF, diluted with DCM, and shaken briefly with 30% aqueous H_2O_2. The resulting bi-phasic mixture was diluted further with DCM and water . The aqueous layer was extracted using DCM (2x) and the combined organics were concentrated. Purification (FCC, SiO_2, 0-50% ethyl acetate/hexanes gradient) afforded the title compound (786 mg,3.58 mmol, 66%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.51 – 4.37 (m, 1H), 4.14 (t, *J* = 8.4 Hz, 2H), 3.70 (dd, *J* = 8.6, 6.0 Hz, 2H), 3.39 – 3.27 (m, 1H), 1.44 (d, *J* = 0.7 Hz, 9H).

Step B. 3-(2,2-Difluorovinyl)azetidine•HCl salt. *tert*-Butyl 3-(2,2-difluorovinyl)azetidine-1-carboxylate (75 mg, 0.34 mmol) was dissolved in 4 N HCl in dioxane (1 mL) and the reaction

mixture was stirred for 2 hours at room temperature. The mixture was concentrated, and the hydrochloride salt of the title compound was used directly in the next step.

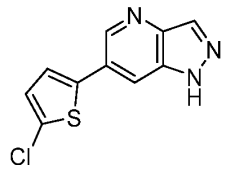
Intermediate 36: (*Z*)-3-(2-fluorovinyl)azetidine•HCl salt.



Step A. *tert*-Butyl (Z)-3-(2-fluorovinyl)azetidine-1-carboxylate. *tert*-Butyl 3-(2,2-difluorovinyl)azetidine-1-carboxylate (500 mg, 2.28 mmol), bis(neopentyl glycolato)diboron (1.6 g, 6.8 mmol), and water (120 μL, 6.8 mmol) were dissolved in dimethylacetamide (10 mL) and the solution was degassed by sparging with N_2. Copper thiophene-2-carboxylate (43 mg, 0.23 mmol), 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (Xantphos®) (135 mg, 0.23 mmol), and lithium tert-butoxide (565 mg, 6.8 mmol) were added (a strong exotherm occurred upon addition of base). The reaction mixture was stirred overnight at 40 °C, then partitioned between water and a mixture of 3:1 ethyl acetate/hexanes. The organic layer was extracted using water (2x). The organic layer was concentrated. Purification (FCC, SiO_2, 0-50% ethyl acetate/hexanes gradient) afforded the title compound (319 mg, 1.59 mmol, 70%) contaminated with approximately 20 mol% starting material and 7 mol% of the *E* isomer. The title compound was carried as is to the next step. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.66 – 6.30 (m, 1H), 5.17 – 4.86 (m, 1H), 4.19 – 4.12 (m, 2H), 3.74 – 3.67 (m, 2H), 3.66 – 3.53 (m, 1H), 1.44 (s, 9H).

Step B. (Z)-3-(2-fluorovinyl)azetidine•HCl salt. *tert*-Butyl (Z)-3-(2-fluorovinyl)azetidine-1-carboxylate (319 mg, 1.59 mmol) was dissolved in 4 N HCl in dioxane (5 mL) and the reaction mixture was stirred for 2 hours at room temperature. The mixture was concentrated, and the hydrochloride salt of the title compound was used directly without further purification.

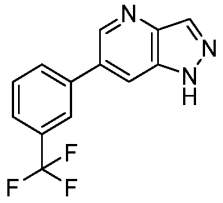
Intermediate 37: 6-(5-Chloro-2-thienyl)-1*H*-pyrazolo[4,3-*b*]pyridine.



To a solution of 6-bromo-1*H*-pyrazolo[4,3-*b*]pyridine (500 mg, 2.52 mmol) in degassed 1,4-dioxane (39.4 mL) and water (9.55 mL) was added 5-chlorothiophene-2-boronic acid (431 mg,

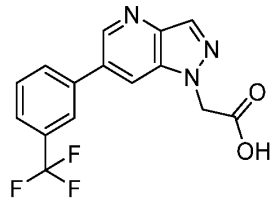
2.654 mmol), potassium fluoride (440 mg, 7.57 mmol) and *tetrakis*(triphenylphosphine)palladium(0) (205 mg, 0.177 mmol). The reaction mixture was stirred at 80 °C for 1 h under argon. Additional 5-chlorothiophene-2-boronic acid (123 mg, 0.757 mmol) and *tetrakis*(triphenylphosphine)palladium(0) (87 mg, 0.075 mmol) was introduced and the reaction mixture was stirred at 80 °C for 2 h under argon. 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 (Na_2SO_4), filtered and concentrated under reduced pressure. 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 38: 6-(3-(Trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine.



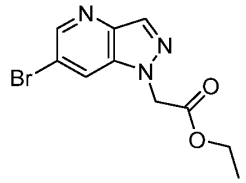
A suspension of 6-bromo-1H-pyrazolo[4,3-b]pyridine (5.0 g, 25.3 mmol), 3-(trifluoromethyl)phenylboronic acid (5.8 g, 30.3 mmol) and palladium-tetrakis(triphenylphosphine) (1.5 g, 1.3 mmol) in aqueous sodium carbonate (2M, 32.5 mL, 64.9 mmol) and 1,4-dioxane (96.9 mL) was stirred at 120 °C under a nitrogen atmosphere. After 48 hours, EtOAc was added and the mixture was washed with H_2O (2x). The organic layer was dried (Na_2SO_4) and concentrated in vacuo. The residue was purified (FCC, SiO_2, 0-50 % EtOAc in heptane) to afford a yellowish solid. The solid was triturated using Et_2O and collected by filtration to afford 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 39: 2-(6-(3-(Trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid.



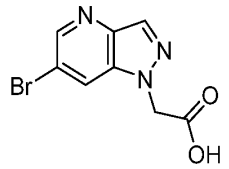
Sodium hydride (60% dispersion in mineral oil, 387.5 mg, 9.7 mmol) was added to a stirred solution of 6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 38, 850 mg, 3.2 mmol) in DMF (20 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 10 minutes. Then, ethyl bromoacetate (0.54 mL, 4.8 mmol) was added and the reaction mixture was allowed to warm to room temperature. After 16 hours, aqueous potassium hydroxide (1M, 16.1 mL, 16.1 mmol) was added to the reaction mixture and stirred for 1 hour. The reaction mixture was concentrated in vacuo and the residue was dissolved in water and washed with EtOAc. The aqueous layer was separated and acidified using 1M HCl. The solid was filtered and washed with water, dried and triturated from Et_2O to afford the title product (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 $[M+H]^+$.

Intermediate 40: Ethyl 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)acetate.



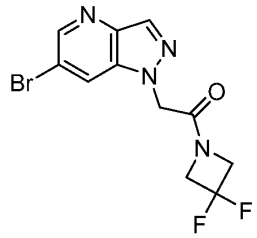
6-Bromo-1H-pyrazolo[4,3-b]pyridine (639.5 mg, 3.2 mmol) was added to a suspension of NaH (60% dispersion in mineral oil, 180.8 mg, 4.5 mmol) in DMF (33.7 mL) at room temperature under a nitrogen atmosphere. After 10 minutes, ethyl bromoacetate (0.5 mL, 4.5 mmol) was added to the reaction mixture. After 16 hours, water (80 mL) was added and precipitation slowly occurred. The solids were collected by filtration and were purified (FCC, SiO_2, 0-90 % EtOAc in hexanes) to afford the title compound (917 mg, 3.2 mmol, 100%). MS (ESI): mass calcd. for $C_{10}H_{10}BrN_3O_2$, 283.0; m/z found, 284.0 $[M+H]^+$.

Intermediate 41: 2-(6-Bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid.



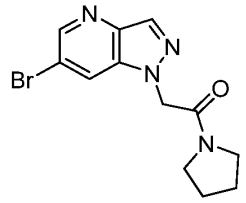
Lithium hydroxide (4M in water, 1.9 mL, 7.6 mmol) was added to a mixture of ethyl 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)acetate (Intermediate 40, 1.54 g, 5.4 mmol) in THF (65.9 mL) at room temperature. After 16 hours, complete conversion was observed, and the precipitates were collected by filtration, rinsed with THF and dried under vacuum to afford the title compound (1.16 g, 4.5 mmol, 83.6 %). MS (ESI): mass calcd. for $C_8H_6BrN_3O_2$, 255.0; m/z found, 256.0 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.50 (d, J = 2.0 Hz, 1H), 8.26 – 8.24 (m, 1H), 8.17 – 8.15 (m, 1H), 4.66 (s, 2H).

Intermediate 42: 2-(6-Bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3,3-difluoroazetidin-1-yl)ethan-1-one.



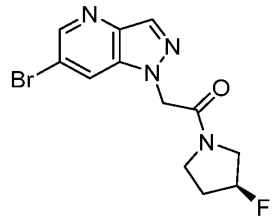
A mixture of 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid (Intermediate 41, 300 mg, 1.2 mmol), 3,3-difluoroazetidine hydrochloride (182 mg, 1.4 mmol), T3P® (50% solution in DMF, 2.1 mL, 3.5 mmol) and DIPEA (0.4 mL, 2.5 mmol) in DCM (11.7 mL) was stirred at room temperature. After 16 hours, complete conversion was observed and water (20 mL) was added. The mixture was extracted with EtOAc (3 x 35 mL). The combined organics were dried ($MgSO_4$), filtered and concentrated under vacuum to afford the title compound (287 mg, 0.9 mmol, 74.0%). MS (ESI): mass calcd. for $C_{11}H_9BrF_2N_4O$, 330.0; m/z found, 331.0 $[M+H]^+$.

Intermediate 43: 2-(6-Bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(pyrrolidin-1-yl)ethan-1-one.



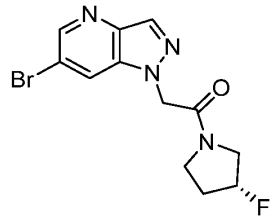
The title compound was prepared in a manner analogous to Intermediate 42, using pyrrolidine in place of 3,3-difluoroazetidine hydrochloride. MS (ESI): mass calcd. for $C_{12}H_{13}BrN_4O$, 308.0; m/z found, 309.0 $[M+H]^+$.

Intermediate 44: (*S*)-2-(6-Bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoropyrrolidin-1-yl)ethan-1-one.



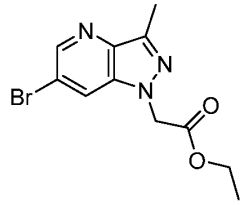
The title compound was prepared in a manner analogous to Intermediate 42, using (*S*)-3-fluoropyrrolidine hydrochloride in place of 3,3-difluoroazetidine hydrochloride. MS (ESI): mass calcd. for $C_{12}H_{12}BrFN_4O$, 326.0; m/z found, 327.0 $[M+H]^+$.

Intermediate 45: (*R*)-2-(6-Bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoropyrrolidin-1-yl)ethan-1-one.



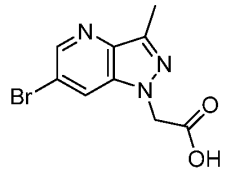
The title compound was prepared in a manner analogous to Intermediate 42, using (*R*)-3-fluoropyrrolidine hydrochloride in place of 3,3-difluoroazetidine hydrochloride. MS (ESI): mass calcd. for $C_{12}H_{12}BrFN_4O$, 326.0; m/z found, 327.0 $[M+H]^+$.

Intermediate 46: Ethyl 2-(6-bromo-3-methyl-1H-pyrazolo[4,3-b]pyridin-1-yl)acetate.



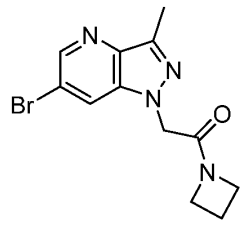
The title compound was prepared in a manner analogous to Intermediate 40, using 6-bromo-3-methyl-1H-pyrazolo[4,3-b]pyridine in place of 6-bromo-1H-pyrazolo[4,3-b]pyridine. MS (ESI): mass calcd. for $C_{11}H_{12}BrN_3O_2$, 297.0; m/z found, 298.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.57 (d, J = 1.9 Hz, 1H), 8.53 (d, J = 1.9 Hz, 1H), 5.33 (s, 2H), 4.14 (q, J = 7.1 Hz, 2H), 2.52 (s, 3H), 1.20 (t, J = 7.1 Hz, 3H).

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



The title compound was prepared in a manner analogous to Intermediate 41, using ethyl 2-(6-bromo-3-methyl-1H-pyrazolo[4,3-b]pyridin-1-yl)acetate (Intermediate 46) in place of ethyl 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)acetate. MS (ESI): mass calcd. for $C_9H_8BrN_3O_2$, 269.0; m/z found, 270.0 $[M+H]^+$.

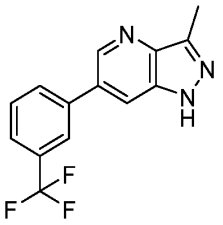
Intermediate 48: 1-(Azetidin-1-yl)-2-(6-bromo-3-methyl-1H-pyrazolo[4,3-b]pyridin-1-yl)ethan-1-one.



The title compound was prepared in a manner analogous to Intermediate 13 using 2-(6-bromo-3-methyl-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid (Intermediate 47) in place of 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid. MS (ESI): mass calcd. for $C_{12}H_{13}BrN_4O$, 308.0; m/z found, 309.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.54 – 8.53 (m, 1H), 8.42 – 8.41 (m,

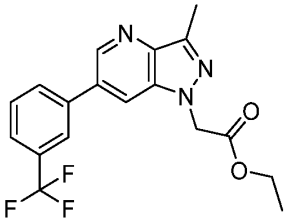
1H), 5.09 (s, 2H), 4.19 (t, J = 7.7 Hz, 2H), 3.90 (t, J = 7.8 Hz, 2H), 2.50 (s, 3H), 2.30 – 2.22 (m, 2H).

Intermediate 49: 3-Methyl-6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine.



A mixture of 6-bromo-3-methyl-1H-pyrazolo[4,3-b]pyridine (200 mg, 0.9 mmol), (3-(trifluoromethyl)phenyl)boronic acid (358 mg, 1.9 mmol), cesium carbonate (614.6 mg, 1.9 mmol) and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (48.3 mg, 0.07 mmol) in 1,4-dioxane (8.7 mL) and distilled water (1.9 mL) was heated to 90 °C. After 16 hours, the reaction mixture was concentrated under vacuum. Purification (FCC, SiO_2, 0-90 % EtOAc in hexanes) afforded the title compound (229 mg, 0.8 mmol, 87.6%). MS (ESI): mass calcd. for $C_{14}H_{10}F_3N_3$, 277.1; m/z found, 278.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 13.06 (s, 1H), 8.83 (d, J = 2.0 Hz, 1H), 8.23 (d, J = 2.0 Hz, 1H), 8.15 – 8.10 (m, 2H), 7.84 – 7.74 (m, 2H), 2.57 (s, 3H).

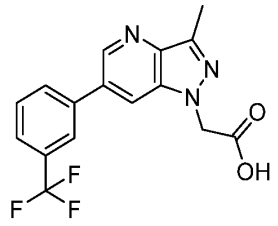
Intermediate 50: Ethyl 2-(3-methyl-6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetate.



The title compound was prepared in a manner analogous to Intermediate 40, using 3-methyl-6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 49) in place of 6-bromo-1H-pyrazolo[4,3-b]pyridine. MS (ESI): mass calcd. for $C_{18}H_{16}F_3N_3O_2$, 363.1; m/z found, 364.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.85 (d, J = 2.1 Hz, 1H), 8.35 (d, J = 2.1 Hz, 1H),

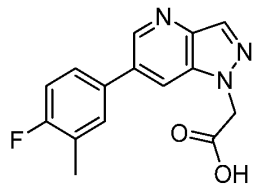
8.16 – 8.10 (m, 2H), 7.83 – 7.73 (m, 2H), 5.48 (s, 2H), 4.21 (q, *J* = 7.1 Hz, 2H), 2.66 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H).

Intermediate 51: 2-(3-Methyl-6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid.



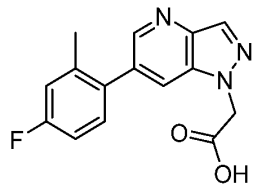
The title compound was prepared in a manner analogous to Intermediate 41, using ethyl 2-(3-methyl-6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetate (Intermediate 50) in place of ethyl 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)acetate. MS (ESI): mass calcd. for $C_{16}H_{12}F_3N_3O_2$, 335.1; m/z found, 336.1 $[M+H]^+$.

Intermediate 52: 2-(6-(4-Fluoro-3-methylphenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid.



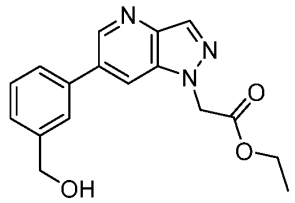
A mixture of 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid (Intermediate 41, 90 mg, 0.27 mmol), 4-fluoro-3-methylboronic acid (63 mg, 0.41 mmol), bis(diphenylphosphino)ferrocene]dichloropalladium(II) complex with dichloromethane (9.9 mg, 0.014 mmol), sodium carbonate (86 mg, 0.82 mmol), 1,4-dioxane (1.4 mL) and water (0.8 mL) was heated at 110 °C for 16 hours. The reaction mixture was diluted with water and washed ethyl acetate (3x). The aqueous layer was acidified with 1N HCl and extracted with ethyl acetate (3x). The combined organics were dried ($MgSO_4$) and concentrated to afford the title compound (71 mg, 0.25 mmol, 92%) in sufficient purity for use in subsequent transformations. MS (ESI): mass calcd. for $C_{15}H_{12}FN_3O_2$, 285.1; m/z found, 286.1 $[M+H]^+$.

Intermediate 53: 2-(6-(4-Fluoro-2-methylphenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid.



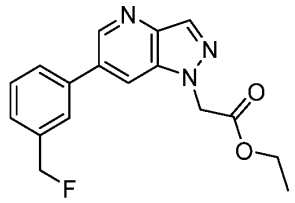
The title compound was prepared in a manner analogous to Intermediate 52, using 4-fluoro-2-methylboronic acid in place of 4-fluoro-3-methylboronic acid. MS (ESI): mass calcd. for $C_{15}H_{12}FN_3O_2$, 285.1; m/z found, 286.1 $[M+H]^+$.

Intermediate 54: Ethyl 2-(6-(3-(hydroxymethyl)phenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetate.



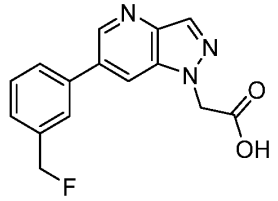
A mixture of ethyl 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)acetate (Intermediate 40, 1.5 g, 5.3 mmol), (3-(hydroxymethyl)phenyl)boronic acid (1.6 g, 10.6 mmol), cesium carbonate (3.4 g, 10.6 mmol) and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (270 mg, 0.4 mmol) in 1,4-dioxane (49 mL) was heated to 90 °C. After 3 days, water (100 mL) was added and the mixture was extracted using EtOAc (3 x 150 mL). The combined organics were dried ($MgSO_4$), filtered and concentrated under vacuum. Purification (FCC, SiO_2, 0-90 % EtOAc in hexanes) afforded the title compound (325 mg, 1.0 mmol, 20%). MS (ESI): mass calcd. for $C_{17}H_{17}N_3O_3$, 311.1; m/z found, 312.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.89 (d, J = 1.9 Hz, 1H), 8.50 – 8.48 (m, 1H), 8.38 – 8.36 (m, 1H), 7.78 – 7.75 (m, 1H), 7.71 – 7.67 (m, 1H), 7.50 (t, J = 7.6 Hz, 1H), 7.43 – 7.39 (m, 1H), 5.49 (s, 2H), 4.61 (s, 2H), 4.16 (q, J = 7.1 Hz, 2H), 1.21 (t, J = 7.1 Hz, 3H).

Intermediate 55: Ethyl 2-(6-(3-(fluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetate.



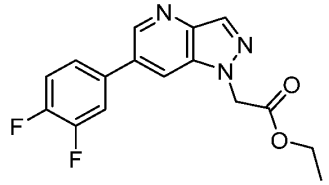
Bis(2-methoxyethyl)aminosulfur trifluoride (Deoxo-Fluor®) (0.2 mL, 1.2 mmol) was added to a mixture of ethyl 2-(6-(3-(hydroxymethyl)phenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetate (Intermediate 54, 300 mg, 1.0 mmol) in DCM (6.6 mL) at 0 °C under a nitrogen atmosphere. After 3 hours, the reaction mixture was slowly poured into a mixture of saturated aqueous $NaHCO_3$ (20 mL) and DCM (20 mL) at 0 °C. The mixture was extracted with DCM (3 x 30 mL). The combined organics were dried ($MgSO_4$), filtered and concentrated under vacuum to afford the title compound. MS (ESI): mass calcd. for $C_{17}H_{16}FN_3O_2$, 313.1; m/z found, 314.2 $[M+H]^+$.

Intermediate 56: 2-(6-(3-(Fluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid.



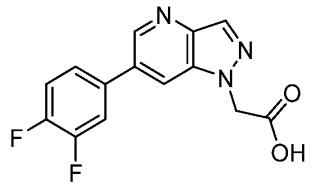
The title compound was prepared in a manner analogous to Intermediate 41, using ethyl 2-(6-(3-(fluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetate (Intermediate 55) in place of ethyl 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)acetate. MS (ESI): mass calcd. for $C_{15}H_{12}FN_3O_2$, 285.1; m/z found, 286.1 $[M+H]^+$.

Intermediate 57: Ethyl 2-(6-(3,4-difluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetate.



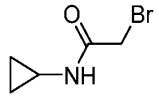
The title compound was prepared in a manner analogous to Intermediate 54, using 3,4-difluorophenylboronic acid in place of (3-(hydroxymethyl)phenyl)boronic acid. MS (ESI): mass calcd. for $C_{16}H_{13}F_2N_3O_2$, 317.1; m/z found, 318.1 $[M+H]^+$.

Intermediate 58: 2-(6-(3,4-Difluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid.



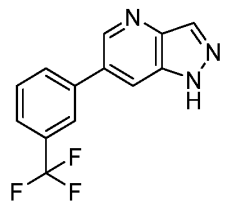
The title compound was prepared in a manner analogous to Intermediate 41 using ethyl 2-(6-(3,4-difluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetate (Intermediate 57) in place of ethyl 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)acetate. MS (ESI): mass calcd. for $C_{14}H_9FN_3O_2$, 289.1; m/z found, 290.1 $[M+H]^+$.

Intermediate 59: 2-Bromo-N-cyclopropylacetamide.



Bromoacetyl chloride (1 mL, 12.0 mmol) was added to a mixture of TEA (1.7 mL) and cyclopropylamine (0.8 mL, 12.0 mmol) in acetonitrile (15 mL) at -78 °C. The iced reaction mixture was slowly warmed to room temperature. After 2h, water (30 mL) was added and the mixture was extracted with DCM (3 x 40 mL). The combined organics were concentrated under vacuum to afford a mixture of the title compound contaminated with the chloro derivative. MS (ESI): mass calcd. for C_5H_8BrNO, 177.0; m/z found, 178.0 $[M+H]^+$.

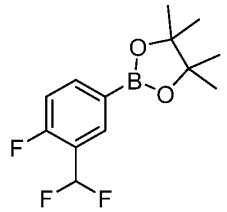
Intermediate 60: 6-(3-(Trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine.



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 sodium carbonate (2M, 32.5 mL, 64.9

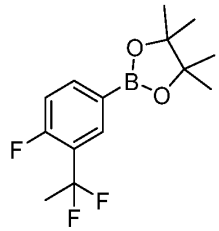
mmol) and 1,4-dioxane (96.9 mL) was stirred at 120 °C under a nitrogen atmosphere. After 48 hours, EtOAc was added and the mixture was washed with H_2O (2x). The organic layer was dried (Na_2SO_4) and concentrated in vacuo. The residue was purified (FCC, SiO_2, 0-50 % EtOAc in heptane) to afford a yellowish solid. The solid was triturated using Et_2O and collected by filtration 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 61: 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 °C 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 $[M+H]^+$.

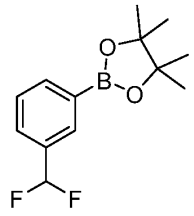
Intermediate 62: 2-(3-(1,1-Difluoroethyl)-4-fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.



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, 1 equiv) and DAST (1.9 mL, 14.4 mmol, 1.25 equiv) 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).

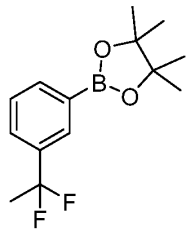
Step B: 2-(3-(1,1-Difluoroethyl)-4-fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. In a round bottom flask, bis(pinacolato)diboron (2.87 g, 11.3 mmol), potassium acetate (2.22 g, 22.6 mmol), and [1,1′-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (615 mg, 0.75 mmol) were added to a solution of 4-bromo-2-(1,1-difluoroethyl)-1-fluorobenzene (3 g, 7.5 mmol) 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 63: 2-(3-(Difluoromethyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.



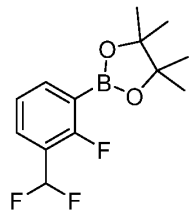
The title compound was prepared in a manner analogous to Intermediate 61 using 1-bromo-3-(difluoromethyl)benzene instead of 4-bromo-2-(difluoromethyl)-1-fluorobenzene. No mass observed.

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



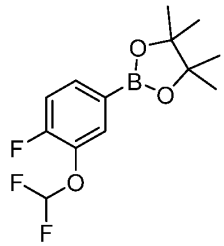
The title compound was prepared in a manner analogous to Intermediate 61 using 1-bromo-3-(1,1-difluoroethyl)benzene instead of 4-bromo-2-(difluoromethyl)-1-fluorobenzene. No mass observed.

Intermediate 65: 2-(3-(Difluoromethyl)-2-fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.



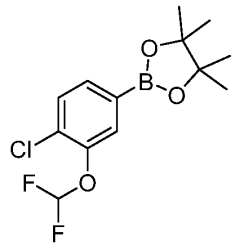
The title compound was prepared in a manner analogous to Intermediate 61 using 1-bromo-3-(1,1-difluoroethyl)benzene instead of 4-bromo-2-(difluoromethyl)-1-fluorobenzene. MS (ESI): mass calcd. for $C_{13}H_{16}BF_3O_2$, 272.1; m/z found, 273.2 [M+H]+.

Intermediate 66: 2-(3-(Difluoromethoxy)-4-fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.



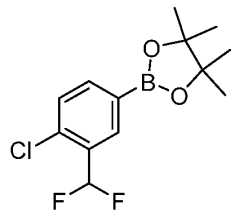
The title compound was prepared in a manner analogous to Intermediate 61 using 4-bromo-2-(difluoromethoxy)-1-fluorobenzene instead of 4-bromo-2-(difluoromethyl)-1-fluorobenzene. MS (ESI): mass calcd. for $C_{13}H_{16}BF_3O_3$, 288.1; m/z found, 289.0 [M+H]+.

Intermediate 67: 2-(4-Chloro-3-(difluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.



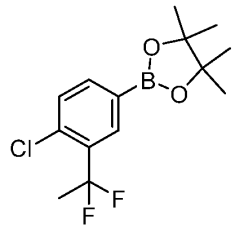
The title compound was prepared in a manner analogous to Intermediate 61 using 4-bromo-1-chloro-2-(difluoromethoxy)benzene instead of 4-bromo-2-(difluoromethyl)-1-fluorobenzene. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 – 7.56 (m, 2H), 7.44 (d, J = 7.9 Hz, 1H), 6.56 (t, J = 73.6 Hz, 1H), 1.34 (s, 12H).

Intermediate 68: 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 62 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 $[M+H]^+$.

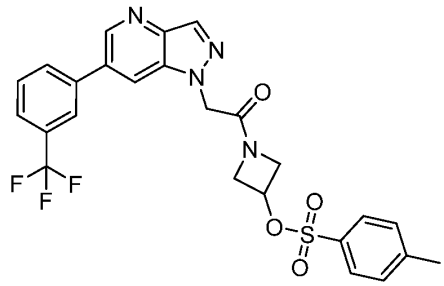
Intermediate 69: 2-(4-Chloro-3-(1,1-difluoroethyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.



The title compound was prepared in a manner analogous to Intermediate 62 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).

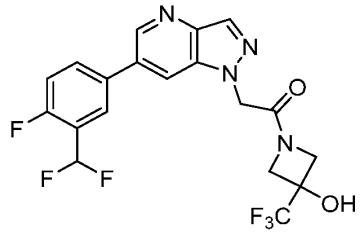
Intermediate 70: 1-(2-(6-(3-(Trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetyl)azetidin-3-yl 4-methylbenzenesulfonate.



To a solution of 1-(3-hydroxyazetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone trifluoroacetate salt (Example 113, 32 mg, 0.085 mmol) in DCM (2 mL) was added triethylamine (0.06 mL, 0.42 mmol), N,N-dimethylpyridin-4-amine (1 mg, 0.0085 mmol), and 4-methylbenzenesulfonyl chloride (24 mg, 0.13 mmol). The resulting mixture was stirred at rt for 15 h. The mixture was then diluted with EtOAc (20 mL) and washed with brine (20 mL), then water (2x20 mL), and dried over Na_2SO_4 and concentrated. The residue was purified by FCC (hexanes/EtOAc, 0 to 100%) to afford the title compound (36 mg, 0.067 mmol). MS (ESI): mass calcd. for $C_{25}H_{21}F_3N_4O_4S$, 530.1; m/z found, 531.2 $[M+H]^+$. ^1H NMR (400 MHz, Chloroform-*d*) δ 8.83 (d, *J* = 1.8 Hz, 1H), 8.31 (d, *J* = 1.0 Hz, 1H), 8.10 – 8.04 (m, 1H), 7.90 – 7.85 (m, 1H), 7.85 – 7.79 (m, 1H), 7.78 – 7.73 (m, 2H), 7.73 – 7.68 (m, 1H), 7.67 – 7.60 (m, 1H), 7.40 – 7.32 (m, 2H), 5.15 – 5.01 (m, 3H), 4.38 – 4.29 (m, 1H), 4.28 – 4.19 (m, 1H), 4.19 – 4.12 (m, 1H), 4.04 – 3.94 (m, 1H), 2.46 (s, 3H).

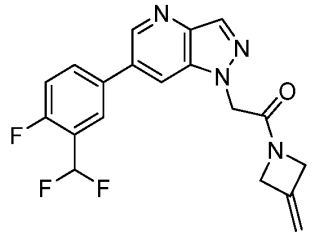
EXAMPLES

Example 1: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-[3-hydroxy-3-(trifluoromethyl)azetidin-1-yl]ethanone.



A stock solution of active ester was prepared by dissolving 2-(6-(3-(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-*b*]pyridin-1-yl)acetic acid (Intermediate 27, 180 mg, 0.56 mmol), DIPEA (290 µL, 1.7 mmol), HOBt (113 mg, 0.84 mmol), and EDCI (161 mg, 1.04 mmol) in dry ACN (6 mL). A 1 mL aliquot (30 mg carboxylic acid, 0.93 mmol) was added to a vial containing 3-(trifluoromethyl)azetidine-3-ol (15.8 mg, 0.112 mmol). The reaction mixture was stirred overnight and purified by reverse phase HPLC (METHOD D) to afford the title compound (3.4 mg, 8%). MS (ESI): mass calcd. for $C_{19}H_{14}F_6N_4O_2$, 444.1; m/z found, 445.0 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, J = 1.9 Hz, 1H), 8.30 (d, J = 1.0 Hz, 1H), 7.95 – 7.91 (m, 1H), 7.89 – 7.84 (m, 1H), 7.78 – 7.70 (m, 1H), 7.32 – 7.27 (m, 1H), 6.98 (t, J = 54.9 Hz, 1H), 5.12 (d, J = 7.2 Hz, 2H), 4.37 – 4.29 (m, 2H), 4.13 – 4.01 (m, 2H).

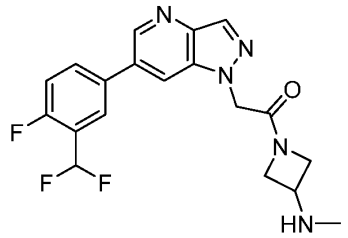
Example 2: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-(3-methyleneazetidin-1-yl)ethanone.



A solution of 2-(6-(3-(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-*b*]pyridin-1-yl)acetic acid (Intermediate 27, 50 mg, 0.156 mmol), 3-methyleneazetidine hydrochloride (33 mg, 0.31 mmol), (benzotriazol-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate (PyBOP®) (97 mg, 0.19 mmol), and DIPEA (110 µL, 0.62 mmol) in dry DCM (2 mL) was stirred at r.t. for 30 minutes. The reaction mixture was injected directly onto a silica gel column and purified chromatographically (FCC, SiO_2, 0-10% MeOH/DCM gradient) to yield 24.9 mg (0.0669 mmol, 43% yield) of the title compound. MS (ESI): mass calcd. for $C_{19}H_{15}F_3N_4O$, 372.1; m/z found, 373.0 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, J = 1.9 Hz, 1H), 8.31 (d, J = 1.0 Hz, 1H),

7.95 (dd, *J* = 1.9, 1.0 Hz, 1H), 7.89 – 7.85 (m, 1H), 7.74 (d, *J* = 5.1 Hz, 1H), 7.30 (d, *J* = 9.3 Hz, 1H), 6.98 (t, *J* = 54.9 Hz, 1H), 5.12 (s, 2H), 5.10 – 5.01 (m, 2H), 4.63 – 4.55 (m, 4H).

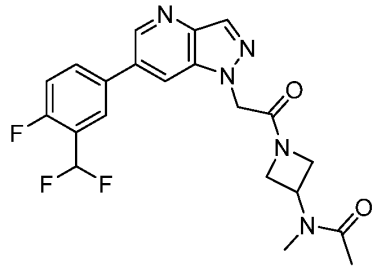
Example 3: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-[3-(methylamino)azetidin-1-yl]ethanone.



Step A. *tert*-Butyl (1-(2-(6-(3-(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetyl)azetidin-3-yl)(methyl)carbamate. The title compound was prepared in a manner analogous to Example 1 using *tert*-butyl azetidin-3-yl(methyl)carbamate in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{24}H_{26}F_3N_5O_3$, 489.2; m/z found, 490.0 $[M+H]^+$.

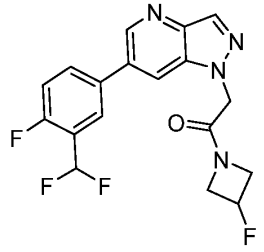
Step B. 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-[3-(methylamino)azetidin-1-yl]ethanone. *tert*-Butyl (1-(2-(6-(3-(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetyl)azetidin-3-yl)(methyl)carbamate (151 mg, 0.309 mmol) was dissolved in 4 mL of a 1:1 mixture of trifluoroacetic acid (TFA) and DCM. The reaction mixture was stirred at r.t. for 1 hour, concentrated, partitioned between DCM and saturated aqueous $NaHCO_3$. The aqueous layer was extracted using DCM (2x) and the combined organics were concentrated and purified on silica gel (non-polar phase DCM, polar phase 10% NH_4OH/MeOH, 0-10% gradient) to yield the title compound (45 mg, 0.116 mmol, 37% yield). MS (ESI): mass calcd. for $C_{19}H_{18}F_3N_5O$, 389.1; m/z found, 390.0 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, *J* = 1.9 Hz, 1H), 8.29 (d, *J* = 1.0 Hz, 1H), 7.95 (dd, *J* = 2.0, 1.0 Hz, 1H), 7.89 – 7.84 (m, 1H), 7.78 – 7.71 (m, 1H), 7.32 – 7.27 (m, 1H), 6.98 (t, *J* = 54.9 Hz, 1H), 5.08 (s, 2H), 4.32 – 4.16 (m, 2H), 3.89 – 3.70 (m, 2H), 3.66 – 3.55 (m, 1H), 2.37 (s, 3H).

Example 4: *N*-[1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]acetyl]azetidin-3-yl]-*N*-methyl-acetamide.



To a solution of 2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-[3-(methylamino)azetidin-1-yl]ethanone (Example 3, 36.5 mg, 0.094 mmol) and triethylamine (40 µL, 0.28 mmol) in dry DCM (1 mL) was added acetyl chloride (10 µL, 0.14 mmol). The reaction mixture was stirred at r.t. for 15 minutes, then injected directly onto a silica gel column and purified chromatographically (0-10% MeOH/DCM), yielding 28.8 mg (0.067 mmol, 71% yield) of the title compound. MS (ESI): mass calcd. for $C_{21}H_{20}F_3N_5O_2$, 431.2; m/z found, 432.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, J = 1.9 Hz, 1H), 8.30 (d, J = 1.0 Hz, 1H), 7.95 (dd, J = 1.9, 1.0 Hz, 1H), 7.91 – 7.83 (m, 1H), 7.79 – 7.64 (m, 1H), 7.34 – 7.27 (m, 1H), 6.98 (t, J = 54.9 Hz, 1H), 5.33 – 5.19 (m, 1H), 5.13 – 5.00 (m, 2H), 4.39 – 4.21 (m, 2H), 4.19 – 4.02 (m, 2H), 3.01 (s, 3H), 2.10 (s, 3H).

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

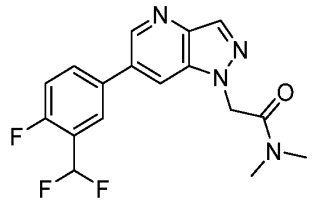


Method A. To a mixture of 6-[3-(difluoromethyl)-4-fluoro-phenyl]-1H-pyrazolo[4,3-b]pyridine (Intermediate 16, 1.10 g, 4.18 mmol) and Cs_2CO_3 (2.05 g, 6.29 mmol) in dry DMF (22 mL) was added 2-chloro-1-(3-fluoroazetidin-1-yl)ethanone (Intermediate 1, 697 mg, 4.60 mmol) and the reaction mixture was stirred at room temperature for 2 h. The reaction mixture was diluted with water (100 mL) and extracted with EtOAc (3 x 60 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by gradient silica gel column chromatography eluting with n-heptane:EtOAc (100:0 → 0:100). The

product was recrystallized from ethanol (20 mL) and triturated with water (20 mL) to afford the title compound (950 mg, 2.51 mmol, 60%) as a white powder. MS (ESI): mass calcd. for $C_{18}H_{14}F_4N_4O$, 378.1; m/z found, 379.1 $[M+H]^+$.

Method B. A solution of 2-(6-bromo-1H-pyrazolo[4,3-*b*]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 12, 8.33 g, 26.6 mmol) in dioxane (200 mL) was treated with 2-(3-(difluoromethyl)-4-fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (8.7 g, 32 mmol), cesium carbonate (26 g, 80 mmol) and (2-dicyclohexylphosphino-2′,6′-diisopropoxy-1,1′-biphenyl)[2-(2′-amino-1,1′-biphenyl)]palladium(II) methanesulfonate (RuPhos Pd G3) (1.1 g, 1.3 mmol, 5 mol%) and the reaction mixture was stirred at reflux for 16 hours. The mixture was allowed to cool to room temperature, concentrated to remove dioxane, partitioned between DCM and water, and the aqueous layer extracted using DCM (2x). The combined organics were washed with 4 N LiOH, dried ($MgSO_4$), filtered, and stirred overnight with SiliaMetSH thiol scavenger. Filtered through Celite®, purified on silica gel (0-10% MeOH/DCM gradient), recrystallized from hot ethanol then recrystallized from hot ethyl acetate. Isolated 4.78 g (12.6 mmol, 47% yield) of the title compound. MS (ESI): mass calcd. for $C_{18}H_{14}F_4N_4O$, 378.1; m/z found, 379.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.88 (d, J = 2.0 Hz, 1H), 8.43 (dd, J = 2.0, 1.0 Hz, 1H), 8.37 (d, J = 0.9 Hz, 1H), 8.10 – 8.01 (m, 2H), 7.62 – 7.54 (m, 1H), 7.30 (t, J = 54.1 Hz, 1H), 5.55 – 5.37 (m, 1H), 5.36 (d, J = 17.0 Hz, 1H), 5.32 (d, J = 17.0 Hz, 1H), 4.60 – 4.47 (m, 1H), 4.36 – 4.20 (m, 2H), 4.03 – 3.91 (m, 1H).

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

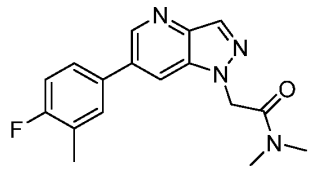


Method A. To a suspension of sodium hydride (60% in mineral oil, 164 mg, 4.10 mmol) in dry DMF (8.9 mL) was added a solution of 6-[3-(difluoromethyl)-4-fluoro-phenyl]-1*H*-pyrazolo[4,3-*b*]pyridine (Intermediate 16, 900 mg, 3.42 mmol) in dry DMF (8.9 mL) at 0 °C under argon. The reaction mixture was stirred at 0 °C for 0.5 h. To the reaction mixture was added 2-chloro-*N*,*N*-

dimethylacetamide (387 µL, 3.76 mmol, 1.18 g/mL). The reaction mixture was allowed to reach room temperature and stirred for 3 h. The reaction was then poured into water (20 mL) and was diluted with ethyl acetate (10 mL). The layers were separated, and the aqueous layer was extracted with ethyl acetate (2 x 20 mL). The combined organics were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification (FCC, SiO_2, 1 to 20% EtOAc/EtOH) afforded a solid that was recrystallized from ethanol (8 mL) to afford the title compound (708 mg, 2.03 mmol, 59%) as a white powder. MS (ESI): mass calcd. for $C_{17}H_{15}F_3N_4O$, 348.1; m/z found,349.2 $[M+H]^+$.

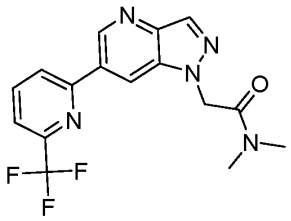
Method B. To a solution of 2-(6-bromo-1H-pyrazolo[4,3-*b*]pyridin-1-yl)-*N*,*N*-dimethylacetamide (Intermediate 10, 14.0 g, 49.5 mmol) in dioxane (400 mL) were added 2-(3-(difluoromethyl)-4-fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (16.2 g, 59.4 mmol), cesium carbonate (48.4 g, 149 mmol), and RuPhos Pd G3 (2.35 g, 2.81 mmol). The reaction mixture was stirred at reflux for 4 hours, let cool to room temperature, concentrated to ~25 mL dioxane, and diluted with water (300 mL). The resulting precipitate was collected by filtration, then adsorbed onto Celite®, and purified by silica gel chromatography (FCC; 0-10% MeOH/DCM). The product obtained this way was recrystallized from hot ethyl acetate, then recrystallized a second time from hot ethanol. The crystals were re-dissolved in hot ethyl acetate and re-concentrated; this process was repeated 3x until all remaining traces of ethanol were removed. The product was dried in a vacuum oven at 60 °C for 72 h to yield 6.97 g (20.0 mmol, 40% yield) of the title compound. MS (ESI): mass calcd. for $C_{17}H_{15}F_3N_4O$, 348.1; m/z found, 349.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.87 (d, J = 2.0 Hz, 1H), 8.42 – 8.39 (m, 1H), 8.33 (d, J = 1.0 Hz, 1H), 8.08 – 8.01 (m, 2H), 7.60 – 7.54 (m, 1H), 7.30 (t, J = 54.1 Hz, 1H), 5.53 (s, 2H), 3.13 (s, 3H), 2.85 (s, 3H).

Example 7: 2-[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-*N*,*N*-dimethyl-acetamide.



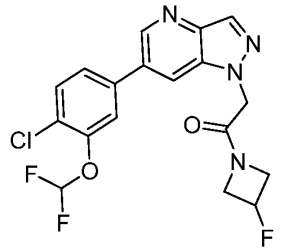
A mixture of 2-(6-bromopyrazolo[4,3-b]pyridin-1-yl)-*N*,*N*-dimethyl-acetamide (Intermediate 10, 583 mg, 2.06 mmol), 4-fluoro-3-methylphenylboronic acid (381 mg, 2.47 mmol), sodium carbonate (655 mg, 6.18 mmol) and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (196 mg, 0.268 mmol) in water (1.72 mL) and acetonitrile (11.2 mL) in a capped vial flushed with argon was stirred at 120 °C for 2 h under microwave irradiation. The reaction mixture was evaporated and the residue was purified by gradient silica gel column chromatography eluting with n-hexane:ethyl acetate:methanol (1:3:0 → 0:1:0 → 0:98:2 → 0:9:1). The product thus obtained from FCC was then recrystallized from ethanol (20 mL) to afford the title compound (380 mg, 1.22 mmol, 59%) as an off-white crystalline solid. MS (ESI): mass calcd. for $C_{17}H_{17}FN_4O$, 312.1; m/z found, 313.2 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.83 (d, J = 1.9 Hz, 1H), 8.36 – 8.29 (m, 1H), 8.30 (s, 1H), 7.79 – 7.70 (m, 1H), 7.69 – 7.59 (m, 1H), 7.31 (t, J = 9.1 Hz, 1H), 5.51 (s, 2H), 3.13 (s, 3H), 2.85 (s, 3H), 2.40 – 2.27 (m, 3H).

Example 8: *N*,*N*-Dimethyl-2-[6-[6-(trifluoromethyl)-2-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide.



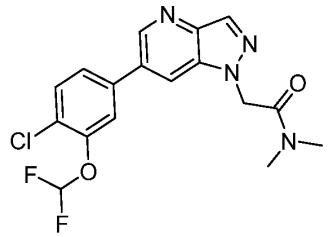
To a solution of 2-(6-bromopyrazolo[4,3-*b*]pyridin-1-yl)-*N*,*N*-dimethyl-acetamide (Intermediate 10, 50 mg, 0.177 mmol) in degassed 1,4-dioxane (550 µL) was added 2-(tributylstannyl)-6-(trifluoromethyl)pyridine (85 mg, 0.195 mmol) and *bis*(triphenylphosphine)palladium(II)chloride (13.0 mg, 0.0185 mmol). The reaction mixture was stirred at 100 °C for 17 h. The reaction mixture was evaporated. Purification (FCC, SiO_2, 10 to 100% hexanes/EtOAc) afforded the title compound (35 mg, 0.100 mmol, 56%) as a white powder after triturating with diethyl ether (4 mL). MS (ESI): mass calcd. for $C_{16}H_{14}F_3N_5O$, 349.1; m/z found, 350.2 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 9.26 (d, J = 1.9 Hz, 1H), 8.79 – 8.67 (m, 1H), 8.44 (d, J = 8.1 Hz, 1H), 8.38 (s, 1H), 8.28 (t, J = 7.9 Hz, 1H), 7.96 (d, J = 7.7 Hz, 1H), 5.59 (s, 2H), 3.15 (s, 3H), 2.86 (s, 3H).

Example 9: 2-[6-[4-Chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone.



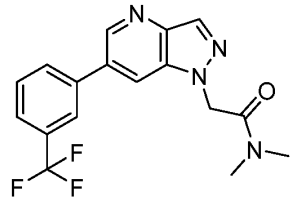
To a solution of 2-(6-bromopyrazolo[4,3-*b*]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethanone (Intermediate 12, 400 mg, 1.28 mmol) in degassed 1,4-dioxane (24.7 mL) and water (7.38 mL) was added 2-[4-chloro-3-(difluoromethoxy)phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (408 mg, 1.34 mmol), potassium fluoride (223 mg, 3.84 mmol) and *tetrakis*(triphenylphosphine)palladium(0) (104 mg, 0.090 mmol). The reaction mixture was stirred at 80 °C for 2 h under argon. Additional 2-[4-chloro-3-(difluoromethoxy)phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (117 mg, 0.384 mmol), potassium fluoride (223 mg, 3.84 mmol) and *tetrakis*(triphenylphosphine)palladium(0) (104 mg, 0.090 mmol) were added and the reaction mixture was stirred at 80 °C for 15 h. The mixture was diluted with water (32 mL) and DCM (50 mL) and the layers were separated. The aqueous layer was extracted with DCM (2 x 40 mL) and the combined organics were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by gradient silica gel column chromatography eluting with *n*-heptane:ethyl acetate:methanol (1:1:0 → 0:1:0 → 0:95:5). The residue obtained was recrystallized from ethanol (30 mL) to afford the title compound (288 mg, 0.701 mmol, 55%) as a white powder. MS (ESI): mass calcd. for $C_{18}H_{14}ClF_3N_4O_2$, 410.1; m/z found, 411.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.91 (d, J = 1.9 Hz, 1H), 8.47 – 8.40 (m, 1H), 8.41 – 8.34 (m, 1H), 7.85 – 7.77 (m, 2H), 7.73 (dd, J = 8.4, 2.0 Hz, 1H), 7.45 (t, J = 73.2 Hz, 1H), 5.61 – 5.34 (m, 2H), 5.31 (d, J = 17.2 Hz, 1H), 4.66 – 4.45 (m, 1H), 4.39 – 4.15 (m, 2H), 4.07 – 3.88 (m, 1H).

Example 10: 2-[6-[4-Chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-*N*,*N*-dimethyl-acetamide.



A mixture of 2-(6-bromopyrazolo[4,3-*b*]pyridin-1-yl)-*N*,*N*-dimethyl-acetamide (Intermediate 10, 46 mg, 0.162 mmol), 2-[4-chloro-3-(difluoromethoxy)phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (59 mg, 0.194 mmol), 1,1'-*bis*(diphenylphosphino)ferrocenepalladium (II) dichloride (12 mg, 0.0164 mmol) and K_2CO_3 (45 mg, 0.326 mmol) in degassed 1,4-dioxane (920 µL) and water (92 µL) was stirred at 80 °C for 4 h under argon. The reaction mixture was evaporated. Purification (FCC, SiO_2, 0 to 5% EtOAc/EtOH) afforded the title compound (32 mg, 0.084 mmol, 52%) as an off-white powder. MS (ESI): mass calcd. for $C_{17}H_{15}ClF_2N_4O_2$, 380.1; m/z found, 381.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.90 (d, J = 1.9 Hz, 1H), 8.44 – 8.39 (m, 1H), 8.34 (s, 1H), 7.82 – 7.79 (m, 1H), 7.76 (d, J = 8.6 Hz, 1H), 7.72 (dd, J = 8.4, 1.9 Hz, 1H), 7.44 (t, J = 73.2 Hz, 1H), 5.52 (s, 2H), 3.13 (s, 3H), 2.85 (s, 3H).

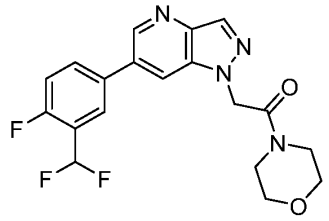
Example 11: *N*,*N*-Dimethyl-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide.



A mixture of 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-*N*,*N*-dimethylacetamide (Intermediate 10, 100 mg, 0.35 mmol), 3-(trifluoromethyl)phenylboronic acid (100 mg, 0.53 mmol), cesium carbonate (230 mg 0.71 mmol), $PdCl_2$(dppf) (18 mg, 0.07 mmol) was suspended in dioxane/water (1:1). The resulting reaction mixture was heated to 90 °C and stirred for 3 hours then cooled to room temperature and diluted with water and extracted with ethyl acetate (x3). The combined organic layers were dried using $MgSO_4$, filtered and concentrated under vacuum. Purification (METHOD A) afforded the title compound (95mg, 77%). MS (ESI): mass calcd. for $C_{17}H_{15}F_3N_4O$, 348.1; m/z found, 349.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.83 (d, J = 1.8

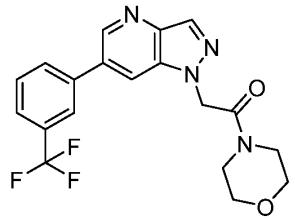
Hz, 1H), 8.32 (d, *J* = 0.9 Hz, 1H), 7.97 (dd, *J* = 1.9, 1.0 Hz, 1H), 7.89 (s, 1H), 7.84 (d, *J* = 7.7 Hz, 1H), 7.70 (d, *J* = 7.8 Hz, 1H), 7.63 (t, *J* = 7.7 Hz, 1H), 5.31 (d, *J* = 5.0 Hz, 2H), 3.20 (s, 3H), 3.00 (s, 3H).

Example 12: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-morpholino-ethanone.



To 6-(3-(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 16, 31.2 mg, 0.117 mmol) stirring in DMF (1 mL) at rt was added Cs_2CO_3 (114.7 mg, 0.352 mmol) followed by 4-(2-chloroacetyl)morpholine (34.1 mg, 0.208 mmol). The reaction was stirred at rt overnight, then filtered through a 0.45 μM syringe filter and purified by prep HPLC (METHOD D). Re-purification (FCC, SiO_2, 0 – 5% MeOH in DCM) afforded the title compound. MS (ESI): mass calcd. for $C_{19}H_{17}F_3N_4O_2$, 390.1; m/z found, 391.0 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.79 (d, *J* = 1.9 Hz, 1H), 8.30 (d, *J* = 1.0 Hz, 1H), 7.93 (dd, *J* = 1.9, 1.0 Hz, 1H), 7.88 – 7.82 (m, 1H), 7.78 – 7.69 (m, 1H), 7.31 – 7.24 (m, 1H), 6.97 (t, *J* = 54.9 Hz, 1H), 5.29 (s, 2H), 3.72 – 3.56 (m, 8H).

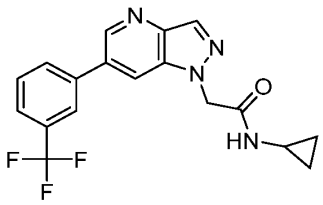
Example 13: 1-Morpholino-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



DIPEA (0.11 mL, 0.6 mmol) was added to a stirred solution of 2-(6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid (Intermediate 39, 100 mg, 0.3 mmol), morpholine (40.7 mg, 0.5 mmol) and HATU (177.5 mg, 0.5 mmol) in DMF (1.4 mL) at room temperature.

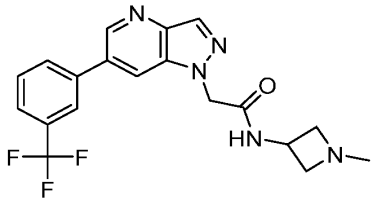
After 16 hours, EtOAc was added and the mixture was washed with brine (2x). The residue was purified (FCC, SiO_2, 0-10 % MeOH in DCM) to afford a yellowish solid. Purification according to Method F. (Stationary phase: C18 XBridge 30 x 100 mm 5 um), Mobile phase: Gradient from 60% 0.1% NH_4CO_3H/NH_4OH pH 9 solution in Water, 40% CH_3CN to 43% 0.1% NH_4CO_3H/NH_4OH pH 9 solution in Water, 57% CH_3CN) afforded the title compound (55 mg, 45%). MS (ESI): mass calcd. for $C_{19}H_{17}F_3N_4O_2$, 390.1; m/z found, 391.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.84 (d, *J*=1.85 Hz, 1 H), 8.32 (d, *J*=0.92 Hz, 1 H), 7.98 (dd, *J*=1.85, 1.16 Hz, 1 H), 7.89 (s, 1 H), 7.84 (d, *J*=7.63 Hz, 1 H), 7.73 – 7.68 (m, 1 H), 7.67 – 7.60 (m, 1 H), 5.31 (s, 2 H), 3.74 – 3.58 (m, 8 H).

Example 14: *N*-Cyclopropyl-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide.



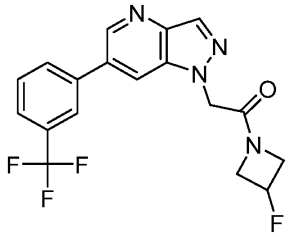
6-(3-(Trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 60, 170 mg, 0.65 mmol) was dissolved in DMF (5 mL) and placed under a nitrogen atmosphere. Sodium hydride (60% dispersion in mineral oil, 78 mg, 1.94 mmol) was added and the reaction mixture was stirred for 10 minutes, at which point 2-bromo-*N*-cyclopropylacetamide (Intermediate 59, 230 mg, 1.29 mmol) was added. The reaction mixture was stirred at 80 °C for 5 hours, cooled to room temperature, and diluted with water. The mixture was extracted with ethyl acetate (3x), the combined organics were dried ($MgSO_4$) and concentrated. Purification (FCC, SiO_2, 0 to 90% EtOAc/hexanes) afforded 44.2 mg (0.123 mmol, 19% yield) of the title compound. MS (ESI): mass calcd. for $C_{18}H_{15}F_3N_4O$, 360.1; m/z found, 361.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.94 (d, *J* = 2.0 Hz, 1H), 8.57 – 8.54 (m, 1H), 8.40 – 8.33 (m, 2H), 8.18 – 8.13 (m, 2H), 7.85 – 7.76 (m, 2H), 5.15 (s, 2H), 2.69 – 2.62 (m, 1H), 0.66 – 0.61 (m, 2H), 0.48 – 0.42 (m, 2H).

Example 15: *N*-(1-Methylazetidin-3-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide.



A mixture of 2-(6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid (Intermediate 39, 78.8 mg, 0.2 mmol), 1-methylazetidin-3-amine (25.4 mg, 0.3 mmol), HATU (102.6, 0.3 mmol) and DIPEA (0.13 mL, 0.7 mmol) in DMF (1.5 mL) was stirred at room temperature. Upon completion the reaction mixture was purified using reversed phase HPLC (METHOD C) to afford the desired product with trace impurities. The material was loaded on a catch and release column (Agilent Bond Elut SCX). The column was washed with MeOH and the filtrate was discarded. Then, the column was washed with a solution of ~5% NH_3 in MeOH to provide title compound (28.3 mg, 0.07 mmol, 29.6 %). (ESI): mass calcd. for $C_{19}H_{18}F_3N_5O$, 389.2; m/z found, 390.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.94 (d, J = 1.9 Hz, 1H), 8.83 – 8.77 (m, 1H), 8.58 – 8.55 (m, 1H), 8.36 – 8.34 (m, 1H), 8.18 – 8.13 (m, 2H), 7.84 – 7.76 (m, 2H), 5.21 (s, 2H), 4.29 – 4.20 (m, 1H), 3.54 (t, J = 7.0 Hz, 2H), 3.01 – 2.88 (m, 2H), 2.29 – 2.23 (s, 3H).

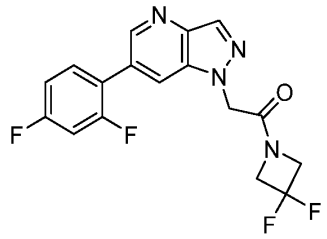
Example 16: 1-(3-Fluoroazetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone trifluoroacetate salt.



A mixture of 2-(6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid (Intermediate 39, 78.8 mg, 0.2 mmol), 3-fluoroazetidine hydrochloride (32.8 mg, 0.3 mmol), T_3P® (50% solution in DMF, 0.44 mL, 0.7 mmol), DIPEA (0.13 mL, 0.7 mmol) in DMF (2.0 mL) was stirred at room temperature. Upon completion, the reaction mixture was purified using reversed phase HPLC (METHOD C) to provide title compound (29.4 mg, 0.06 mmol, 24.3%). MS (ESI): mass calcd. for $C_{18}H_{14}F_4N_4O$, 378.1; m/z found, 379.2 $[M+H]^+$. ^1H NMR (400 MHz,

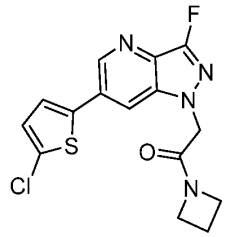
DMSO-d_6) δ 8.94 (d, J = 1.9 Hz, 1H), 8.51 – 8.49 (m, 1H), 8.39 – 8.38 (m, 1H), 8.17 – 8.12 (m, 2H), 7.86 – 7.76 (m, 2H), 5.56 – 5.29 (m, 3H), 4.61 – 4.48 (m, 1H), 4.37 – 4.18 (m, 2H), 4.04 – 3.90 (m, 1H).

Example 17: 1-(3,3-Difluoroazetidin-1-yl)-2-[6-(2,4-difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone.



A mixture of 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3,3-difluoroazetidin-1-yl)ethan-1-one (Intermediate 42, 116 mg, 0.4 mmol), (2,4-difluorophenyl)boronic acid (111 mg, 0.7 mmol), [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (18.0 mg, 0.02 mmol) and cesium carbonate (229.0 mg, 0.7 mmol) in 1,4-dioxane (3.2 mL) was heated to 75 °C. After 16 hours, the reaction mixture was concentrated under vacuum. The crude material was purified (FCC, SiO_2, 0-90 % EtOAc in hexanes) to provide title compound (29.7 mg, 0.08 mmol, 23.1%). MS (ESI): mass calcd. for $C_{17}H_{12}F_4N_4O$, 364.1; m/z found, 365.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.68 (t, J = 1.9 Hz, 1H), 8.39 (d, J = 1.0 Hz, 1H), 8.29 – 8.26 (m, 1H), 7.72 (td, J = 8.8, 6.5 Hz, 1H), 7.52 – 7.45 (m, 1H), 7.33 – 7.27 (m, 1H), 5.41 (s, 2H), 4.74 (t, J = 12.3 Hz, 2H), 4.37 (t, J = 12.5 Hz, 2H).

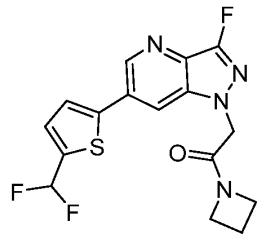
Example 18: 1-(Azetidin-1-yl)-2-[6-(5-chloro-2-thienyl)-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]ethanone.



The title compound was made in a manner analogous to Example 9 using 1-(azetidin-1-yl)-2-(6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)ethan-1-one (Intermediate 14) in place of

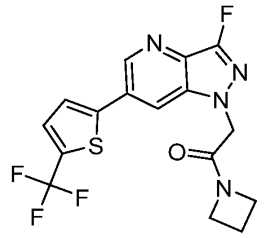
Intermediate 12 and 5-chlorothiophene-2-boronic acid in place of 2-[4-chloro-3-(difluoromethoxy)phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd. for $C_{15}H_{12}ClFN_4OS$, 350.1; m/z found, 351.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.91 (d, J = 1.9 Hz, 1H), 8.39 – 8.28 (m, 1H), 7.68 (d, J = 4.0 Hz, 1H), 7.29 (d, J = 4.0 Hz, 1H), 5.12 (s, 2H), 4.31 – 4.15 (m, 2H), 4.00 – 3.79 (m, 2H), 2.38 – 2.18 (m, 2H).

Example 19: 1-(Azetidin-1-yl)-2-[6-[5-(difluoromethyl)-2-thienyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]ethanone.



The title compound was made in a manner analogous to Example 9 using 1-(azetidin-1-yl)-2-(6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)ethan-1-one (Intermediate 14) in place of Intermediate 12 and 2-(5-(difluoromethyl)thiophen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Intermediate 8) in place of 2-[4-chloro-3-(difluoromethoxy)phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd. for $C_{16}H_{13}F_3N_4OS$, 366.1; m/z found, 367.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.99 (d, J = 1.8 Hz, 1H), 8.52 – 8.42 (m, 1H), 7.83 – 7.74 (m, 1H), 7.64 – 7.54 (m, 1H), 7.38 (t, J = 55.1 Hz, 1H), 5.15 (s, 2H), 4.30 – 4.15 (m, 2H), 3.99 – 3.84 (m, 2H), 2.36 – 2.19 (m, 2H).

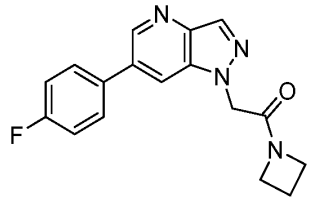
Example 20: 1-(Azetidin-1-yl)-2-[3-fluoro-6-[5-(trifluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



The title compound was made in a manner analogous to Example 9 using 1-(azetidin-1-yl)-2-(6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)ethan-1-one (Intermediate 14) in place of

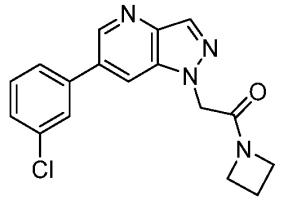
Intermediate 12 and 4,4,5,5-tetramethyl-2-(5-(trifluoromethyl)thiophen-2-yl)-1,3,2-dioxaborolane in place of 4-fluoro-3-methylboronic acid. MS (ESI): mass calcd. for $C_{16}H_{12}F_4N_4OS$, 384.1; m/z found, 385.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 9.01 (d, J = 2.0 Hz, 1H), 8.56 – 8.52 (m, 1H), 7.90 – 7.85 (m, 2H), 5.15 (s, 2H), 4.27 – 4.21 (m, 2H), 3.94 – 3.88 (m, 2H), 2.33 – 2.25 (m, 2H).

Example 21: 1-(Azetidin-1-yl)-2-[6-(4-fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone.



The title compound was prepared in a manner analogous to Example 13, using 2-(6-(4-fluorophenyl)-1H-pyrazolo[4,3-*b*]pyridin-1-yl)acetic acid (Intermediate 31) in place of Intermediate 16 and azetidine in place of 3-(trifluoromethyl)azetidin-3-ol. MS (ESI): mass calcd. for $C_{17}H_{15}FN_4O$, 310.1; m/z found, 311.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.80 (d, J = 1.9 Hz, 1H), 8.27 (d, J = 1.0 Hz, 1H), 7.98-7.96 (m, 1H), 7.67 – 7.61 (m, 2H), 7.24 – 7.17 (m, 2H), 5.06 (s, 2H), 4.13-4.05 (m, 4H), 2.34-2.26 (m, 2H).

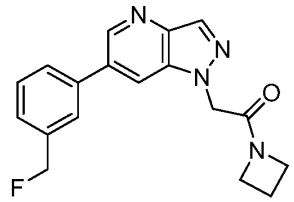
Example 22: 1-(Azetidin-1-yl)-2-[6-(3-chlorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone.



The title compound was prepared in a manner analogous to Example 17, using 1-(azetidin-1-yl)-2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)ethan-1-one (Intermediate 13) in place of Intermediate 42, (3-chlorophenyl)boronic acid in place of 2,4-difluorophenylboronic acid and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). The reaction mixture was heated to 90 °C. MS (ESI): mass calcd. for $C_{17}H_{15}ClN_4O$, 326.1; m/z found, 327.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.90 – 8.89 (m, 1H), 8.47 – 8.45 (m, 1H), 8.36 – 8.34 (m, 1H),

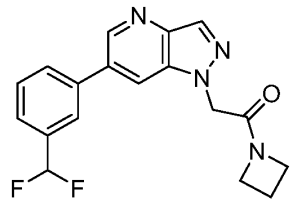
7.93 – 7.89 (m, 1H), 7.84 – 7.79 (m, 1H), 7.61 – 7.56 (m, 1H), 7.55 – 7.51 (m, 1H), 5.26 (s, 2H), 4.20 (t, *J* = 7.7 Hz, 2H), 3.91 (t, *J* = 7.7 Hz, 2H) , 2.31 – 2.22 (m, 2H).

Example 23: 1-(Azetidin-1-yl)-2-[6-[3-(fluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



The title compound was prepared in a manner analogous to Example 16, using azetidine in place of 3-fluoroazetidine hydrochloride, 2-(6-(3-(fluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid (Intermediate 56) in place of Intermediate 39 and DCM in place of DMF. MS (ESI): mass calcd. for $C_{18}H_{17}FN_4O$, 324.1; m/z found, 325.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.89 (d, *J* = 1.9 Hz, 1H), 8.41 – 8.40 (m, 1H), 8.35 – 8.34 (m, 1H), 7.89 – 7.82 (m, 2H), 7.63 – 7.58 (m, 1H), 7.54 – 7.50 (m, 1H), 5.54 (d, *J* = 47.7 Hz, 2H), 5.27 (s, 2H), 4.20 (t, *J* = 7.7 Hz, 2H), 3.91 (t, *J* = 7.7 Hz, 2H), 2.31 – 2.22 (m, 2H).

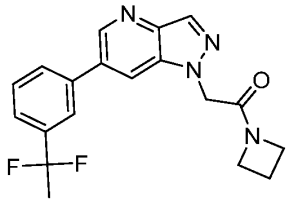
Example 24: 1-(Azetidin-1-yl)-2-[6-[3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



The title compound was prepared in a manner analogous to Example 17 using 1-(azetidin-1-yl)-2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)ethan-1-one (Intermediate 13) in place of Intermediate 42, (3-(difluoromethyl)phenyl)boronic acid in place of 2,4-difluorophenylboronic acid and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). The reaction mixture was heated to 90 °C. MS (ESI): mass calcd. for $C_{18}H_{16}F_2N_4O$, 342.1; m/z found, 343.1 $[M+H]^+$. ^1H NMR (600 MHz, DMSO-d_6) δ 8.90 (d, *J* = 1.9 Hz, 1H), 8.45 – 8.43 (m, 1H),

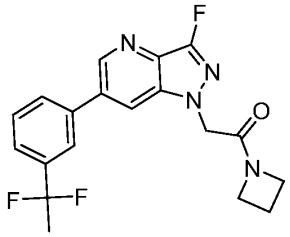
8.37 – 8.35 (m, 1H), 8.02 – 7.99 (m, 2H), 7.73 – 7.65 (m, 2H), 7.14 (t, *J* = 55.8 Hz, 1H), 5.27 (s, 2H), 4.20 (t, *J* = 7.7 Hz, 2H), 3.91 (t, *J* = 7.7 Hz, 2H), 2.30 – 2.23 (m, 2H).

Example 25: 1-(Azetidin-1-yl)-2-[6-[3-(1,1-difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



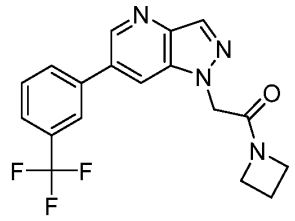
The title compound was made in a manner analogous to Example 6, Method A, using 6-[3-(1,1-difluoroethyl)phenyl]pyrazolo[4,3-b]pyridine (Intermediate 20) in place of Intermediate 16 and 1-(azetidin-1-yl)-2-chloroethan-1-one in place of 2-chloro-*N*,*N*-dimethylacetamide. MS (ESI): mass calcd. for $C_{19}H_{18}F_2N_4O$, 356.1; m/z found, 357.2 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.91 (d, *J* = 1.9 Hz, 1H), 8.48 – 8.40 (m, 1H), 8.36 (s, 1H), 8.05 – 7.88 (m, 2H), 7.74 – 7.57 (m, 2H), 5.27 (s, 2H), 4.27 – 4.13 (m, 2H), 3.97 – 3.83 (m, 2H), 2.33 – 2.19 (m, 2H), 2.07 (t, *J* = 18.9 Hz, 3H).

Example 26: 1-(Azetidin-1-yl)-2-[6-[3-(1,1-difluoroethyl)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]ethanone.



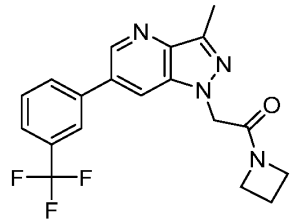
The title compound was made in a manner analogous to Example 5, Method A, using 6-(3-(1,1-difluoroethyl)phenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridine (Intermediate 24) in place of Intermediate 16 and 1-(azetidin-1-yl)-2-chloroethan-1-one in place of Intermediate 1. MS (ESI): mass calcd. for $C_{19}H_{17}F_3N_4O$, 374.1; m/z found, 375.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.96 (d, *J* = 1.8 Hz, 1H), 8.53 – 8.42 (m, 1H), 8.06 – 7.88 (m, 2H), 7.75 – 7.60 (m, 2H), 5.16 (s, 2H), 4.30 – 4.15 (m, 2H), 3.98 – 3.82 (m, 2H), 2.36 – 2.18 (m, 2H), 2.06 (t, *J* = 18.9 Hz, 3H).

Example 27: 1-(Azetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



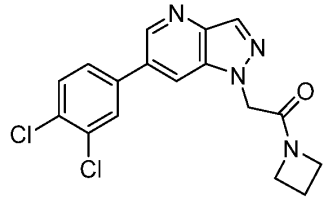
The title compound was prepared in a manner analogous to Example 16, using azetidine in place of 3-fluoroazetidine hydrochloride and DCM in place of DMF. MS (ESI): mass calcd. for $C_{18}H_{15}F_3N_4O$, 360.1; m/z found, 361.2 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.94 (d, J = 1.9 Hz, 1H), 8.52 – 8.50 (m, 1H), 8.38 – 8.36 (m, 1H), 8.18 – 8.12 (m, 2H), 7.85 – 7.76 (m, 2H), 5.27 (s, 2H), 4.20 (t, J = 7.6 Hz, 2H), 3.91 (t, J = 7.7 Hz, 2H), 2.31 – 2.22 (m, 2H).

Example 28: 1-(Azetidin-1-yl)-2-[3-methyl-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



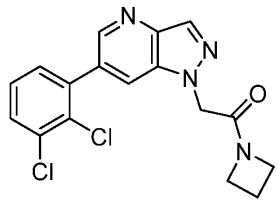
The title compound was prepared in a manner analogous to Example 17, using 1-(azetidin-1-yl)-2-(6-bromo-3-methyl-1H-pyrazolo[4,3-b]pyridin-1-yl)ethan-1-one (Intermediate 48) in place of Intermediate 42, (3-(trifluoromethyl)phenyl)boronic acid in place of 2,4-difluorophenylboronic acid and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). The reaction mixture was heated to 90 °C. MS (ESI): mass calcd. for $C_{19}H_{17}F_3N_4O$, 374.1; m/z found, 375.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.87 (d, J = 1.9 Hz, 1H), 8.43 (d, J = 2.0 Hz, 1H), 8.17 – 8.10 (m, 2H), 7.85 – 7.76 (m, 2H), 5.17 (s, 2H), 4.17 (t, J = 7.7 Hz, 2H), 3.90 (t, J = 7.7 Hz, 2H), 2.56 (s, 3H), 2.30 – 2.21 (m, 2H).

Example 29: 1-(Azetidin-1-yl)-2-[6-(3,4-dichlorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone.



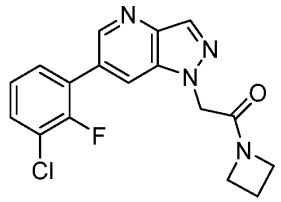
The title compound was prepared in a manner analogous to Example 17, using 1-(azetidin-1-yl)-2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)ethan-1-one (Intermediate 13) in place of Intermediate 42, (3,4-dichlorophenyl)boronic acid in place of 2,4-difluorophenylboronic acid and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). The reaction mixture was heated to 90 °C. MS (ESI): mass calcd. for $C_{17}H_{14}Cl_2N_4O$, 360.1; m/z found, 361.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.91 (d, J = 2.0 Hz, 1H), 8.50 – 8.47 (m, 1H), 8.37 – 8.34 (m, 1H), 8.13 (d, J = 2.1 Hz, 1H), 7.87 – 7.79 (m, 2H), 5.25 (s, 2H), 4.20 (t, J = 7.7 Hz, 2H), 3.91 (t, J = 7.7 Hz, 2H), 2.31 – 2.22 (m, 2H).

Example 30: 1-(Azetidin-1-yl)-2-[6-(2,3-dichlorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone.



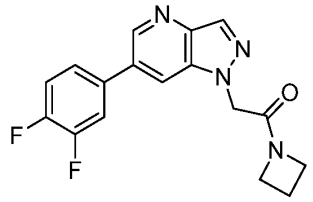
The title compound was prepared in a manner analogous to Example 17, using 1-(azetidin-1-yl)-2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)ethan-1-one (Intermediate 13) in place of Intermediate 42, (2,3-dichlorophenyl)boronic acid in place of 2,4-difluorophenylboronic acid and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). The reaction mixture was heated to 90 °C. MS (ESI): mass calcd. for $C_{17}H_{14}Cl_2N_4O$, 360.1; m/z found, 361.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.59 (d, J = 1.8 Hz, 1H), 8.39 – 8.37 (m, 1H), 8.22 – 8.20 (m, 1H), 7.79 – 7.76 (m, 1H), 7.56 – 7.49 (m, 2H), 5.23 (s, 2H), 4.20 (t, J = 7.7 Hz, 2H), 3.90 (t, J = 7.7 Hz, 2H), 2.30 – 2.20 (m, 2H).

Example 31: 1-(Azetidin-1-yl)-2-[6-(3-chloro-2-fluoro-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone.



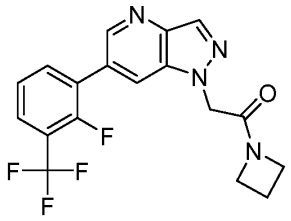
The title compound was prepared in a manner analogous to Example 17, using 1-(azetidin-1-yl)-2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)ethan-1-one (Intermediate 13) in place of Intermediate 42, (3-chloro-2-fluorophenyl)boronic acid in place of 2,4-difluorophenylboronic acid and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). The reaction mixture was heated to 90 °C. MS (ESI): mass calcd. for $C_{17}H_{14}ClFN_4O$, 344.1; m/z found, 345.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.71 (t, J = 1.9 Hz, 1H), 8.39 – 8.37 (m, 1H), 8.35 – 8.33 (m, 1H), 7.73 – 7.68 (m, 1H), 7.65 – 7.61 (m, 1H), 7.44 – 7.39 (m, 1H), 5.25 (s, 2H), 4.21 (t, J = 7.7 Hz, 2H), 3.90 (t, J = 7.7 Hz, 2H), 2.31 – 2.22 (m, 2H).

Example 32: 1-(Azetidin-1-yl)-2-[6-(3,4-difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone.



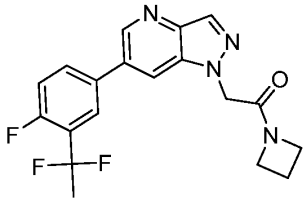
The title compound was prepared in a manner analogous to Example 17, using 1-(azetidin-1-yl)-2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)ethan-1-one (Intermediate 13) in place of Intermediate 42, (3,4-difluorophenyl)boronic acid in place of 2,4-difluorophenylboronic acid and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). The reaction mixture was heated to 90 °C. MS (ESI): mass calcd. for $C_{17}H_{14}F_2N_4O$, 328.1; m/z found, 329.1 $[M+H]^+$. ^1H NMR (600 MHz, DMSO-d_6) δ 8.89 (d, J = 1.9 Hz, 1H), 8.46 – 8.43 (m, 1H), 8.36 – 8.34 (m, 1H), 7.97 (ddd, J = 12.1, 7.8, 2.4 Hz, 1H), 7.73 – 7.68 (m, 1H), 7.66 – 7.60 (m, 1H), 5.25 (s, 2H), 4.20 (t, J = 7.7 Hz, 2H), 3.91 (t, J = 7.7 Hz, 2H), 2.30 – 2.23 (m, 2H).

Example 33: 1-(Azetidin-1-yl)-2-[6-[2-fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



The title compound was prepared in a manner analogous to Example 17, using 1-(azetidin-1-yl)-2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)ethan-1-one (Intermediate 13) in place of Intermediate 42, (2-fluoro-3-(trifluoromethyl)phenyl)boronic acid in place of 2,4-difluorophenylboronic acid and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). The reaction mixture was heated to 90 °C. MS (ESI): mass calcd. for $C_{18}H_{14}F_4N_4O$, 378.1; m/z found, 379.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.72 (t, J = 1.8 Hz, 1H), 8.41 – 8.36 (m, 2H), 8.03 – 7.98 (m, 1H), 7.93 – 7.88 (m, 1H), 7.60 (t, J = 7.8 Hz, 1H), 5.27 (s, 2H), 4.21 (t, J = 7.7 Hz, 2H), 3.90 (t, J = 7.7 Hz, 2H), 2.30 – 2.22 (m, 2H).

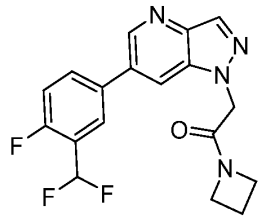
Example 34: 1-(Azetidin-1-yl)-2-[6-[3-(1,1-difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



The title compound was made in a manner analogous to Example 6, Method A, using 6-(3-(1,1-difluoroethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 19) in place of Intermediate 16 and 1-(azetidin-1-yl)-2-chloroethan-1-one in place of 2-chloro-*N*,*N*-dimethylacetamide. MS (ESI): mass calcd. for $C_{19}H_{17}F_3N_4O$, 374.1; m/z found, 375.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.88 (d, J = 2.0 Hz, 1H), 8.45 – 8.39 (m, 1H), 8.37 – 8.33 (m,

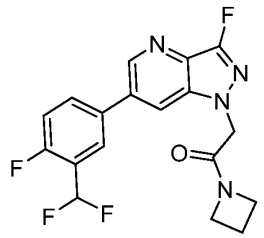
1H), 8.03 – 7.97 (m, 1H), 7.94 (dd, *J* = 7.2, 2.4 Hz, 1H), 7.55 (dd, *J* = 11.0, 8.6 Hz, 1H), 5.26 (s, 2H), 4.24 – 4.14 (m, 2H), 3.96 – 3.87 (m, 2H), 2.32 – 2.22 (m, 2H), 2.10 (t, *J* = 19.2 Hz, 3H).

Example 35: 1-(Azetidin-1-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



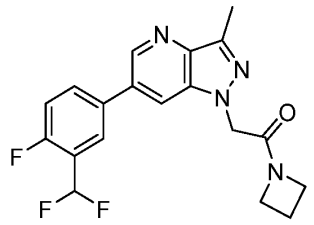
The title compound was made in a manner analogous to Example 5, Method A, using 1-(azetidin-1-yl)-2-chloroethan-1-one in place of 2-chloro-1-(3-fluoroazetidin-1-yl)ethanone. MS (ESI): mass calcd. for $C_{18}H_{15}F_3N_4O$, 360.1; m/z found, 361.2 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.88 (d, *J* = 1.9 Hz, 1H), 8.48 – 8.40 (m, 1H), 8.40 – 8.32 (m, 1H), 8.13 – 8.00 (m, 2H), 7.64 – 7.52 (m, 1H), 7.31 (t, *J* = 54.1 Hz, 1H), 5.27 (s, 2H), 4.20 (t, *J* = 7.7 Hz, 2H), 3.91 (t, *J* = 7.7 Hz, 2H), 2.36 – 2.17 (m, 2H).

Example 36: 1-(Azetidin-1-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]ethanone.



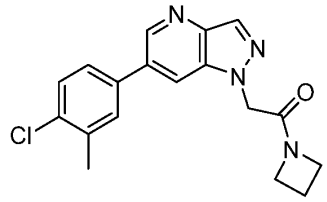
The title compound was made in a manner analogous to Example 6, Method A, using 6-[3-(difluoromethyl)-4-fluorophenyl]-3-fluoro-pyrazolo[4,3-b]pyridine (Intermediate 21) in place of Intermediate 16 and 1-(azetidin-1-yl)-2-chloroethan-1-one in place of 2-chloro-*N*,*N*-dimethylacetamide. MS (ESI): mass calcd. for $C_{18}H_{14}F_4N_4O$, 378.1; m/z found, 379.1 $[M+H]^+$. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.93 (d, *J* = 1.9 Hz, 1H), 8.50 – 8.46 (m, 1H), 8.12 – 8.04 (m, 2H), 7.64 – 7.56 (m, 1H), 7.31 (t, *J* = 54.1 Hz, 1H), 5.15 (s, 2H), 4.27 – 4.17 (m, 2H), 3.94 – 3.86 (m, 2H), 2.33 – 2.22 (m, 2H).

Example 37: 1-(Azetidin-1-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]-3-methyl-pyrazolo[4,3-*b*]pyridin-1-yl]ethanone.



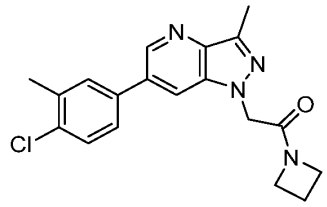
The title compound was prepared in a manner analogous to Example 1 using 2-(6-(3-(difluoromethyl)-4-fluorophenyl)-3-methyl-1H-pyrazolo[4,3-*b*]pyridin-1-yl)acetic acid (Intermediate 32) in place of Intermediate 27 and azetidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{19}H_{17}F_3N_4O$, 374.1; m/z found, 375.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, *J* = 1.9 Hz, 1H), 7.90 – 7.80 (m, 2H), 7.78 – 7.69 (m, 1H), 7.33 – 7.22 (m, 1H), 6.97 (t, *J* = 54.9 Hz, 1H), 4.98 (s, 2H), 4.1 (dt, 4H), 2.70 (s, 3H), 2.39 – 2.23 (m, 2H).

Example 38: 1-(Azetidin-1-yl)-2-[6-(4-chloro-3-methylphenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone.



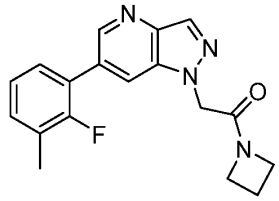
The title compound was prepared in a manner analogous to Example 17, using 1-(azetidin-1-yl)-2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)ethan-1-one (Intermediate 13) in place of Intermediate 42, (4-chloro-3-methylphenyl)boronic acid in place of 2,4-difluorophenylboronic acid and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). The reaction mixture was heated to 90 °C. MS (ESI): mass calcd. for $C_{18}H_{17}ClN_4O$, 340.1; m/z found, 341.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.87 (d, *J* = 1.9 Hz, 1H), 8.40 – 8.37 (m, 1H), 8.35 – 8.32 (m, 1H), 7.85 – 7.83 (m, 1H), 7.69 – 7.65 (m, 1H), 7.60 – 7.57 (m, 1H), 5.25 (s, 2H), 4.20 (t, *J* = 7.7 Hz, 2H), 3.91 (t, *J* = 7.7 Hz, 2H), 2.45 (s, 3H), 2.31 – 2.23 (m, 2H).

Example 39: 1-(Azetidin-1-yl)-2-[6-(4-chloro-3-methylphenyl)-3-methyl-pyrazolo[4,3-b]pyridin-1-yl]ethanone.



The title compound was prepared in a manner analogous to Example 17, using 1-(azetidin-1-yl)-2-(6-bromo-3-methyl-1H-pyrazolo[4,3-b]pyridin-1-yl)ethan-1-one (Intermediate 48) in place of Intermediate 42, (4-chloro-3-methylphenyl)boronic acid in place of 2,4-difluorophenylboronic acid and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). The reaction mixture was heated to 90 °C. MS (ESI): mass calcd. for $C_{19}H_{19}ClN_4O$, 354.1; m/z found, 355.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.81 (d, J = 1.9 Hz, 1H), 8.31 (d, J = 1.9 Hz, 1H), 7.83 – 7.80 (m, 1H), 7.67 – 7.63 (m, 1H), 7.60 – 7.56 (m, 1H), 5.15 (s, 2H), 4.17 (t, J = 7.7 Hz, 2H), 3.90 (t, J = 7.7 Hz, 2H), 2.54 (s, 3H), 2.44 (s, 3H), 2.30 – 2.21 (m, 2H).

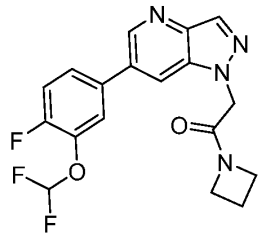
Example 40: 1-(Azetidin-1-yl)-2-[6-(2-fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone.



The title compound was prepared in a manner analogous to Example 17, using 1-(azetidin-1-yl)-2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)ethan-1-one (Intermediate 13) in place of Intermediate 42, (2-fluoro-3-methylphenyl)boronic acid in place of 2,4-difluorophenylboronic acid and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). The reaction mixture was heated to 90 °C. MS (ESI): mass calcd. for $C_{18}H_{17}FN_4O$, 324.1; m/z found, 325.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.68 (t, J = 1.9 Hz, 1H), 8.36 – 8.34 (m, 1H),

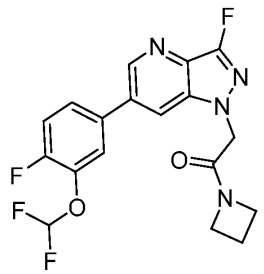
8.27 – 8.24 (m, 1H), 7.47 – 7.42 (m, 1H), 7.41 – 7.37 (m, 1H), 7.29 – 7.24 (m, 1H), 5.24 (s, 2H), 4.20 (t, *J* = 7.7 Hz, 2H), 3.90 (t, *J* = 7.7 Hz, 2H), 2.36 – 2.32 (m, 3H), 2.30 – 2.22 (m, 2H).

Example 41: 1-(Azetidin-1-yl)-2-[6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



The title compound was made in a manner analogous to Example 6, Method A, using 6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridine (Intermediate 17) in place of Intermediate 16 and 1-(azetidin-1-yl)-2-chloroethan-1-one in place of 2-chloro-*N*,*N*-dimethylacetamide. MS (ESI): mass calcd. for $C_{18}H_{15}F_3N_4O_2$, 376.1; m/z found, 377.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.88 (d, *J* = 2.0 Hz, 1H), 8.42 – 8.38 (m, 1H), 8.37 – 8.33 (m, 1H), 7.83 (dd, *J* = 7.6, 2.3 Hz, 1H), 7.78 – 7.73 (m, 1H), 7.60 (dd, *J* = 10.5, 8.6 Hz, 1H), 7.38 (t, *J* = 73.2 Hz, 1H), 5.25 (s, 2H), 4.20 (t, *J* = 7.7 Hz, 2H), 3.91 (t, *J* = 7.7 Hz, 2H), 2.34 – 2.20 (m, 2H).

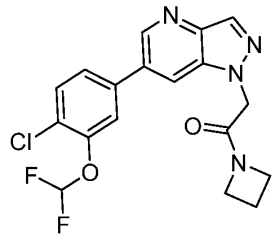
Example 42: 1-(Azetidin-1-yl)-2-[6-[3-(difluoromethoxy)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]ethanone.



The title compound was made in a manner analogous to Example 5, Method A, using 6-(3-(difluoromethoxy)-4-fluorophenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridine (Intermediate 23) in place of Intermediate 16 and 1-(azetidin-1-yl)-2-chloroethan-1-one in place of Intermediate 1. MS (ESI): mass calcd. for $C_{18}H_{14}F_4N_4O_2$, 394.1; m/z found, 395.1 $[M+H]^+$. ^1H NMR (500 MHz,

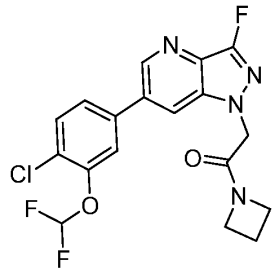
DMSO-d_6) δ 8.93 (d, J = 1.9 Hz, 1H), 8.46 – 8.44 (m, 1H), 7.85 (dd, J = 7.6, 2.3 Hz, 1H), 7.80 – 7.74 (m, 1H), 7.62 (dd, J = 10.5, 8.6 Hz, 1H), 7.38 (t, J = 73.2 Hz, 1H), 5.14 (s, 2H), 4.27 – 4.18 (m, 2H), 3.95 – 3.84 (m, 2H), 2.33 – 2.21 (m, 2H).

Example 43: 1-(Azetidin-1-yl)-2-[6-[4-chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



The title compound was made in a manner analogous to Example 6, Method A, using 6-[4-chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridine (Intermediate 18) in place of Intermediate 16 and 1-(azetidin-1-yl)-2-chloroethan-1-one in place of 2-chloro-*N*,*N*-dimethylacetamide. MS (ESI): mass calcd. for $C_{18}H_{15}ClF_2N_4O_2$, 392.1; m/z found, 393.1 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.91 (d, J = 1.9 Hz, 1H), 8.48 – 8.41 (m, 1H), 8.40 – 8.34 (m, 1H), 7.85 – 7.77 (m, 2H), 7.74 (dd, J = 8.4, 1.9 Hz, 1H), 7.45 (t, J = 73.2 Hz, 1H), 5.26 (s, 2H), 4.20 (t, J = 7.6 Hz, 2H), 3.91 (t, J = 7.7 Hz, 2H), 2.34 – 2.20 (m, 2H).

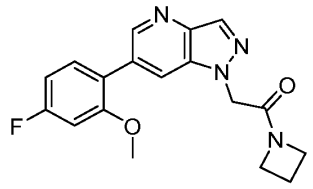
Example 44: 1-(Azetidin-1-yl)-2-[6-[4-chloro-3-(difluoromethoxy)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]ethanone.



The title compound was made in a manner analogous to Example 5, Method A, using 6-(4-chloro-3-(difluoromethoxy)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 22) in place of Intermediate 16 and 1-(azetidin-1-yl)-2-chloroethan-1-one in place of Intermediate 1. MS (ESI): mass calcd. for $C_{18}H_{14}ClF_3N_4O_2$, 410.1; m/z found, 411.1 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-

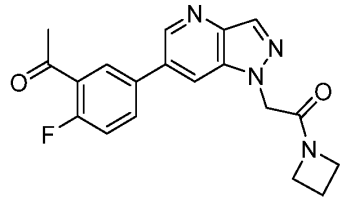
d_6) δ 9.02 – 8.88 (m, 1H), 8.54 – 8.39 (m, 1H), 7.89 – 7.70 (m, 3H), 7.45 (t, J = 73.2 Hz, 1H), 5.15 (s, 2H), 4.33 – 4.12 (m, 2H), 4.01 – 3.80 (m, 2H), 2.37 – 2.18 (m, 2H).

Example 45: 1-(Azetidin-1-yl)-2-[6-(4-fluoro-2-methoxy-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone.



The title compound was prepared in a manner analogous to Example 17, using 1-(azetidin-1-yl)-2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)ethan-1-one (Intermediate 13) in place of Intermediate 42 and (4-fluoro-2-methoxyphenyl)boronic acid in place of 2,4-difluorophenylboronic acid. MS (ESI): mass calcd. for $C_{18}H_{17}FN_4O_2$, 340.1; m/z found, 341.2 $[M+H]^+$. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.60 (d, J = 1.8 Hz, 1H), 8.30 (d, J = 1.0 Hz, 1H), 8.11 – 8.09 (m, 1H), 7.43 (dd, J = 8.5, 6.9 Hz, 1H), 7.11 (dd, J = 11.5, 2.5 Hz, 1H), 6.95 (td, J = 8.4, 2.5 Hz, 1H), 5.21 (s, 2H), 4.18 (t, J = 7.7 Hz, 2H), 3.89 (t, J = 7.7 Hz, 2H), 3.81 (s, 3H), 2.29 – 2.21 (m, 2H).

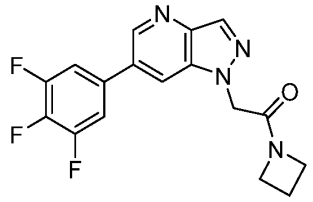
Example 46: 2-[6-(3-Acetyl-4-fluoro-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(azetidin-1-yl)ethanone.



The title compound was prepared in a manner analogous to Example 17, using 1-(azetidin-1-yl)-2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)ethan-1-one (Intermediate 13) in place of Intermediate 42, (3-acetyl-4-fluorophenyl)boronic acid in place of 2,4-difluorophenylboronic acid and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). The reaction mixture was heated to 90 °C. MS (ESI): mass calcd. for $C_{19}H_{17}FN_4O_2$, 352.1; m/z found,

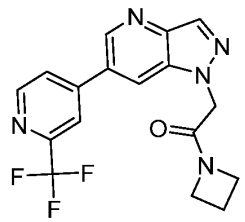
353.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.88 (d, J = 1.9 Hz, 1H), 8.44 – 8.42 (m, 1H), 8.36 – 8.34 (m, 1H), 8.19 – 8.16 (m, 1H), 8.12 – 8.08 (m, 1H), 7.56 (dd, J = 10.9, 8.6 Hz, 1H), 5.27 (s, 2H), 4.20 (t, J = 7.6 Hz, 2H), 3.91 (t, J = 7.7 Hz, 2H), 2.68 (d, J = 4.1 Hz, 3H), 2.31 – 2.23 (m, 2H).

Example 47: 1-(Azetidin-1-yl)-2-[6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone.



The title compound was prepared in a manner analogous to Example 17 using 1-(azetidin-1-yl)-2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)ethan-1-one (Intermediate 13) in place of Intermediate 42, (3,4,5-trifluorophenyl)boronic acid in place of 2,4-difluorophenylboronic acid and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). The reaction mixture was heated to 90 °C. MS (ESI): mass calcd. for $C_{17}H_{13}F_3N_4O$, 346.1; m/z found, 347.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.93 (d, J = 2.0 Hz, 1H), 8.52 – 8.48 (m, 1H), 8.38 – 8.35 (m, 1H), 7.94 – 7.85 (m, 2H), 5.24 (s, 2H), 4.20 (t, J = 7.7 Hz, 2H), 3.91 (t, J = 7.8 Hz, 2H), 2.32 – 2.22 (m, 2H).

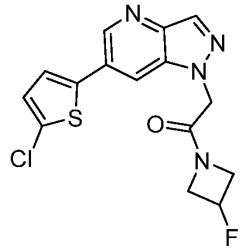
Example 48: 1-(Azetidin-1-yl)-2-[6-[2-(trifluoromethyl)-4-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



The title compound was made in a manner analogous to Example 7 using 1-(azetidin-1-yl)-2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)ethan-1-one (Intermediate 13) in place of Intermediate 10 and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(trifluoromethyl)pyridine in place of 4-

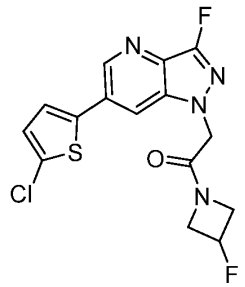
fluoro-3-methylphenylboronic acid. MS (ESI): mass calcd. for $C_{17}H_{14}F_3N_5O$, 361.1; m/z found, 362.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 9.08 (d, J = 2.0 Hz, 1H), 8.91 (d, J = 5.1 Hz, 1H), 8.72 (dd, J = 2.0, 1.0 Hz, 1H), 8.42 (d, J = 0.9 Hz, 1H), 8.38 – 8.35 (m, 1H), 8.23 (dd, J = 5.1, 1.7 Hz, 1H), 5.29 (s, 2H), 4.26 – 4.16 (m, 2H), 3.95 – 3.88 (m, 2H), 2.32 – 2.23 (m, 2H).

Example 49: 2-[6-(5-Chloro-2-thienyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone.



The title compound was made in a manner analogous to Example 5, Method A, using 6-(5-chloro-2-thienyl)pyrazolo[4,3-b]pyridine (Intermediate 37) in place of Intermediate 16. MS (ESI): mass calcd. for $C_{15}H_{12}ClFN_4OS$, 350.0; m/z found, 351.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.87 (d, J = 2.0 Hz, 1H), 8.37 – 8.32 (m, 1H), 8.32 – 8.28 (m, 1H), 7.62 (d, J = 4.0 Hz, 1H), 7.27 (d, J = 4.0 Hz, 1H), 5.63 – 5.32 (m, 1H), 5.39 – 5.31 (m, 1H), 5.28 (d, J = 16.4 Hz, 1H), 4.65 – 4.46 (m, 1H), 4.40 – 4.16 (m, 2H), 4.08 – 3.87 (m, 1H).

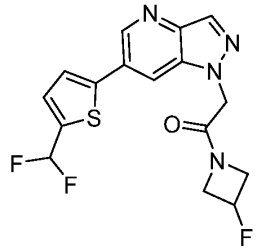
Example 50: 2-[6-(5-Chloro-2-thienyl)-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone.



The title compound was made in a manner analogous to Example 9 using 2-(6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 15) and 5-chlorothiophene-2-boronic acid in place of 2-[4-chloro-3-(difluoromethoxy)phenyl]-4,4,5,5-

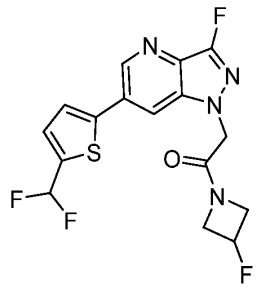
tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd. for $C_{15}H_{11}ClF_2N_4OS$, 368.0; m/z found, 369.0 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.92 (d, J = 1.9 Hz, 1H), 8.36 – 8.29 (m, 1H), 7.67 (d, J = 3.9 Hz, 1H), 7.29 (d, J = 3.9 Hz, 1H), 5.56 – 5.37 (m, 1H), 5.22 (d, J = 17.1 Hz, 1H), 5.17 (d, J = 17.0 Hz, 1H), 4.63 – 4.52 (m, 1H), 4.39 – 4.19 (m, 2H), 4.03 – 3.91 (m, 1H).

Example 51: 2-[6-[5-(Difluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone.



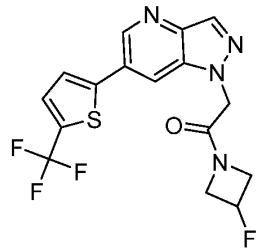
The title compound was made in a manner analogous to Example 9 using Intermediate 12 and 2-(5-(difluoromethyl)thiophen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Intermediate 8) in place of 2-[4-chloro-3-(difluoromethoxy)phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd. for $C_{16}H_{13}F_3N_4OS$, 366.1; m/z found, 367.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.95 (d, J = 2.0 Hz, 1H), 8.42 (dd, J = 2.0, 1.0 Hz, 1H), 8.36 (d, J = 1.0 Hz, 1H), 7.76 – 7.71 (m, 1H), 7.63 – 7.54 (m, 1H), 7.37 (t, J = 55.2 Hz, 1H), 5.56 – 5.37 (m, 1H), 5.35 (d, J = 16.7 Hz, 1H), 5.31 (d, J = 17.0 Hz, 1H), 4.62 – 4.50 (m, 1H), 4.40 – 4.19 (m, 2H), 4.05 – 3.92 (m, 1H).

Example 52: 2-[6-[5-(Difluoromethyl)-2-thienyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone.



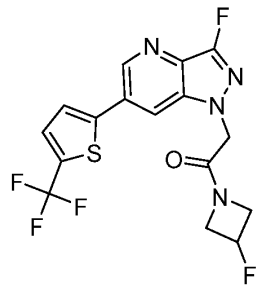
The title compound was made in a manner analogous to Example 9 using 2-(6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 15) and 2-(5-(difluoromethyl)thiophen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Intermediate 8) in place of 2-[4-chloro-3-(difluoromethoxy)phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd. for $C_{16}H_{12}F_4N_4OS$, 384.1; m/z found, 385.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 9.05 – 8.94 (m, 1H), 8.52 – 8.40 (m, 1H), 7.85 – 7.71 (m, 1H), 7.63 – 7.56 (m, 1H), 7.39 (t, J = 55.3 Hz, 1H), 5.65 – 5.32 (m, 1H), 5.26 (d, J = 17.2 Hz, 1H), 5.19 (d, J = 17.7 Hz, 1H), 4.73 – 4.46 (m, 1H), 4.46 – 4.15 (m, 2H), 4.10 – 3.85 (m, 1H).

Example 53: 1-(3-Fluoroazetidin-1-yl)-2-[6-[5-(trifluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



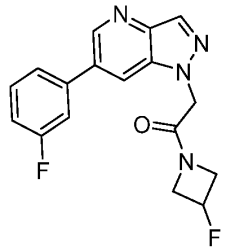
The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 12) in place of Intermediate 10 and 4,4,5,5-tetramethyl-2-(5-(trifluoromethyl)thiophen-2-yl)-1,3,2-dioxaborolane in place of 4-fluoro-3-methylboronic acid. MS (ESI): mass calcd. for $C_{16}H_{12}F_4N_4OS$, 384.1; m/z found, 385.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.98 (d, J = 2.0 Hz, 1H), 8.51 – 8.46 (m, 1H), 8.38 (d, J = 1.0 Hz, 1H), 7.88 – 7.79 (m, 2H), 5.56 – 5.39 (m, 1H), 5.36 (d, J = 16.8 Hz, 1H), 5.31 (d, J = 16.8 Hz, 1H), 4.62 – 4.50 (m, 1H), 4.40 – 4.19 (m, 2H), 4.04 – 3.91 (m, 1H).

Example 54: 1-(3-Fluoroazetidin-1-yl)-2-[3-fluoro-6-[5-(trifluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



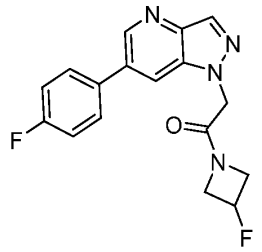
The title compound was made in a manner analogous to Example 9 using 2-(6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 15) and 4,4,5,5-tetramethyl-2-(5-(trifluoromethyl)thiophen-2-yl)-1,3,2-dioxaborolane in place of 4-fluoro-3-methylboronic acid. MS (ESI): mass calcd. for $C_{16}H_{11}F_5N_4OS$, 402.1; m/z found, 403.0 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 9.02 (d, J = 1.9 Hz, 1H), 8.56 – 8.49 (m, 1H), 7.91 – 7.82 (m, 2H), 5.58 – 5.37 (m, 1H), 5.25 (d, J = 17.1 Hz, 1H), 5.20 (d, J = 17.1 Hz, 1H), 4.65 – 4.52 (m, 1H), 4.41 – 4.19 (m, 2H), 4.06 – 3.91 (m, 1H).

Example 55: 1-(3-Fluoroazetidin-1-yl)-2-[6-(3-fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone.



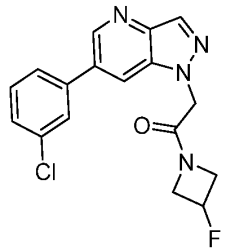
The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 12) in place of Intermediate 10 and 3-fluorophenylboronic acid in place of 4-fluoro-3-methylboronic acid. MS (ESI): mass calcd. for $C_{17}H_{14}F_2N_4O$, 328.1; m/z found, 329.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.91 (d, J = 1.9 Hz, 1H), 8.47 – 8.42 (m, 1H), 8.38 – 8.33 (m, 1H), 7.72 – 7.67 (m, 1H), 7.70 – 7.66 (m, 1H), 7.60 (dt, J = 8.1, 6.2 Hz, 1H), 7.34 – 7.26 (m, 1H), 5.55 – 5.37 (m, 1H), 5.35 (d, J = 17.0 Hz, 1H), 5.31 (d, J = 17.1 Hz, 1H), 4.61 – 4.48 (m, 1H), 4.36 – 4.18 (m, 2H), 4.04 – 3.90 (m, 1H).

Example 56: 1-(3-Fluoroazetidin-1-yl)-2-[6-(4-fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone.



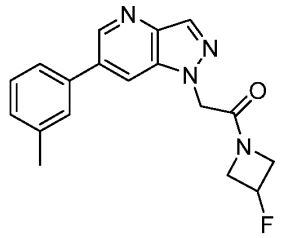
The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 12) in place of Intermediate 10 and 4-fluorophenylboronic acid in place of 4-fluoro-3-methylboronic acid. MS (ESI): mass calcd. for $C_{17}H_{14}F_2N_4O$, 328.1; m/z found, 329.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.86 (d, J = 1.9 Hz, 1H), 8.36 (d, J = 1.9 Hz, 1H), 8.34 (s, 1H), 7.91 – 7.82 (m, 2H), 7.44 – 7.34 (m, 2H), 5.54 – 5.37 (m, 1H), 5.34 (d, J = 17.0 Hz, 1H), 5.30 (d, J = 17.1 Hz, 1H), 4.60 – 4.48 (m, 1H), 4.35 – 4.19 (m, 2H), 4.03 – 3.91 (m, 1H).

Example 57: 2-[6-(3-Chlorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone.



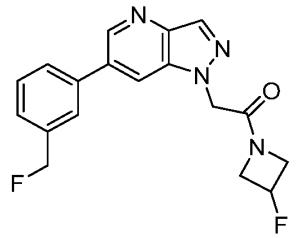
The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 12) in place of Intermediate 10 and 3-chlorophenylboronic acid in place of 4-fluoro-3-methylphenylboronic acid. MS (ESI): mass calcd. for $C_{17}H_{14}ClFN_4O$, 344.1; m/z found, 345.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.90 (d, J = 1.9 Hz, 1H), 8.48 – 8.42 (m, 1H), 8.39 – 8.32 (m, 1H), 7.92 – 7.87 (m, 1H), 7.84 – 7.77 (m, 1H), 7.58 (t, J = 7.8 Hz, 1H), 7.55 – 7.49 (m, 1H), 5.55 – 5.36 (m, 1H), 5.36 (d, J = 17.1 Hz, 1H), 5.31 (d, J = 17.1 Hz, 1H), 4.60 – 4.49 (m, 1H), 4.35 – 4.19 (m, 2H), 4.04 – 3.90 (m, 1H).

Example 58: 1-(3-Fluoroazetidin-1-yl)-2-[6-(m-tolyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone.



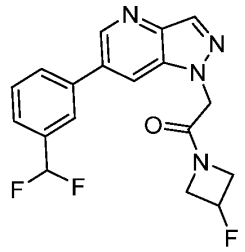
The title compound was prepared in a manner analogous to Example 17, using 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 12) in place of Intermediate 42, *m*-tolylboronic acid in place of 2,4-difluorophenylboronic acid and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). MS (ESI): mass calcd. for $C_{18}H_{17}FN_4O$, 324.1; m/z found, 325.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.86 (d, J = 1.9 Hz, 1H), 8.36 – 8.33 (m, 2H), 7.65 – 7.62 (m, 1H), 7.62 – 7.58 (m, 1H), 7.43 (t, J = 7.6 Hz, 1H), 7.30 – 7.25 (m, 1H), 5.54 – 5.28 (m, 3H), 4.60 – 4.50 (m, 1H), 4.35 – 4.20 (m, 2H), 4.02 – 3.92 (m, 1H), 2.42 (s, 3H).

Example 59: 1-(3-Fluoroazetidin-1-yl)-2-[6-[3-(fluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



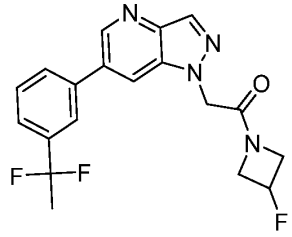
The title compound was prepared in a manner analogous to Example 16, using 2-(6-(3-(fluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid (Intermediate 56) in place of Intermediate 39 and DCM in place of DMF. MS (ESI): mass calcd. for $C_{18}H_{16}F_2N_4O$, 342.1; m/z found, 343.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.89 (d, J = 1.9 Hz, 1H), 8.41 – 8.39 (m, 1H), 8.36 – 8.35 (m, 1H), 7.88 – 7.82 (m, 2H), 7.64 – 7.58 (m, 1H), 7.54 – 7.49 (m, 1H), 5.60 – 5.29 (m, 5H), 4.59 – 4.50 (m, 1H), 4.36 – 4.20 (m, 2H), 4.04 – 3.92 (m, 1H).

Example 60: 2-[6-[3-(Difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone.



The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 12) in place of Intermediate 10 and 2-(3-(difluoromethyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in place of 4-fluoro-3-methylboronic acid. MS (ESI): mass calcd. for $C_{18}H_{15}F_3N_4O$, 360.1; m/z found, 361.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.90 (d, J = 1.9 Hz, 1H), 8.53 – 8.41 (m, 1H), 8.40 – 8.31 (m, 1H), 8.09 – 7.90 (m, 2H), 7.77 – 7.62 (m, 2H), 7.15 (t, J = 55.8 Hz, 1H), 5.62 – 5.32 (m, 1H), 5.38 (d, J = 16.8 Hz, 1H), 5.32 (d, J = 16.9 Hz, 1H), 4.64 – 4.45 (m, 1H), 4.40 – 4.15 (m, 2H), 4.08 – 3.85 (m, 1H).

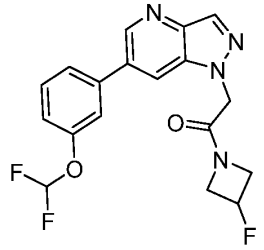
Example 61: 2-[6-[3-(1,1-Difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone.



The title compound was made in a manner analogous to Example 6, Method A, using 3-(1,1-difluoroethyl)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 20) in place of Intermediate 16 and 2-chloro-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 1) in place of 2-chloro-*N*,*N*-dimethylacetamide. MS (ESI): mass calcd. for $C_{19}H_{17}F_3N_4O$, 374.1; m/z found, 375.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.92 (d, J = 1.9 Hz, 1H), 8.50 – 8.40 (m, 1H), 8.40 – 8.31 (m, 1H), 8.02 – 7.85 (m, 2H), 7.76 – 7.58 (m, 2H), 5.61 – 5.29 (m, 1H), 5.36 (d, J = 17.1 Hz, 1H),

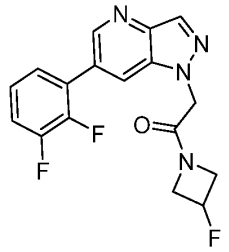
5.35 (d, J = 17.2 Hz, 1H), 4.63 – 4.45 (m, 1H), 4.39 – 4.15 (m, 2H), 4.07 – 3.85 (m, 1H), 2.06 (t, J = 18.9 Hz, 3H).

Example 62: 2-[6-[3-(Difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone.



The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 12) in place of Intermediate 10 and 2-(3-(difluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in place of 4-fluoro-3-methylphenylboronic acid. MS (ESI): mass calcd. for $C_{18}H_{15}F_3N_4O_2$, 376.1; m/z found, 377.1 $[M+H]^+$. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.90 (d, J = 1.9 Hz, 1H), 8.45 – 8.39 (m, 1H), 8.39 – 8.33 (m, 1H), 7.74 – 7.67 (m, 1H), 7.65 – 7.57 (m, 2H), 7.37 (t, J = 74.0 Hz, 1H), 7.30 – 7.25 (m, 1H), 5.55 – 5.38 (m, 1H), 5.36 (d, J = 17.2 Hz, 1H), 5.31 (d, J = 17.2 Hz, 1H), 4.60 – 4.49 (m, 1H), 4.36 – 4.19 (m, 2H), 4.04 – 3.90 (m, 1H).

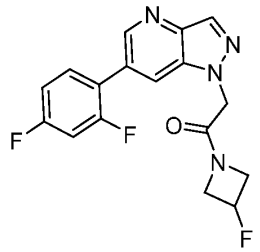
Example 63: 2-[6-(2,3-Difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone.



The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 12) in place of Intermediate 10 and (2,3-difluorophenyl)boronic acid in place of 4-fluoro-3-methylphenylboronic acid. MS (ESI): mass calcd. for $C_{17}H_{13}F_3N_4O$, 346.1; m/z found, 347.1

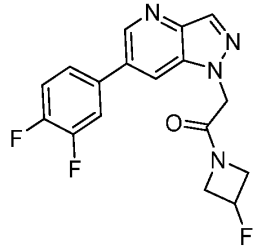
$[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.77 – 8.69 (m, 1H), 8.42 – 8.38 (m, 1H), 8.37 – 8.30 (m, 1H), 7.62 – 7.45 (m, 2H), 7.44 – 7.34 (m, 1H), 5.61 – 5.29 (m, 1H), 5.42 – 5.34 (m, 1H), 5.33 (d, J = 17.1 Hz, 1H), 4.65 – 4.48 (m, 1H), 4.40 – 4.18 (m, 2H), 4.05 – 3.88 (m, 1H).

Example 64: 2-[6-(2,4-Difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone.



The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 12) in place of Intermediate 10 and 2,4-difluorophenylboronic acid in place of 4-fluoro-3-methylboronic acid. MS (ESI): mass calcd. for $C_{17}H_{13}F_3N_4O$, 346.1; m/z found, 347.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.71 – 8.66 (m, 1H), 8.41 – 8.34 (m, 1H), 8.30 – 8.24 (m, 1H), 7.72 (dt, J = 8.8, 6.5 Hz, 1H), 7.52 – 7.44 (m, 1H), 7.34 – 7.25 (m, 1H), 5.54 – 5.37 (m, 1H), 5.35 (d, J = 17.1 Hz, 1H), 5.30 (d, J = 17.1 Hz, 1H), 4.61 – 4.50 (m, 1H), 4.37 – 4.18 (m, 2H), 4.03 – 3.90 (m, 1H).

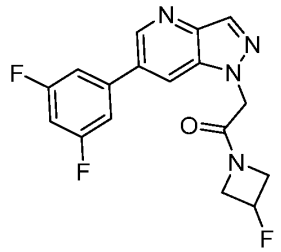
Example 65: 2-[6-(3,4-Difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone.



The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 12) in place of Intermediate 10 and 3,4-difluorophenylboronic acid in place of 4-fluoro-3-methylboronic acid. MS (ESI): mass calcd. for $C_{17}H_{13}F_3N_4O$, 346.1; m/z found, 347.1 $[M+H]^+$. ^1H NMR (300 MHz,

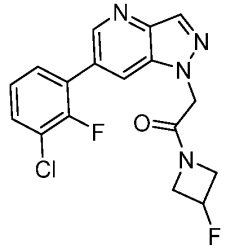
DMSO-d_6) δ 8.93 – 8.87 (m, 1H), 8.46 – 8.41 (m, 1H), 8.36 (s, 1H), 8.01 – 7.90 (m, 1H), 7.75 – 7.57 (m, 2H), 5.58 – 5.36 (m, 1H), 5.39 – 5.33 (m, 1H), 5.32 (d, J = 17.1 Hz, 1H), 4.64 – 4.46 (m, 1H), 4.38 – 4.17 (m, 2H), 4.05 – 3.90 (m, 1H).

Example 66: 2-[6-(3,5-Difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone.



The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 12) in place of Intermediate 10 and 3,5-difluorophenylboronic acid in place of 4-fluoro-3-methylboronic acid. MS (ESI): mass calcd. for $C_{17}H_{13}F_3N_4O$, 346.1; m/z found, 347.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 9.00 – 8.90 (m, 1H), 8.56 – 8.47 (m, 1H), 8.42 – 8.33 (m, 1H), 7.72 – 7.57 (m, 2H), 7.42 – 7.28 (m, 1H), 5.63 – 5.28 (m, 1H), 5.39 – 5.33 (m, 1H), 5.30 (d, J = 17.5 Hz, 1H), 4.66 – 4.45 (m, 1H), 4.40 – 4.13 (m, 2H), 4.08 – 3.85 (m, 1H).

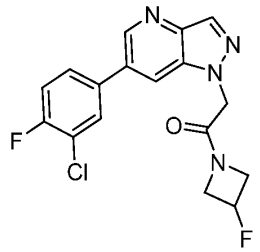
Example 67: 2-[6-(3-Chloro-2-fluoro-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone.



The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 12) in place of Intermediate 10 and 3-chloro-2-fluorophenylboronic acid in place of 4-fluoro-3-methylboronic acid. MS (ESI): mass calcd. for $C_{17}H_{13}ClF_2N_4O$, 362.1; m/z found, 363.1 $[M+H]^+$. ^1H NMR (300

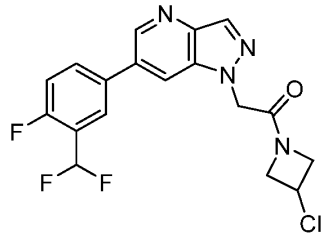
MHz, DMSO-d_6) δ 8.74 – 8.69 (m, 1H), 8.40 (s, 1H), 8.37 – 8.31 (m, 1H), 7.75 – 7.67 (m, 1H), 7.67 – 7.59 (m, 1H), 7.45 – 7.37 (m, 1H), 5.59 – 5.36 (m, 1H), 5.39 – 5.33 (m, 1H), 5.33 (d, J = 17.1 Hz, 1H), 4.66 – 4.45 (m, 1H), 4.42 – 4.16 (m, 2H), 4.06 – 3.88 (m, 1H).

Example 68: 2-[6-(3-Chloro-4-fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone.



The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 12) in place of Intermediate 10 and 3-chloro-4-fluorophenylboronic acid in place of 4-fluoro-3-methylboronic acid. MS (ESI): mass calcd. for $C_{17}H_{13}ClF_2N_4O$, 362.1; m/z found, 363.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.90 (d, J = 1.9 Hz, 1H), 8.48 – 8.41 (m, 1H), 8.39 – 8.32 (m, 1H), 8.07 (dd, J = 7.1, 2.3 Hz, 1H), 7.90 – 7.80 (m, 1H), 7.61 (t, J = 9.0 Hz, 1H), 5.60 – 5.33 (m, 1H), 5.39 – 5.33 (m, 1H), 5.30 (d, J = 17.3 Hz, 1H), 4.64 – 4.44 (m, 1H), 4.39 – 4.15 (m, 2H), 4.07 – 3.86 (m, 1H).

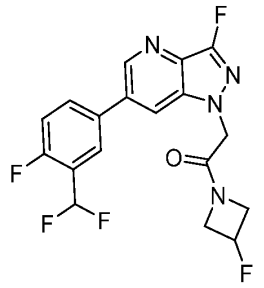
Example 69: 1-(3-Chloroazetidin-1-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]ethanone.



The title compound was prepared in a manner analogous to Example 1 using 3-chloroazetidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{18}H_{14}ClF_3N_4O$, 394.1; m/z found, 395.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.82 (d, J = 1.9 Hz, 1H), 8.31 (d, J = 1.0

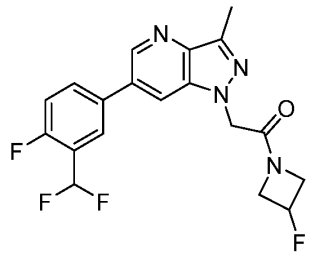
Hz, 1H), 7.93 (dd, *J* = 1.9, 1.0 Hz, 1H), 7.93 – 7.84 (m, 1H), 7.82 – 7.67 (m, 1H), 7.35 – 7.27 (m, 1H), 6.98 (t, *J* = 54.8 Hz, 1H), 5.34 – 4.90 (m, 2H), 4.72 – 4.41 (m, 3H), 4.26 – 4.14 (m, 2H).

Example 70: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone.



The title compound was made in a manner analogous to Example 6, Method A, using 6-[3-(difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridine (Intermediate 21) in place of Intermediate 16 and 2-chloro-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 1) in place of 2-chloro-*N*,*N*-dimethylacetamide. MS (ESI): mass calcd. for $C_{18}H_{13}F_5N_4O$, 396.1; m/z found, 397.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.93 (d, *J* = 1.8 Hz, 1H), 8.52 – 8.42 (m, 1H), 8.14 – 8.01 (m, 2H), 7.66 – 7.54 (m, 1H), 7.31 (t, *J* = 54.1 Hz, 1H), 5.62 – 5.31 (m, 1H), 5.27 (d, *J* = 17.1 Hz, 1H), 5.20 (d, *J* = 17.2 Hz, 1H), 4.66 – 4.49 (m, 1H), 4.43 – 4.15 (m, 2H), 4.07 – 3.87 (m, 1H).

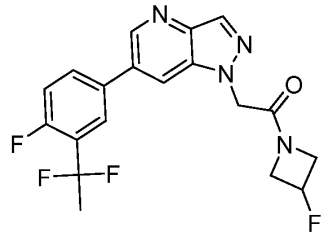
Example 71: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-methyl-pyrazolo[4,3-*b*]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone.



The title compound was prepared in a manner analogous to Example 13 using 2-(6-(3-(difluoromethyl)-4-fluorophenyl)-3-methyl-1H-pyrazolo[4,3-*b*]pyridin-1-yl)acetic acid (Intermediate 32) in place of Intermediate 27 and 3-fluoroazetidine in place of 3-

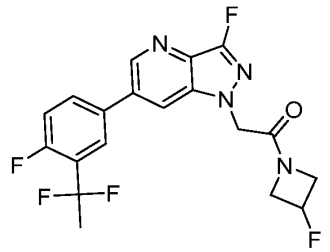
(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{19}H_{16}F_4N_4O$, 392.1; m/z found, 393.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.75 (d, J = 1.9 Hz, 1H), 7.93 – 7.79 (m, 2H), 7.78 – 7.69 (m, 1H), 7.36 – 7.21 (m, 1H), 6.97 (t, J = 54.8 Hz, 1H), 5.47 – 5.13 (m, 1H), 5.02 (s, 2H), 4.44 – 4.25 (m, 2H), 4.25 – 4.07 (m, 2H), 2.69 (s, 3H).

Example 72: 2-[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone.



The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 12) in place of Intermediate 10 and 2-(3-(1,1-difluoroethyl)-4-fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in place of 4-fluoro-3-methylphenylboronic acid. MS (ESI): mass calcd. for $C_{19}H_{16}F_4N_4O$, 392.1; m/z found, 393.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.89 (d, J = 1.9 Hz, 1H), 8.46 – 8.39 (m, 1H), 8.39 – 8.34 (m, 1H), 8.08 – 7.96 (m, 1H), 7.97 – 7.89 (m, 1H), 7.56 (dd, J = 11.0, 8.6 Hz, 1H), 5.62 – 5.33 (m, 2H), 5.31 (d, J = 16.8 Hz, 1H), 4.64 – 4.45 (m, 1H), 4.39 – 4.15 (m, 2H), 4.07 – 3.87 (m, 1H), 2.10 (t, J = 19.1 Hz, 3H).

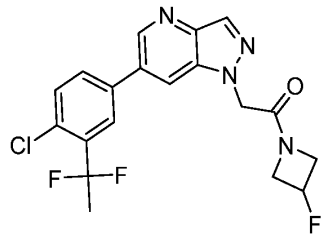
Example 73: 2-[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone.



The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 15) in place

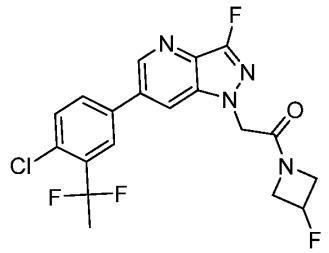
of Intermediate 10 and 2-(3-(1,1-difluoroethyl)-4-fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in place of 4-fluoro-3-methylphenylboronic acid. MS (ESI): mass calcd. for $C_{19}H_{15}F_5N_4O$, 410.1; m/z found, 411.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.93 (d, J = 1.8 Hz, 1H), 8.51 – 8.42 (m, 1H), 8.08 – 7.98 (m, 1H), 7.98 – 7.91 (m, 1H), 7.58 (dd, J = 11.0, 8.6 Hz, 1H), 5.61 – 5.31 (m, 1H), 5.27 (d, J = 17.2 Hz, 1H), 5.20 (d, J = 17.2 Hz, 1H), 4.67 – 4.47 (m, 1H), 4.42 – 4.15 (m, 2H), 4.07 – 3.88 (m, 1H), 2.10 (t, J = 19.1 Hz, 3H).

Example 74: 2-[6-[4-Chloro-3-(1,1-difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone.



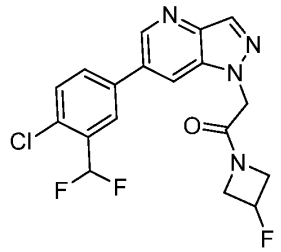
The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 12) in place of Intermediate 10 and 2-(4-chloro-3-(1,1-difluoroethyl))-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in place of 4-fluoro-3-methylphenylboronic acid. MS (ESI): mass calcd. for $C_{19}H_{16}ClF_3N_4O$, 408.1; m/z found, 409.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.91 (d, J = 1.9 Hz, 1H), 8.49 – 8.41 (m, 1H), 8.38 (s, 1H), 8.04 – 7.98 (m, 1H), 7.99 – 7.90 (m, 1H), 7.77 (d, J = 8.3 Hz, 1H), 5.61 – 5.35 (m, 2H), 5.32 (d, J = 17.0 Hz, 1H), 4.66 – 4.46 (m, 1H), 4.40 – 4.14 (m, 2H), 4.07 – 3.88 (m, 1H), 2.13 (t, J = 19.0 Hz, 3H).

Example 75: 2-[6-[4-Chloro-3-(1,1-difluoroethyl)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone.



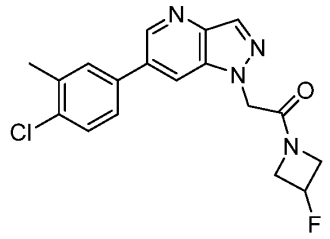
The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 15) in place of Intermediate 10 and 2-(4-chloro-3-(1,1-difluoroethyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in place of 4-fluoro-3-methylphenylboronic acid. MS (ESI): mass calcd. for $C_{19}H_{15}ClF_4N_4O$, 426.1; m/z found, 427.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.95 (d, J = 1.8 Hz, 1H), 8.54 – 8.44 (m, 1H), 8.05 – 7.92 (m, 2H), 7.79 (d, J = 8.3 Hz, 1H), 5.62 – 5.32 (m, 1H), 5.27 (d, J = 17.0 Hz, 1H), 5.21 (d, J = 17.0 Hz, 1H), 4.68 – 4.47 (m, 1H), 4.43 – 4.14 (m, 2H), 4.06 – 3.87 (m, 1H), 2.13 (t, J = 19.0 Hz, 3H).

Example 76: 2-[6-[4-Chloro-3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone.



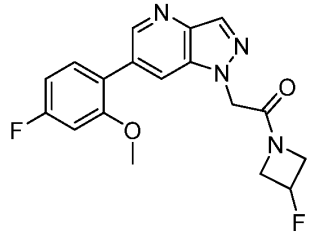
The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 12) in place of Intermediate 10 and 2-(4-chloro-3-(difluoromethyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in place of 4-fluoro-3-methylboronic acid. MS (ESI): mass calcd. for $C_{18}H_{14}ClF_3N_4O$, 394.1; m/z found, 395.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.91 (d, J = 2.0 Hz, 1H), 8.48 (dd, J = 2.0, 1.0 Hz, 1H), 8.38 (d, J = 1.0 Hz, 1H), 8.10 (d, J = 2.3 Hz, 1H), 8.06 – 8.01 (m, 1H), 7.82 – 7.77 (m, 1H), 7.31 (t, J = 54.1 Hz, 1H), 5.56 – 5.37 (m, 1H), 5.39 – 5.35 (m, 1H), 5.33 (d, J = 17.2 Hz, 1H), 4.60 – 4.47 (m, 1H), 4.36 – 4.19 (m, 2H), 4.03 – 3.91 (m, 1H).

Example 77: 2-[6-(4-Chloro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone.



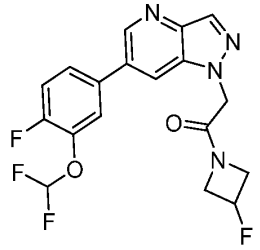
The title compound was prepared in a manner analogous to Example 17, using 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 12) in place of Intermediate 42, (4-chloro-3-methylphenyl)boronic acid in place of 2,4-difluorophenylboronic acid, and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). The reaction mixture was heated to 90 °C. MS (ESI): mass calcd. for $C_{18}H_{16}ClFN_4O$, 358.1; m/z found, 359.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.88 (d, J = 1.9 Hz, 1H), 8.40 – 8.38 (m, 1H), 8.36 – 8.34 (m, 1H), 7.85 – 7.82 (m, 1H), 7.68 – 7.65 (m, 1H), 7.60 – 7.57 (m, 1H), 5.55 – 5.27 (m, 3H), 4.61 – 4.49 (m, 1H), 4.37 – 4.19 (m, 2H), 4.03 – 3.91 (m, 1H), 2.45 (s, 3H).

Example 78: 1-(3-Fluoroazetidin-1-yl)-2-[6-(4-fluoro-2-methoxy-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone.



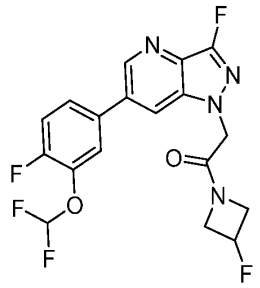
The title compound was prepared in a manner analogous to Example 17, using 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 12) in place of Intermediate 42 and (4-fluoro-2-methoxyphenyl)boronic acid in place of 2,4-difluorophenylboronic acid. MS (ESI): mass calcd. for $C_{18}H_{16}F_2N_4O_2$, 358.1; m/z found, 359.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.60 (d, J = 1.8 Hz, 1H), 8.31 (d, J = 1.0 Hz, 1H), 8.11 – 8.09 (m, 1H), 7.43 (dd, J = 8.4, 6.9 Hz, 1H), 7.11 (dd, J = 11.5, 2.5 Hz, 1H), 6.95 (td, J = 8.4, 2.5 Hz, 1H), 5.53 – 5.35 (m, 1H), 5.34 – 5.23 (m, 2H), 4.58 – 4.47 (m, 1H), 4.35 – 4.17 (m, 2H), 4.01 – 3.90 (m, 1H), 3.81 (s, 3H).

Example 79: 2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone.



The title compound was made in a manner analogous to Example 5, Method A, using 6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 17) in place of Intermediate 16. MS (ESI): mass calcd. for $C_{18}H_{14}F_4N_4O_2$, 394.1; m/z found, 395.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.88 (d, J = 1.9 Hz, 1H), 8.44 – 8.39 (m, 1H), 8.36 (d, J = 1.1 Hz, 1H), 7.83 (dd, J = 7.5, 2.3 Hz, 1H), 7.78 – 7.71 (m, 1H), 7.60 (dd, J = 10.5, 8.6 Hz, 1H), 7.38 (t, J = 73.2 Hz, 1H), 5.54 – 5.38 (m, 1H), 5.33 (d, J = 17.4 Hz, 1H), 5.30 (d, J = 17.1 Hz, 1H), 4.59 – 4.50 (m, 1H), 4.35 – 4.19 (m, 2H), 4.03 – 3.91 (m, 1H).

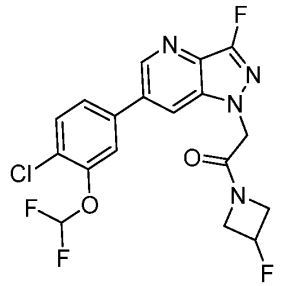
Example 80: 2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone.



The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 15) in place of Intermediate 10 and 2-(3-(difluoromethoxy)-4-fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in place of 4-fluoro-3-methylphenylboronic acid. MS (ESI): mass calcd. for $C_{18}H_{13}F_5N_4O_2$, 412.1; m/z found, 413.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.93 (d, J = 1.8 Hz, 1H), 8.51 – 8.36 (m, 1H), 7.90 – 7.81 (m, 1H), 7.81 – 7.71 (m, 1H), 7.68 – 7.58 (m, 1H),

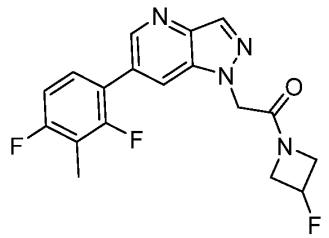
7.38 (t, J = 73.2 Hz, 1H), 5.62 – 5.30 (m, 1H), 5.26 (d, J = 17.3 Hz, 1H), 5.19 (d, J = 17.7 Hz, 1H), 4.68 – 4.46 (m, 1H), 4.44 – 4.15 (m, 2H), 4.07 – 3.86 (m, 1H).

Example 81: 2-[6-[4-Chloro-3-(difluoromethoxy)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone.



The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 15) in place of Intermediate 10 and 2-(4-chloro-3-(difluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in place of 4-fluoro-3-methylphenylboronic acid. MS (ESI): mass calcd. for $C_{18}H_{13}ClF_4N_4O_2$, 428.1; m/z found, 429.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.95 (d, J = 1.9 Hz, 1H), 8.51 – 8.44 (m, 1H), 7.83 (d, J = 2.1 Hz, 1H), 7.80 (d, J = 8.3 Hz, 1H), 7.74 (dd, J = 8.4, 2.1 Hz, 1H), 7.44 (t, J = 73.2 Hz, 1H), 5.56 – 5.35 (m, 1H), 5.25 (d, J = 17.2 Hz, 1H), 5.20 (d, J = 17.0 Hz, 1H), 4.64 – 4.52 (m, 1H), 4.39 – 4.19 (m, 2H), 4.04 – 3.91 (m, 1H).

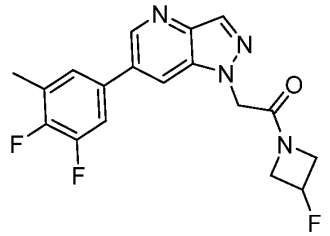
Example 82: 2-[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone.



The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 12) in place of Intermediate 10 and 2-(2,4-difluoro-3-methylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in place of 4-fluoro-3-methylboronic acid. MS (ESI): mass calcd. for $C_{18}H_{15}F_3N_4O$, 360.1; m/z

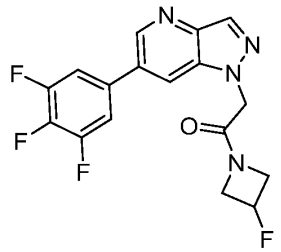
found, 361.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.72 – 8.60 (m, 1H), 8.42 – 8.32 (m, 1H), 8.30 – 8.21 (m, 1H), 7.61 – 7.45 (m, 1H), 7.32 – 7.19 (m, 1H), 5.63 – 5.29 (m, 1H), 5.41 – 5.33 (m, 1H), 5.29 (d, J = 17.7 Hz, 1H), 4.65 – 4.44 (m, 1H), 4.42 – 4.13 (m, 2H), 4.07 – 3.83 (m, 1H), 2.26 (s, 3H).

Example 83: 2-[6-(3,4-Difluoro-5-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone.



The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 12) in place of Intermediate 10 and 2-(3,4-difluoro-5-methylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in place of 4-fluoro-3-methylboronic acid. MS (ESI): mass calcd. for $C_{18}H_{15}F_3N_4O$, 360.1; m/z found, 361.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.88 (d, J = 2.0 Hz, 1H), 8.43 – 8.38 (m, 1H), 8.37 – 8.33 (m, 1H), 7.79 – 7.71 (m, 1H), 7.64 – 7.58 (m, 1H), 5.54 – 5.37 (m, 1H), 5.34 (d, J = 17.0 Hz, 1H), 5.29 (d, J = 17.0 Hz, 1H), 4.60 – 4.48 (m, 1H), 4.36 – 4.19 (m, 2H), 4.04 – 3.92 (m, 1H), 2.43 – 2.38 (m, 3H).

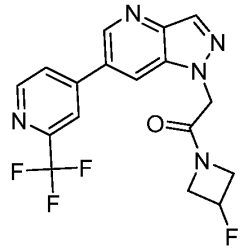
Example 84: 1-(3-Fluoroazetidin-1-yl)-2-[6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone.



The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 12) in place of

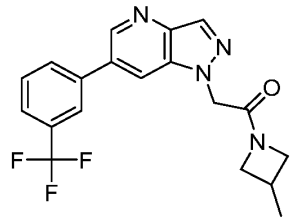
Intermediate 10 and 3,4,5-trifluorophenylboronic acid in place of 4-fluoro-3-methylboronic acid. MS (ESI): mass calcd. for $C_{17}H_{12}F_4N_4O$, 364.1; m/z found, 365.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.93 (d, J = 2.0 Hz, 1H), 8.51 – 8.46 (m, 1H), 8.41 – 8.35 (m, 1H), 7.92 – 7.84 (m, 2H), 5.54 – 5.37 (m, 1H), 5.34 (d, J = 17.1 Hz, 1H), 5.29 (d, J = 17.1 Hz, 1H), 4.60 – 4.49 (m, 1H), 4.35 – 4.19 (m, 2H), 4.04 – 3.91 (m, 1H).

Example 85: 1-(3-Fluoroazetidin-1-yl)-2-[6-[2-(trifluoromethyl)-4-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoroazetidin-1-yl)ethan-1-one (Intermediate 12) in place of Intermediate 10 and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(trifluoromethyl)pyridine in place of 4-fluoro-3-methylphenylboronic acid. MS (ESI): mass calcd. for $C_{17}H_{13}F_4N_5O$, 379.1; m/z found, 380.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 9.08 (d, J = 2.0 Hz, 1H), 8.92 (d, J = 5.1 Hz, 1H), 8.73 – 8.68 (m, 1H), 8.45 – 8.41 (m, 1H), 8.38 – 8.33 (m, 1H), 8.22 (dd, J = 5.2, 1.7 Hz, 1H), 5.55 – 5.38 (m, 1H), 5.40 – 5.36 (m, 1H), 5.35 (d, J = 17.2 Hz, 1H), 4.61 – 4.49 (m, 1H), 4.37 – 4.20 (m, 2H), 4.03 – 3.92 (m, 1H).

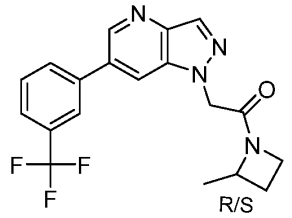
Example 86: 1-(3-Methylazetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone trifluoroacetate salt.



The title compound was prepared in a manner analogous to Example 16, using 3-methylazetidine in place of 3-fluoroazetidine hydrochloride and DCM in place of DMF. MS (ESI): mass calcd.

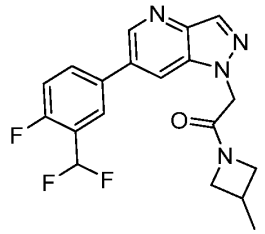
for $C_{19}H_{17}F_3N_4O$, 374.1; m/z found, 375.2 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.95 (d, J = 1.9 Hz, 1H), 8.52 – 8.50 (m, 1H), 8.38 – 8.36 (m, 1H), 8.17 – 8.13 (m, 2H), 7.86 – 7.77 (m, 2H), 5.28 (s, 2H), 4.30 (t, J = 8.4 Hz, 1H), 4.04 – 3.98 (m, 1H), 3.78 – 3.73 (m, 1H), 3.49 – 3.44 (m, 1H), 2.79 – 2.69 (m, 1H), 1.21 (d, J = 6.9 Hz, 3H).

Example 87: (Racemic) 1-(2-Methylazetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



The title compound was prepared in a manner analogous to Example 15, using 2-methylazetidine hydrochloride in place of 1-methylazetidin-3-amine and DCM in place of DMF. MS (ESI): mass calcd. for $C_{19}H_{17}F_3N_4O$, 374.1; m/z found, 375.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.95 – 8.92 (m, 1H), 8.53 – 8.49 (m, 1H), 8.38 – 8.35 (m, 1H), 8.17 – 8.12 (m, 2H), 7.85 – 7.76 (m, 2H), 5.38 – 5.16 (m, 2H), 4.79 – 3.77 (m, 3H), 2.48 – 2.34 (m, 1H), 1.92 – 1.81 (m, 1H), 1.58 – 1.31 (m, 3H).

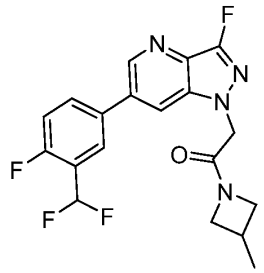
Example 88: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methylazetidin-1-yl)ethanone.



The title compound was made in a manner analogous to Example 5, Method A, using 2-chloro-1-(3-methylazetidin-1-yl)ethan-1-one (Intermediate 6) in place of 2-chloro-1-(3-fluoroazetidin-1-yl)ethanone. MS (ESI): mass calcd. for $C_{19}H_{17}F_3N_4O$, 374.1; m/z found, 375.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.88 (d, J = 2.0 Hz, 1H), 8.43 (dd, J = 2.0, 1.0 Hz, 1H), 8.35 (d, J = 0.9 Hz, 1H), 8.08 – 8.03 (m, 2H), 7.62 – 7.54 (m, 1H), 7.30 (t, J = 54.1 Hz, 1H), 5.26 (s, 2H), 4.32 –

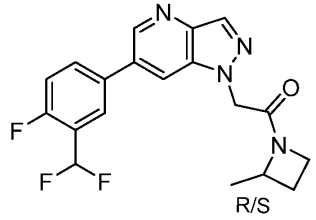
4.26 (m, 1H), 4.04 – 3.99 (m, 1H), 3.78 – 3.73 (m, 1H), 3.49 – 3.43 (m, 1H), 2.78 – 2.68 (m, 1H), 1.21 (d, J = 6.9 Hz, 3H).

Example 89: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methylazetidin-1-yl)ethanone.



The title compound was made in a manner analogous to Example 6, Method A, using 6-(3-(difluoromethyl)-4-fluorophenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridine (Intermediate 21) in place of Intermediate 10 and 2-chloro-1-(3-methylazetidin-1-yl)ethan-1-one (Intermediate 6) in place of 4-fluoro-3-methylphenylboronic acid. MS (ESI): mass calcd. for $C_{19}H_{16}F_4N_4O$, 392.1; m/z found, 393.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.93 (d, J = 1.8 Hz, 1H), 8.52 – 8.44 (m, 1H), 8.13 – 8.00 (m, 2H), 7.65 – 7.55 (m, 1H), 7.31 (t, J = 54.1 Hz, 1H), 5.16 (s, 2H), 4.37 – 4.28 (m, 1H), 4.06 – 3.96 (m, 1H), 3.83 – 3.74 (m, 1H), 3.51 – 3.41 (m, 1H), 2.82 – 2.67 (m, 1H), 1.21 (d, J = 6.9 Hz, 3H).

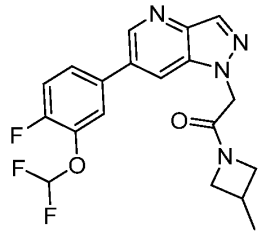
Example 90: (Racemic) 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-(2-methylazetidin-1-yl)ethanone.



The title compound was prepared in a manner analogous to Example 1 using 2-methylazetidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{19}H_{17}F_3N_4O$, 374.1; m/z found, 375.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.82 – 8.76 (m, 1H), 8.33 – 8.26 (m, 1H), 7.98 (d, J = 13.5 Hz, 1H), 7.89 – 7.84 (m, 1H), 7.79 – 7.72 (m, 1H), 7.32 – 7.25 (m, 1H), 6.98 (t,

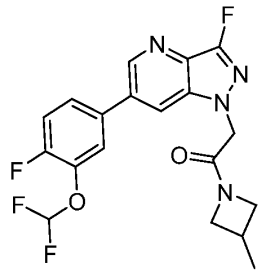
J = 54.8 Hz, 1H), 5.16 – 4.88 (m, 2H), 4.71 – 4.48 (m, 1H), 4.18 – 3.88 (m, 2H), 2.62 – 2.38 (m, 1H), 1.98 – 1.84 (m, 1H), 1.64 (d, *J* = 6.3 Hz, 1H), 1.45 (d, *J* = 6.3 Hz, 2H).

Example 91: 2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methylazetidin-1-yl)ethanone.



The title compound was made in a manner analogous to Example 6, Method A, using 6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridine (Intermediate 17) in place of Intermediate 16 and 2-chloro-1-(3-methylazetidin-1-yl)ethan-1-one (Intermediate 6) in place of 2-chloro-*N*,*N*-dimethylacetamide. MS (ESI): mass calcd. for $C_{19}H_{17}F_3N_4O_2$, 390.1; m/z found, 391.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.88 (d, *J* = 1.9 Hz, 1H), 8.42 – 8.39 (m, 1H), 8.35 (d, *J* = 0.9 Hz, 1H), 7.83 (dd, *J* = 7.6, 2.3 Hz, 1H), 7.78 – 7.73 (m, 1H), 7.60 (dd, *J* = 10.5, 8.6 Hz, 1H), 7.38 (t, *J* = 73.2 Hz, 1H), 5.25 (s, 2H), 4.33 – 4.26 (m, 1H), 4.05 – 3.97 (m, 1H), 3.79 – 3.73 (m, 1H), 3.49 – 3.44 (m, 1H), 2.78 – 2.68 (m, 1H), 1.21 (d, *J* = 6.9 Hz, 3H).

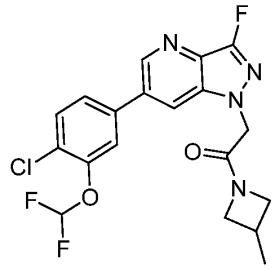
Example 92: 2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methylazetidin-1-yl)ethanone.



The title compound was made in a manner analogous to Example 5, Method A, using 6-(3-(difluoromethoxy)-4-fluorophenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridine (Intermediate 23) in place of Intermediate 16 and 2-chloro-1-(3-methylazetidin-1-yl)ethan-1-one (Intermediate 6) in place of Intermediate 1. MS (ESI): mass calcd. for $C_{19}H_{16}F_4N_4O_2$, 408.1; m/z found, 409.2

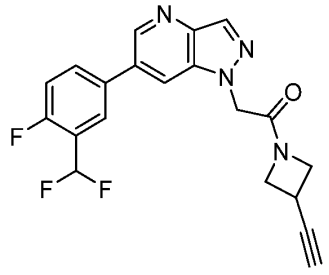
[M+H]$^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.93 (d, J = 1.8 Hz, 1H), 8.51 – 8.38 (m, 1H), 7.89 – 7.82 (m, 1H), 7.82 – 7.72 (m, 1H), 7.62 (dd, J = 10.7, 8.4 Hz, 1H), 7.38 (t, J = 73.2 Hz, 1H), 5.15 (s, 2H), 4.40 – 4.26 (m, 1H), 4.07 – 3.94 (m, 1H), 3.84 – 3.71 (m, 1H), 3.51 – 3.41 (m, 1H), 2.82 – 2.67 (m, 1H), 1.21 (d, J = 6.9 Hz, 3H).

Example 93: 2-[6-[4-Chloro-3-(difluoromethoxy)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methylazetidin-1-yl)ethanone.



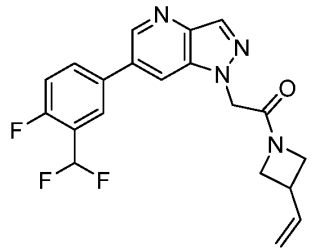
The title compound was made in a manner analogous to Example 5, Method A, using 6-(4-chloro-3-(difluoromethoxy)phenyl)-1H-pyrazolo[4,3-b]pyridine (Intermediate 22) in place of Intermediate 16 and 2-chloro-1-(3-methylazetidin-1-yl)ethan-1-one (Intermediate 6) in place of Intermediate 1. MS (ESI): mass calcd. for $C_{19}H_{16}ClF_3N_4O_2$, 424.1; m/z found, 425.1 [M+H]$^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.95 (d, J = 1.8 Hz, 1H), 8.52 – 8.44 (m, 1H), 7.86 – 7.78 (m, 2H), 7.75 (dd, J = 8.4, 2.0 Hz, 1H), 7.44 (t, J = 73.2 Hz, 1H), 5.15 (s, 2H), 4.38 – 4.27 (m, 1H), 4.06 – 3.94 (m, 1H), 3.84 – 3.74 (m, 1H), 3.51 – 3.41 (m, 1H), 2.82 – 2.67 (m, 1H), 1.21 (d, J = 6.9 Hz, 3H).

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



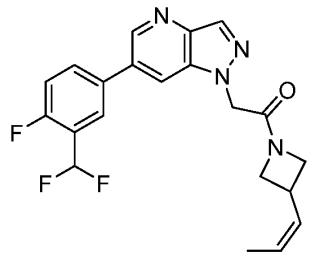
The title compound was prepared in a manner analogous to Example 2 using 3-ethynylazetidine (Intermediate 33) in place of 3-methyleneazetidine. MS (ESI): mass calcd. for $C_{20}H_{15}F_3N_4O$, 384.1; m/z found, 385.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, J = 1.9 Hz, 1H), 8.30 (d, J = 1.0 Hz, 1H), 7.93 (dd, J = 1.9, 1.0 Hz, 1H), 7.90 – 7.84 (m, 1H), 7.78 – 7.71 (m, 1H), 7.32 – 7.27 (m, 1H), 6.98 (t, J = 54.9 Hz, 1H), 5.17 – 4.89 (m, 2H), 4.37 – 4.25 (m, 2H), 4.18 – 4.03 (m, 2H), 3.55 – 3.28 (m, 1H), 2.32 (d, J = 2.4 Hz, 1H).

Example 95: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-(3-vinylazetidin-1-yl)ethanone.



The title compound was prepared in a manner analogous to Example 2 using 3-ethenylazetidine in place of 3-methyleneazetidine. MS (ESI): mass calcd. for $C_{20}H_{17}F_3N_4O$, 386.1; m/z found, 387.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.79 (d, J = 1.9 Hz, 1H), 8.29 (d, J = 1.0 Hz, 1H), 7.95 (dd, J = 1.9, 1.0 Hz, 1H), 7.90 – 7.82 (m, 1H), 7.77 – 7.69 (m, 1H), 7.33 – 7.21 (m, 1H), 6.98 (t, J = 54.8 Hz, 1H), 5.95 (ddd, J = 17.0, 10.4, 7.7 Hz, 1H), 5.16 – 5.08 (m, 2H), 5.07 (s, 2H), 4.31 – 4.18 (m, 2H), 3.96 – 3.82 (m, 2H), 3.37 – 3.24 (m, 1H).

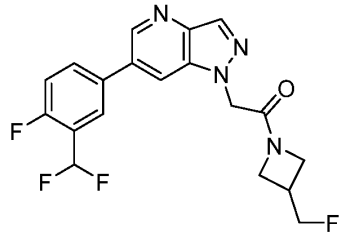
Example 96: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-[3-[(*Z*)-prop-1-enyl]azetidin-1-yl]ethanone.



The title compound was prepared in a manner analogous to Example 2 using (*Z*)-3-(prop-1-en-1-yl)azetidine (Intermediate 34) in place of 3-methyleneazetidine. MS (ESI): mass calcd. for

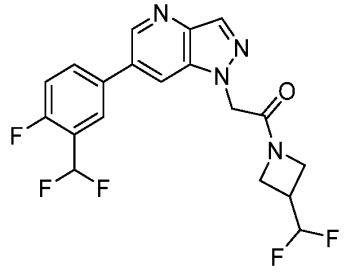
$C_{21}H_{19}F_3N_4O$, 400.2; m/z found, 401.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, J = 1.9 Hz, 1H), 8.29 (d, J = 1.0 Hz, 1H), 7.96 (dd, J = 1.9, 1.0 Hz, 1H), 7.89 – 7.84 (m, 1H), 7.79 – 7.68 (m, 1H), 7.33 – 7.27 (m, 1H), 6.98 (t, J = 54.9 Hz, 1H), 5.65 – 5.49 (m, 2H), 5.06 (t, J = 1.9 Hz, 2H), 4.35 – 4.23 (m, 2H), 3.90 – 3.76 (m, 2H), 3.64 – 3.51 (m, 1H), 1.60 – 1.56 (m, 3H).

Example 97: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-[3-(fluoromethyl)azetidin-1-yl]ethanone.



The title compound was prepared in a manner analogous to Example 1 using 3-fluoromethylazetidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{19}H_{16}F_4N_4O$, 392.1; m/z found, 393.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, J = 1.9 Hz, 1H), 8.30 (d, J = 1.0 Hz, 1H), 7.95 (dd, J = 2.0, 1.0 Hz, 1H), 7.89 – 7.85 (m, 1H), 7.79 – 7.71 (m, 1H), 7.34 – 7.27 (m, 1H), 6.98 (t, J = 54.9 Hz, 1H), 5.08 (d, J = 4.0 Hz, 2H), 4.51 (dd, J = 46.9, 5.2 Hz, 2H), 4.25 – 4.10 (m, 2H), 4.04 – 3.89 (m, 2H), 3.06 – 2.88 (m, 1H).

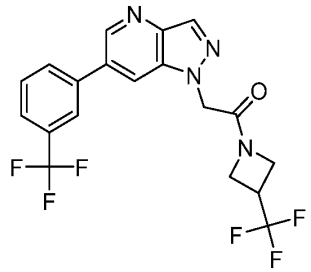
Example 98: 1-[3-(Difluoromethyl)azetidin-1-yl]-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]ethanone.



The title compound was prepared in a manner analogous to Example 1 using 3-(difluoromethyl)azetidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{19}H_{15}F_5N_4O$, 410.1; m/z found, 411.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, J = 1.9 Hz, 1H), 8.30 (d, J = 0.9 Hz, 1H), 7.94 (dd, J = 1.9, 1.0 Hz, 1H), 7.89 – 7.84 (m, 1H), 7.80 –

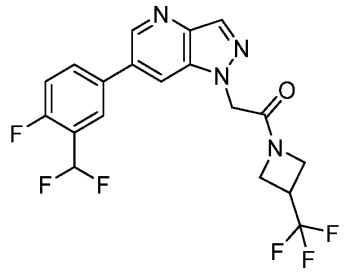
7.70 (m, 1H), 7.34 – 7.28 (m, 1H), 6.98 (t, J = 54.9 Hz, 1H), 5.94 (td, J = 55.9, 3.7 Hz, 1H), 5.22 – 4.98 (m, 2H), 4.25 – 3.97 (m, 4H), 3.15 – 2.93 (m, 1H).

Example 99: 1-[3-(Trifluoromethyl)azetidin-1-yl]-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone trifluoroacetate salt.



The title compound was prepared in a manner analogous to Example 16, using 3-(trifluoromethyl)azetidine hydrochloride in place of 3-fluoroazetidine hydrochloride. MS (ESI): mass calcd. for $C_{19}H_{14}F_6N_4O$, 428.1; m/z found, 429.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.95 (d, J = 1.9 Hz, 1H), 8.50 – 8.49 (m, 1H), 8.40 – 8.38 (m, 1H), 8.16 – 8.12 (m, 2H), 7.85 – 7.77 (m, 2H), 5.43 – 5.31 (m, 2H), 4.48 (t, J = 9.1 Hz, 1H), 4.28 (dd, J = 9.4, 5.4 Hz, 1H), 4.16 (t, J = 9.6 Hz, 1H), 3.91 (dd, J = 10.3, 5.4 Hz, 1H).

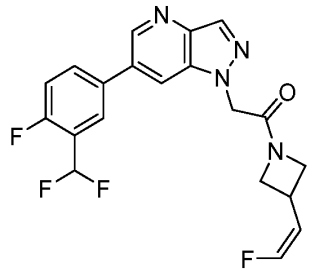
Example 100: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-[3-(trifluoromethyl)azetidin-1-yl]ethanone.



The title compound was prepared in a manner analogous to Example 1 using 3-trifluoromethylazetidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{19}H_{14}F_6N_4O$, 428.1; m/z found, 429.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.82 (d, J = 1.9 Hz, 1H), 8.31 (d, J = 1.0 Hz, 1H), 7.93 (dd, J = 1.9, 1.0 Hz, 1H), 7.89 – 7.83 (m, 1H), 7.79 –

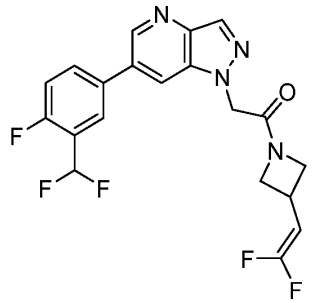
7.71 (m, 1H), 7.34 – 7.26 (m, 1H), 6.98 (t, *J* = 54.8 Hz, 1H), 5.17 – 4.95 (m, 2H), 4.30 – 4.08 (m, 4H), 3.37 – 3.16 (m, 1H).

Example 101: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-[3-[(Z)-2-fluorovinyl]azetidin-1-yl]ethanone.



The title compound was prepared in a manner analogous to Example 2 using (*Z*)-3-(2-fluorovinyl)azetidine (Intermediate 36) in place of 3-methyleneazetidine. MS (ESI): mass calcd. for $C_{20}H_{16}F_4N_4O$, 404.1; m/z found, 405.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.79 (d, *J* = 1.9 Hz, 1H), 8.29 (d, *J* = 1.0 Hz, 1H), 7.95 (dd, *J* = 2.0, 1.0 Hz, 1H), 7.89 – 7.82 (m, 1H), 7.78 – 7.70 (m, 1H), 7.32 – 7.24 (m, 1H), 6.97 (t, *J* = 54.8 Hz, 1H), 6.48 (ddd, *J* = 83.3, 4.7, 1.2 Hz, 1H), 5.06 (s, 2H), 5.05 – 4.91 (m, 1H), 4.36 – 4.24 (m, 2H), 3.88 (ddd, *J* = 30.9, 9.4, 6.2 Hz, 2H), 3.76 – 3.66 (m, 1H).

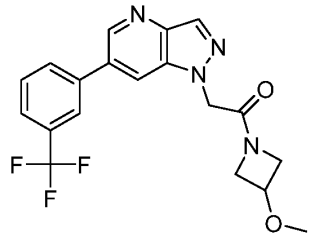
Example 102: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-[3-(2,2-difluorovinyl)azetidin-1-yl]ethanone.



The title compound was prepared in a manner analogous to Example 2 using 3-(2,2-difluorovinyl)azetidine (Intermediate 35) in place of 3-methyleneazetidine. MS (ESI): mass calcd. for $C_{20}H_{15}F_5N_4O$, 422.1; m/z found, 423.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.81

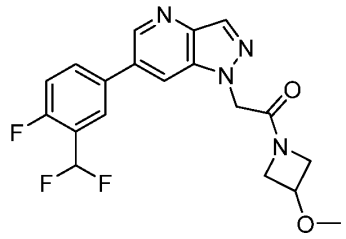
(d, J = 1.9 Hz, 1H), 8.30 (d, J = 1.0 Hz, 1H), 7.94 (dd, J = 1.9, 1.0 Hz, 1H), 7.91 – 7.83 (m, 1H), 7.81 – 7.70 (m, 1H), 7.33 – 7.27 (m, 1H), 6.98 (t, J = 54.9 Hz, 1H), 5.06 (s, 2H), 4.43 (ddd, J = 24.2, 9.6, 1.7 Hz, 1H), 4.35 – 4.24 (m, 2H), 3.95 – 3.80 (m, 2H), 3.53 – 3.40 (m, 1H).

Example 103: 1-(3-Methoxyazetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



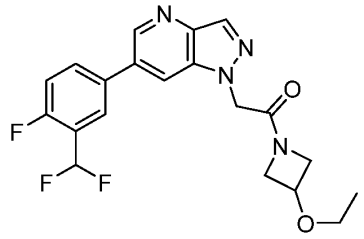
The title compound was prepared in a manner analogous to Example 16, using 3-methoxyazetidine hydrochloride in place of 3-fluoroazetidine hydrochloride and DCM in place of DMF. MS (ESI): mass calcd. for $C_{19}H_{17}F_3N_4O_2$, 390.1; m/z found, 391.2 $[M+H]^+$. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.94 (d, J = 1.9 Hz, 1H), 8.52 – 8.50 (m, 1H), 8.37 (d, J = 1.0 Hz, 1H), 8.17 – 8.12 (m, 2H), 7.86 – 7.75 (m, 2H), 5.40 – 5.25 (m, 2H), 4.42 – 4.35 (m, 1H), 4.30 – 4.23 (m, 1H), 4.13 – 4.01 (m, 2H), 3.72 (dd, J = 10.5, 3.8 Hz, 1H), 3.23 (s, 3H).

Example 104: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-(3-methoxyazetidin-1-yl)ethanone.



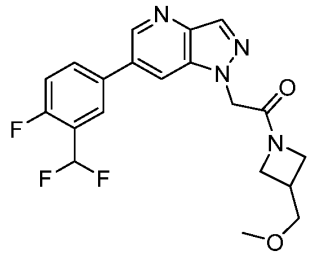
The title compound was prepared in a manner analogous to Example 1 using 3-methoxyazetidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{19}H_{17}F_3N_4O_2$, 390.1; m/z found, 391.2 $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, J = 1.9 Hz, 1H), 8.30 (d, J = 1.0 Hz, 1H), 7.94 (dd, J = 2.0, 1.0 Hz, 1H), 7.86 (d, J = 6.5 Hz, 1H), 7.80 – 7.68 (m, 1H), 7.33 – 7.26 (m, 1H), 6.98 (t, J = 54.9 Hz, 1H), 5.08 (d, J = 2.3 Hz, 2H), 4.29 – 4.13 (m, 3H), 4.00 – 3.88 (m, 2H), 3.28 (s, 3H).

Example 105: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-(3-ethoxyazetidin-1-yl)ethanone.



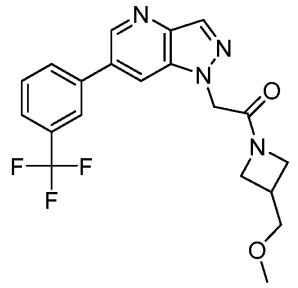
The title compound was prepared in a manner analogous to Example 1 using 3-ethoxyazetidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{20}H_{19}F_3N_4O_2$, 404.1; m/z found, 405.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, J = 1.9 Hz, 1H), 8.29 (d, J = 1.0 Hz, 1H), 7.94 (dd, J = 1.9, 1.0 Hz, 1H), 7.90 – 7.83 (m, 1H), 7.80 – 7.71 (m, 1H), 7.34 – 7.27 (m, 1H), 6.98 (t, J = 54.9 Hz, 1H), 5.15 – 5.00 (m, 2H), 4.34 – 4.16 (m, 3H), 4.02 – 3.89 (m, 2H), 3.47 – 3.37 (m, 2H), 1.20 (t, J = 7.0 Hz, 3H).

Example 106: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-[3-(methoxymethyl)azetidin-1-yl]ethanone.



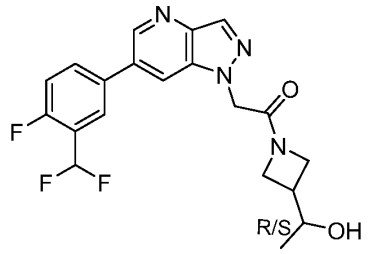
The title compound was prepared in a manner analogous to Example 1 using 3-(methoxymethyl)azetidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{20}H_{19}F_3N_4O_2$, 404.1; m/z found, 405.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, J = 1.9 Hz, 1H), 8.29 (d, J = 1.0 Hz, 1H), 7.95 (dd, J = 1.9, 1.0 Hz, 1H), 7.90 – 7.84 (m, 1H), 7.81 – 7.73 (m, 1H), 7.34 – 7.26 (m, 1H), 6.98 (t, J = 54.8 Hz, 1H), 5.21 – 4.84 (m, 2H), 4.24 – 4.03 (m, 2H), 3.99 – 3.77 (m, 2H), 3.53 – 3.44 (m, 2H), 3.35 (s, 3H), 2.92 – 2.80 (m, 1H).

Example 107: 1-[3-(Methoxymethyl)azetidin-1-yl]-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



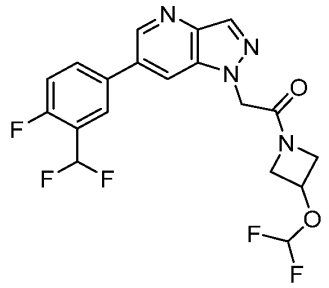
The title compound was prepared in a manner analogous to Example 16, using 3-(methoxymethyl)azetidine hydrochloride in place of 3-fluoroazetidine hydrochloride and DCM in place of DMF. MS (ESI): mass calcd. for $C_{20}H_{19}F_3N_4O_2$, 404.2; m/z found, 405.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.94 (d, J = 2.0 Hz, 1H), 8.51 – 8.49 (m, 1H), 8.38 – 8.36 (m, 1H), 8.17 – 8.13 (m, 2H), 7.85 – 7.77 (m, 2H), 5.28 (s, 2H), 4.23 (t, J = 8.5 Hz, 1H), 3.97 – 3.90 (m, 2H), 3.62 (dd, J = 9.7, 5.6 Hz, 1H), 3.49 (d, J = 6.4 Hz, 2H), 3.28 (s, 3H), 2.92 – 2.82 (m, 1H).

Example 108: (Racemic) 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-[3-(1-hydroxyethyl)azetidin-1-yl]ethanone.



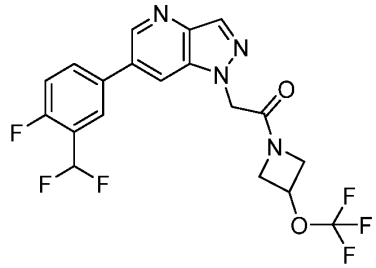
The title compound was prepared in a manner analogous to Example 1 using 1-(azetidine-3-yl)ethan-1-ol in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{20}H_{19}F_3N_4O_2$, 404.1; m/z found, 405.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.79 (d, J = 1.9 Hz, 1H), 8.37 – 8.24 (m, 1H), 8.01 – 7.92 (m, 1H), 7.92 – 7.83 (m, 1H), 7.83 – 7.68 (m, 1H), 7.34 – 7.22 (m, 1H), 6.97 (t, J = 54.9 Hz, 1H), 5.17 – 4.92 (m, 2H), 4.20 – 3.76 (m, 6H), 2.60 (dtd, J = 14.7, 6.1, 2.3 Hz, 1H), 1.14 (dd, J = 6.3, 0.9 Hz, 3H).

Example 109: 1-[3-(Difluoromethoxy)azetidin-1-yl]-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]ethanone.



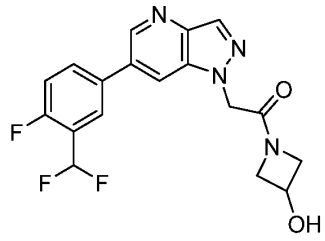
The title compound was prepared in a manner analogous to Example 1 using 3-(difluoromethoxy)azetidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{19}H_{15}F_5N_4O_2$, 426.1; m/z found, 427.0 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, J = 1.9 Hz, 1H), 8.31 (d, J = 1.0 Hz, 1H), 7.93 (dd, J = 1.9, 1.0 Hz, 1H), 7.91 – 7.85 (m, 1H), 7.81 – 7.68 (m, 1H), 7.34 – 7.27 (m, 1H), 6.98 (t, J = 54.8 Hz, 1H), 6.23 (t, J = 72.3 Hz, 1H), 5.08 (d, J = 1.3 Hz, 2H), 5.02 – 4.90 (m, 1H), 4.43 – 4.31 (m, 2H), 4.17 – 4.06 (m, 2H).

Example 110: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-[3-(trifluoromethoxy)azetidin-1-yl]ethanone.



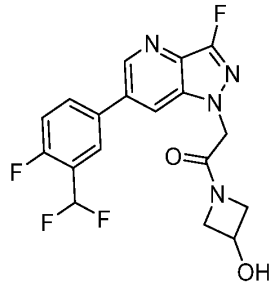
The title compound was prepared in a manner analogous to Example 1 using 3-(trifluoromethoxy)azetidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{19}H_{14}F_6N_4O_2$, 444.1; m/z found, 445.0 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.82 (d, J = 1.9 Hz, 1H), 8.31 (d, J = 1.0 Hz, 1H), 7.93 (dd, J = 1.9, 1.0 Hz, 1H), 7.89 – 7.85 (m, 1H), 7.79 – 7.71 (m, 1H), 7.30 (t, J = 9.1 Hz, 1H), 6.98 (t, J = 54.8 Hz, 1H), 5.09 (d, J = 2.8 Hz, 2H), 4.99 – 4.89 (m, 1H), 4.42 – 4.34 (m, 2H), 4.24 – 4.14 (m, 2H).

Example 111: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-(3-hydroxyazetidin-1-yl)ethanone.



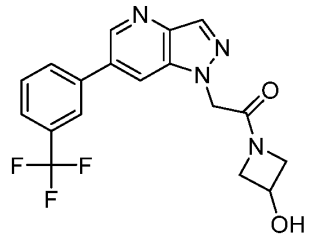
The title compound was prepared in a manner analogous to Example 1 using azetidin-3-ol in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{18}H_{15}F_3N_4O_2$, 376.1; m/z found, 377.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, J = 1.9 Hz, 1H), 8.29 (d, J = 1.0 Hz, 1H), 7.95 – 7.92 (m, 1H), 7.89 – 7.84 (m, 1H), 7.78 – 7.71 (m, 1H), 7.32 – 7.26 (m, 1H), 6.98 (t, J = 54.9 Hz, 1H), 5.08 (s, 2H), 4.73 – 4.63 (m, 1H), 4.34 – 4.27 (m, 2H), 3.98 – 3.89 (m, 2H).

Example 112: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-hydroxyazetidin-1-yl)ethanone.



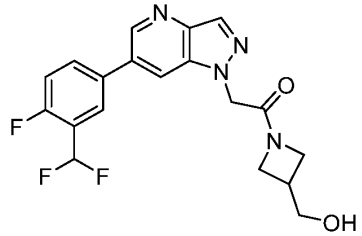
The title compound was prepared in a manner analogous to Example 1 using 2-(6-(3-(difluoromethyl)-4-fluorophenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid (Intermediate 28) in place of Intermediate 27 and azetidin-3-ol in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{18}H_{14}F_4N_4O_2$, 394.1; m/z found, 395.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.93 (d, J = 1.9 Hz, 1H), 8.52 – 8.45 (m, 1H), 8.13 – 8.03 (m, 2H), 7.63 – 7.55 (m, 1H), 7.31 (t, J = 54.1 Hz, 1H), 5.79 (d, J = 5.8 Hz, 1H), 5.20 (d, J = 17.0 Hz, 1H), 5.16 (d, J = 16.7 Hz, 1H), 4.56 – 4.49 (m, 1H), 4.42 – 4.36 (m, 1H), 4.13 – 4.06 (m, 1H), 4.00 – 3.92 (m, 1H), 3.68 – 3.59 (m, 1H).

Example 113: 1-(3-Hydroxyazetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone trifluoroacetate salt.



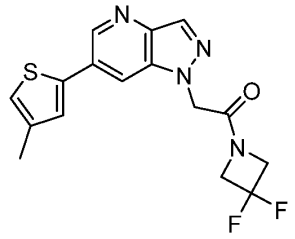
The title compound was prepared in a manner analogous to Example 15, using azetidin-3-ol hydrochloride in place of 1-methylazetidin-3-amine. MS (ESI): mass calcd. for $C_{18}H_{15}F_3N_4O_2$, 376.1; m/z found, 377.0 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.95 (d, J = 1.9 Hz, 1H), 8.54 – 8.51 (m, 1H), 8.39 – 8.36 (m, 1H), 8.17 – 8.13 (m, 2H), 7.86 – 7.76 (m, 2H), 5.31 (d, J = 2.7 Hz, 2H), 4.56 – 4.48 (m, 1H), 4.39 – 4.32 (m, 1H), 4.13 – 4.08 (m, 1H), 3.96 – 3.91 (m, 1H), 3.68 – 3.62 (m, 1H).

Example 114: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-[3-(hydroxymethyl)azetidin-1-yl]ethanone.



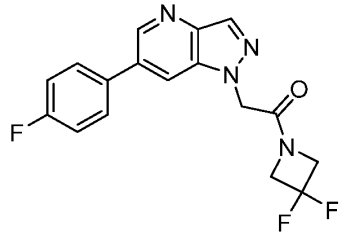
The title compound was prepared in a manner analogous to Example 1 using 3-(hydroxymethyl)azetidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{19}H_{17}F_3N_4O_2$, 390.1; m/z found, 391.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.79 (d, J = 1.9 Hz, 1H), 8.29 (d, J = 0.9 Hz, 1H), 7.96 (dd, J = 1.9, 1.0 Hz, 1H), 7.88 – 7.84 (m, 1H), 7.78 – 7.71 (m, 1H), 7.32 – 7.27 (m, 1H), 6.97 (t, J = 54.8 Hz, 1H), 5.07 (s, 2H), 4.16 (t, J = 8.6 Hz, 1H), 4.09 (dd, J = 10.1, 8.6 Hz, 1H), 3.97 (dd, J = 8.8, 5.4 Hz, 1H), 3.86 (dd, J = 10.3, 5.5 Hz, 1H), 3.75 (d, J = 5.9 Hz, 2H), 2.81 (tt, J = 8.5, 5.6 Hz, 1H), 2.08 (s, 1H).

Example 115: 1-(3,3-Difluoroazetidin-1-yl)-2-[6-(4-methyl-2-thienyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone.



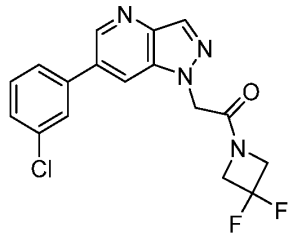
The title compound was prepared in a manner analogous to Example 17, using 4-methylthiophene-2-boronic acid pinacol ester in place of 2,4-difluorophenylboronic acid and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane in place of [1,1′-Bis(diphenylphosphino)ferrocene]dichloropalladium(II). The reaction mixture was heated to 90 °C. MS (ESI): mass calcd. for $C_{16}H_{14}F_2N_4OS$, 348.1; m/z found, 349.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.86 (d, J = 1.9 Hz, 1H), 8.33 – 8.31 (m, 1H), 8.27 – 8.25 (m, 1H), 7.57 – 7.54 (m, 1H), 7.28 – 7.25 (m, 1H), 5.39 (s, 2H), 4.75 (t, J = 12.4 Hz, 2H), 4.39 (t, J = 12.5 Hz, 2H), 2.30 – 2.26 (m, 3H).

Example 116: 1-(3,3-Difluoroazetidin-1-yl)-2-[6-(4-fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone.



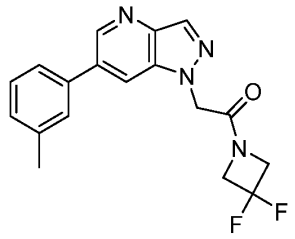
The title compound was prepared in a manner analogous to Example 1 using 2-(6-(4-fluorophenyl)-1H-pyrazolo[4,3-*b*]pyridin-1-yl)acetic acid (Intermediate 31) in place of Intermediate 16 and 3,3-difluoroazetidine in place of 3-(trifluoromethyl)azetidin-3-ol. MS (ESI): mass calcd. for $C_{17}H_{13}F_3N_4O$, 346.1; m/z found, 347.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.83 (d, J = 1.9 Hz, 1H), 8.31 (d, J = 1.0 Hz, 1H), 7.89 (dd, J = 1.9, 1.0 Hz, 1H), 7.66 – 7.60 (m, 2H), 7.25 – 7.18 (m, 2H), 5.14 (s, 2H), 4.42-4.26 (m, 4H).

Example 117: 2-[6-(3-Chlorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3,3-difluoroazetidin-1-yl)ethanone.



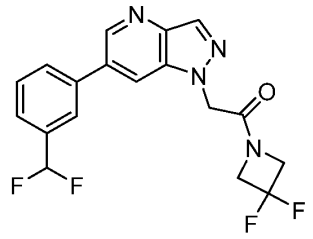
The title compound was prepared in a manner analogous to Example 17, using (3-chlorophenyl)boronic acid in place of 2,4-difluorophenylboronic acid and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II) complex with dichloromethane in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). MS (ESI): mass calcd. for $C_{17}H_{13}ClF_2N_4O$, 362.1; m/z found, 363.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.90 (d, J = 1.9 Hz, 1H), 8.45 – 8.43 (m, 1H), 8.38 – 8.37 (m, 1H), 7.89 (t, J = 1.8 Hz, 1H), 7.82 – 7.78 (m, 1H), 7.61 – 7.51 (m, 2H), 5.42 (s, 2H), 4.74 (t, J = 12.4 Hz, 2H), 4.38 (t, J = 12.6 Hz, 2H).

Example 118: 1-(3,3-Difluoroazetidin-1-yl)-2-[6-(m-tolyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone.



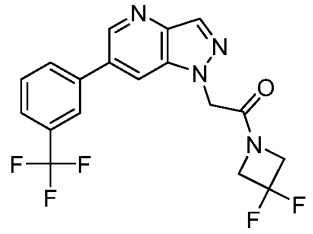
The title compound was prepared in a manner analogous to Example 17, using *m*-tolylboronic acid in place of 2,4-difluorophenylboronic acid and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). The reaction mixture was heated to 90 °C. MS (ESI): mass calcd. for $C_{18}H_{16}F_2N_4O$, 342.1; m/z found, 343.2 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.89 – 8.83 (m, 1H), 8.39 – 8.31 (m, 2H), 7.66 – 7.56 (m, 2H), 7.44 (t, J = 7.6 Hz, 1H), 7.32 – 7.24 (m, 1H), 5.41 (s, 2H), 4.74 (t, J = 12.5 Hz, 2H), 4.38 (t, J = 12.4 Hz, 2H), 2.42 (s, 3H).

Example 119: 1-(3,3-Difluoroazetidin-1-yl)-2-[6-[3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



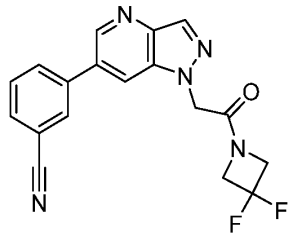
The title compound was prepared in a manner analogous to Example 17, using (3-(difluoromethyl)phenyl)boronic acid in place of 2,4-difluorophenylboronic acid and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II) complex with dichloromethane in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). MS (ESI): mass calcd. for $C_{18}H_{14}F_4N_4O$, 378.1; m/z found, 379.0 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.90 (d, J = 2.0 Hz, 1H), 8.44 – 8.42 (m, 1H), 8.39 – 8.37 (m, 1H), 8.01 – 7.97 (m, 2H), 7.74 – 7.65 (m, 2H), 7.14 (t, J = 55.8 Hz, 1H), 5.43 (s, 2H), 4.74 (t, J = 12.4 Hz, 2H), 4.38 (t, J = 12.5 Hz, 2H).

Example 120: 1-(3,3-Difluoroazetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone trifluoroacetate salt.



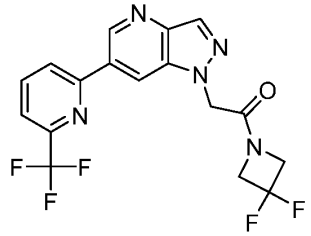
The title compound was prepared in a manner analogous to Example 15, using 3,3-difluoroazetidine hydrochloride in place of 1-methylazetidin-3-amine. MS (ESI): mass calcd. for $C_{18}H_{13}F_5N_4O$, 396.1; m/z found, 397.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.95 (d, J = 1.9 Hz, 1H), 8.50 – 8.47 (m, 1H), 8.40 (d, J = 0.9 Hz, 1H), 8.16 – 8.11 (m, 2H), 7.86 – 7.77 (m, 2H), 5.43 (s, 2H), 4.73 (t, J = 12.4 Hz, 2H), 4.38 (t, J = 12.5 Hz, 2H).

Example 121: 3-[1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]pyrazolo[4,3-b]pyridin-6-yl]benzonitrile.



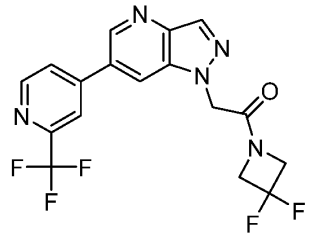
The title compound was prepared in a manner analogous to Example 17, using (3-cyanophenyl)boronic acid in place of 2,4-difluorophenylboronic acid, [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II) complex with dichloromethane in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), and sodium carbonate in place of cesium carbonate. MS (ESI): mass calcd. for $C_{18}H_{13}F_2N_5O$, 353.1; m/z found, 354.2 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ8.98 – 8.93 (m, 1H), 8.52 – 8.49 (m, 1H), 8.41 – 8.39 (m, 1H), 8.34 – 8.31 (m, 1H), 8.21 – 8.16 (m, 1H), 7.97 – 7.92 (m, 1H), 7.81 – 7.73 (t, J = 7.9 Hz, 1H), 5.42 (s, 2H), 4.75 (t, J = 12.1 Hz, 2H), 4.39 (t, J = 12.6 Hz, 2H).

Example 122: 1-(3,3-Difluoroazetidin-1-yl)-2-[6-[6-(trifluoromethyl)-2-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone trifluoroacetate salt



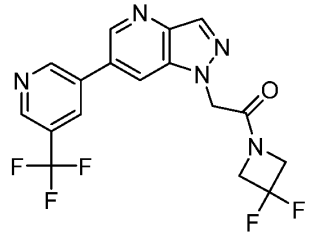
The title compound was prepared in a manner analogous to Example 17, using 6-(trifluoromethyl)pyridine-2-boronic acid pinacol ester in place of 2,4-difluorophenylboronic acid and palladium-tetrakis(triphenylphosphine) in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). MS (ESI): mass calcd. for $C_{17}H_{12}F_5N_5O$, 397.1; m/z found, 398.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 9.28 (s, 1H), 8.74 (s, 1H), 8.48 – 8.41 (m, 2H), 8.29 (t, J = 7.9 Hz, 1H), 7.97 (d, J = 7.7 Hz, 1H), 5.48 (s, 2H), 4.77 (t, J = 13.0 Hz, 2H), 4.39 (t, J = 12.5 Hz, 2H).

Example 123: 1-(3,3-Difluoroazetidin-1-yl)-2-[6-[2-(trifluoromethyl)-4-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



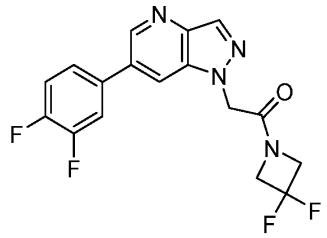
The title compound was prepared in a manner analogous to Example 17, using (2-(trifluoromethyl)pyridin-4-yl)boronic acid in place of 2,4-difluorophenylboronic acid and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). The reaction mixture was heated to 90 °C. MS (ESI): mass calcd. for $C_{17}H_{12}F_5N_5O$, 397.1; m/z found, 398.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 9.08 (d, J = 1.9 Hz, 1H), 8.94 – 8.91 (m, 1H), 8.70 – 8.67 (m, 1H), 8.46 – 8.44 (m, 1H), 8.37 – 8.34 (m, 1H), 8.23 – 8.20 (m, 1H), 5.45 (s, 2H), 4.75 (t, J = 12.3 Hz, 2H), 4.39 (t, J = 12.5 Hz, 2H).

Example 124: 1-(3,3-Difluoroazetidin-1-yl)-2-[6-[5-(trifluoromethyl)-3-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



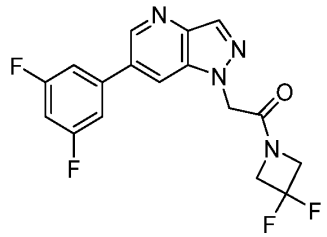
The title compound was prepared in a manner analogous to Example 17, using (5-(trifluoromethyl)pyridin-3-yl)boronic acid in place of 2,4-difluorophenylboronic acid and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). The reaction mixture was heated to 90 °C. MS (ESI): mass calcd. for $C_{17}H_{12}F_5N_5O$, 397.1; m/z found, 398.2 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 9.36 – 9.34 (m, 1H), 9.08 – 9.06 (m, 1H), 9.04 (d, J = 1.9 Hz, 1H), 8.66 – 8.63 (m, 1H), 8.62 – 8.59 (m, 1H), 8.44 – 8.42 (m, 1H), 5.43 (s, 2H), 4.74 (t, J = 12.6 Hz, 2H), 4.38 (t, J = 12.5 Hz, 2H).

Example 125: 1-(3,3-Difluoroazetidin-1-yl)-2-[6-(3,4-difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone.



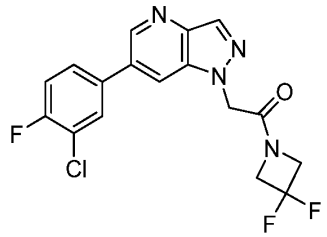
The title compound was prepared in a manner analogous to Example 17, using (3,4-difluorophenyl)boronic acid in place of 2,4-difluorophenylboronic acid and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II) complex with dichloromethane in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). MS (ESI): mass calcd. for $C_{17}H_{12}F_4N_4O$, 364.1; m/z found, 365.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.92 – 8.88 (m, 1H), 8.43 – 8.41 (m, 1H), 8.38 – 8.37 (m, 1H), 7.98 – 7.91 (m, 1H), 7.71 – 7.60 (m, 2H), 5.40 (s, 2H), 4.74 (t, J = 12.5 Hz, 2H), 4.38 (t, J = 12.5 Hz, 2H).

Example 126: 1-(3,3-Difluoroazetidin-1-yl)-2-[6-(3,5-difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone.



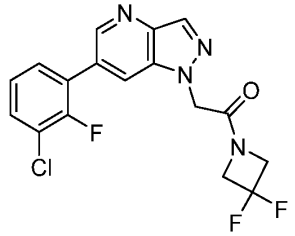
The title compound was prepared in a manner analogous to Example 17, using (3,5-difluorophenyl)boronic acid in place of 2,4-difluorophenylboronic acid. MS (ESI): mass calcd. for $C_{17}H_{12}F_4N_4O$, 364.1; m/z found, 365.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.95 (d, J = 2.0 Hz, 1H), 8.50 – 8.48 (m, 1H), 8.40 – 8.38 (m, 1H), 7.67 – 7.58 (m, 2H), 7.35 (tt, J = 9.3, 2.4 Hz, 1H), 5.41 (s, 2H), 4.73 (t, J = 12.4 Hz, 2H), 4.38 (t, J = 12.6 Hz, 2H).

Example 127: 2-[6-(3-Chloro-4-fluoro-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3,3-difluoroazetidin-1-yl)ethanone.



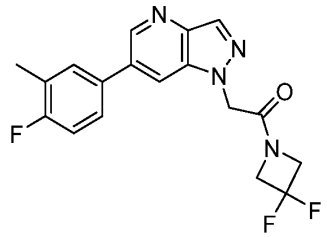
The title compound was prepared in a manner analogous to Example 17, using (3-chloro-4-fluorophenyl)boronic acid in place of 2,4-difluorophenylboronic acid and palladium-tetrakis(triphenylphosphine) in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). MS (ESI): mass calcd. for $C_{17}H_{12}ClF_3N_4O$, 380.1; m/z found, 381.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.89 (d, J = 1.9 Hz, 1H), 8.44 – 8.41 (m, 1H), 8.38 – 8.36 (m, 1H), 8.06 (dd, J = 7.1, 2.3 Hz, 1H), 7.85 (ddd, J = 8.6, 4.6, 2.4 Hz, 1H), 7.61 (t, J = 8.9 Hz, 1H), 5.41 (s, 2H), 4.73 (t, J = 12.4 Hz, 2H), 4.38 (t, J = 12.5 Hz, 2H).

Example 128: 2-[6-(3-Chloro-2-fluoro-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3,3-difluoroazetidin-1-yl)ethanone.



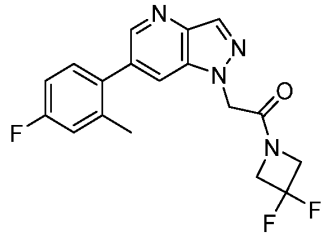
The title compound was prepared in a manner analogous to Example 17, using (3-chloro-2-fluorophenyl)boronic acid in place of 2,4-difluorophenylboronic acid and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). MS (ESI): mass calcd. for $C_{17}H_{12}ClF_3N_4O$, 380.1; m/z found, 381.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.72 (t, J = 1.9 Hz, 1H), 8.42 – 8.40 (m, 1H), 8.35 – 8.33 (m, 1H), 7.74 – 7.68 (m, 1H), 7.66 – 7.61 (m, 1H), 7.42 (td, J = 7.9, 1.0 Hz, 1H), 5.42 (s, 2H), 4.75 (t, J = 12.5 Hz, 2H), 4.37 (t, J = 12.6 Hz, 2H).

Example 129: 1-(3,3-Difluoroazetidin-1-yl)-2-[6-(4-fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone trifluoroacetate salt.



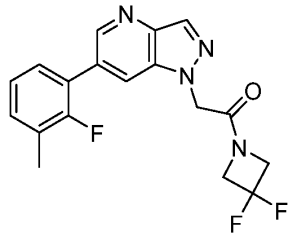
The title compound was prepared in a manner analogous to Example 13, using 2-(6-(4-fluoro-3-methylphenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid (Intermediate 52) in place of Intermediate 39 and 3,3-difluoroazetidine hydrochloride in place of morpholine. MS (ESI): mass calcd. for $C_{18}H_{15}F_3N_4O$, 360.1; m/z found, 361.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.85 (d, J = 1.9 Hz, 1H), 8.36 – 8.33 (m, 2H), 7.76 – 7.72 (m, 1H), 7.67 – 7.63 (m, 1H), 7.34 – 7.29 (m, 1H), 5.40 (s, 2H), 4.73 (t, J = 12.4 Hz, 2H), 4.38 (t, J = 12.6 Hz, 2H), 2.35 – 2.34 (m, 3H).

Example 130: 1-(3,3-Difluoroazetidin-1-yl)-2-[6-(4-fluoro-2-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone trifluoroacetate salt.



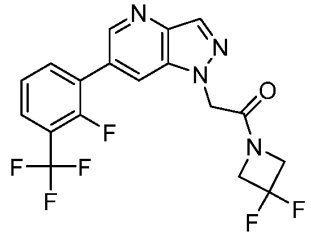
The title compound was prepared in a manner analogous to Example 1, using 2-(6-(4-fluoro-2-methylphenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid (Intermediate 53) in place of Intermediate 39 and 3,3-difluoropyrrolidine hydrochloride in place of morpholine. MS (ESI): mass calcd. for $C_{18}H_{15}F_3N_4O$, 360.1; m/z found, 361.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.54 – 8.50 (m, 1H), 8.38 – 8.35 (m, 1H), 8.11 – 8.09 (m, 1H), 7.36 (dd, J = 8.5, 6.0 Hz, 1H), 7.26 (dd, J = 10.1, 2.8 Hz, 1H), 7.17 (td, J = 8.6, 2.8 Hz, 1H), 5.38 (s, 2H), 4.72 (t, J = 12.4 Hz, 2H), 4.36 (t, J = 12.5 Hz, 2H), 2.27 (s, 3H).

Example 131: 1-(3,3-Difluoroazetidin-1-yl)-2-[6-(2-fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone.



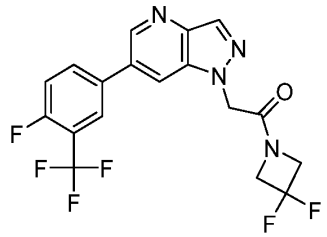
The title compound was prepared in a manner analogous to Example 17, using (2-fluoro-3-methylphenyl)boronic acid in place of 2,4-difluorophenylboronic acid and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). The reaction mixture was heated to 90 ºC. MS (ESI): mass calcd. for $C_{18}H_{15}F_3N_4O$, 360.1; m/z found, 361.2 $[M+H]^+$. ^1H NMR (600 MHz, DMSO-d_6) δ 8.69 (t, J = 1.9 Hz, 1H), 8.39 – 8.36 (m, 1H), 8.28 – 8.25 (m, 1H), 7.46 – 7.42 (m, 1H), 7.42 – 7.37 (m, 1H), 7.27 (t, J = 7.6 Hz, 1H), 5.41 (s, 2H), 4.74 (t, J = 12.4 Hz, 2H), 4.37 (t, J = 12.5 Hz, 2H), 2.35 – 2.32 (m, 3H).

Example 132: 1-(3,3-Difluoroazetidin-1-yl)-2-[6-[2-fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



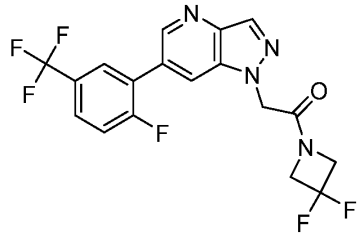
The title compound was prepared in a manner analogous to Example 17, using (2-fluoro-3-(trifluoromethyl)phenyl)boronic acid in place of 2,4-difluorophenylboronic acid. MS (ESI): mass calcd. for $C_{18}H_{12}F_6N_4O$, 414.1; m/z found, 415.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.73 (t, J = 1.7 Hz, 1H), 8.43 – 8.42 (m, 1H), 8.38 – 8.36 (m, 1H), 8.04 – 7.98 (m, 1H), 7.94 – 7.88 (t, J = 7.3 Hz, 1H), 7.60 (t, J = 7.8 Hz, 1H), 5.43 (s, 2H), 4.75 (t, J = 12.4 Hz, 2H), 4.37 (t, J = 12.6 Hz, 2H).

Example 133: 1-(3,3-Difluoroazetidin-1-yl)-2-[6-[4-fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



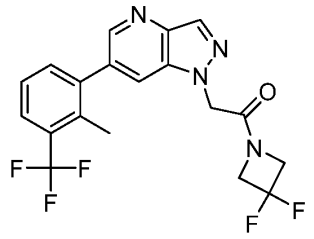
The title compound was prepared in a manner analogous to Example 17, using (4-fluoro-3-(trifluoromethyl)phenyl)boronic acid in place of 2,4-difluorophenylboronic acid and palladium-tetrakis(triphenylphosphine) in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). MS (ESI): mass calcd. for $C_{18}H_{12}F_6N_4O$, 414.1; m/z found, 415.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.93 (d, J = 1.9 Hz, 1H), 8.47 – 8.46 (m, 1H), 8.40 – 8.38 (m, 1H), 8.22 – 8.14 (m, 2H), 7.76 – 7.69 (m, 1H), 5.42 (s, 2H), 4.73 (t, J = 12.3 Hz, 2H), 4.38 (t, J = 12.6 Hz, 2H).

Example 134: 1-(3,3-Difluoroazetidin-1-yl)-2-[6-[2-fluoro-5-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



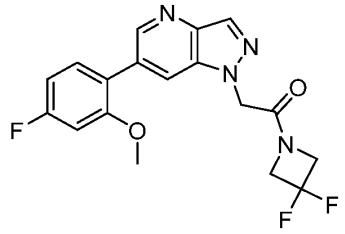
The title compound was prepared in a manner analogous to Example 17, using (2-fluoro-5-(trifluoromethyl)phenyl)boronic acid in place of 2,4-difluorophenylboronic acid and palladium-tetrakis(triphenylphosphine) in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). MS (ESI): mass calcd. for $C_{18}H_{12}F_6N_4O$, 414.1; m/z found, 415.2 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.57 (t, J = 2.0 Hz, 1H), 8.24 – 8.21 (m, 1H), 8.20 – 8.16 (m, 1H), 7.88 – 7.83 (m, 1H), 7.77 – 7.71 (m, 1H), 7.48 (t, J = 9.4 Hz, 1H), 5.23 (s, 2H), 4.54 (t, J = 12.5 Hz, 2H), 4.17 (t, J = 12.5 Hz, 2H).

Example 135: 1-(3,3-Difluoroazetidin-1-yl)-2-[6-[2-methyl-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



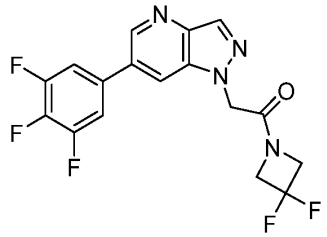
The title compound was prepared in a manner analogous to Example 17, using (2-methyl-3-(trifluoromethyl)phenyl)boronic acid in place of 2,4-difluorophenylboronic acid and palladium-tetrakis(triphenylphosphine) in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). MS (ESI): mass calcd. for $C_{19}H_{15}F_5N_4O$, 410.1; m/z found, 411.2 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.54 (d, J = 1.8 Hz, 1H), 8.40 (d, J = 1.0 Hz, 1H), 8.16 – 8.14 (m, 1H), 7.84 – 7.79 (m, 1H), 7.65 – 7.51 (m, 2H), 5.38 (s, 2H), 4.72 (t, J = 12.4 Hz, 2H), 4.36 (t, J = 12.5 Hz, 2H), 2.35 – 2.29 (m, 3H).

Example 136: 1-(3,3-Difluoroazetidin-1-yl)-2-[6-(4-fluoro-2-methoxy-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone.



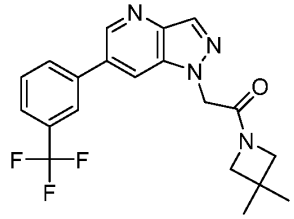
The title compound was prepared in a manner analogous to Example 17, using (4-fluoro-2-methoxyphenyl)boronic acid in place of 2,4-difluorophenylboronic acid. The reaction mixture was heated to 90 °C in place of 75 °C. MS (ESI): mass calcd. for $C_{18}H_{15}F_3N_4O_2$, 376.1; m/z found, 377.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.60 (d, J = 1.8 Hz, 1H), 8.33 (d, J = 1.0 Hz, 1H), 8.12 – 8.10 (m, 1H), 7.43 (dd, J = 8.4, 6.9 Hz, 1H), 7.11 (dd, J = 11.4, 2.5 Hz, 1H), 6.95 (td, J = 8.4, 2.5 Hz, 1H), 5.37 (s, 2H), 4.72 (t, J = 12.4 Hz, 2H), 4.36 (t, J = 12.5 Hz, 2H), 3.81 (s, 3H).

Example 137: 1-(3,3-Difluoroazetidin-1-yl)-2-[6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone.



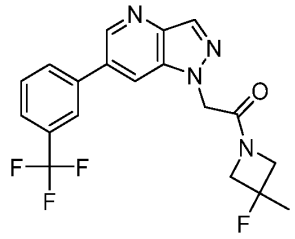
The title compound was prepared in a manner analogous to Example 17, using (3,4,5-trifluorophenyl)boronic acid in place of 2,4-difluorophenylboronic acid and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). The reaction mixture was heated to 90 °C. MS (ESI): mass calcd. for $C_{17}H_{11}F_5N_4O$, 382.1; m/z found, 383.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.93 (d, J = 2.0 Hz, 1H), 8.48 – 8.46 (m, 1H), 8.39 (d, J = 1.0 Hz, 1H), 7.91 – 7.83 (m, 2H), 5.40 (s, 2H), 4.73 (t, J = 12.4 Hz, 2H), 4.38 (t, J = 12.5 Hz, 2H).

Example 138: 1-(3,3-Dimethylazetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone trifluoroacetate salt.



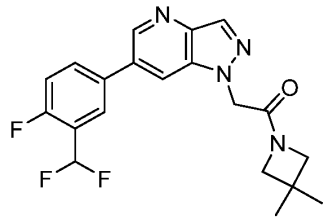
The title compound was prepared in a manner analogous to Example 16, using 3,3-dimethylazetidine hydrochloride in place of 3-fluoroazetidine hydrochloride. MS (ESI): mass calcd. for $C_{20}H_{19}F_3N_4O$, 388.2; m/z found, 389.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.94 (d, J = 1.9 Hz, 1H), 8.52 – 8.50 (m, 1H), 8.38 – 8.36 (m, 1H), 8.17 – 8.13 (m, 2H), 7.85 – 7.77 (m, 2H), 5.29 (s, 2H), 3.89 (s, 2H), 3.59 (s, 2H), 1.26 (s, 6H).

Example 139: 1-(3-Fluoro-3-methyl-azetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



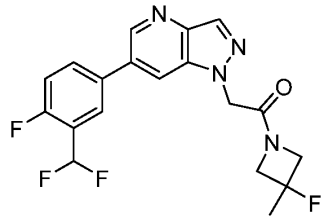
The title compound was prepared in a manner analogous to Example 16, using 3-fluoro-3-methylazetidine in place of 3-fluoroazetidine hydrochloride and DCM in place of DMF. MS (ESI): mass calcd. for $C_{19}H_{16}F_4N_4O$, 392.1; m/z found, 393.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.94 (d, J = 1.9 Hz, 1H), 8.51 – 8.49 (m, 1H), 8.39 – 8.37 (m, 1H), 8.17 – 8.12 (m, 2H), 7.85 – 7.77 (m, 2H), 5.42 – 5.30 (m, 2H), 4.40 – 4.26 (m, 2H), 4.07 – 3.96 (m, 2H), 1.61 (d, J = 22.1 Hz, 3H).

Example 140: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-(3,3-dimethylazetidin-1-yl)ethanone.



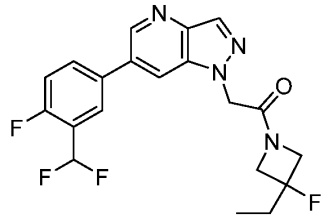
The title compound was prepared in a manner analogous to Example 1 using 3,3-dimethylazetidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{20}H_{19}F_3N_4O$, 388.2; m/z found, 389.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, J = 1.9 Hz, 1H), 8.29 (d, J = 1.0 Hz, 1H), 7.96 (dd, J = 1.9, 1.0 Hz, 1H), 7.93 – 7.84 (m, 1H), 7.81 – 7.68 (m, 1H), 7.37 – 7.27 (m, 1H), 6.98 (t, J = 54.9 Hz, 1H), 5.06 (s, 2H), 3.79 (s, 2H), 3.73 (s, 2H), 1.27 (s, 6H).

Example 141: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-(3-fluoro-3-methyl-azetidin-1-yl)ethanone.



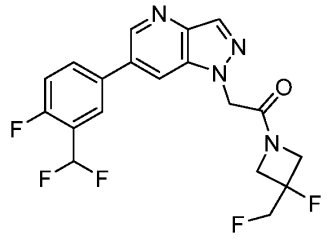
The title compound was prepared in a manner analogous to Example 1 using 3-fluoro-3-methylazetidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{19}H_{16}F_4N_4O$, 392.1; m/z found, 393.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, J = 1.9 Hz, 1H), 8.31 (d, J = 1.0 Hz, 1H), 7.94 (dd, J = 2.0, 1.0 Hz, 1H), 7.93 – 7.83 (m, 1H), 7.79 – 7.71 (m, 1H), 7.34 – 7.26 (m, 1H), 6.98 (t, J = 54.8 Hz, 1H), 5.10 (s, 2H), 4.32 – 4.15 (m, 2H), 4.12 – 3.88 (m, 2H), 1.61 (d, J = 21.4 Hz, 3H).

Example 142: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-(3-ethyl-3-fluoro-azetidin-1-yl)ethanone.



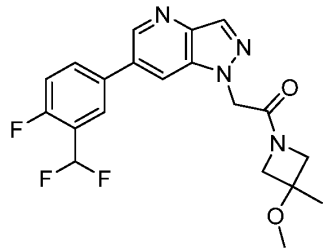
The title compound was prepared in a manner analogous to Example 2 using 3-ethyl-3-fluoroazetidine in place of 3-methyleneazetidine. MS (ESI): mass calcd. for $C_{20}H_{18}F_4N_4O$, 406.1; m/z found, 407.3 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, J = 1.9 Hz, 1H), 8.31 (d, J = 1.0 Hz, 1H), 7.94 (dd, J = 1.9, 1.0 Hz, 1H), 7.92 – 7.83 (m, 1H), 7.81 – 7.68 (m, 1H), 7.37 – 7.28 (m, 1H), 6.98 (t, J = 54.9 Hz, 1H), 5.10 (s, 2H), 4.25 – 3.94 (m, 4H), 1.95 – 1.75 (m, 2H), 0.97 (t, J = 7.4 Hz, 3H).

Example 143: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-[3-fluoro-3-(fluoromethyl)azetidin-1-yl]ethanone.



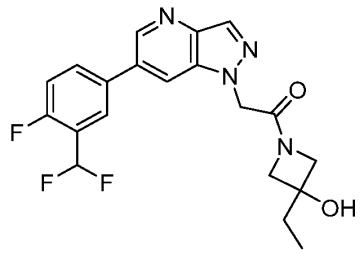
The title compound was prepared in a manner analogous to Example 1 using 3-fluoro-3-(fluoromethyl)azetidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{19}H_{15}F_5N_4O$, 410.1; m/z found, 411.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.82 (d, J = 1.9 Hz, 1H), 8.32 (d, J = 1.0 Hz, 1H), 7.93 (dd, J = 1.9, 1.0 Hz, 1H), 7.90 – 7.85 (m, 1H), 7.80 – 7.66 (m, 1H), 7.37 – 7.29 (m, 1H), 6.98 (t, J = 54.8 Hz, 1H), 5.12 (s, 2H), 4.58 (dd, J = 46.8, 18.2 Hz, 2H), 4.32 – 4.13 (m, 4H).

Example 144: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-(3-methoxy-3-methyl-azetidin-1-yl)ethanone.



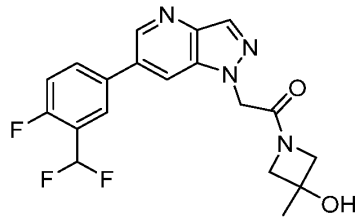
The title compound was prepared in a manner analogous to Example 1 using 3-methoxy-3-methylazetidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{20}H_{19}F_3N_4O_2$, 404.1; m/z found, 405.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, J = 1.9 Hz, 1H), 8.30 (d, J = 1.0 Hz, 1H), 7.96 – 7.93 (m, 1H), 7.88 – 7.84 (m, 1H), 7.78 – 7.72 (m, 1H), 7.32 – 7.26 (m, 1H), 6.98 (t, J = 54.9 Hz, 1H), 5.09 (s, 2H), 4.03 (dd, J = 14.6, 9.7 Hz, 2H), 3.83 (ddd, J = 24.8, 9.7, 1.3 Hz, 2H), 3.21 (s, 3H), 1.46 (s, 3H).

Example 145: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-(3-ethyl-3-hydroxy-azetidin-1-yl)ethanone.



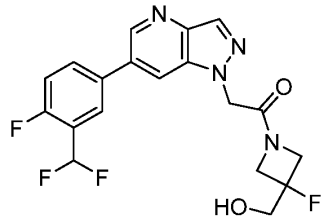
The title compound was prepared in a manner analogous to Example 1 using 3-ethyl-3-hydroxyazetidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{20}H_{19}F_3N_4O_2$, 404.1; m/z found, 405.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, J = 1.9 Hz, 1H), 8.30 (d, J = 1.0 Hz, 1H), 7.96 – 7.93 (m, 1H), 7.89 – 7.84 (m, 1H), 7.78 – 7.72 (m, 1H), 7.33 – 7.26 (m, 1H), 6.98 (t, J = 54.8 Hz, 1H), 5.09 (s, 2H), 4.06 – 3.85 (m, 4H), 2.01 (s, 1H), 1.77 (q, J = 7.4 Hz, 2H), 0.95 (t, J = 7.4 Hz, 3H).

Example 146: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-(3-hydroxy-3-methyl-azetidin-1-yl)ethanone.



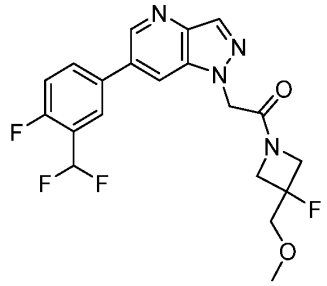
The title compound was prepared in a manner analogous to Example 1 using 3-hydroxy-3-methylazetidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{19}H_{17}F_3N_4O_2$, 390.1; m/z found, 391.2 $[M+H]^+$ [M+H]+. ^1H NMR (400 MHz, Methanol-d4) δ 8.79 (d, J = 1.8 Hz, 1H), 8.29 (d, J = 0.9 Hz, 1H), 8.16 (dd, J = 1.9, 1.0 Hz, 1H), 7.97 – 7.90 (m, 1H), 7.90 – 7.79 (m, 1H), 7.42 – 7.30 (m, 1H), 7.02 (t, J = 54.8 Hz, 1H), 5.19 (s, 2H), 4.12 (s, 2H), 3.95 (s, 2H), 1.53 (s, 3H).

Example 147: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-[3-fluoro-3-(hydroxymethyl)azetidin-1-yl]ethanone.



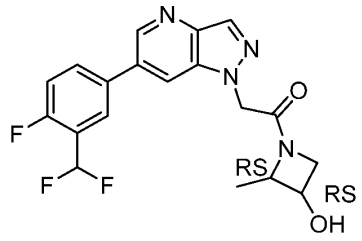
The title compound was prepared in a manner analogous to Example 1 using 3-fluoro-3-hydroxymethylazetidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{19}H_{16}F_4N_4O_2$, 408.1; m/z found, 409.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, J = 1.9 Hz, 1H), 8.31 (d, J = 1.0 Hz, 1H), 7.93 (dd, J = 2.0, 1.0 Hz, 1H), 7.87 (d, J = 6.5 Hz, 1H), 7.75 (s, 1H), 7.33 – 7.26 (m, 1H), 6.98 (t, J = 54.9 Hz, 1H), 5.11 (s, 2H), 4.29 – 4.12 (m, 4H), 3.94 – 3.78 (m, 2H), 1.98 – 1.88 (m, 1H).

Example 148: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-[3-fluoro-3-(methoxymethyl)azetidin-1-yl]ethanone.



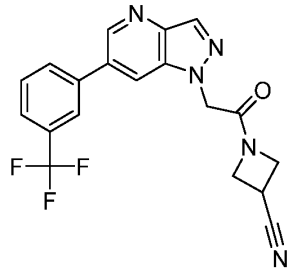
The title compound was prepared in a manner analogous to Example 1 using 3-fluoro-3-methoxymethylazetidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{20}H_{18}F_4N_4O_2$, 422.1; m/z found, 423.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, J = 1.9 Hz, 1H), 8.31 (d, J = 1.0 Hz, 1H), 7.93 (dd, J = 1.9, 1.0 Hz, 1H), 7.90 – 7.84 (m, 1H), 7.80 – 7.71 (m, 1H), 7.32 – 7.27 (m, 1H), 6.98 (t, J = 54.8 Hz, 1H), 5.11 (s, 2H), 4.28 – 4.07 (m, 4H), 3.60 (d, J = 17.5 Hz, 2H), 3.41 (s, 3H).

Example 149: [6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-(3-hydroxy-2-methyl-azetidin-1-yl)ethanone.



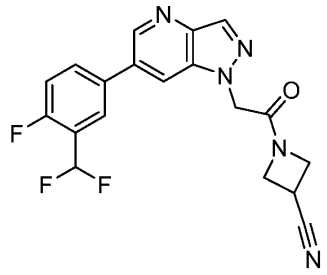
The title compound was prepared in a manner analogous to Example 1 using a diastereomeric mixture of 3-hydroxy-2-methylazetidines in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{19}H_{17}F_3N_4O_2$, 390.1; m/z found, 391.0 $[M+H]^+$. ^1H NMR (400 MHz, Chloroform-*d*) δ 8.81 – 8.77 (m, 1H), 8.32 – 8.27 (m, 1H), 8.00 – 7.92 (m, 1H), 7.89 – 7.83 (m, 1H), 7.78 – 7.71 (m, 1H), 7.31 – 7.26 (m, 1H), 6.98 (t, *J* = 54.9 Hz, 1H), 5.21 – 4.93 (m, 2H), 4.78 – 4.11 (m, 3H), 3.96 – 3.75 (m, 1H), 2.59 – 2.06 (m, 1H), 1.50 – 1.35 (m, 3H).

Example 150: 1-[2-[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]azetidine-3-carbonitrile.



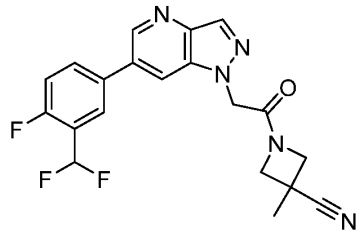
The title compound was prepared in a manner analogous to Example 16, using azetidine-3-carbonitrile hydrochloride in place of 3-fluoroazetidine hydrochloride and DCM in place of DMF. MS (ESI): mass calcd. for $C_{19}H_{14}F_3N_5O$, 385.1; m/z found, 386.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.95 (d, *J* = 1.9 Hz, 1H), 8.50 – 8.47 (m, 1H), 8.40 – 8.38 (m, 1H), 8.18 – 8.11 (m, 2H), 7.87 – 7.77 (m, 2H), 5.40 – 5.28 (m, 2H), 4.54 – 4.39 (m, 2H), 4.25 – 4.16 (m, 1H), 4.13 – 4.05 (m, 1H), 3.91 – 3.82 (m, 1H).

Example 151: 1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]acetyl]azetidine-3-carbonitrile.



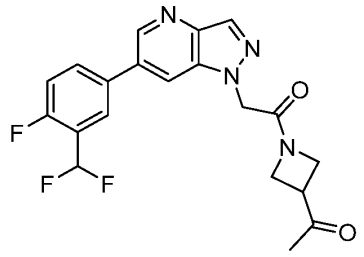
The title compound was prepared in a manner analogous to Example 2 using 3-cyanoazetidine in place of 3-methyleneazetidine. MS (ESI): mass calcd. for $C_{19}H_{14}F_3N_5O$, 385.1; m/z found, 386.0 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.83 (d, J = 1.9 Hz, 1H), 8.32 (d, J = 1.0 Hz, 1H), 7.92 (dd, J = 2.0, 1.0 Hz, 1H), 7.90 – 7.84 (m, 1H), 7.80 – 7.69 (m, 1H), 7.34 – 7.28 (m, 1H), 6.98 (t, J = 54.8 Hz, 1H), 5.09 (d, J = 3.1 Hz, 2H), 4.44 – 4.17 (m, 3H), 3.58 – 3.42 (m, 2H).

Example 152: 1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]acetyl]-3-methyl-azetidine-3-carbonitrile.



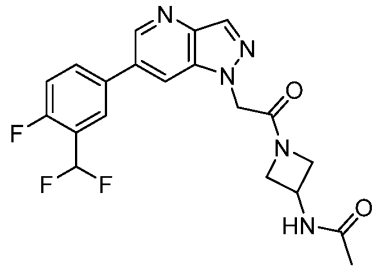
The title compound was prepared in a manner analogous to Example 1 using 3-cyano-3-methylazetidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{20}H_{16}F_3N_5O$, 399.1; m/z found, 400.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.83 (d, J = 1.9 Hz, 1H), 8.32 (d, J = 1.0 Hz, 1H), 7.92 (dd, J = 1.9, 1.0 Hz, 1H), 7.90 – 7.85 (m, 1H), 7.79 – 7.72 (m, 1H), 7.34 – 7.27 (m, 1H), 6.98 (t, J = 54.9 Hz, 1H), 5.09 (s, 2H), 4.45 – 4.34 (m, 2H), 3.97 (t, J = 9.0 Hz, 2H), 1.67 (s, 3H).

Example 153: 1-(3-Acetylazetidin-1-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]ethanone.



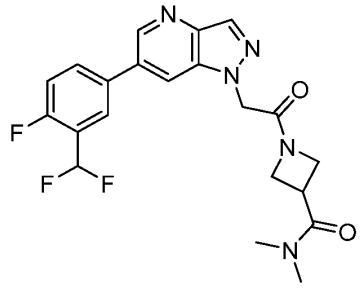
The title compound was prepared in a manner analogous to Example 1 using 1-(azetidine-3-yl)ethan-1-one in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{20}H_{17}F_3N_4O_2$, 402.1; m/z found, 403.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, J = 1.9 Hz, 1H), 8.30 (d, J = 1.0 Hz, 1H), 7.93 (dd, J = 1.9, 1.0 Hz, 1H), 7.89 – 7.84 (m, 1H), 7.78 – 7.72 (m, 1H), 7.32 – 7.27 (m, 1H), 6.98 (t, J = 54.8 Hz, 1H), 5.21 – 4.94 (m, 2H), 4.33 (dd, J = 8.8, 6.0 Hz, 1H), 4.27 – 4.08 (m, 3H), 3.57 – 3.43 (m, 1H), 2.18 (s, 3H).

Example 154: *N*-[1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]acetyl]azetidin-3-yl]acetamide.



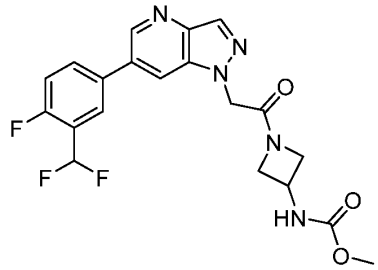
The title compound was prepared in a manner analogous to Example 1 using 3-acetamidoazetidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{20}H_{18}F_3N_5O_2$, 417.1; m/z found, 418.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, J = 1.9 Hz, 1H), 8.30 (d, J = 1.0 Hz, 1H), 7.93 (dd, J = 1.9, 1.0 Hz, 1H), 7.90 – 7.83 (m, 1H), 7.81 – 7.70 (m, 1H), 7.32 – 7.27 (m, 1H), 6.98 (t, J = 54.8 Hz, 1H), 5.96 (d, J = 7.1 Hz, 1H), 5.19 – 5.01 (m, 2H), 4.76 – 4.61 (m, 1H), 4.47 – 4.30 (m, 2H), 4.01 – 3.83 (m, 2H), 1.96 (s, 3H).

Example 155: 1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]acetyl]-*N*,*N*-dimethyl-azetidine-3-carboxamide.



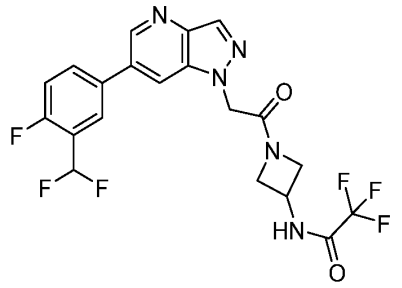
The title compound was prepared in a manner analogous to Example 1 using *N,N*-dimethylazetidine-3-carboxamide in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{21}H_{20}F_3N_5O_2$, 431.2; m/z found, 432.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.79 (d, J = 1.9 Hz, 1H), 8.29 (d, J = 1.0 Hz, 1H), 7.95 (dd, J = 2.0, 1.0 Hz, 1H), 7.89 – 7.83 (m, 1H), 7.79 – 7.71 (m, 1H), 7.33 – 7.23 (m, 1H), 6.98 (t, J = 54.8 Hz, 1H), 5.20 – 4.89 (m, 2H), 4.57 – 4.47 (m, 1H), 4.31 – 4.07 (m, 3H), 3.59 (tt, J = 9.0, 6.2 Hz, 1H), 2.97 (s, 3H), 2.89 (s, 3H).

Example 156: Methyl *N*-[1-[2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]acetyl]azetidin-3-yl]carbamate.



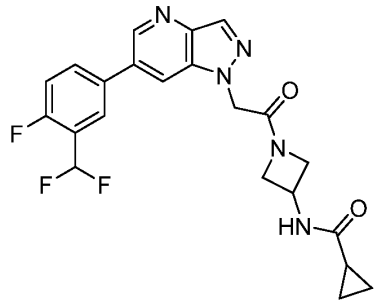
The title compound was prepared in a manner analogous to Example 1 using methyl azetidin-3-ylcarbamate in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{20}H_{18}F_3N_5O_3$, 433.1; m/z found, 434.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, J = 1.9 Hz, 1H), 8.30 (d, J = 1.0 Hz, 1H), 7.93 (dd, J = 2.0, 1.0 Hz, 1H), 7.91 – 7.85 (m, 1H), 7.80 – 7.73 (m, 1H), 7.33 – 7.27 (m, 1H), 6.98 (t, J = 54.9 Hz, 1H), 5.12 – 5.07 (m, 3H), 4.58 – 4.45 (m, 1H), 4.41 – 4.31 (m, 2H), 4.03 – 3.83 (m, 2H), 3.68 (s, 3H).

Example 157: *N*-[1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]acetyl]azetidin-3-yl]-2,2,2-trifluoro-acetamide.



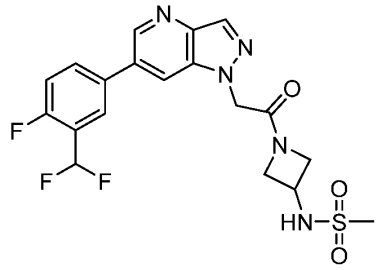
The title compound was prepared in a manner analogous to Example 1 using 3-(2,2,2-trifluoroacetamido)azetidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{20}H_{15}F_6N_5O_2$, 471.1; m/z found, 472.0 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.82 (d, J = 1.9 Hz, 1H), 8.31 (d, J = 1.0 Hz, 1H), 7.93 (dd, J = 1.9, 1.0 Hz, 1H), 7.89 – 7.85 (m, 1H), 7.79 – 7.73 (m, 1H), 7.33 – 7.26 (m, 1H), 6.98 (t, J = 54.8 Hz, 1H), 5.24 – 5.00 (m, 2H), 4.82 – 4.63 (m, 1H), 4.57 – 4.29 (m, 2H), 4.16 – 3.97 (m, 2H).

Example 158: *N*-[1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]acetyl]azetidin-3-yl]cyclopropanecarboxamide.



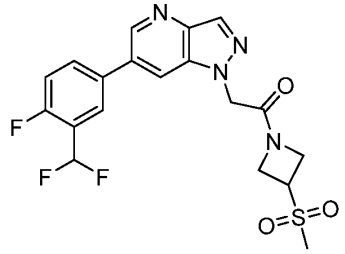
The title compound was prepared in a manner analogous to Example 1 using *N*-(azetidin-3-yl)cyclopropanecarboxamide in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{22}H_{20}F_3N_5O_2$, 443.2; m/z found, 444.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 – 8.77 (m, 1H), 8.32 – 8.25 (m, 1H), 7.96 – 7.91 (m, 1H), 7.88 – 7.83 (m, 1H), 7.77 – 7.71 (m, 1H), 7.31 – 7.27 (m, 1H), 6.98 (t, J = 54.9 Hz, 1H), 5.21 (s, 2H), 3.86 – 3.41 (m, 4H), 3.38 – 3.22 (m, 4H), 2.71 – 2.43 (m, 1H), 2.22 – 1.96 (m, 1H), 1.94 – 1.64 (m, 1H).

Example 159: *N*-[1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]acetyl]azetidin-3-yl]methanesulfonamide.



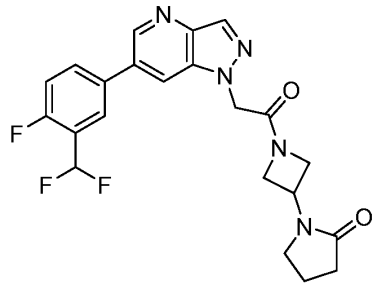
The title compound was prepared in a manner analogous to Example 1 using *N*-(azetidin-3-yl)methanesulfonamide in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{19}H_{18}F_3N_5O_3S$, 453.1; m/z found, 454.0 $[M+H]^+$. ^1H NMR (400 MHz, Methanol-d4) δ 8.79 (d, J = 1.9 Hz, 1H), 8.30 (d, J = 1.0 Hz, 1H), 8.15 (dd, J = 1.9, 1.0 Hz, 1H), 7.96 – 7.89 (m, 1H), 7.88 – 7.81 (m, 1H), 7.35 (ddd, J = 9.8, 8.6, 1.2 Hz, 1H), 7.02 (t, J = 54.8 Hz, 1H), 5.18 (s, 2H), 4.59 – 4.49 (m, 1H), 4.42 – 4.27 (m, 2H), 4.24 – 4.16 (m, 1H), 4.04 – 3.95 (m, 1H), 2.96 (s, 3H).

Example 160: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-(3-methylsulfonylazetidin-1-yl)ethanone.



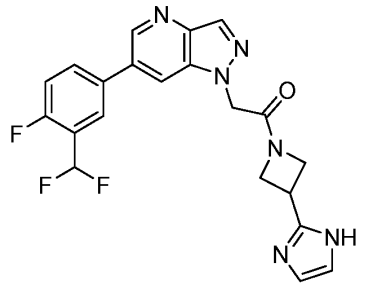
The title compound was prepared in a manner analogous to Example 1 using 3-(methylsulfonyl)azetidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{19}H_{17}F_3N_4O_3S$, 438.1; m/z found, 439.0 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.90 (d, J = 2.0 Hz, 1H), 8.44 (dd, J = 2.0, 1.0 Hz, 1H), 8.39 (d, J = 1.0 Hz, 1H), 8.12 – 7.98 (m, 2H), 7.59 (t, J = 9.8 Hz, 1H), 7.31 (t, J = 54.1 Hz, 1H), 5.48 – 5.25 (m, 2H), 4.60 – 4.52 (m, 1H), 4.50 – 4.44 (m, 1H), 4.44 – 4.35 (m, 1H), 4.26 – 4.17 (m, 1H), 4.16 – 4.07 (m, 1H), 3.07 (s, 3H).

Example 161: 1-[1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]acetyl]azetidin-3-yl]pyrrolidin-2-one.



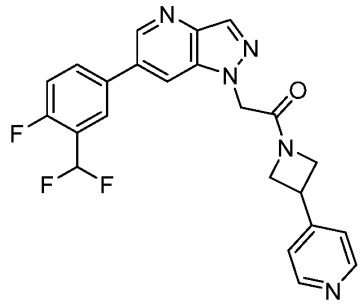
The title compound was prepared in a manner analogous to Example 1 using 1-(azetidin-3-yl)pyrrolidin-2-one in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{22}H_{20}F_3N_5O_2$, 443.2; m/z found, 444.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, J = 1.9 Hz, 1H), 8.30 (d, J = 1.0 Hz, 1H), 7.95 (dd, J = 2.0, 1.0 Hz, 1H), 7.89 – 7.82 (m, 1H), 7.81 – 7.67 (m, 1H), 7.37 – 7.27 (m, 1H), 6.98 (t, J = 54.8 Hz, 1H), 5.09 (s, 2H), 5.06 – 4.96 (m, 1H), 4.31 – 4.11 (m, 4H), 3.57 – 3.30 (m, 2H), 2.50 – 2.26 (m, 2H), 2.13 – 2.04 (m, 2H).

Example 162: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-[3-(1*H*-imidazol-2-yl)azetidin-1-yl]ethanone.



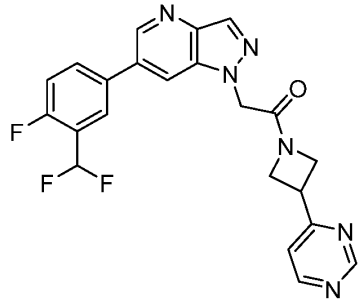
The title compound was prepared in a manner analogous to Example 2 using 2-(azetidine-3-yl)-1*H*-imidazole in place of 3-methyleneazetidine. MS (ESI): mass calcd. for $C_{21}H_{17}F_3N_6O$, 426.1; m/z found, 427.2. ^1H NMR (400 MHz, $CDCl_3$) δ 8.92 – 8.60 (m, 1H), 8.21 (s, 1H), 7.96 (s, 1H), 7.88 – 7.82 (m, 1H), 7.73 (t, J = 6.7 Hz, 1H), 7.30 – 7.22 (m, 1H), 6.96 (t, J = 54.9 Hz, 1H), 6.76 (s, 2H), 5.40 – 5.02 (m, 3H), 4.51 – 4.36 (m, 2H), 4.34 – 4.22 (m, 2H), 4.00 – 3.84 (m, 1H).

Example 163: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-[3-(4-pyridyl)azetidin-1-yl]ethanone.



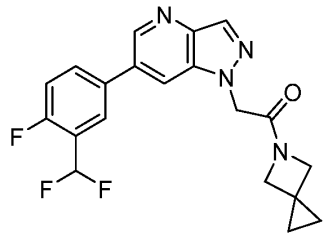
The title compound was prepared in a manner analogous to Example 2 using 4-(azetidin-3-yl)pyridine in place of 3-methyleneazetidine. MS (ESI): mass calcd. for $C_{23}H_{18}F_3N_5O$, 437.1; m/z found, 438.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, J = 1.9 Hz, 1H), 8.62 – 8.55 (m, 2H), 8.31 (d, J = 1.0 Hz, 1H), 7.98 (dd, J = 2.0, 1.0 Hz, 1H), 7.91 – 7.84 (m, 1H), 7.81 – 7.68 (m, 1H), 7.36 – 7.25 (m, 1H), 7.21 – 7.15 (m, 2H), 6.98 (t, J = 54.8 Hz, 1H), 5.13 (d, J = 1.0 Hz, 2H), 4.56 – 4.43 (m, 2H), 4.13 (dt, J = 10.3, 6.7 Hz, 2H), 3.83 (tt, J = 8.9, 6.0 Hz, 1H).

Example 164: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-(3-pyrimidin-4-ylazetidin-1-yl)ethanone.



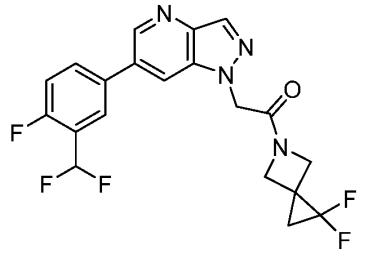
The title compound was prepared in a manner analogous to Example 2 using 4-(azetidin-3-yl)pyrimidine in place of 3-methyleneazetidine. MS (ESI): mass calcd. for $C_{22}H_{17}F_3N_6O$, 438.1; m/z found, 439.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 9.19 (d, J = 1.5 Hz, 1H), 8.80 (d, J = 1.9 Hz, 1H), 8.68 (d, J = 5.1 Hz, 1H), 8.30 (d, J = 1.0 Hz, 1H), 8.05 – 7.97 (m, 1H), 7.93 – 7.83 (m, 1H), 7.81 – 7.69 (m, 1H), 7.34 – 7.25 (m, 1H), 7.18 (dd, J = 5.1, 1.4 Hz, 1H), 6.98 (t, J = 54.8 Hz, 1H), 5.23 – 5.04 (m, 2H), 4.47 – 4.38 (m, 3H), 4.33 – 4.24 (m, 1H), 3.96 – 3.85 (m, 1H).

Example 165: 1-(5-Azaspiro[2.3]hexan-5-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]ethanone.



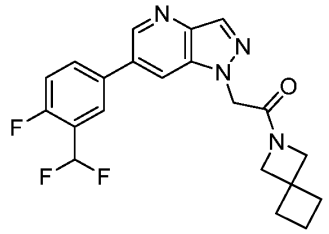
The title compound was prepared in a manner analogous to Example 1 using 5-azaspiro[3.2]hexane in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{20}H_{17}F_3N_4O$, 386.1; m/z found, 387.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, J = 1.9 Hz, 1H), 8.29 (d, J = 1.0 Hz, 1H), 7.97 (dd, J = 1.9, 1.0 Hz, 1H), 7.90 – 7.85 (m, 1H), 7.80 – 7.71 (m, 1H), 7.32 – 7.27 (m, 1H), 6.98 (t, J = 54.8 Hz, 1H), 5.11 (s, 2H), 4.22 – 4.07 (m, 4H), 0.79 – 0.56 (m, 4H).

Example 166: 1-(2,2-Difluoro-5-azaspiro[2.3]hexan-5-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]ethanone.



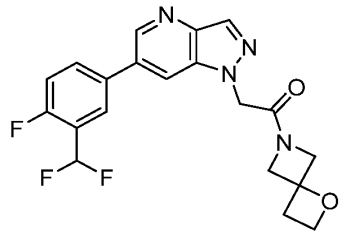
The title compound was prepared in a manner analogous to Example 1 using 1,1-difluoro-5-azaspiro[2.3]hexane in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{20}H_{15}F_5N_4O$, 422.1; m/z found, 423.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.82 (d, J = 1.9 Hz, 1H), 8.31 (d, J = 1.1 Hz, 1H), 7.95 (dd, J = 2.0, 1.1 Hz, 1H), 7.90 – 7.84 (m, 1H), 7.80 – 7.73 (m, 1H), 7.33 – 7.27 (m, 1H), 6.98 (t, J = 54.9 Hz, 1H), 5.21 – 5.00 (m, 2H), 4.32 – 4.19 (m, 2H), 4.17 – 4.03 (m, 2H), 1.53 – 1.42 (m, 2H).

Example 167: 1-(6-Azaspiro[3.3]heptan-6-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]ethanone.



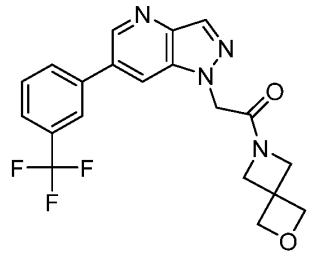
The title compound was prepared in a manner analogous to Example 1 using-azaspiro[3.3]heptane in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{21}H_{19}F_3N_4O$, 400.2; m/z found, 401.3 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.79 (d, J = 1.9 Hz, 1H), 8.29 (d, J = 0.9 Hz, 1H), 7.95 (dd, J = 2.0, 1.0 Hz, 1H), 7.89 – 7.82 (m, 1H), 7.78 – 7.70 (m, 1H), 7.33 – 7.24 (m, 1H), 6.97 (t, J = 54.8 Hz, 1H), 5.05 (s, 2H), 4.05 (s, 2H), 4.00 (s, 2H), 2.22 – 2.04 (m, 3H), 1.91 – 1.70 (m, 3H).

Example 168: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-(3-oxa-6-azaspiro[3.3]heptan-6-yl)ethanone.



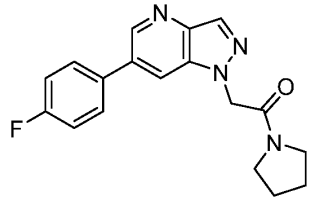
The title compound was prepared in a manner analogous to Example 1 using 1-oxa-6-azaspiro[3.3]heptane in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{20}H_{17}F_3N_4O_2$, 402.1; m/z found, 403.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, J = 1.9 Hz, 1H), 8.30 (d, J = 1.0 Hz, 1H), 7.92 (dd, J = 1.9, 1.0 Hz, 1H), 7.90 – 7.82 (m, 1H), 7.80 – 7.68 (m, 1H), 7.34 – 7.27 (m, 1H), 6.98 (t, J = 54.8 Hz, 1H), 5.08 (s, 2H), 4.58 – 4.42 (m, 2H), 4.31 – 4.11 (m, 4H), 2.91 – 2.76 (m, 2H).

Example 169: 1-(6-Oxa-2-azaspiro[3.3]heptan-2-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



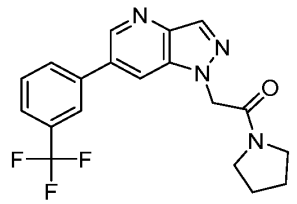
The title compound was prepared in a manner analogous to Example 16, using 2-oxa-6-azaspiro[3.3]heptane in place of 3-fluoroazetidine hydrochloride and DCM in place of DMF. MS (ESI): mass calcd. for $C_{20}H_{17}F_3N_4O_2$, 402.1; m/z found, 403.2 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.94 (d, J = 1.9 Hz, 1H), 8.48 – 8.45 (m, 1H), 8.38 – 8.36 (m, 1H), 8.16 – 8.12 (m, 2H), 7.86 – 7.76 (m, 2H), 5.28 (s, 2H), 4.73 – 4.65 (m, 4H), 4.38 (s, 2H), 4.10 (s, 2H).

Example 170: 2-[6-(4-Fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-pyrrolidin-1-yl-ethanone.



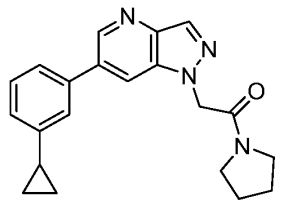
The title compound was prepared in a manner analogous to Example 1 using 2-(6-(4-fluorophenyl)-1H-pyrazolo[4,3-*b*]pyridin-1-yl)acetic acid (Intermediate 31) in place of Intermediate 16 and pyrrolidine in place of 3-(trifluoromethyl)azetidin-3-ol. MS (ESI): mass calcd. for $C_{18}H_{17}FN_4O$, 324.1; m/z found, 325.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.78 (d, J = 1.9 Hz, 1H), 8.28-8.26 (m, 1H), 7.96-7.94 (m, 1H), 7.65 – 7.59 (m, 2H), 7.23 – 7.15 (m, 2H), 5.20 (s, 2H), 3.61-3.47 (m, 4H), 2.06-1.99 (m, 2H), 1.92-1.85 (m, 2H).

Example 171: 1-Pyrrolidin-1-yl-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



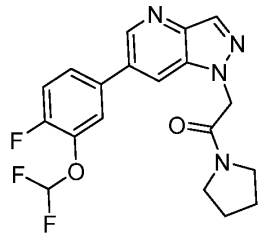
The title compound was prepared in a manner analogous to Example 17, using 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(pyrrolidin-1-yl)ethan-1-one (Intermediate 43) in place of Intermediate 42, (3-(trifluoromethyl)phenyl)boronic acid in place of 2,4-difluorophenylboronic acid and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II).The reaction mixture was heated to 90 °C. MS (ESI): mass calcd. for $C_{19}H_{17}F_3N_4O$, 374.1; m/z found, 375.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.93 (d, J = 2.0 Hz, 1H), 8.51 – 8.48 (m, 1H), 8.37 – 8.34 (m, 1H), 8.16 – 8.12 (m, 2H), 7.85 – 7.77 (m, 2H), 5.45 (s, 2H), 3.61 (t, J = 6.8 Hz, 2H), 2.00 – 1.93 (m, 2H), 1.85 – 1.77 (m, 2H).

Example 172: 2-[6-(3-Cyclopropylphenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-pyrrolidin-1-yl-ethanone.



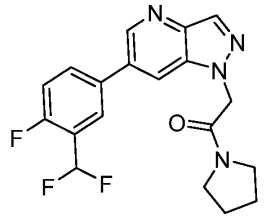
The title compound was prepared in a manner analogous to Example 17, using 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(pyrrolidin-1-yl)ethan-1-one (Intermediate 43) in place of Intermediate 42, 2-(3-cyclopropylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in place of 2,4-difluorophenylboronic acid and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). The reaction mixture was heated to 90 °C. MS (ESI): mass calcd. for $C_{21}H_{22}N_4O$, 346.2; m/z found, 347.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ8.84 (d, J = 1.9 Hz, 1H), 8.34 – 8.32 (m, 1H), 8.32 – 8.30 (m, 1H), 7.55 – 7.52 (m, 1H), 7.50 – 7.47 (m, 1H), 7.41 (t, J = 7.7 Hz, 1H), 7.16 – 7.12 (m, 1H), 5.43 (s, 2H), 3.60 (t, J = 6.8 Hz, 2H), 2.06 – 1.92 (m, 3H), 1.84 – 1.77 (m, 2H), 1.02 – 0.98 (m, 2H), 0.82 – 0.78 (m, 2H).

Example 173: 2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-pyrrolidin-1-yl-ethanone.



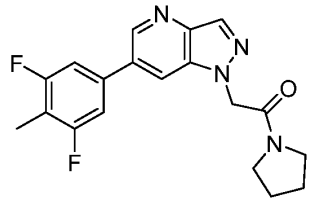
The title compound was made in a manner analogous to Example 5, Method A, using 6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridine (Intermediate 17) in place of Intermediate 16 and 2-chloro-1-(pyrrolidin-1-yl)ethan-1-one in place of Intermediate 1. MS (ESI): mass calcd. for $C_{19}H_{17}F_3N_4O_2$, 390.1; m/z found, 391.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.96 – 8.80 (m, 1H), 8.45 – 8.36 (m, 1H), 8.34 (s, 1H), 7.89 – 7.78 (m, 1H), 7.81 – 7.70 (m, 1H), 7.68 – 7.53 (m, 1H), 7.38 (t, J = 73.3 Hz, 1H), 5.43 (s, 2H), 3.72 – 3.47 (m, 2H), 3.37 – 3.22 (m, 2H), 2.05 – 1.88 (m, 2H), 1.88 – 1.72 (m, 2H).

Example 174: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-pyrrolidin-1-yl-ethanone.



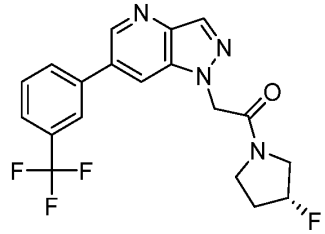
The title compound was made in a manner analogous to Example 5, Method A, using 2-chloro-1-(pyrrolidin-1-yl)ethan-1-one in place of Intermediate 1. MS (ESI): mass calcd. for $C_{19}H_{17}F_3N_4O$, 374.1; m/z found, 375.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.93 – 8.83 (m, 1H), 8.47 – 8.39 (m, 1H), 8.34 (s, 1H), 8.09 – 8.01 (m, 2H), 7.62 – 7.53 (m, 1H), 7.30 (t, J = 55.2 Hz, 1H), 5.44 (s, 2H), 3.66 – 3.54 (m, 2H), 3.38 – 3.27 (m, 2H), 2.03 – 1.92 (m, 2H), 1.87 – 1.76 (m, 2H).

Example 175: 2-[6-(3,5-Difluoro-4-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-pyrrolidin-1-yl-ethanone trifluoroacetate salt.



The title compound was prepared in a manner analogous to Example 17, using 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(pyrrolidin-1-yl)ethan-1-one (Intermediate 43) in place of Intermediate 42, (3,5-difluoro-4-methylphenyl)boronic acid in place of 2,4-difluorophenylboronic acid and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). The reaction mixture was heated to 90 °C. MS (ESI): mass calcd. for $C_{19}H_{18}F_2N_4O$, 356.1; m/z found, 357.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.93 (d, J = 2.0 Hz, 1H), 8.50 – 8.48 (m, 1H), 8.34 – 8.32 (m, 1H), 7.65 – 7.58 (m, 2H), 5.42 (s, 2H), 3.61 (t, J = 6.8 Hz, 2H), 3.31 (t, J = 6.9 Hz, 2H), 2.24 – 2.20 (m, 3H), 2.01 – 1.93 (m, 2H), 1.85 – 1.78 (m, 2H).

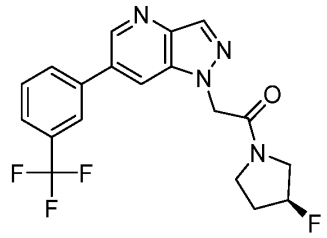
Example 176: 1-[(3R)-3-Fluoropyrrolidin-1-yl]-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



The title compound was prepared in a manner analogous to Example 17, using (*R*)-2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoropyrrolidin-1-yl)ethan-1-one (Intermediate 45) in place of Intermediate 42, (3-(trifluoromethyl)phenyl)boronic acid in place of 2,4-difluorophenylboronic acid and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). The reaction mixture was heated to 90 °C. MS (ESI): mass calcd. for $C_{19}H_{16}F_4N_4O$, 392.1; m/z found, 393.0 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.93 (d, J = 2.0 Hz, 1H), 8.52 – 8.49 (m, 1H), 8.39 – 8.35 (m, 1H), 8.16 –

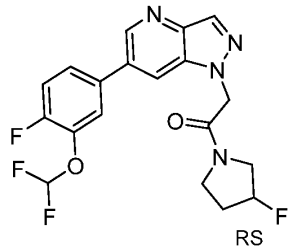
8.10 (m, 2H), 7.85 – 7.76 (m, 2H), 5.59 – 5.27 (m, 3H), 4.02 – 3.41 (m, 4H), 2.38 – 1.94 (m, 2H).

Example 177: 1-[(3*S*)-3-Fluoropyrrolidin-1-yl]-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



The title compound was prepared in a manner analogous to Example 17, using (*S*)-2-6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-fluoropyrrolidin-1-yl)ethan-1-one (Intermediate 44) in place of Intermediate 42, (3-(trifluoromethyl)phenyl)boronic acid in place of 2,4-difluorophenylboronic acid and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane in place of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II). The reaction mixture was heated to 90 °C. MS (ESI): mass calcd. for $C_{19}H_{16}F_4N_4O$, 392.1; m/z found, 393.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.93 (d, J = 1.9 Hz, 1H), 8.52 – 8.49 (m, 1H), 8.38 – 8.35 (m, 1H), 8.16 – 8.11 (m, 2H), 7.85 – 7.76 (m, 2H), 5.59 – 5.28 (m, 3H), 4.03 – 3.40 (m, 4H), 2.38 – 1.93 (m, 2H).

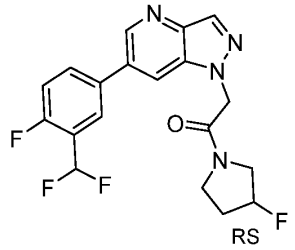
Example 178: (R,S)-2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoropyrrolidin-1-yl)ethanone.



The title compound was made in an analogous manner to Example 5, Method A, using 6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridine (Intermediate 17) in place of

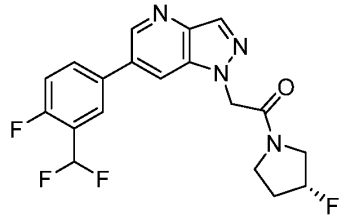
Intermediate 16 and racemic 2-chloro-1-(3-fluoropyrrolidin-1-yl)ethan-1-one (Intermediate 5) in place of Intermediate 1. MS (ESI): mass calcd. for $C_{19}H_{16}F_4N_4O_2$, 408.1; m/z found, 409.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.88 (d, J = 1.9 Hz, 1H), 8.45 – 8.38 (m, 1H), 8.35 (s, 1H), 7.86 – 7.78 (m, 1H), 7.79 – 7.70 (m, 1H), 7.60 (dd, J = 10.2, 8.8 Hz, 1H), 7.38 (t, J = 73.2 Hz, 1H), 5.63 – 5.22 (m, 3H), 4.10 – 3.23 (m, 4H), 2.41 – 1.89 (m, 2H).

Example 179: (R,S)-2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoropyrrolidin-1-yl)ethanone.



The title compound was made in an analogous manner to Example 5, Method A, using racemic 2-chloro-1-(3-fluoropyrrolidin-1-yl)ethan-1-one (Intermediate 5) in place of Intermediate 1. MS (ESI): mass calcd. for $C_{19}H_{16}F_4N_4O$, 392.1; m/z found, 393.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.91 – 8.84 (m, 1H), 8.48 – 8.40 (m, 1H), 8.36 (s, 1H), 8.11 – 7.97 (m, 2H), 7.64 – 7.52 (m, 1H), 7.30 (t, J = 54.2 Hz, 1H), 5.65 – 5.23 (m, 3H), 4.08 – 3.21 (m, 4H), 2.39 – 2.21 (m, 1H), 2.21 – 2.03 (m, 1H).

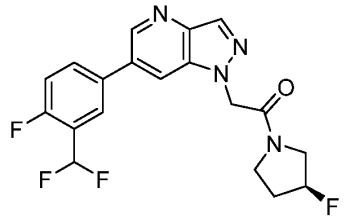
Example 180: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-[(3*R*)-3-fluoropyrrolidin-1-yl]ethanone.



The title compound was prepared in a manner analogous to Example 1 using (*R*)-3-fluoropyrrolidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{19}H_{16}F_4N_4O$, 392.1; m/z found, 393.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.87 – 8.70 (m,

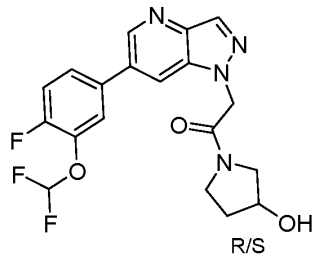
1H), 8.36 – 8.26 (m, 1H), 7.97 – 7.93 (m, 1H), 7.89 – 7.85 (m, 1H), 7.79 – 7.72 (m, 1H), 7.32 – 7.26 (m, 1H), 6.98 (t, *J* = 54.9 Hz, 1H), 5.47 – 5.12 (m, 3H), 4.02 – 3.45 (m, 4H), 2.54 – 1.85 (m, 2H).

Example 181: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-[(3*S*)-3-fluoropyrrolidin-1-yl]ethanone.



The title compound was prepared in a manner analogous to Example 1 using (*S*)-3-fluoropyrrolidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{19}H_{16}F_4N_4O$, 392.1; m/z found, 393.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.85 – 8.74 (m, 1H), 8.36 – 8.26 (m, 1H), 7.98 – 7.91 (m, 1H), 7.89 – 7.84 (m, 1H), 7.79 – 7.71 (m, 1H), 7.33 – 7.26 (m, 1H), 6.98 (t, *J* = 54.9 Hz, 1H), 5.48 – 5.06 (m, 3H), 4.05 – 3.48 (m, 4H), 2.53 – 1.88 (m, 2H).

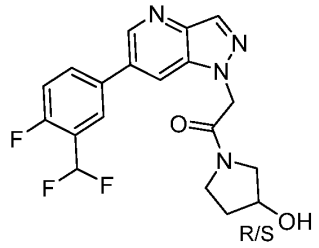
Example 182: (R,S)-2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-hydroxypyrrolidin-1-yl)ethanone.



The title compound was made in an analogous manner to Example 5, Method A, using 6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridine (Intermediate 17) in place of Intermediate 16 and racemic 2-chloro-1-(3-hydroxypyrrolidin-1-yl)ethan-1-one (Intermediate 4) in place of Intermediate 1. MS (ESI): mass calcd. for $C_{19}H_{17}F_3N_4O_3$, 406.1; m/z found, 407.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.88 (d, *J* = 1.9 Hz, 1H), 8.46 – 8.36 (m, 1H), 8.34

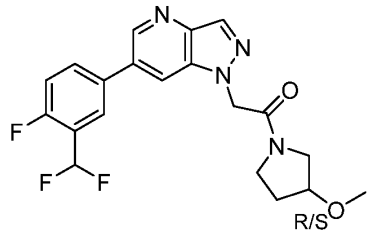
(s, 1H), 7.87 – 7.78 (m, 1H), 7.79 – 7.70 (m, 1H), 7.59 (dd, *J* = 10.2, 8.7 Hz, 1H), 7.38 (t, *J* = 73.2 Hz, 1H), 5.49 (d, *J* = 17.1 Hz, 1H), 5.46 – 5.39 (m, 1H), 4.99 (d, *J* = 3.3 Hz, 1H), 4.33 – 4.24 (m, 1H), 3.80 – 3.64 (m, 2H), 3.53 – 3.19 (m, 2H), 2.10 – 1.70 (m, 2H).

Example 183: (R,S)-2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-hydroxypyrrolidin-1-yl)ethanone.



The title compound was made in a manner analogous to Example 5, Method A, using racemic 2-chloro-1-(3-hydroxypyrrolidin-1-yl)ethan-1-one (Intermediate 4) in place of Intermediate 1. MS (ESI): mass calcd. for $C_{19}H_{17}F_3N_4O_2$, 390.1; m/z found, 391.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.85 (d, *J* = 1.9 Hz, 1H), 8.45 – 8.37 (m, 1H), 8.32 (s, 1H), 8.07 – 7.97 (m, 2H), 7.59 – 7.50 (m, 1H), 7.27 (t, *J* = 54.1 Hz, 1H), 5.49 – 5.42 (m, 1H), 5.41 – 5.33 (m, 1H), 4.97 (d, *J* = 3.2 Hz, 1H), 4.29 – 4.23 (m, 1H), 3.74 – 3.61 (m, 2H), 3.49 – 3.38 (m, 1H), 3.31 – 3.20 (m, 1H), 2.04 – 1.69 (m, 2H).

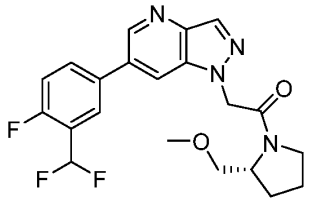
Example 184: (Racemic) 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-(3-methoxypyrrolidin-1-yl)ethanone.



The title compound was prepared in a manner analogous to Example 1 using racemic 3-methoxypyrrolidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{20}H_{19}F_3N_4O_2$, 404.1; m/z found, 405.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 – 8.68 (m, 1H), 8.37 – 8.20 (m, 1H), 7.99 – 7.92 (m, 1H), 7.92 – 7.81 (m, 1H), 7.81 – 7.70 (m, 1H), 7.36 –

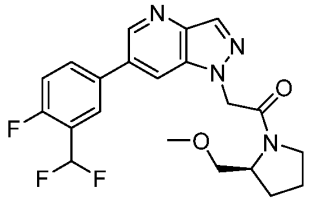
7.26 (m, 1H), 6.97 (t, J = 54.9 Hz, 1H), 5.31 – 5.08 (m, 2H), 4.12 – 3.89 (m, 1H), 3.80 – 3.58 (m, 3H), 3.58 – 3.42 (m, 1H), 3.34 (d, J = 12.3 Hz, 3H), 2.35 – 1.87 (m, 2H).

Example 185: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-[(2*R*)-2-(methoxymethyl)pyrrolidin-1-yl]ethanone.



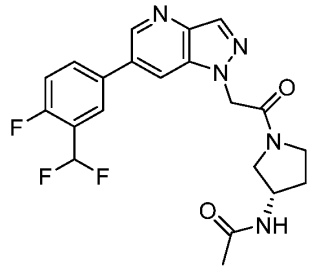
The title compound was prepared in a manner analogous to Example 1 using (*R*)-2-(methoxymethyl)pyrrolidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{21}H_{21}F_3N_4O_2$, 418.2; m/z found, 419.2 $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 – 8.71 (m, 1H), 8.35 – 8.23 (m, 1H), 7.97 – 7.90 (m, 1H), 7.90 – 7.83 (m, 1H), 7.75 (s, 1H), 7.26 (s, 1H), 6.98 (t, J = 54.8 Hz, 1H), 5.56 – 5.10 (m, 2H), 4.33 (d, J = 61.3 Hz, 1H), 3.75 – 3.23 (m, 7H), 2.29 – 1.77 (m, 4H).

Example 186: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-[(2*S*)-2-(methoxymethyl)pyrrolidin-1-yl]ethanone.



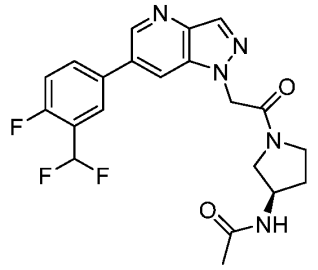
The title compound was prepared in a manner analogous to Example 1 using (*S*)-2-(methoxymethyl)pyrrolidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{21}H_{21}F_3N_4O_2$, 418.2; m/z found, 419.2 $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 – 8.70 (m, 1H), 8.35 – 8.25 (m, 1H), 7.97 – 7.89 (m, 1H), 7.89 – 7.84 (m, 1H), 7.80 – 7.68 (m, 1H), 7.33 – 7.24 (m, 1H), 6.98 (t, J = 54.9 Hz, 1H), 5.53 – 5.14 (m, 2H), 4.44 – 4.20 (m, 1H), 3.75 – 3.19 (m, 7H), 2.26 – 1.76 (m, 4H).

Example 187: *N*-[(3*S*)-1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]acetyl]pyrrolidin-3-yl]acetamide.



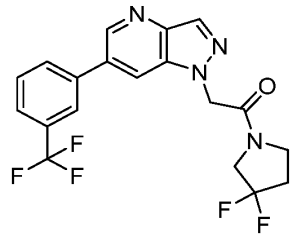
The title compound was prepared in a manner analogous to Example 1 using (*S*)-3-acetamidopyrrolidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{21}H_{20}F_3N_5O_2$, 431.2; m/z found, 432.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.82 – 8.78 (m, 1H), 8.34 – 8.29 (m, 1H), 7.96 – 7.90 (m, 1H), 7.89 – 7.81 (m, 1H), 7.79 – 7.71 (m, 1H), 7.32 – 7.26 (m, 1H), 6.98 (t, *J* = 54.9 Hz, 1H), 5.71 – 5.58 (m, 1H), 5.37 – 5.10 (m, 2H), 4.64 – 4.43 (m, 1H), 4.02 – 3.36 (m, 5H), 2.43 – 1.79 (m, 4H).

Example 188: *N*-[(3*R*)-1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]acetyl]pyrrolidin-3-yl]acetamide.



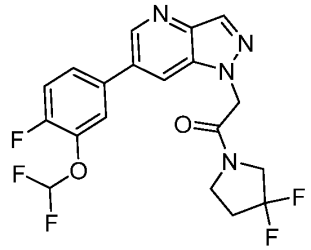
The title compound was prepared in a manner analogous to Example 1 using (*R*)-3-acetamidopyrrolidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{21}H_{20}F_3N_5O_2$, 431.2; m/z found, 432.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 – 8.78 (m, 1H), 8.32 – 8.28 (m, 1H), 7.94 – 7.90 (m, 1H), 7.88 – 7.85 (m, 1H), 7.78 – 7.70 (m, 1H), 7.35 – 7.28 (m, 1H), 6.98 (t, *J* = 54.9 Hz, 1H), 5.74 – 5.62 (m, 1H), 5.36 – 5.10 (m, 2H), 4.60 – 4.45 (m, 1H), 3.99 – 3.39 (m, 5H), 2.39 – 1.80 (m, 4H).

Example 189: 1-(3,3-Difluoropyrrolidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



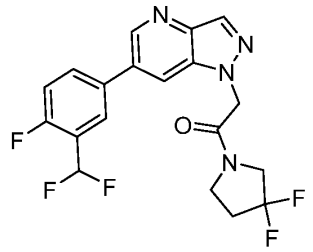
The title compound was prepared in a manner analogous to Example 13, using 3,3-difluoropyrrolidine hydrochloride in place of morpholine. MS (ESI): mass calcd. for $C_{19}H_{15}F_5N_4O$, 410.1; m/z found, 411.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.84 (d, *J*=1.16 Hz, 1H), 8.32 (s, 1H), 7.97 (br. s, 1H), 7.89 (s, 1H), 7.84 (d, *J*=7.63 Hz, 1H), 7.74 – 7.68 (m, 1H), 7.67 – 7.60 (m, 1H), 5.30 – 5.14 (m, 2H), 4.05 – 3.70 (m, 4H), 2.61 – 2.29 (m, 2H).

Example 190: 2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3,3-difluoropyrrolidin-1-yl)ethanone.



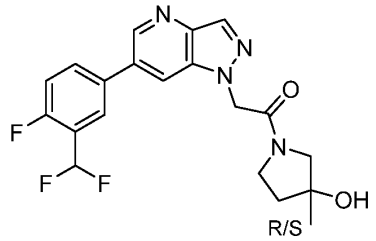
The title compound was made in a manner analogous to Example 5, Method A, using 6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridine (Intermediate 17) in place of Intermediate 16 and 2-chloro-1-(3,3-difluoropyrrolidin-1-yl)ethan-1-one (Intermediate 3) in place of Intermediate 1. MS (ESI): mass calcd. for $C_{19}H_{15}F_5N_4O_2$, 426.1; m/z found, 427.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.88 (d, *J* = 1.9 Hz, 1H), 8.43 – 8.32 (m, 1H), 8.36 (s, 1H), 7.87 – 7.77 (m, 1H), 7.78 – 7.68 (m, 1H), 7.66 – 7.55 (m, 1H), 7.38 (t, *J* = 73.2 Hz, 1H), 5.59 – 5.49 (m, 1H), 5.51 – 5.38 (m, 1H), 4.24 – 4.09 (m, 1H), 4.01 – 3.85 (m, 1H), 3.82 – 3.65 (m, 1H), 3.63 – 3.49 (m, 1H), 2.71 – 2.50 (m, 1H), 2.49 – 2.30 (m, 1H).

Example 191: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3,3-difluoropyrrolidin-1-yl)ethanone.



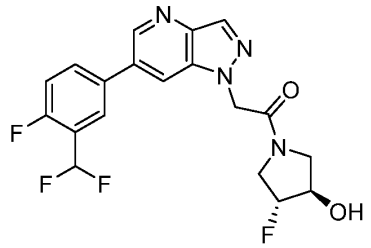
The title compound was made in a manner analogous to Example 5, Method A, using 2-chloro-1-(3,3-difluoropyrrolidin-1-yl)ethan-1-one (Intermediate 3) in place of Intermediate 1. MS (ESI): mass calcd. for $C_{19}H_{15}F_5N_4O$, 410.1; m/z found, 411.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.88 (d, J = 1.9 Hz, 1H), 8.43 – 8.38 (m, 1H), 8.36 (s, 1H), 8.07 – 8.01 (m, 2H), 7.61 – 7.55 (m, 1H), 7.30 (t, J = 54.1 Hz, 1H), 5.54, 5.47 (s, 2H), 4.20 – 4.12, 3.78 – 3.70 (m, 2H), 3.92, 3.56 (t, J = 7.4 Hz, 2H), 2.62 – 2.38 (m, 2H)* mixture of rotamers.

Example 192: (Racemic) 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-(3-hydroxy-3-methyl-pyrrolidin-1-yl)ethanone.



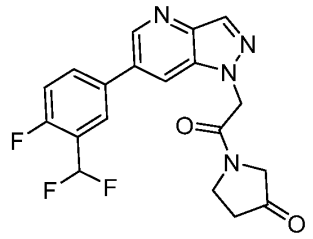
The title compound was prepared in a manner analogous to Example 1 using racemic 3-methylpyrrolidin-3-ol in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{20}H_{19}F_3N_4O_2$, 404.1; m/z found, 405.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 – 8.72 (m, 1H), 8.34 – 8.22 (m, 1H), 8.00 – 7.92 (m, 1H), 7.90 – 7.85 (m, 1H), 7.79 – 7.69 (m, 1H), 7.33 – 7.27 (m, 1H), 6.97 (t, J = 54.9 Hz, 1H), 5.33 – 5.09 (m, 2H), 3.91 – 3.77 (m, 1H), 3.74 – 3.59 (m, 2H), 3.57 – 3.28 (m, 1H), 2.22 – 1.81 (m, 2H), 1.52 – 1.44 (m, 3H).

Example 193: (Racemic) *Trans*-2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-(3-fluoro-4-hydroxy-pyrrolidin-1-yl)ethanone.



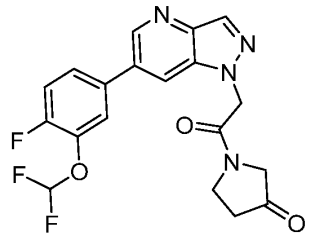
The title compound was prepared in a manner analogous to Example 1 using racemic *trans*-4-fluoropyrrolidin-3-ol in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{19}H_{16}F_4N_4O_2$, 408.1; m/z found, 409.1 $[M+H]^+$. ^1H NMR (400 MHz, Methanol-d4) δ 8.78 (d, *J* = 1.9 Hz, 1H), 8.29 (t, *J* = 0.9 Hz, 1H), 8.25 – 8.16 (m, 1H), 7.98 – 7.92 (m, 1H), 7.92 – 7.84 (m, 1H), 7.41 – 7.29 (m, 1H), 7.02 (t, *J* = 54.8 Hz, 1H), 5.50 – 5.29 (m, 2H), 5.20 – 4.87 (m, 1H), 4.54 – 4.32 (m, 1H), 4.11 – 3.55 (m, 5H)* mixture of trans.

Example 194: 1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]pyrrolidin-3-one.



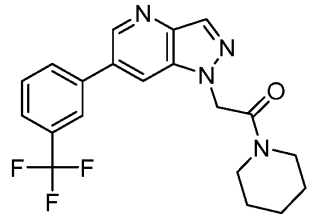
The title compound was prepared in a manner analogous to Example 1 using pyrrolidin-3-one in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{19}H_{15}F_3N_4O_2$, 388.1; m/z found, 389.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.88 (d, *J* = 1.9 Hz, 1H), 8.43 – 8.36 (m, 1H), 8.38 – 8.34 (m, 1H), 8.08 – 8.00 (m, 2H), 7.61 – 7.54 (m, 1H), 7.30 (t, *J* = 54.1 Hz, 1H), 5.46 (s, 2H), 4.16 (s, 2H), 3.77 – 3.70 (m, 2H), 2.60 (t, *J* = 7.9 Hz, 2H).

Example 195: 1-[2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]pyrrolidin-3-one.



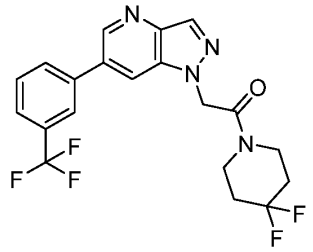
The title compound was prepared in a manner analogous to Example 1 using 2-(6-(3-(difluoromethoxy)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid (Intermediate 29) in place of Intermediate 27 and pyrrolidin-3-one in place of 3-(trifluoromethyl)azetidine-3-. MS (ESI): mass calcd. for $C_{19}H_{15}F_3N_4O_3$, 404.1; m/z found, 405.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.88 (d, J = 1.9 Hz, 1H), 8.40 – 8.33 (m, 2H), 7.84 – 7.79 (m, 1H), 7.77 – 7.71 (m, 1H), 7.60 (dd, J = 10.5, 8.6 Hz, 1H), 7.38 (t, J = 73.2 Hz, 1H), 5.45 (s, 2H), 4.16 (s, 2H), 3.76 – 3.70 (m, 2H), 2.61 (t, J = 7.9 Hz, 2H).

Example 196: 1-(1-Piperidyl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone trifluoroacetate salt.



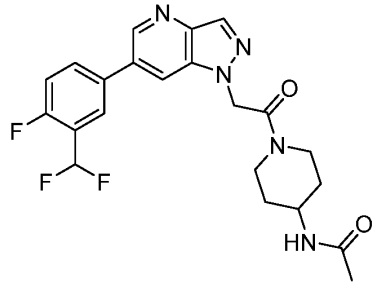
The title compound was prepared in a manner analogous to Example 16, using piperidine in place of 3-fluoroazetidine hydrochloride and DCM in place of DMF. MS (ESI): mass calcd. for $C_{20}H_{19}F_3N_4O$, 388.2; m/z found, 389.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.92 (d, J = 2.0 Hz, 1H), 8.48 – 8.46 (m, 1H), 8.35 – 8.34 (m, 1H), 8.16 – 8.11 (m, 2H), 7.84 – 7.76 (m, 2H), 5.55 (s, 2H), 3.43 – 3.39 (m, 2H), 1.66 – 1.57 (m, 4H), 1.51 – 1.40 (s, 2H).

Example 197: 1-(4,4-Difluoro-1-piperidyl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone.



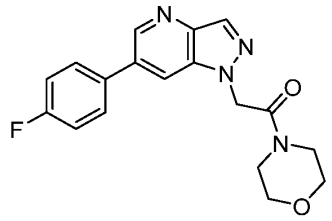
The title compound was prepared in a manner analogous to Example 13, using 4,4-difluoropiperidine in place of morpholine. MS (ESI): mass calcd. for $C_{20}H_{17}F_5N_4O$, 424.1; m/z found, 425.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.84 (d, *J*=1.85 Hz, 1H), 8.33 (d, *J*=0.92 Hz, 1H), 7.98 (dd, *J*=1.85, 0.92 Hz, 1H), 7.89 (s, 1H), 7.84 (d, *J*=7.63 Hz, 1H), 7.74 – 7.68 (m, 1H), 7.67 – 7.60 (m, 1H), 5.34 (s, 2H), 3.86 – 3.78 (m, 2H), 3.74 (t, *J*=5.90 Hz, 2H), 2.07 – 1.86 (m, 4H).

Example 198: *N*-[1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]acetyl]-4-piperidyl]acetamide.



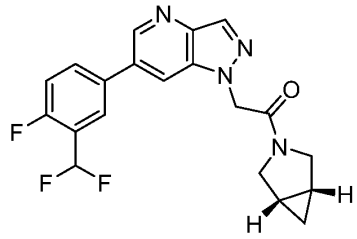
The title compound was prepared in a manner analogous to Example 1 using 4-acetamidopiperidine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{22}H_{22}F_3N_5O_2$, 445.2; m/z found, 446.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, *J* = 1.9 Hz, 1H), 8.30 (d, *J* = 1.0 Hz, 1H), 7.93 (dd, *J* = 1.9, 1.0 Hz, 1H), 7.90 – 7.81 (m, 1H), 7.77 – 7.72 (m, 1H), 7.34 – 7.27 (m, 1H), 6.98 (t, *J* = 54.9 Hz, 1H), 5.44 – 5.14 (m, 3H), 4.55 – 4.40 (m, 1H), 4.21 – 4.10 (m, 1H), 4.04 – 3.95 (m, 1H), 3.35 – 3.20 (m, 1H), 2.85 – 2.72 (m, 1H), 2.14 – 1.89 (m, 5H), 1.32 – 1.15 (m, 2H).

Example 199: 2-[6-(4-Fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-morpholino-ethanone.



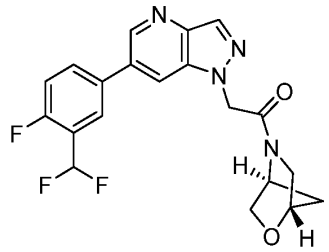
The title compound was prepared in a manner analogous to Example 1 using 2-(6-(4-fluorophenyl)-1H-pyrazolo[4,3-*b*]pyridin-1-yl)acetic acid (Intermediate 31) in place of Intermediate 16 and morpholine in place of 3-(trifluoromethyl)azetidin-3-ol. MS (ESI): mass calcd. for $C_{18}H_{17}FN_4O_2$, 340.1; m/z found, 341.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.80 (d, *J* = 1.9 Hz, 1H), 8.28 (d, *J* = 1.1 Hz, 1H), 7.93 (dd, *J* = 1.9, 1.0 Hz, 1H), 7.65 – 7.59 (m, 2H), 7.23 – 7.17 (m, 2H), 5.28 (s, 2H), 3.72 – 3.59 (m, 8H).

Example 200: 1-[(1*R*,5*S*)-3-Azabicyclo[3.1.0]hexan-3-yl]-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]ethanone.



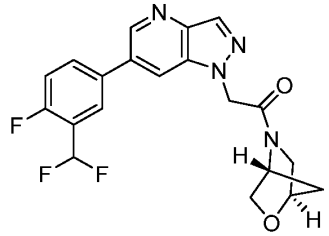
The title compound was prepared in a manner analogous to Example 1 using (1*R*,5*S*)-3-azabicyclo[3.1.0]hexane in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{20}H_{17}F_3N_4O$, 386.1; m/z found, 387.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.78 (d, *J* = 1.9 Hz, 1H), 8.29 (d, *J* = 1.0 Hz, 1H), 7.96 – 7.89 (m, 1H), 7.89 – 7.80 (m, 1H), 7.78 – 7.70 (m, 1H), 7.35 – 7.26 (m, 1H), 6.97 (t, *J* = 54.8 Hz, 1H), 5.16 (d, *J* = 2.3 Hz, 2H), 3.87 – 3.74 (m, 2H), 3.68 (dd, *J* = 9.9, 4.3 Hz, 1H), 3.45 (dd, *J* = 12.0, 4.5 Hz, 1H), 1.66 (tt, *J* = 7.9, 4.2 Hz, 1H), 1.59 (dd, *J* = 8.0, 4.1 Hz, 1H), 0.83 – 0.76 (m, 1H), 0.20 (q, *J* = 4.5 Hz, 1H).

Example 201: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-[(1*S*,4*S*)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl]ethanone.



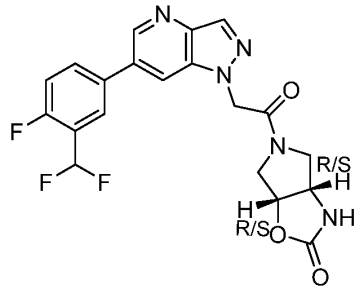
The title compound was prepared in a manner analogous to Example 1 using (1*S*,4*S*)-2-oxa-5-azabicyclo[2.2.1]heptane in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{20}H_{17}F_3N_4O_2$, 402.1; m/z found, 403.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.83 – 8.76 (m, 1H), 8.33 – 8.26 (m, 1H), 8.04 – 7.90 (m, 1H), 7.89 – 7.85 (m, 1H), 7.79 – 7.72 (m, 1H), 7.33 – 7.26 (m, 1H), 7.14 – 6.79 (m, 1H), 5.34 – 5.07 (m, 2H), 4.98 – 4.81 (m, 1H), 4.76 – 4.63 (m, 1H), 3.97 – 3.38 (m, 4H), 2.03 – 1.79 (m, 2H).

Example 202: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-1-[(1*R*,4*R*)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl]ethanone.



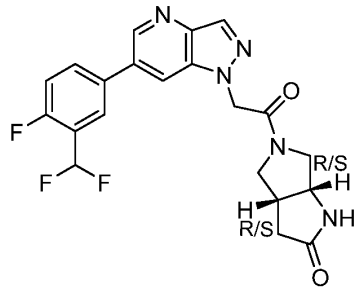
The title compound was prepared in a manner analogous to Example 1 using (1*R*,4*R*)-2-oxa-5-azabicyclo[2.2.1]heptane in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{20}H_{17}F_3N_4O_2$, 402.1; m/z found, 403.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.83 – 8.77 (m, 1H), 8.31 – 8.28 (m, 1H), 8.04 – 7.91 (m, 1H), 7.89 – 7.84 (m, 1H), 7.80 – 7.70 (m, 1H), 7.32 – 7.26 (m, 1H), 7.14 – 6.81 (m, 1H), 5.33 – 5.09 (m, 2H), 4.97 – 4.79 (m, 1H), 4.76 – 4.62 (m, 1H), 3.92 – 3.74 (m, 2H), 3.70 – 3.53 (m, 1H), 3.51 – 3.37 (m, 1H), 2.01 – 1.78 (m, 2H).

Example 203: (Racemic) *Cis*-5-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]acetyl]-3a,4,6,6a-tetrahydro-3H-pyrrolo[3,4-d]oxazol-2-one.



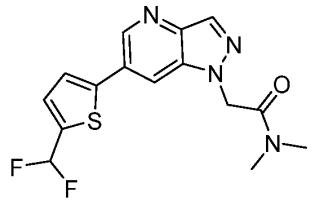
The title compound was prepared in a manner analogous to Example 2 using racemic *cis*-hexahydro-2H-pyrrolo[3,4-d]oxazol-2-one in place of 3-methyleneazetidine. MS (ESI): mass calcd. for $C_{20}H_{16}F_3N_5O_3$, 431.1; m/z found, 432.1 $[M+H]^+$. ^1H NMR (400 MHz,DMSO-d6) δ 8.72 (d, J = 1.9 Hz, 1H), 8.27 – 8.13 (m, 2H), 7.97 – 7.83 (m, 3H), 7.33 (t, J = 9.3 Hz, 1H), 7.02 (t, J = 54.5 Hz, 1H), 5.63 – 4.96 (m, 3H), 4.41 (dd, J = 48.3, 6.4 Hz, 2H), 3.97 – 3.71 (m, 3H)* cis.

Example 204: (Racemic) *Cis*-5-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]acetyl]-1,3,3a,4,6,6a-hexahydropyrrolo[2,3-c]pyrrol-2-one.



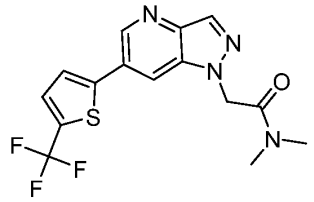
The title compound was prepared in a manner analogous to Example 2 using racemic *cis*-hexahydropyrrolo[3,4-*b*]pyrrol-2(1H)-one in place of 3-methyleneazetidine. MS (ESI): mass calcd. for $C_{21}H_{18}F_3N_5O_2$, 429.1; m/z found, 430.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 10.47 (s, 1H), 8.73 (s, 1H), 8.29 – 8.21 (m, 1H), 8.13 – 8.05 (m, 1H), 7.90 – 7.65 (m, 2H), 7.29 – 7.23 (m, 1H), 7.15 – 6.79 (m, 1H), 5.48 – 5.10 (m, 2H), 4.30 (dt, *J* = 46.8, 5.8 Hz, 1H), 4.09 – 3.99 (m, 1H), 3.80 (dd, *J* = 12.9, 9.7 Hz, 1H), 3.28 – 2.95 (m, 3H), 2.71 – 2.53 (m, 1H), 2.35 – 2.10 (m, 1H).

Example 205: 2-[6-[5-(Difluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]-*N*,*N*-dimethyl-acetamide.



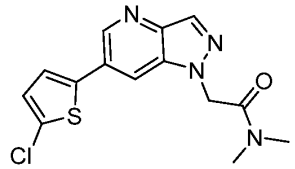
The title compound was made in a manner analogous to Example 9 using 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-*N*,*N*-dimethylacetamide (Intermediate 10) in place of Intermediate 12 and 2-(5-(difluoromethyl)thiophen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Intermediate 8) in place of 2-[4-chloro-3-(difluoromethoxy)phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd. for $C_{15}H_{14}F_2N_4OS$, 336.1; m/z found, 337.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.93 (d, J = 2.0 Hz, 1H), 8.47 – 8.37 (m, 1H), 8.36 – 8.28 (m, 1H), 7.77 – 7.68 (m, 1H), 7.62 – 7.53 (m, 1H), 7.37 (t, J = 55.4 Hz, 1H), 5.52 (s, 2H), 3.13 (s, 3H), 2.86 (s, 3H).

Example 206: *N*,*N*-Dimethyl-2-[6-[5-(trifluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide.



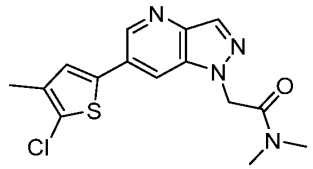
The title compound was made in a manner analogous to Example 7 using 4,4,5,5-tetramethyl-2-(5-(trifluoromethyl)thiophen-2-yl)-1,3,2-dioxaborolane in place of 4-fluoro-3-methylboronic acid. MS (ESI): mass calcd. for $C_{15}H_{13}F_3N_4OS$, 354.1; m/z found, 355.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.96 (d, J = 1.9 Hz, 1H), 8.52 – 8.45 (m, 1H), 8.35 (s, 1H), 7.89 – 7.76 (m, 2H), 5.52 (s, 2H), 3.14 (s, 3H), 2.86 (s, 3H).

Example 207: 2-[6-(5-Chloro-2-thienyl)pyrazolo[4,3-b]pyridin-1-yl]-*N*,*N*-dimethyl-acetamide.



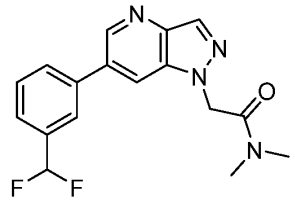
The title compound was made in a manner analogous to Example 9 using 2-(6-bromo-1H-pyrazolo[4,3-b]pyridin-1-yl)-*N*,*N*-dimethylacetamide (Intermediate 10) in place of Intermediate 12 and 5-chlorothiophene-2-boronic acid in place of 2-[4-chloro-3-(difluoromethoxy)phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. MS (ESI): mass calcd. for $C_{14}H_{13}ClN_4OS$, 320.1; m/z found, 321.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.85 (d, J = 1.9 Hz, 1H), 8.35 – 8.23 (m, 2H), 7.61 (d, J = 4.0 Hz, 1H), 7.26 (d, J = 4.0 Hz, 1H), 5.50 (s, 2H), 3.13 (s, 3H), 2.86 (s, 3H).

Example 208: 2-[6-(5-Chloro-4-methyl-2-thienyl)pyrazolo[4,3-b]pyridin-1-yl]-*N*,*N*-dimethyl-acetamide.



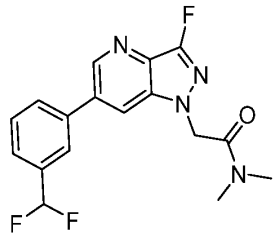
The title compound was prepared in a manner analogous to Example 11 using 2-(5-chloro-4-methylthiophene-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in place of 3-(trifluoromethyl)phenylboronic acid. MS (ESI): mass calcd. for $C_{15}H_{15}ClN_4OS$, 334.1; m/z found, 335.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.75 (d, J = 1.9 Hz, 1H), 8.24 (d, J = 1.0 Hz, 1H), 7.80 (dd, J = 2.0, 1.0 Hz, 1H), 7.12 (s, 1H), 5.24 (s, 2H), 3.17 (s, 3H), 2.99 (s, 3H), 2.23 (s, 3H).

Example 209: 2-[6-[3-(Difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-*N*,*N*-dimethyl-acetamide.



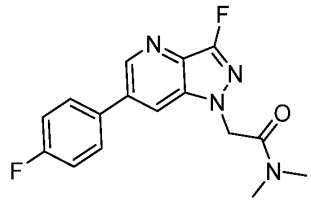
The title compound was prepared in a manner analogous to Example 11 using 3-(difluoromethyl)phenylboronic acid in place of 3-(trifluoromethyl)phenylboronic acid. MS (ESI): mass calcd. for $C_{17}H_{16}F_2N_4O$, 330.1; m/z found, 331.0 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.83 (d, J = 1.9 Hz, 1H), 8.30 (d, J = 1.1 Hz, 1H), 7.95 (dd, J = 1.9, 1.0 Hz, 1H), 7.80 – 7.74 (m, 2H), 7.63 – 7.54 (m, 2H), 6.86 - 6.63 (m, 1H), 5.30 (s, 2H), 3.19 (s, 3H), 2.99 (s, 3H).

Example 210: 2-[6-[3-(Difluoromethyl)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-*N*,*N*-dimethyl-acetamide.



The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)-N,N-dimethylacetamide (Intermediate 11) in place of Intermediate 10 and 2-(3-(difluoromethyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in place of 4-fluoro-3-methylphenylboronic acid. MS (ESI): mass calcd. for $C_{17}H_{15}F_3N_4O$, 348.1; m/z found, 349.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.93 (d, J = 1.8 Hz, 1H), 8.51 – 8.42 (m, 1H), 8.06 – 7.95 (m, 2H), 7.77 – 7.64 (m, 2H), 7.14 (t, J = 55.7 Hz, 1H), 5.43 (s, 2H), 3.10 (s, 3H), 2.84 (s, 3H).

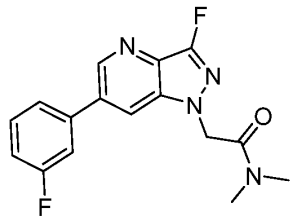
Example 211: 2-[3-Fluoro-6-(4-fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-*N*,*N*-dimethyl-acetamide.



The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)-*N*,*N*-dimethylacetamide (Intermediate 11) in place of Intermediate 10 and 4-fluorophenylboronic acid in place of 4-fluoro-3-methylphenylboronic

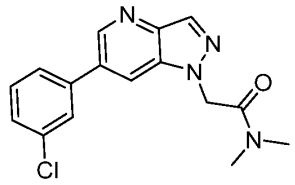
acid. MS (ESI): mass calcd. for $C_{16}H_{14}F_2N_4O$, 316.1; m/z found, 317.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.89 (d, J = 1.8 Hz, 1H), 8.42 – 8.36 (m, 1H), 7.91 – 7.83 (m, 2H), 7.45 – 7.35 (m, 2H), 5.40 (s, 2H), 3.10 (s, 3H), 2.84 (s, 3H).

Example 212: 2-[3-Fluoro-6-(3-fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-*N*,*N*-dimethyl-acetamide.



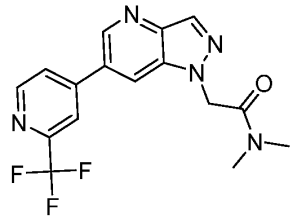
The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)-*N*,*N*-dimethylacetamide (Intermediate 11) in place of Intermediate 10 and 3-fluorophenylboronic acid in place of 4-fluoro-3-methylphenylboronic acid. MS (ESI): mass calcd. for $C_{16}H_{14}F_2N_4O$, 316.1; m/z found, 317.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.95 (d, J = 1.8 Hz, 1H), 8.52 – 8.44 (m, 1H), 7.76 – 7.66 (m, 2H), 7.65 – 7.55 (m, 1H), 7.38 – 7.27 (m, 1H), 5.41 (s, 2H), 3.10 (s, 3H), 2.84 (s, 3H).

Example 213: 2-[6-(3-Chlorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-*N*,*N*-dimethyl-acetamide.



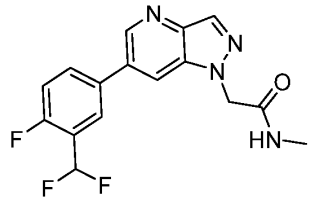
The title compound was made in a manner analogous to Example 7 using 3-chlorophenylboronic acid in place of 4-fluoro-3-methylboronic acid. MS (ESI): mass calcd. for $C_{16}H_{15}ClN_4O$, 314.1; m/z found, 315.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.89 (d, J = 1.9 Hz, 1H), 8.43 (dd, J = 2.0, 1.0 Hz, 1H), 8.32 (d, J = 1.0 Hz, 1H), 7.91 – 7.88 (m, 1H), 7.82 – 7.78 (m, 1H), 7.57 (t, J = 7.8 Hz, 1H), 7.54 – 7.50 (m, 1H), 5.52 (s, 2H), 3.13 (s, 3H), 2.85 (s, 3H).

Example 214: *N*,*N*-Dimethyl-2-[6-[2-(trifluoromethyl)-4-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide.



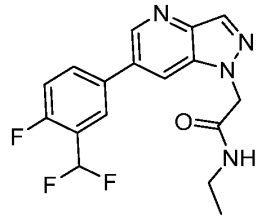
The title compound was made in a manner analogous to Example 7 using 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(trifluoromethyl)pyridine in place of 4-fluoro-3-methylphenylboronic acid. MS (ESI): mass calcd. for $C_{16}H_{14}F_3N_5O$, 349.1; m/z found, 350.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 9.07 (d, J = 2.0 Hz, 1H), 8.91 (d, J = 5.2 Hz, 1H), 8.74 – 8.63 (m, 1H), 8.42 – 8.37 (m, 1H), 8.37 – 8.32 (m, 1H), 8.26 – 8.16 (m, 1H), 5.56 (s, 2H), 3.15 (s, 3H), 2.86 (s, 3H).

Example 215: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-*N*-methyl-acetamide.



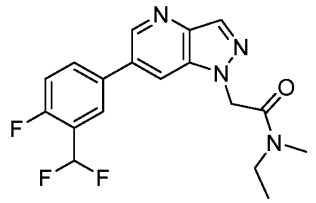
The title compound was made in a manner analogous to Example 5, Method A, using 2-chloro-*N*-methylacetamide in place of Intermediate 1. MS (ESI): mass calcd. for $C_{16}H_{13}F_3N_4O$, 334.1; m/z found, 335.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.89 (d, J = 1.9 Hz, 1H), 8.55 – 8.46 (m, 1H), 8.35 (s, 1H), 8.17 – 8.01 (m, 3H), 7.63 – 7.51 (m, 1H), 7.30 (t, J = 54.1 Hz, 1H), 5.19 (s, 2H), 2.62 (d, J = 4.6 Hz, 3H).

Example 216: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-*N*-ethyl-acetamide.



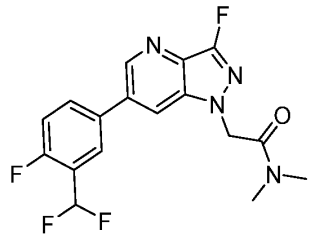
The title compound was made in a manner analogous to Example 5, Method A, using 2-chloro-*N*-ethylacetamide in place of Intermediate 1. MS (ESI): mass calcd. for $C_{17}H_{15}F_3N_4O$, 348.1; m/z found, 349.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.89 (d, J = 1.9 Hz, 1H), 8.54 – 8.46 (m, 1H), 8.38 – 8.31 (m, 1H), 8.23 (t, J = 5.6 Hz, 1H), 8.12 – 8.01 (m, 2H), 7.64 – 7.52 (m, 1H), 7.30 (t, J = 54.1 Hz, 1H), 5.18 (s, 2H), 3.18 – 3.03 (m, 2H), 1.04 (t, J = 7.2 Hz, 3H).

Example 217: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-*N*-ethyl-*N*-methyl-acetamide.



The title compound was prepared in a manner analogous to Example 1 using *N*-methylethanamine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{18}H_{17}F_3N_4O$, 362.1; m/z found, 363.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.78 (d, J = 1.9 Hz, 1H), 8.30 (dd, J = 2.4, 1.0 Hz, 1H), 7.92 (ddd, J = 16.9, 2.0, 1.0 Hz, 1H), 7.89 – 7.83 (m, 1H), 7.79 – 7.72 (m, 1H), 6.97 (t, J = 54.9 Hz, 1H), 5.38 – 5.23 (m, 2H), 3.63 – 3.40 (m, 2H), 3.20 – 2.91 (m, 3H), 1.33 – 1.06 (m, 3H).

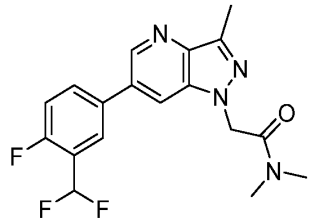
Example 218: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-*N*,*N*-dimethyl-acetamide.



The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)-*N*,*N*-dimethylacetamide (Intermediate 11) in place of Intermediate 10 and 2-(3-(difluoromethyl)-4-fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in place of 4-fluoro-3-methylphenylboronic acid. MS (ESI): mass calcd. for

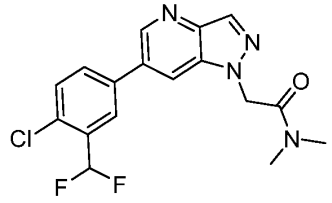
$C_{17}H_{14}F_4N_4O$, 366.1; m/z found, 367.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.89 (d, J = 1.9 Hz, 1H), 8.48 – 8.38 (m, 1H), 8.10 – 7.97 (m, 2H), 7.60 – 7.53 (m, 1H), 7.28 (t, J = 54.1 Hz, 1H), 5.39 (s, 2H), 3.07 (s, 3H), 2.81 (s, 3H).

Example 219: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-methyl-pyrazolo[4,3-*b*]pyridin-1-yl]-N,N-dimethyl-acetamide.



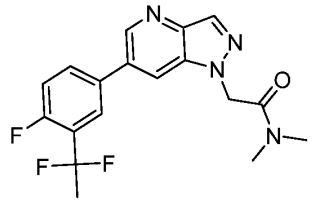
The title compound was prepared in a manner analogous to Example 1 using 2-(6-(3-(difluoromethyl)-4-fluorophenyl)-3-methyl-1H-pyrazolo[4,3-*b*]pyridin-1-yl)acetic acid (Intermediate 32) in place of Intermediate 27 and dimethylamine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{18}H_{17}F_3N_4O$, 362.1; m/z found, 363.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, J = 1.9 Hz, 1H), 7.88 – 7.79 (m, 2H), 7.77 – 7.69 (m, 1H), 7.26 (s, 1H), 6.97 (t, J = 54.9 Hz, 1H), 5.22 (s, 2H), 3.18 (s, 3H), 2.99 (s, 3H), 2.70 (s, 3H).

Example 220: 2-[6-[4-Chloro-3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-*N*,*N*-dimethyl-acetamide.



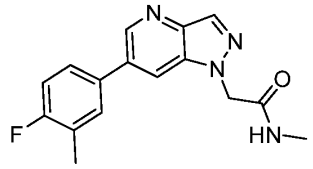
The title compound was made in a manner analogous to Example 7 using 2-(4-chloro-3-(difluoromethyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in place of 4-fluoro-3-methylboronic acid. MS (ESI): mass calcd. for $C_{17}H_{15}ClF_2N_4O$, 364.1; m/z found, 365.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.89 (d, J = 2.0 Hz, 1H), 8.45 (dd, J = 2.0, 1.0 Hz, 1H), 8.34 (d, J = 1.0 Hz, 1H), 8.08 (d, J = 2.2 Hz, 1H), 8.05 – 8.00 (m, 1H), 7.81 – 7.76 (m, 1H), 7.30 (t, J = 54.1 Hz, 1H), 5.54 (s, 2H), 3.13 (s, 3H), 2.85 (s, 3H).

Example 221: 2-[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-*N*,*N*-dimethyl-acetamide.



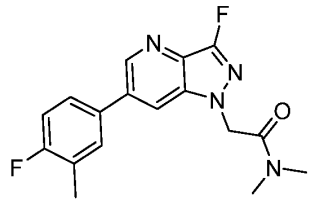
The title compound was made in a manner analogous to Example 6, Method A, using 6-[3-(1,1-difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridine (Intermediate 19) in place of Intermediate 16. MS (ESI): mass calcd. for $C_{18}H_{17}F_3N_4O$, 362.1; m/z found, 363.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.87 (d, J = 1.9 Hz, 1H), 8.43 – 8.36 (m, 1H), 8.36 – 8.30 (m, 1H), 8.04 – 7.96 (m, 1H), 7.92 (dd, J = 7.2, 2.3 Hz, 1H), 7.55 (dd, J = 11.0, 8.6 Hz, 1H), 5.53 (s, 2H), 3.13 (s, 3H), 2.85 (s, 3H), 2.09 (t, J = 19.2 Hz, 3H).

Example 222: 2-[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-*N*-methyl-acetamide.



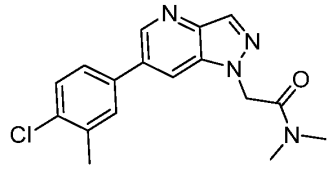
The title compound was made in a manner analogous to Example 5, Method A, using 6-(4-fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridine (Intermediate 25) in place of Intermediate 16 and 2-chloro-*N*-methylacetamide in place of Intermediate 1. MS (ESI): mass calcd. for $C_{16}H_{15}FN_4O$, 298.1; m/z found, 299.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.85 (d, J = 1.9 Hz, 1H), 8.41 – 8.37 (m, 1H), 8.34 – 8.30 (m, 1H), 8.11 – 8.04 (m, 1H), 7.77 (dd, J = 7.4, 2.4 Hz, 1H), 7.70 – 7.64 (m, 1H), 7.33 – 7.27 (m, 1H), 5.17 (s, 2H), 2.62 (d, J = 4.6 Hz, 3H), 2.34 (d, J = 1.8 Hz, 3H).

Example 223: 2-[3-Fluoro-6-(4-fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-*N*,*N*-dimethyl-acetamide.



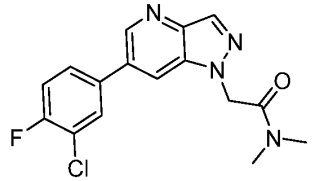
The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)-*N*,*N*-dimethylacetamide (Intermediate 11) in place of Intermediate 10. MS (ESI): mass calcd. for $C_{17}H_{16}F_2N_4O$, 330.1; m/z found, 331.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.88 (d, J = 1.8 Hz, 1H), 8.39 – 8.35 (m, 1H), 7.78 – 7.74 (m, 1H), 7.69 – 7.65 (m, 1H), 7.35 – 7.30 (m, 1H), 5.40 (s, 2H), 3.10 (s, 3H), 2.84 (s, 3H), 2.35 (d, J = 1.8 Hz, 3H).

Example 224: 2-[6-(4-Chloro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-*N*,*N*-dimethyl-acetamide.



The title compound was made in a manner analogous to Example 7 using 4-chloro-3-methylphenylboronic acid in place of 4-fluoro-3-methylboronic acid. MS (ESI): mass calcd. for $C_{17}H_{17}ClN_4O$, 328.1; m/z found, 329.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.86 (d, J = 1.9 Hz, 1H), 8.39 – 8.34 (m, 1H), 8.31 (s, 1H), 7.86 – 7.79 (m, 1H), 7.66 (dd, J = 8.3, 2.3 Hz, 1H), 7.57 (d, J = 8.3 Hz, 1H), 5.52 (s, 2H), 3.13 (s, 3H), 2.85 (s, 3H), 2.44 (s, 3H).

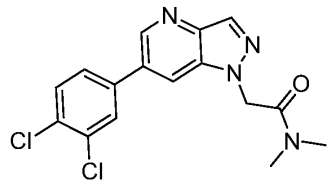
Example 225: 2-[6-(3-Chloro-4-fluoro-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-*N*,*N*-dimethyl-acetamide.



The title compound was made in a manner analogous to Example 7 using 3-chloro-4-fluorophenylboronic acid in place of 4-fluoro-3-methylboronic acid. MS (ESI): mass calcd. for

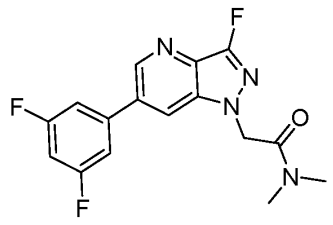
$C_{16}H_{14}ClFN_4O$, 332.1; m/z found, 333.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.88 (d, J = 2.0 Hz, 1H), 8.45 – 8.39 (m, 1H), 8.32 (d, J = 0.9 Hz, 1H), 8.06 (dd, J = 7.1, 2.4 Hz, 1H), 7.88 – 7.81 (m, 1H), 7.60 (t, J = 8.9 Hz, 1H), 5.51 (s, 2H), 3.13 (s, 3H), 2.85 (s, 3H).

Example 226: 2-[6-(3,4-Dichlorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-*N*,*N*-dimethyl-acetamide.



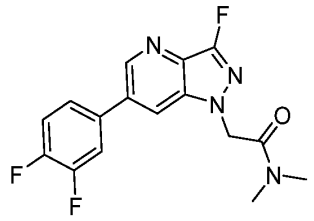
The title compound was made in a manner analogous to Example 7 using 3,4-dichlorophenylboronic acid in place of 4-fluoro-3-methylboronic acid. MS (ESI): mass calcd. for $C_{16}H_{14}Cl_2N_4O$, 348.1; m/z found, 349.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.91 (d, J = 1.9 Hz, 1H), 8.50 – 8.42 (m, 1H), 8.33 (s, 1H), 8.11 (d, J = 1.9 Hz, 1H), 7.85 (dd, J = 8.4, 2.0 Hz, 1H), 7.80 (d, J = 8.4 Hz, 1H), 5.52 (s, 2H), 3.13 (s, 3H), 2.85 (s, 3H).

Example 227: 2-[6-(3,5-Difluorophenyl)-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-*N*,*N*-dimethyl-acetamide.



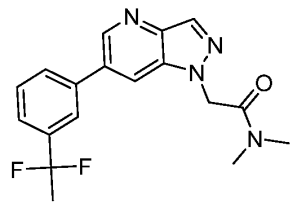
The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)-*N*,*N*-dimethylacetamide (Intermediate 11) in place of Intermediate 10 and 3,5-difluorophenylboronic acid in place of 4-fluoro-3-methylphenylboronic acid. MS (ESI): mass calcd. for $C_{16}H_{13}F_3N_4O$, 334.1; m/z found, 335.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.98 (d, J = 1.9 Hz, 1H), 8.57 – 8.51 (m, 1H), 7.70 – 7.60 (m, 2H), 7.43 – 7.31 (m, 1H), 5.40 (s, 2H), 3.11 (s, 3H), 2.84 (s, 3H).

Example 228: 2-[6-(3,4-Difluorophenyl)-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-*N*,*N*-dimethyl-acetamide.



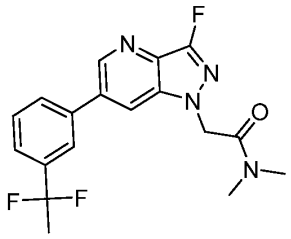
The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)-*N*,*N*-dimethylacetamide (Intermediate 11) in place of Intermediate 10 and 3,4-difluorophenylboronic acid in place of 4-fluoro-3-methylphenylboronic acid. MS (ESI): mass calcd. for $C_{16}H_{13}F_3N_4O$, 334.1; m/z found, 335.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.93 (d, J = 1.9 Hz, 1H), 8.48 – 8.43 (m, 1H), 8.00 – 7.94 (m, 1H), 7.73 – 7.68 (m, 1H), 7.64 (dt, J = 10.5, 8.5 Hz, 1H), 5.40 (s, 2H), 3.10 (s, 3H), 2.84 (s, 3H).

Example 229: 2-[6-[3-(1,1-Difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-*N*,*N*-dimethyl-acetamide.



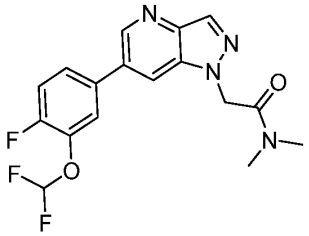
The title compound was made in a manner analogous to Example 6, Method A, using 6-[3-(1,1-difluoroethyl)phenyl]pyrazolo[4,3-b]pyridine (Intermediate 20) in place of Intermediate 16. MS (ESI): mass calcd. for $C_{18}H_{18}F_2N_4O$, 344.1; m/z found, 345.2 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.90 (d, J = 1.9 Hz, 1H), 8.43 – 8.37 (m, 1H), 8.37 – 8.31 (m, 1H), 7.97 – 7.88 (m, 2H), 7.72 – 7.61 (m, 2H), 5.54 (s, 2H), 3.13 (s, 3H), 2.85 (s, 3H), 2.06 (t, J = 18.9 Hz, 3H).

Example 230: 2-[6-[3-(1,1-Difluoroethyl)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-*N*,*N*-dimethyl-acetamide.



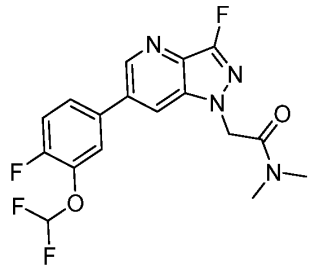
The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)-*N*,*N*-dimethylacetamide (Intermediate 11) in place of Intermediate 10 and 2-(3-(1,1-difluoroethyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in place of 4-fluoro-3-methylphenylboronic acid. MS (ESI): mass calcd. for $C_{18}H_{17}F_3N_4O$, 362.1; m/z found, 363.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.94 (d, J = 1.9 Hz, 1H), 8.48 – 8.44 (m, 1H), 7.99 – 7.91 (m, 2H), 7.72 – 7.64 (m, 2H), 5.43 (s, 2H), 3.10 (s, 3H), 2.84 (s, 3H), 2.06 (t, J = 18.9 Hz, 3H).

Example 231: 2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-*N*,*N*-dimethyl-acetamide.



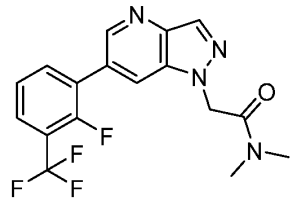
The title compound was made in a manner analogous to Example 6, Method A, using 6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridine (Intermediate 17) in place of Intermediate 16. MS (ESI): mass calcd. for $C_{17}H_{15}F_3N_4O_2$, 364.1; m/z found, 365.2 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.92 – 8.83 (m, 1H), 8.43 – 8.35 (m, 1H), 8.35 – 8.30 (m, 1H), 7.87 – 7.79 (m, 1H), 7.79 – 7.70 (m, 1H), 7.63 – 7.55 (m, 1H), 7.38 (t, J = 73.3 Hz, 1H), 5.52 (s, 2H), 3.13 (s, 3H), 2.85 (s, 3H).

Example 232: 2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-*N*,*N*-dimethyl-acetamide.



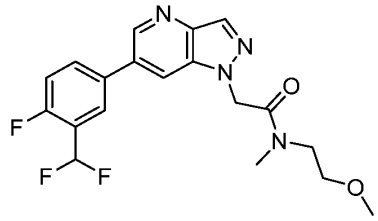
The title compound was made in a manner analogous to Example 7 using 2-(6-bromo-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)-*N*,*N*-dimethylacetamide (Intermediate 11) in place of Intermediate 10 and 2-(3-(difluoromethoxy)-4-fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in place of 4-fluoro-3-methylphenylboronic acid. MS (ESI): mass calcd. for $C_{17}H_{14}F_4N_4O_2$, 382.1; m/z found, 383.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.92 (d, J = 1.8 Hz, 1H), 8.44 – 8.41 (m, 1H), 7.86 – 7.82 (m, 1H), 7.79 – 7.73 (m, 1H), 7.61 (dd, J = 10.5, 8.6 Hz, 1H), 7.38 (t, J = 73.2 Hz, 1H), 5.41 (s, 2H), 3.10 (s, 3H), 2.84 (s, 3H).

Example 233: 2-[6-[2-Fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-*N*,*N*-dimethyl-acetamide.



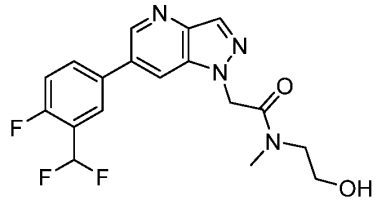
The title compound was prepared in a manner analogous to Example 11 using 2-fluoro-3-(trifluoromethyl)phenylboronic acid in place of 3-(trifluoromethyl)phenylboronic acid. MS (ESI): mass calcd. for $C_{17}H_{14}F_4N_4O$, 366.1; m/z found, 367.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.73 (t, J = 1.6 Hz, 1H), 8.32 (d, J = 1.0 Hz, 1H), 7.99 (q, J = 1.6 Hz, 1H), 7.76 – 7.64 (m, 2H), 7.38 (t, J = 7.8 Hz, 1H), 5.30 (s, 2H), 3.18 (s, 3H), 2.98 (s, 3H).

Example 234: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-*N*-(2-methoxyethyl)-*N*-methyl-acetamide.



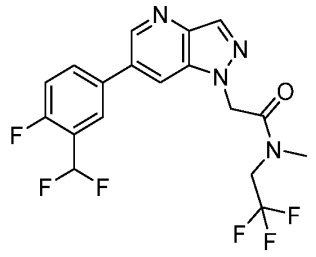
The title compound was prepared in a manner analogous to Example 1 using 2-methoxy-*N*-methylethan-1-amine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{19}H_{19}F_3N_4O_2$, 392.1; m/z found, 393.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.82 – 8.71 (m, 1H), 8.36 – 8.25 (m, 1H), 7.92 – 7.82 (m, 2H), 7.80 – 7.67 (m, 1H), 7.29 (d, *J* = 9.4 Hz, 1H), 6.97 (t, *J* = 54.9 Hz, 1H), 5.51 – 5.17 (m, 2H), 3.73 – 3.50 (m, 4H), 3.46 – 3.27 (m, 3H), 3.26 – 2.92 (m, 3H).

Example 235: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-*N*-(2-hydroxyethyl)-*N*-methyl-acetamide.



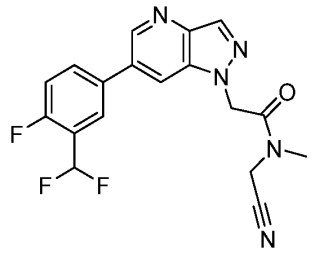
The title compound was prepared in a manner analogous to Example 1 using 2-(methylamino)ethan-1-ol in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{18}H_{17}F_3N_4O_2$, 378.1; m/z found, 379.0 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.86 – 8.70 (m, 1H), 8.37 – 8.21 (m, 1H), 7.98 – 7.80 (m, 2H), 7.78 – 7.68 (m, 1H), 7.34 – 7.24 (m, 1H), 7.16 – 6.76 (m, 1H), 5.48 – 5.29 (m, 2H), 3.95 – 3.75 (m, 2H), 3.74 – 3.53 (m, 2H), 3.28 – 2.95 (m, 3H), 2.42 – 2.20 (m, 1H).

Example 236: 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-*N*-methyl-*N*-(2,2,2-trifluoroethyl)acetamide.



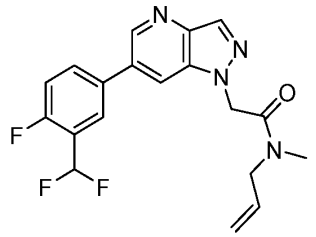
The title compound was prepared in a manner analogous to Example 1 using *N*-methyl-2,2,2-trifluoroethylamine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{18}H_{14}F_6N_4O$, 416.1; m/z found, 417.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, *J* = 1.9 Hz, 1H), 8.32 (d, *J* = 1.0 Hz, 1H), 7.93 – 7.80 (m, 2H), 7.73 (s, 1H), 7.30 (d, *J* = 9.2 Hz, 1H), 6.98 (t, *J* = 54.9 Hz, 1H), 5.34 (d, *J* = 20.7 Hz, 2H), 4.28 – 3.97 (m, 2H), 3.38 – 2.90 (m, 3H).

Example 237: *N*-(Cyanomethyl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-*N*-methyl-acetamide.



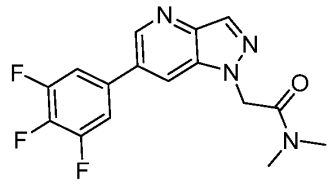
The title compound was prepared in a manner analogous to Example 1 using 2-(methylamino)acetonitrile in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{18}H_{14}F_3N_5O$, 373.1; m/z found, 374.1 $[M+H]^+$. ^1H NMR (400 MHz, Methanol-d4) δ 8.78 (d, *J* = 1.9 Hz, 1H), 8.30 (d, *J* = 1.0 Hz, 1H), 8.16 (dd, *J* = 1.9, 1.0 Hz, 1H), 7.96 – 7.89 (m, 1H), 7.85 (dddd, *J* = 7.4, 4.9, 2.5, 1.3 Hz, 1H), 7.45 – 7.29 (m, 1H), 7.01 (t, *J* = 54.8 Hz, 1H), 5.52 (s, 2H), 4.43 (s, 2H), 3.35 (s, 3H).

Example 238: *N*-Allyl-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-*N*-methyl-acetamide.



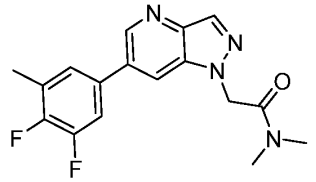
The title compound was prepared in a manner analogous to Example 1 using *N*-methylallylamine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{19}H_{17}F_3N_4O$, 374.1; m/z found, 375.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.80 – 8.77 (m, 1H), 8.32 – 8.26 (m, 1H), 7.93 – 7.89 (m, 1H), 7.88 – 7.83 (m, 1H), 7.78 – 7.72 (m, 1H), 7.32 – 7.27 (m, 1H), 6.98 (t, *J* = 54.9 Hz, 1H), 5.91 – 5.66 (m, 1H), 5.38 – 5.08 (m, 4H), 4.19 – 3.90 (m, 2H), 3.21 – 2.88 (m, 3H).

Example 239: *N*,*N*-Dimethyl-2-[6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]acetamide.



The title compound was made in a manner analogous to Example 7 using 3,4,5-trifluorophenylboronic acid in place of 4-fluoro-3-methylboronic acid. MS (ESI): mass calcd. for $C_{16}H_{13}F_3N_4O$, 334.1; m/z found, 335.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.92 (d, *J* = 2.0 Hz, 1H), 8.49 – 8.45 (m, 1H), 8.35 – 8.32 (m, 1H), 7.92 – 7.82 (m, 2H), 5.50 (s, 2H), 3.14 (s, 3H), 2.86 (s, 3H).

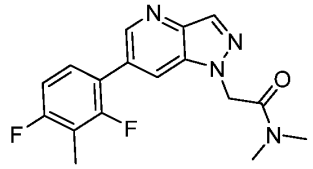
Example 240: 2-[6-(3,4-Difluoro-5-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-*N*,*N*-dimethyl-acetamide.



The title compound was made in a manner analogous to Example 7 using 2-(3,4-difluoro-5-methylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in place of 4-fluoro-3-methylboronic

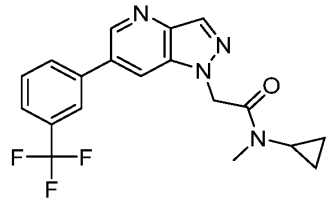
acid. MS (ESI): mass calcd. for $C_{17}H_{16}F_2N_4O$, 330.1; m/z found, 331.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.87 (d, J = 1.9 Hz, 1H), 8.38 (dd, J = 2.0, 1.0 Hz, 1H), 8.31 (d, J = 1.0 Hz, 1H), 7.78 – 7.70 (m, 1H), 7.64 – 7.58 (m, 1H), 5.50 (s, 2H), 3.13 (s, 3H), 2.85 (s, 3H), 2.39 (d, J = 2.1 Hz, 3H).

Example 241: 2-[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-*N*,*N*-dimethyl-acetamide.



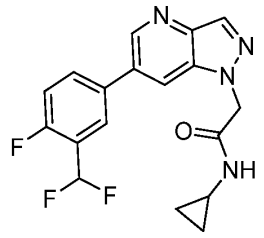
The title compound was made in a manner analogous to Example 7 using 2-(2,4-difluoro-3-methylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in place of 4-fluoro-3-methylboronic acid. MS (ESI): mass calcd. for $C_{17}H_{16}F_2N_4O$, 330.1; m/z found, 331.2 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.69 – 8.60 (m, 1H), 8.34 (s, 1H), 8.27 – 8.18 (m, 1H), 7.58 – 7.43 (m, 1H), 7.31 – 7.18 (m, 1H), 5.51 (s, 2H), 3.11 (s, 3H), 2.84 (s, 3H), 2.32 – 2.18 (m, 3H).

Example 242: *N*-Cyclopropyl-*N*-methyl-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide.



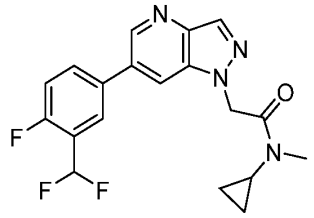
The title compound was prepared in a manner analogous to Example 16, using *N*-methylcyclopropanamine hydrochloride in place of 3-fluoroazetidine hydrochloride and DCM in place of DMF. MS (ESI): mass calcd. for $C_{19}H_{17}F_3N_4O$, 374.1; m/z found, 375.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d6) □ 8.95 – 8.90 (m, 1H), 8.54 – 8.45 (m, 1H), 8.37 – 8.32 (m, 1H), 8.17 – 8.10 (m, 2H), 7.86 – 7.76 (m, 2H), 5.62 (s, 1.84H), 5.48 (s, 0.14H), 3.04 (s, 0.23H), 3.02 – 2.95 (m, 1H), 2.83 (s, 2.81), 1.02 – 0.90 (m, 3.74H), 0.70 – 0.55 (m, 0.32H).

Example 243: *N*-Cyclopropyl-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide.



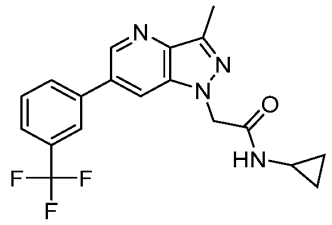
The title compound was made in a manner analogous to Example 6, Method A, using 2-chloro-*N*-cyclopropylacetamide in place of 2-chloro-*N*,*N*-dimethylacetamide. MS (ESI): mass calcd. for $C_{18}H_{15}F_3N_4O$, 360.1; m/z found, 361.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.89 (d, J = 2.0 Hz, 1H), 8.53 – 8.46 (m, 1H), 8.38 (d, J = 4.2 Hz, 1H), 8.34 (s, 1H), 8.11 – 8.01 (m, 2H), 7.63 – 7.52 (m, 1H), 7.30 (t, J = 54.1 Hz, 1H), 5.14 (s, 2H), 2.72 – 2.56 (m, 1H), 0.69 – 0.58 (m, 2H), 0.50 – 0.39 (m, 2H).

Example 244: *N*-Cyclopropyl-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-*N*-methyl-acetamide.



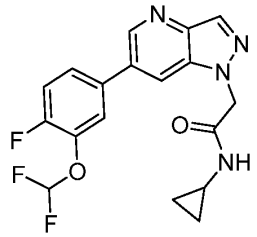
The title compound was prepared in a manner analogous to Example 1 using *N*-methylcycloproanamine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{19}H_{17}F_3N_4O$, 374.1; m/z found, 375.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, J = 1.9 Hz, 1H), 8.30 (d, J = 1.0 Hz, 1H), 7.88 – 7.84 (m, 2H), 7.80 – 7.69 (m, 1H), 7.32 – 7.26 (m, 1H), 6.98 (t, J = 54.9 Hz, 1H), 5.48 (s, 2H), 2.97 (s, 3H), 2.89 (tt, J = 7.1, 3.9 Hz, 1H), 1.13 – 1.03 (m, 2H), 1.00 – 0.92 (m, 2H).

Example 245: *N*-Cyclopropyl-2-[3-methyl-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide.



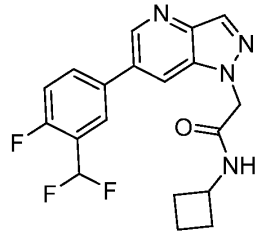
The title compound was prepared in a manner analogous to Example 15, using 2-(3-methyl-6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid (Intermediate 51) in place of Intermediate 39 and cyclopropanamine in place of 1-methylazetidin-3-amine. MS (ESI): mass calcd. for $C_{19}H_{17}F_3N_4O$, 374.1; m/z found, 375.2 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.88 (d, J = 1.9 Hz, 1H), 8.47 (d, J = 1.9 Hz, 1H), 8.33 (d, J = 4.2 Hz, 1H), 8.16 – 8.11 (m, 2H), 7.85 – 7.75 (m, 2H), 5.06 (s, 2H), 2.69 – 2.61 (m, 1H), 2.55 (s, 3H), 0.66 – 0.59 (m, 2H), 0.47 – 0.42 (m, 2H).

Example 246: *N*-Cyclopropyl-2-[6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide.



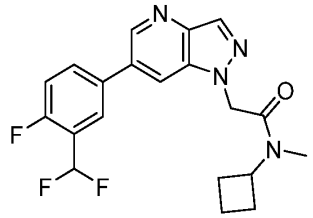
The title compound was made in a manner analogous to Example 6, Method A, using 6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridine (Intermediate 17) in place of Intermediate 16 and 2-chloro-*N*-cyclopropylacetamide in place of 2-chloro-*N*,*N*-dimethylacetamide. MS (ESI): mass calcd. for $C_{18}H_{15}F_3N_4O_2$, 376.1; m/z found, 377.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.89 (d, J = 1.9 Hz, 1H), 8.50 – 8.40 (m, 1H), 8.39 (d, J = 4.1 Hz, 1H), 8.34 (s, 1H), 7.87 – 7.80 (m, 1H), 7.81 – 7.73 (m, 1H), 7.60 (dd, J = 10.6, 8.4 Hz, 1H), 7.39 (t, J = 73.2 Hz, 1H), 5.13 (s, 2H), 2.70 – 2.59 (m, 1H), 0.69 – 0.58 (m, 2H), 0.50 – 0.38 (m, 2H).

Example 247: *N*-Cyclobutyl-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide.



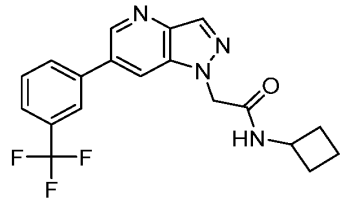
The title compound was made in a manner analogous to Example 5, Method A, using 2-chloro-*N*-cyclobutylacetamide (Intermediate 7) in place of Intermediate 1. MS (ESI): mass calcd. for $C_{19}H_{17}F_3N_4O$, 374.1; m/z found, 375.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.88 (d, J = 1.9 Hz, 1H), 8.56 (d, J = 7.7 Hz, 1H), 8.52 – 8.46 (m, 1H), 8.33 (s, 1H), 8.11 – 8.00 (m, 2H), 7.63 – 7.51 (m, 1H), 7.30 (t, J = 54.1 Hz, 1H), 5.16 (s, 2H), 4.28 – 4.10 (m, 1H), 2.23 – 2.07 (m, 2H), 2.03 – 1.83 (m, 2H), 1.74 – 1.51 (m, 2H).

Example 248: *N*-Cyclobutyl-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-*N*-methyl-acetamide.



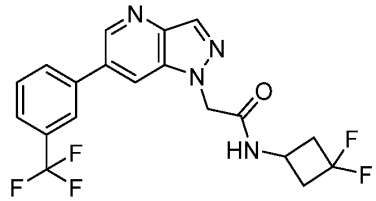
The title compound was prepared in a manner analogous to Example 1 using *N*-methylcyclobutylamine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{20}H_{19}F_3N_4O$, 388.2; m/z found, 389.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, J = 1.9 Hz, 1H), 8.30 (d, J = 1.0 Hz, 1H), 7.90 – 7.81 (m, 2H), 7.78 – 7.72 (m, 1H), 7.31 – 7.26 (m, 1H), 6.97 (t, J = 54.9 Hz, 1H), 5.33 – 5.21 (m, 2H), 4.93 – 4.46 (m, 1H), 3.14 – 2.92 (m, 3H), 2.40 – 2.06 (m, 4H), 1.72 (dq, J = 28.5, 9.8 Hz, 2H).

Example 249: *N*-Cyclobutyl-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide.



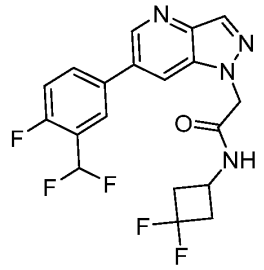
The title compound was prepared in a manner analogous to Example 16, using cyclobutanamine in place of 3-fluoroazetidine hydrochloride and DCM in place of DMF. MS (ESI): mass calcd. for $C_{19}H_{17}F_3N_4O$, 374.1; m/z found, 375.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.94 (d, J = 2.0 Hz, 1H), 8.58 – 8.53 (m, 2H), 8.36 – 8.33 (m, 1H), 8.18 – 8.13 (m, 2H), 7.84 – 7.76 (m, 2H), 5.17 (s, 2H), 4.24 – 4.14 (m, 1H), 2.20 – 2.12 (m, 2H), 1.98 – 1.88 (m, 2H), 1.70 – 1.56 (m, 2H).

Example 250: *N*-(3,3-Difluorocyclobutyl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide.



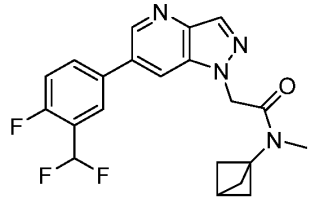
The title compound was prepared in a manner analogous to Example 13, using 3,3-difluorocyclobutan-1-amine hydrochloride in place of morpholine. MS (ESI): mass calcd. for $C_{19}H_{15}F_5N_4O$, 410.1; m/z found, 411.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.89 (d, J=1.85 Hz, 1 H), 8.42 (d, J=0.92 Hz, 1 H), 7.93 (dd, J=1.85, 0.92 Hz, 1 H), 7.89 (s, 1 H), 7.84 (d, J=7.63 Hz, 1 H), 7.76 – 7.71 (m, 1 H), 7.70 – 7.64 (m, 1 H), 6.45 (d, J=6.01 Hz, 1 H), 5.09 (s, 2 H), 4.31 – 4.18 (m, 1 H), 3.05 – 2.89 (m, 2 H), 2.52 – 2.34 (m, 2 H).

Example 251: *N*-(3,3-Difluorocyclobutyl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide.



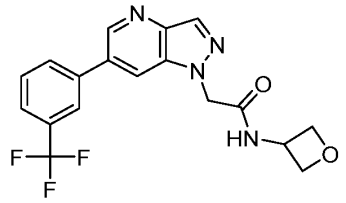
The title compound was made in a manner analogous to Example 5, Method A, using 2-chloro-*N*-(3,3-difluorocyclobutyl)acetamide (Intermediate 2) in place of Intermediate 1. MS (ESI): mass calcd. for $C_{19}H_{15}F_5N_4O$, 410.1; m/z found, 411.1 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.89 (d, J = 1.9 Hz, 1H), 8.76 (d, J = 6.7 Hz, 1H), 8.54 – 8.47 (m, 1H), 8.36 (s, 1H), 8.15 – 7.99 (m, 2H), 7.64 – 7.51 (m, 1H), 7.30 (t, J = 54.1 Hz, 1H), 5.21 (s, 2H), 4.18 – 3.97 (m, 1H), 3.01 – 2.81 (m, 2H), 2.69 – 2.39 (m, 2H).

Example 252: *N*-(3-Bicyclo[1.1.1]pentanyl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-*b*]pyridin-1-yl]-*N*-methyl-acetamide.



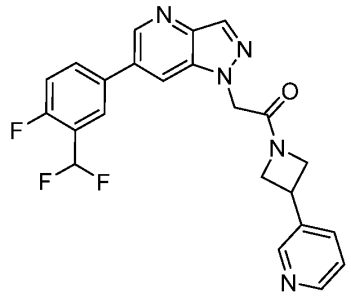
The title compound was prepared in a manner analogous to Example 1 using *N*-methyl bicyclo[1.1.1]pentan-1-amine in place of 3-(trifluoromethyl)azetidine-3-ol. MS (ESI): mass calcd. for $C_{21}H_{19}F_3N_4O$, 400.2; m/z found, 401.3 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, J = 1.9 Hz, 1H), 8.34 – 8.24 (m, 1H), 7.89 – 7.80 (m, 2H), 7.79 – 7.71 (m, 1H), 7.31 – 7.27 (m, 1H), 6.98 (t, J = 54.9 Hz, 1H), 5.37 – 5.18 (m, 2H), 3.12 – 2.87 (m, 3H), 2.66 – 2.42 (m, 1H), 2.36 – 2.09 (m, 6H).

Example 253: *N*-(Oxetan-3-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide.



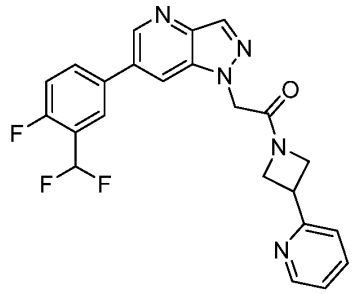
The title compound was prepared in a manner analogous to Example 15, using 3-oxetanamine in place of 1-methylazetidin-3-amine. MS (ESI): mass calcd. for $C_{18}H_{15}F_3N_4O_2$, 376.1; m/z found, 377.1 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 9.06 (d, J = 6.8 Hz, 1H), 8.95 (d, J = 1.9 Hz, 1H), 8.58 – 8.55 (m, 1H), 8.37 – 8.35 (m, 1H), 8.18 – 8.13 (m, 2H), 7.84 – 7.76 (m, 2H), 5.25 (s, 2H), 4.86 – 4.78 (m, 1H), 4.74 – 4.69 (m, 2H), 4.48 – 4.44 (m, 2H).

Example 254: 2-(6-(3-(Difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-(pyridin-3-yl)azetidin-1-yl)ethan-1-one.



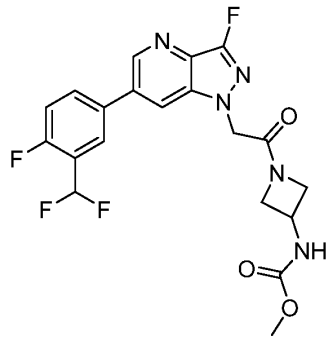
To a solution of 2-(6-(3-(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid (Intermediate 27, 40 mg, 0.125 mmol) in DCM (1 mL) were added DIPEA (170 µL, 0.62 mmol) and 3-(azetidin-3-yl)pyridine dihydrochloride (52 mg, 0.25 mmol), followed by PyBOP (84 mg, 0.16 mmol). The reaction mixture was stirred for two hours and purified on silica gel (0-10% MeOH/DCM) followed by reverse phase HPLC (METHOD D) to afford the title compound (24.2 mg, 44%). MS (ESI): mass calcd. for $C_{23}H_{18}F_3N_5O$, 437.1; m/z found, 438.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, J = 1.9 Hz, 1H), 8.65 – 8.50 (m, 2H), 8.31 (d, J = 1.0 Hz, 1H), 8.00 (dd, J = 2.0, 1.0 Hz, 1H), 7.95 – 7.81 (m, 1H), 7.82 – 7.73 (m, 1H), 7.72 – 7.58 (m, 1H), 7.40 – 7.28 (m, 2H), 6.98 (t, J = 54.9 Hz, 1H), 5.14 (s, 2H), 4.62 – 4.45 (m, 2H), 4.19 – 4.09 (m, 2H), 3.96 – 3.82 (m, 1H).

Example 255: 2-(6-(3-(Difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-(pyridin-2-yl)azetidin-1-yl)ethan-1-one.



The title compound was prepared in a manner analogous to Example 254, using 2-(azetidin-3-yl)pyridine dihydrochloride in place of 3-(azetidin-3-yl)pyridine dihydrochloride. MS (ESI): mass calcd. for $C_{23}H_{18}F_3N_5O$, 437.1; m/z found, 438.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, J = 1.9 Hz, 1H), 8.66 – 8.54 (m, 1H), 8.30 (d, J = 1.0 Hz, 1H), 7.99 (dd, J = 1.9, 1.0 Hz, 1H), 7.92 – 7.85 (m, 1H), 7.85 – 7.72 (m, 1H), 7.70 – 7.57 (m, 1H), 7.33 – 7.27 (m, 1H), 7.23 – 7.18 (m, 1H), 7.16 – 7.13 (m, 1H), 6.98 (t, J = 54.8 Hz, 1H), 5.24 – 5.04 (m, 2H), 4.50 – 4.39 (m, 3H), 4.34 – 4.23 (m, 1H), 4.02 – 3.89 (m, 1H).

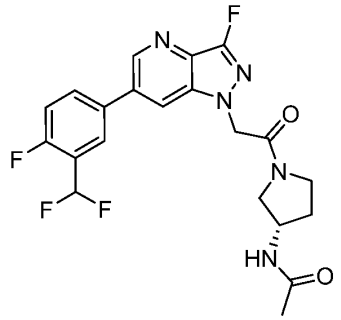
Example 256: Methyl (1-(2-(6-(3-(Difluoromethyl)-4-fluorophenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)acetyl)azetidin-3-yl)carbamate.



The title compound was prepared in a manner analogous to Example 254, using 2-(6-(3-(difluoromethyl)-4-fluorophenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid (Intermediate 28) in place of 2-(6-(3-(difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid (Intermediate 27) and methyl azetidin-3-ylcarbamate in place of 3-(azetidin-3-yl)pyridine dihydrochloride. MS (ESI): mass calcd. for $C_{20}H_{17}F_4N_5O_3$, 451.1; m/z

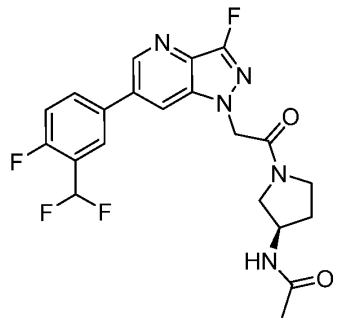
found, 452.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.94 (d, J = 1.9 Hz, 1H), 8.48 (t, J = 2.0 Hz, 1H), 8.07 (dd, J = 5.1, 2.4 Hz, 2H), 7.90 (d, J = 6.9 Hz, 1H), 7.68 – 7.55 (m, 1H), 7.32 (t, J = 54.1 Hz, 1H), 5.37 – 5.07 (m, 2H), 4.49 – 4.26 (m, 2H), 4.20 – 3.98 (m, 2H), 3.79 (dd, J = 9.8, 5.4 Hz, 1H), 3.56 (s, 3H).

Example 257: (*S*)-*N*-(1-(2-(6-(3-(Difluoromethyl)-4-fluorophenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)acetyl)pyrrolidin-3-yl)acetamide.



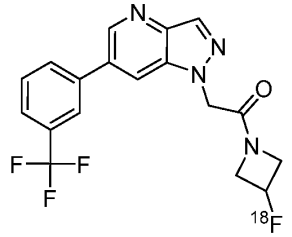
To a solution of 2-(6-(3-(difluoromethyl)-4-fluorophenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)acetic acid (Intermediate 28, 25 mg, 0.074 mmol) in DMF (1 mL) were added DIPEA (40 μL, 0.22 mmol) and (*S*)-*N*-(pyrrolidin-3-yl)acetamide (19 mg, 0.15 mmol), followed by COMU ((1-cyano-2-ethoxy-2-oxoethylidenaminooxy)dimethylamino-morpholino-carbenium hexafluorophosphate) (38 mg, 0.088 mmol). The reaction mixture was stirred for 90 minutes and purified by reverse phase HPLC (METHOD D) to afford the title compound (4.9 mg, 0.011 mmol, 15%). MS (ESI): mass calcd. for $C_{21}H_{19}F_4N_5O_2$, 449.1; m/z found, 472.2 $[M+Na]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.83 – 8.75 (m, 1H), 7.91 – 7.80 (m, 2H), 7.79 – 7.69 (m, 1H), 7.34 – 7.27 (m, 1H), 6.97 (t, J = 54.8 Hz, 1H), 6.16 – 5.91 (m, 1H), 5.33 – 4.94 (m, 2H), 4.67 – 4.40 (m, 1H), 4.20 – 3.40 (m, 4H), 2.50 – 1.20 (m, 5H).

Example 258: (*R*)-*N*-(1-(2-(6-(3-(Difluoromethyl)-4-fluorophenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)acetyl)pyrrolidin-3-yl)acetamide.



The title compound was prepared in a manner analogous to Example 257, using (*R*)-*N*-(pyrrolidin-3-yl)acetamide in place of (*S*)-*N*-(pyrrolidin-3-yl)acetamide. MS (ESI): mass calcd. for $C_{21}H_{19}F_4N_5O_2$, 449.1; m/z found, 450.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 – 8.72 (m, 1H), 7.89 – 7.80 (m, 2H), 7.77 – 7.69 (m, 1H), 7.34 – 7.27 (m, 1H), 7.14 – 6.74 (m, 1H), 6.43 – 6.08 (m, 1H), 5.38 – 4.93 (m, 2H), 4.65 – 4.37 (m, 1H), 3.94 – 3.41 (m, 4H), 2.32 – 1.61 (m, 5H).

Example 259: 1-(3-(Fluoro-18F)azetidin-1-yl)-2-(6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)ethan-1-one.



[^{18}F]fluoride in a shipping vial (obtained from the cyclotron facility) was transferred onto and trapped on an ion exchange cartridge, then eluted into a reaction vessel 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 to the reaction vessel 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 1-(2-(6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)acetyl)azetidin-3-yl 4-methylbenzenesulfonate (Intermediate 70, 3.0 mg, 0.0053 mmol) in anhydrous MeCN (0.7 mL) was added to the reaction vessel. The reaction mixture was heated at 90 °C for 5 min. The

reactor was cooled to 70 °C and 0.5 mL HCl (1.0 M) was added to the solution. The reaction was heated at 90 °C for 2 min before the reactor was cooled to 40 °C and 1.0 mL Na_2HPO_4 (0.5M) was added to the mixture. The solution was further diluted with water (2.8 mL) and the mixture 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) eluted with a mixture of 10 mM NH4OAc and MeCN (62:38 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).

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.

Example #	Compound Name	GluN2B IC_{50} (μM) standard assay
1	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-hydroxy-3-(trifluoromethyl)azetidin-1-yl]ethanone;	0.444
2	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methyleneazetidin-1-yl)ethanone;	0.070
3	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-(methylamino)azetidin-1-yl]ethanone;	0.635
4	N-[1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]azetidin-3-yl]-N-methyl-acetamide;	0.110
5	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;	0.016
6	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;	0.018
7	2-[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;	0.025
8	N,N-Dimethyl-2-[6-[6-(trifluoromethyl)-2-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;	0.395
9	2-[6-[4-Chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;	0.022
10	2-[6-[4-Chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;	0.024

Example #	Compound Name	GluN2B IC_{50} (μM) standard assay
11	N,N-Dimethyl-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;	0.125
12	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-morpholino-ethanone;	0.068
13	1-Morpholino-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.219
14	N-Cyclopropyl-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;	0.437
15	N-(1-Methylazetidin-3-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;	8.110
16	1-(3-Fluoroazetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.042
17	1-(3,3-Difluoroazetidin-1-yl)-2-[6-(2,4-difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.356
18	1-(Azetidin-1-yl)-2-[6-(5-chloro-2-thienyl)-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.012
19	1-(Azetidin-1-yl)-2-[6-[5-(difluoromethyl)-2-thienyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.013
20	1-(Azetidin-1-yl)-2-[3-fluoro-6-[5-(trifluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.021
21	1-(Azetidin-1-yl)-2-[6-(4-fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.299
22	1-(Azetidin-1-yl)-2-[6-(3-chlorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.027
23	1-(Azetidin-1-yl)-2-[6-[3-(fluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.020
24	1-(Azetidin-1-yl)-2-[6-[3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.048
25	1-(Azetidin-1-yl)-2-[6-[3-(1,1-difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.044
26	1-(Azetidin-1-yl)-2-[6-[3-(1,1-difluoroethyl)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.066

Example #	Compound Name	GluN2B IC_{50} (μM) standard assay
27	1-(Azetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.037
28	1-(Azetidin-1-yl)-2-[3-methyl-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.187
29	1-(Azetidin-1-yl)-2-[6-(3,4-dichlorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.028
30	1-(Azetidin-1-yl)-2-[6-(2,3-dichlorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.040
31	1-(Azetidin-1-yl)-2-[6-(3-chloro-2-fluoro-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.070
32	1-(Azetidin-1-yl)-2-[6-(3,4-difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.044
33	1-(Azetidin-1-yl)-2-[6-[2-fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.045
34	1-(Azetidin-1-yl)-2-[6-[3-(1,1-difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.066
35	1-(Azetidin-1-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.017
36	1-(Azetidin-1-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.020
37	1-(Azetidin-1-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]-3-methyl-pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.064
38	1-(Azetidin-1-yl)-2-[6-(4-chloro-3-methylphenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.024
39	1-(Azetidin-1-yl)-2-[6-(4-chloro-3-methylphenyl)-3-methyl-pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.088
40	1-(Azetidin-1-yl)-2-[6-(2-fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.038
41	1-(Azetidin-1-yl)-2-[6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.028
42	1-(Azetidin-1-yl)-2-[6-[3-(difluoromethoxy)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.040

Example #	Compound Name	GluN2B IC_{50} (μM) standard assay
43	1-(Azetidin-1-yl)-2-[6-[4-chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.024
44	1-(Azetidin-1-yl)-2-[6-[4-chloro-3-(difluoromethoxy)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.040
45	1-(Azetidin-1-yl)-2-[6-(4-fluoro-2-methoxy-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.118
46	2-[6-(3-Acetyl-4-fluoro-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(azetidin-1-yl)ethanone;	0.161
47	1-(Azetidin-1-yl)-2-[6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.047
48	1-(Azetidin-1-yl)-2-[6-[2-(trifluoromethyl)-4-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.286
49	2-[6-(5-Chloro-2-thienyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;	0.025
50	2-[6-(5-Chloro-2-thienyl)-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;	0.018
51	2-[6-[5-(Difluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;	0.032
52	2-[6-[5-(Difluoromethyl)-2-thienyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;	0.022
53	1-(3-Fluoroazetidin-1-yl)-2-[6-[5-(trifluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.012
54	1-(3-Fluoroazetidin-1-yl)-2-[3-fluoro-6-[5-(trifluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.040
55	1-(3-Fluoroazetidin-1-yl)-2-[6-(3-fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.106
56	1-(3-Fluoroazetidin-1-yl)-2-[6-(4-fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.053
57	2-[6-(3-Chlorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;	0.019
58	1-(3-Fluoroazetidin-1-yl)-2-[6-(m-tolyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.045

Example #	Compound Name	GluN2B IC_{50} (μM) standard assay
59	1-(3-Fluoroazetidin-1-yl)-2-[6-[3-(fluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.040
60	2-[6-[3-(Difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;	0.030
61	2-[6-[3-(1,1-Difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;	0.029
62	2-[6-[3-(Difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;	0.097
63	2-[6-(2,3-Difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;	0.525
64	2-[6-(2,4-Difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;	0.189
65	2-[6-(3,4-Difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;	0.111
66	2-[6-(3,5-Difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;	0.065
67	2-[6-(3-Chloro-2-fluoro-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;	0.183
68	2-[6-(3-Chloro-4-fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;	0.017
69	1-(3-Chloroazetidin-1-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.032
70	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;	0.027
71	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-methyl-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;	0.030
72	2-[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;	0.044
73	2-[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;	0.092
74	2-[6-[4-Chloro-3-(1,1-difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;	0.047

Example #	Compound Name	GluN2B IC_{50} (μM) standard assay
75	2-[6-[4-Chloro-3-(1,1-difluoroethyl)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;	0.124
76	2-[6-[4-Chloro-3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;	0.016
77	2-[6-(4-Chloro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;	0.041
78	1-(3-Fluoroazetidin-1-yl)-2-[6-(4-fluoro-2-methoxy-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.129
79	2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;	0.016
80	2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;	0.032
81	2-[6-[4-Chloro-3-(difluoromethoxy)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;	0.037
82	2-[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;	0.023
83	2-[6-(3,4-Difluoro-5-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;	0.017
84	1-(3-Fluoroazetidin-1-yl)-2-[6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.068
85	1-(3-Fluoroazetidin-1-yl)-2-[6-[2-(trifluoromethyl)-4-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.291
86	1-(3-Methylazetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.038
87	(Racemic) 1-(2-Methylazetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.216
88	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methylazetidin-1-yl)ethanone;	0.073
89	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methylazetidin-1-yl)ethanone;	0.038
90	(Racemic) 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(2-methylazetidin-1-yl)ethanone;	0.098

Example #	Compound Name	GluN2B IC_{50} (μM) standard assay
91	2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methylazetidin-1-yl)ethanone;	0.063
92	2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methylazetidin-1-yl)ethanone;	0.092
93	2-[6-[4-Chloro-3-(difluoromethoxy)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methylazetidin-1-yl)ethanone;	0.173
94	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-ethynylazetidin-1-yl)ethanone;	0.068
95	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-vinylazetidin-1-yl)ethanone;	0.096
96	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-[(Z)-prop-1-enyl]azetidin-1-yl]ethanone;	0.107
97	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-(fluoromethyl)azetidin-1-yl]ethanone;	0.067
98	1-[3-(Difluoromethyl)azetidin-1-yl]-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.114
99	1-[3-(Trifluoromethyl)azetidin-1-yl]-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.660
100	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-(trifluoromethyl)azetidin-1-yl]ethanone;	0.537
101	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-[(Z)-2-fluorovinyl]azetidin-1-yl]ethanone;	0.130
102	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-(2,2-difluorovinyl)azetidin-1-yl]ethanone;	0.147
103	1-(3-Methoxyazetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.402
104	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methoxyazetidin-1-yl)ethanone;	0.078
105	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-ethoxyazetidin-1-yl)ethanone;	0.215
106	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-(methoxymethyl)azetidin-1-yl]ethanone;	0.152

Example #	Compound Name	GluN2B IC_{50} (μM) standard assay
107	1-[3-(Methoxymethyl)azetidin-1-yl]-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.126
108	(Racemic) 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-(1-hydroxyethyl)azetidin-1-yl]ethanone;	0.623
109	1-[3-(Difluoromethoxy)azetidin-1-yl]-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.115
110	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-(trifluoromethoxy)azetidin-1-yl]ethanone;	0.491
111	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-hydroxyazetidin-1-yl)ethanone;	0.042
112	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-hydroxyazetidin-1-yl)ethanone;	0.033
113	1-(3-Hydroxyazetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.133
114	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-(hydroxymethyl)azetidin-1-yl]ethanone;	0.083
115	1-(3,3-Difluoroazetidin-1-yl)-2-[6-(4-methyl-2-thienyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.053
116	1-(3,3-Difluoroazetidin-1-yl)-2-[6-(4-fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.194
117	2-[6-(3-Chlorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3,3-difluoroazetidin-1-yl)ethanone;	0.039
118	1-(3,3-Difluoroazetidin-1-yl)-2-[6-(m-tolyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.052
119	1-(3,3-Difluoroazetidin-1-yl)-2-[6-[3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.046
120	1-(3,3-Difluoroazetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.092
121	3-[1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]pyrazolo[4,3-b]pyridin-6-yl]benzonitrile;	2.480
122	1-(3,3-Difluoroazetidin-1-yl)-2-[6-[6-(trifluoromethyl)-2-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.405

Example #	Compound Name	GluN2B IC_{50} (μM) standard assay
123	1-(3,3-Difluoroazetidin-1-yl)-2-[6-[2-(trifluoromethyl)-4-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.293
124	1-(3,3-Difluoroazetidin-1-yl)-2-[6-[5-(trifluoromethyl)-3-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.459
125	1-(3,3-Difluoroazetidin-1-yl)-2-[6-(3,4-difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.092
126	1-(3,3-Difluoroazetidin-1-yl)-2-[6-(3,5-difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.070
127	2-[6-(3-Chloro-4-fluoro-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3,3-difluoroazetidin-1-yl)ethanone;	0.020
128	2-[6-(3-Chloro-2-fluoro-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3,3-difluoroazetidin-1-yl)ethanone;	0.048
129	1-(3,3-Difluoroazetidin-1-yl)-2-[6-(4-fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.068
130	1-(3,3-Difluoroazetidin-1-yl)-2-[6-(4-fluoro-2-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.310
131	1-(3,3-Difluoroazetidin-1-yl)-2-[6-(2-fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.031
132	1-(3,3-Difluoroazetidin-1-yl)-2-[6-[2-fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.037
133	1-(3,3-Difluoroazetidin-1-yl)-2-[6-[4-fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.065
134	1-(3,3-Difluoroazetidin-1-yl)-2-[6-[2-fluoro-5-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.262
135	1-(3,3-Difluoroazetidin-1-yl)-2-[6-[2-methyl-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	2.099
136	1-(3,3-Difluoroazetidin-1-yl)-2-[6-(4-fluoro-2-methoxy-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.160
137	1-(3,3-Difluoroazetidin-1-yl)-2-[6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.039
138	1-(3,3-Dimethylazetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.263

Example #	Compound Name	GluN2B IC_{50} (μM) standard assay
139	1-(3-Fluoro-3-methyl-azetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.059
140	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3,3-dimethylazetidin-1-yl)ethanone;	0.119
141	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoro-3-methyl-azetidin-1-yl)ethanone;	0.069
142	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-ethyl-3-fluoro-azetidin-1-yl)ethanone;	0.237
143	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-fluoro-3-(fluoromethyl)azetidin-1-yl]ethanone;	0.082
144	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methoxy-3-methyl-azetidin-1-yl)ethanone;	0.469
145	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-ethyl-3-hydroxy-azetidin-1-yl)ethanone;	0.433
146	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-hydroxy-3-methyl-azetidin-1-yl)ethanone;	0.073
147	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-fluoro-3-(hydroxymethyl)azetidin-1-yl]ethanone;	0.121
148	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-fluoro-3-(methoxymethyl)azetidin-1-yl]ethanone;	0.155
149	[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-hydroxy-2-methyl-azetidin-1-yl)ethanone;	0.456
150	1-[2-[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]azetidine-3-carbonitrile;	0.330
151	1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]azetidine-3-carbonitrile;	0.063
152	1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]-3-methyl-azetidine-3-carbonitrile;	0.075
153	1-(3-Acetylazetidin-1-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.336
154	N-[1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]azetidin-3-yl]acetamide;	0.064

Example #	Compound Name	GluN2B IC_{50} (μM) standard assay
155	1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]-N,N-dimethyl-azetidine-3-carboxamide;	0.727
156	MethylN-[1-[2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]azetidin-3-yl]carbamate;	0.038
157	N-[1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]azetidin-3-yl]-2,2,2-trifluoro-acetamide;	0.122
158	N-[1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]azetidin-3-yl]cyclopropanecarboxamide;	0.066
159	N-[1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]azetidin-3-yl]methanesulfonamide;	0.157
160	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methylsulfonylazetidin-1-yl)ethanone;	3.250
161	1-[1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]azetidin-3-yl]pyrrolidin-2-one;	0.246
162	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-(1H-imidazol-2-yl)azetidin-1-yl]ethanone;	0.041
163	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-(4-pyridyl)azetidin-1-yl]ethanone;	0.067
164	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-pyrimidin-4-ylazetidin-1-yl)ethanone;	0.111
165	1-(5-Azaspiro[2.3]hexan-5-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.133
166	1-(2,2-Difluoro-5-azaspiro[2.3]hexan-5-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.197
167	1-(6-Azaspiro[3.3]heptan-6-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.397
168	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-oxa-6-azaspiro[3.3]heptan-6-yl)ethanone;	0.141
169	1-(6-Oxa-2-azaspiro[3.3]heptan-2-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.400
170	2-[6-(4-Fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-pyrrolidin-1-yl-ethanone;	0.304

Example #	Compound Name	GluN2B IC_{50} (μM) standard assay
171	1-Pyrrolidin-1-yl-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.101
172	2-[6-(3-Cyclopropylphenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-pyrrolidin-1-yl-ethanone;	0.375
173	2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-pyrrolidin-1-yl-ethanone;	0.084
174	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-pyrrolidin-1-yl-ethanone;	0.022
175	2-[6-(3,5-Difluoro-4-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-pyrrolidin-1-yl-ethanone;	1.322
176	1-[(3R)-3-Fluoropyrrolidin-1-yl]-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.270
177	1-[(3S)-3-Fluoropyrrolidin-1-yl]-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.393
178	(Racemic) (R,S)-2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoropyrrolidin-1-yl)ethanone;	0.235
179	(Racemic) (R,S)-2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoropyrrolidin-1-yl)ethanone;	0.062
180	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[(3R)-3-fluoropyrrolidin-1-yl]ethanone;	0.036
181	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[(3S)-3-fluoropyrrolidin-1-yl]ethanone;	0.044
182	(Racemic) (R,S)-2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-hydroxypyrrolidin-1-yl)ethanone;	0.394
183	(Racemic) (R,S)-2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-hydroxypyrrolidin-1-yl)ethanone;	0.089
184	(Racemic) 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methoxypyrrolidin-1-yl)ethanone;	0.193
185	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[(2R)-2-(methoxymethyl)pyrrolidin-1-yl]ethanone;	>2.99

Example #	Compound Name	GluN2B IC_{50} (μM) standard assay
186	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[(2S)-2-(methoxymethyl)pyrrolidin-1-yl]ethanone;	>2.99
187	N-[(3S)-1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]pyrrolidin-3-yl]acetamide;	0.106
188	N-[(3R)-1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]pyrrolidin-3-yl]acetamide;	0.083
189	1-(3,3-Difluoropyrrolidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.200
190	2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3,3-difluoropyrrolidin-1-yl)ethanone;	0.177
191	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3,3-difluoropyrrolidin-1-yl)ethanone;	0.027
192	(Racemic) 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-hydroxy-3-methyl-pyrrolidin-1-yl)ethanone;	0.318
193	(Racemic) Trans-2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoro-4-hydroxy-pyrrolidin-1-yl)ethanone;	0.212
194	1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]pyrrolidin-3-one;	0.146
195	1-[2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]pyrrolidin-3-one;	0.351
196	1-(1-Piperidyl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.200
197	1-(4,4-Difluoro-1-piperidyl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	1.280
198	N-[1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]-4-piperidyl]acetamide;	0.230
199	2-[6-(4-Fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-morpholino-ethanone;	0.800
200	1-[(1R,5S)-3-Azabicyclo[3.1.0]hexan-3-yl]-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;	0.063

Example #	Compound Name	GluN2B IC_{50} (μM) standard assay
201	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[(1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl]ethanone;	0.361
202	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[(1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl]ethanone;	0.184
203	(Racemic) Cis-5-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]-3a,4,6,6a-tetrahydro-3H-pyrrolo[3,4-d]oxazol-2-one;	4.839
204	(Racemic) Cis-5-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]-1,3,3a,4,6,6a-hexahydropyrrolo[2,3-c]pyrrol-2-one;	0.795
205	2-[6-[5-(Difluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;	0.066
206	N,N-Dimethyl-2-[6-[5-(trifluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;	0.020
207	2-[6-(5-Chloro-2-thienyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;	0.036
208	2-[6-(5-Chloro-4-methyl-2-thienyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;	0.014
209	2-[6-[3-(Difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;	0.061
210	2-[6-[3-(Difluoromethyl)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;	0.033
211	2-[3-Fluoro-6-(4-fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;	0.098
212	2-[3-Fluoro-6-(3-fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;	0.089
213	2-[6-(3-Chlorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;	0.071
214	N,N-Dimethyl-2-[6-[2-(trifluoromethyl)-4-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;	0.324
215	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N-methyl-acetamide;	0.155

Example #	Compound Name	GluN2B IC_{50} (μM) standard assay
216	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N-ethyl-acetamide;	0.046
217	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N-ethyl-N-methyl-acetamide;	0.070
218	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;	0.024
219	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-methyl-pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;	0.043
220	2-[6-[4-Chloro-3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;	0.028
221	2-[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;	0.102
222	2-[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-N-methyl-acetamide;	0.315
223	2-[3-Fluoro-6-(4-fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;	0.024
224	2-[6-(4-Chloro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;	0.035
225	2-[6-(3-Chloro-4-fluoro-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;	0.027
226	2-[6-(3,4-Dichlorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;	0.041
227	2-[6-(3,5-Difluorophenyl)-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;	0.094
228	2-[6-(3,4-Difluorophenyl)-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;	0.035
229	2-[6-[3-(1,1-Difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;	0.062
230	2-[6-[3-(1,1-Difluoroethyl)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;	0.078
231	2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;	0.020

Example #	Compound Name	GluN2B IC_{50} (μM) standard assay
232	2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;	0.042
233	2-[6-[2-Fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;	0.039
234	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N-(2-methoxyethyl)-N-methyl-acetamide;	1.030
235	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N-(2-hydroxyethyl)-N-methyl-acetamide;	0.387
236	2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;	1.470
237	N-(Cyanomethyl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N-methyl-acetamide;	0.311
238	N-Allyl-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N-methyl-acetamide;	0.166
239	N,N-Dimethyl-2-[6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]acetamide;	0.093
240	2-[6-(3,4-Difluoro-5-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;	0.016
241	2-[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;	0.014
242	N-Cyclopropyl-N-methyl-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;	0.145
243	N-Cyclopropyl-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;	0.031
244	N-Cyclopropyl-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N-methyl-acetamide;	0.086
245	N-Cyclopropyl-2-[3-methyl-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;	0.561
246	N-Cyclopropyl-2-[6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;	0.085
247	N-Cyclobutyl-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;	0.049

Example #	Compound Name	GluN2B IC_{50} (μM) standard assay
248	N-Cyclobutyl-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N-methyl-acetamide;	0.150
249	N-Cyclobutyl-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;	1.120
250	N-(3,3-Difluorocyclobutyl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;	0.900
251	N-(3,3-Difluorocyclobutyl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;	0.160
252	N-(3-Bicyclo[1.1.1]pentanyl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N-methyl-acetamide;	0.394
253	N-(Oxetan-3-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;	2.210
254	2-(6-(3-(Difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-(pyridin-3-yl)azetidin-1-yl)ethan-1-one;	0.066
255	2-(6-(3-(Difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-(pyridin-2-yl)azetidin-1-yl)ethan-1-one;	0.096
256	Methyl (1-(2-(6-(3-(Difluoromethyl)-4-fluorophenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)acetyl)azetidin-3-yl)carbamate;	0.044
257	(S)-N-(1-(2-(6-(3-(Difluoromethyl)-4-fluorophenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)acetyl)pyrrolidin-3-yl)acetamide;	0.13
258	(R)-N-(1-(2-(6-(3-(Difluoromethyl)-4-fluorophenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)acetyl)pyrrolidin-3-yl)acetamide; and	0.12
259	1-(3-(Fluoro-18F)azetidin-1-yl)-2-(6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)ethan-1-one.	NT

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- position 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.

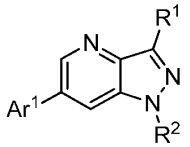
Example #	Extraction Ratio @ 1 μM
5	<0.298
6	0.42
7	0.63
9	<0.298
35	0.42
41	0.30
70	<0.298

Example #	Extraction Ratio @ 1 μM
76	<0.298
79	<0.298
141	<0.298

Specific Embodiments

The present disclosure is exemplified by the specific embodiments 1-40 below.

1. A compound, having the structure of Formula (I):



(I)

wherein

R^1 is H, halo, or CH_3;

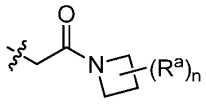
Ar^1 is selected from the group consisting of:

(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, OC_{1-6}perhaloalkyl, CN, and C_{3-6}cycloalkyl;

(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}alkyl, OC_{1-6}perhaloalkyl, and $(C=O)CH_3$; and

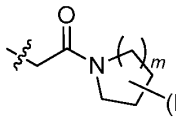
(c) thienyl independently substituted with one or two members selected from: halo, C_{1-6}alkyl, and C_{1-6}perhaloalkyl; and pyridine substituted with CF_3;

R^2 is selected from the group consisting of:

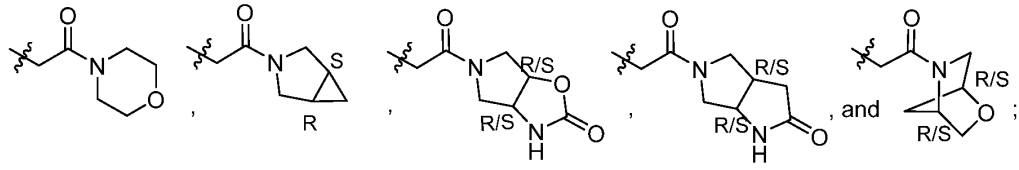
(d)  ; wherein

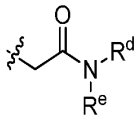
R^a is each independently selected from the group consisting of: H, halo, OH, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}haloalkenyl, C_{2-6}alkynyl, CH_2OH, $CH(OH)(CH_3)$, CH_2OCH_3, OC_{1-6}haloalkyl, OC_{1-6}alkyl, $NH(CH_3)$, $NHCO_2CH_3$, $NHC(=O)CH_3$, $NHC(=O)CF_3$, NHC(=O)cyclopropyl, $N(CH_3)C(=O)CH_3$, $C(=O)N(CH_3)_2$, $C(=O)CH_3$, CN, $NHSO_2CH_3$, SO_2CH_3,

1H-imidazol-2-yl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrimidin-4-yl, and pyrrolidine-2-one; or two R^a members combine to form a C_{3-6}cycloalkyl or heterocycloalkyl, wherein the cycloalkyl and heterocycloalkyl is optionally substituted one or two F members;

(e)  ; wherein

R^b is each independently selected from the group consisting of: H, OH, F, OCH_3, CH_2OCH_3, and $NHC(=O)CH_3$; or two R^b members come together to form =O;

(f)  and

(g)  , wherein

R^d is selected from the group consisting of: C_{1-6}alkyl; C_{2-6}alkenyl; C_{1-6}haloalkyl; $CH_2CH_2OCH_3$; CH_2CH_2OH; CH_2CN; NH_2; $NH\text{-}C(=O)CH_3$; C_{3-6}cycloalkyl; C_{3-6}cycloalkyl substituted with two F members; 1-methylazetidin-3-yl; and oxetan-3-yl;

R^e is H or CH_3;

n is 1 or 2; and

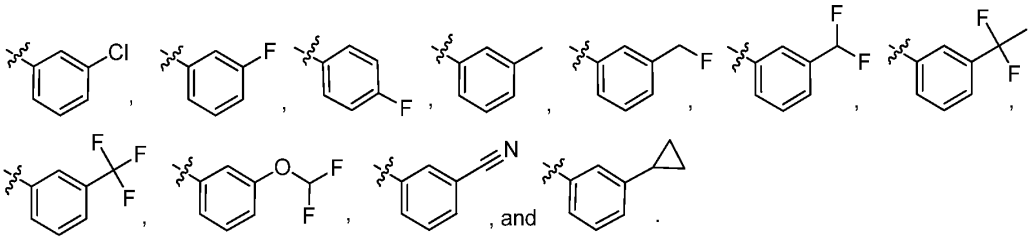
m is 1 or 2;

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

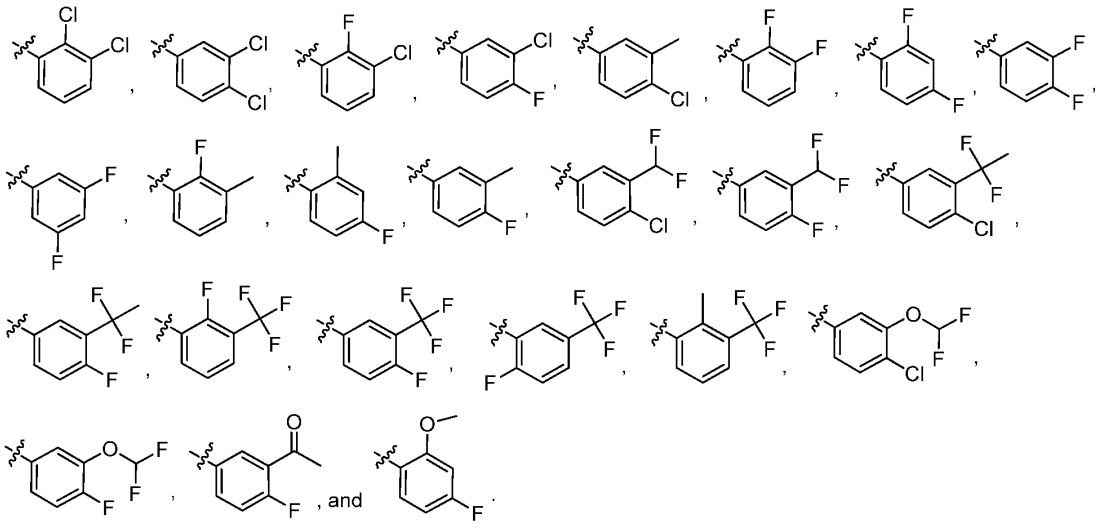
2. The compound of embodiment 1, wherein R^1 is H.

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 phenyl substituted with one member selected from the group consisting of: Cl, F, CH_3, OCH_3, CH_2F, CHF_2, CF_3, CHF_2CH_3, $OCHF_2$, CN, and cyclopropyl.
6. The compound of embodiment 1, wherein Ar^1 is selected from the group consisting of:

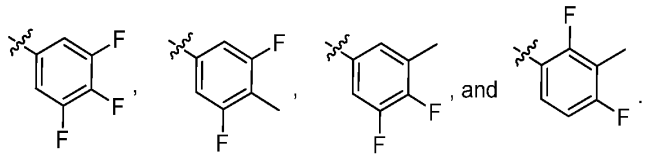


7. The compound of embodiment 1, wherein Ar^1 is phenyl substituted with two members each independently selected from the group consisting of: Cl, F, CH_3, CHF_2, CF_3, CHF_2CH_3, OCH_3, $OCHF_2$, and $(C=O)CH_3$.
8. The compound of embodiment 1, wherein Ar^1 is selected from the group consisting of:



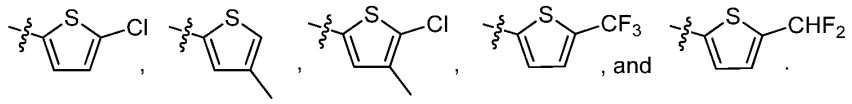
9. The compound of embodiment 1, wherein Ar^1 is phenyl substituted with three members each independently selected from the group consisting of: halo, and CH_3.

10. The compound of embodiment 1, wherein Ar^1 is selected from the group consisting of:

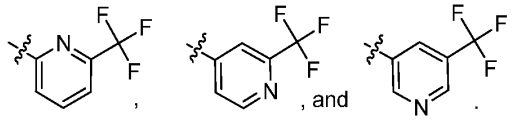


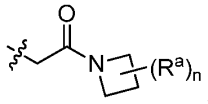
11. The compound of embodiment 1, wherein Ar^1 is thienyl independently substituted with one or two members selected from: Cl, CH_3, CF_3 and CHF_2.

12. The compound of embodiment 1, wherein Ar^1 is selected from the group consisting of:



13. The compound of embodiment 1, wherein Ar^1 is selected from the group consisting of:

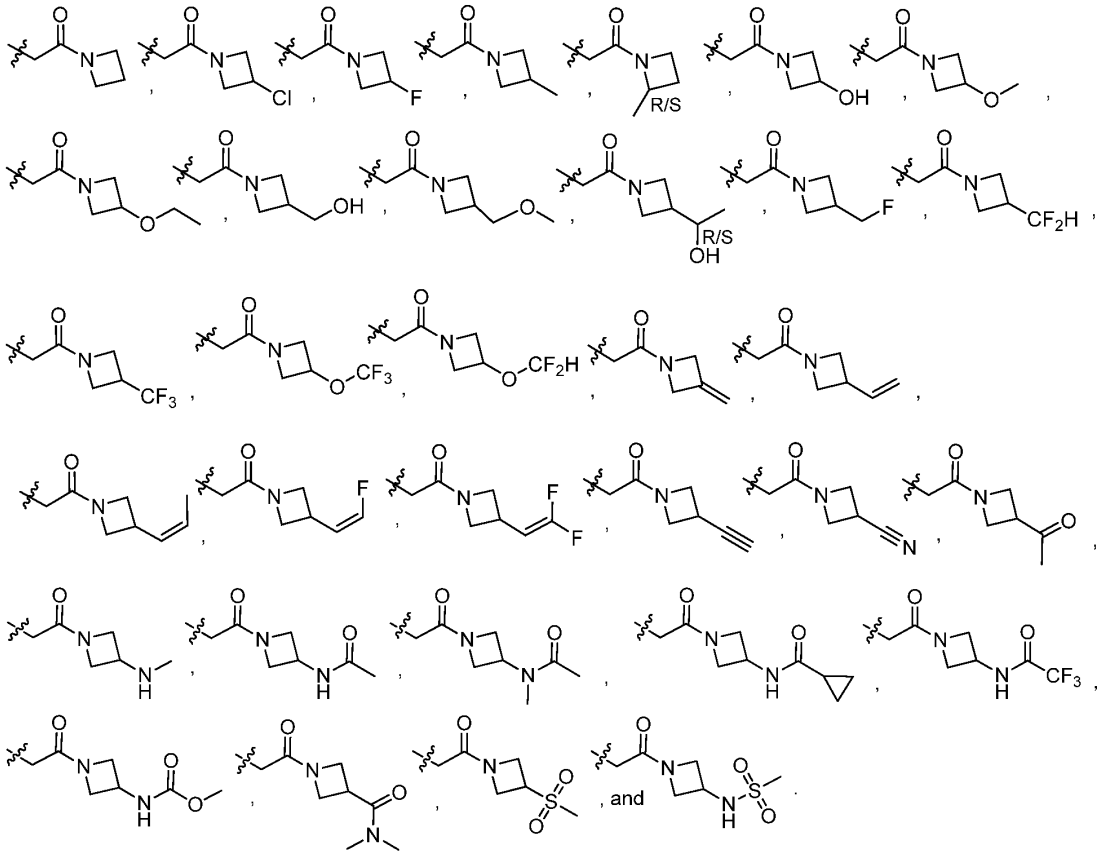


14. The compound of embodiment 1, wherein R^2 is ; wherein

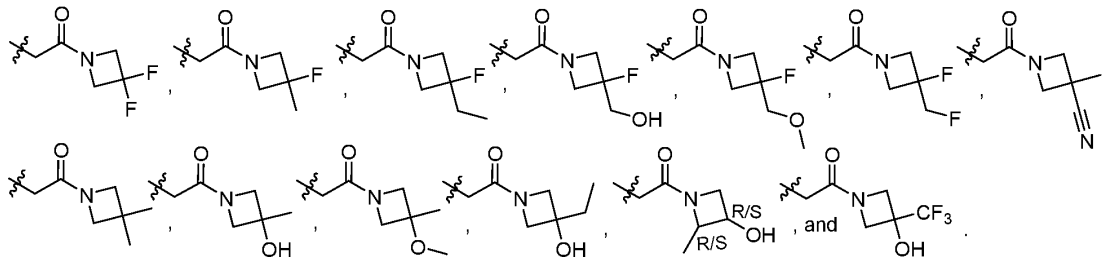
R^a is each independently selected from the group consisting of: H, Cl, F, OH, CH_3, CH_2CH_3, CH_2F, CHF_2, CF_3, $=CH_2$, $CH=CH_2$, $CH=CH(CH_3)$, CH=CH(F), CH=CF(F), C≡CH, CH_2OH, $CH(OH)(CH_3)$, CH_2OCH_3, $OCHF_2$, OCF_3, OCH_3, OCH_2CH_3, $NH(CH_3)$, $NHCO_2CH_3$, $NHC(=O)CH_3$, $NHC(=O)CF_3$, NHC(=O)cyclopropyl, $N(CH_3)C(=O)CH_3$, $C(=O)N(CH_3)_2$, $C(=O)CH_3$, CN, $NHSO_2CH_3$, SO_2CH_3, 1H-imidazol-2-yl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrimidin-4-yl, and pyrrolidine-2-one; or two R^a members combine to form a cyclopropyl, cyclobutyl, or oxetanyl; wherein the cyclopropyl is optionally substituted one or two F members;

and n is 1 or 2.

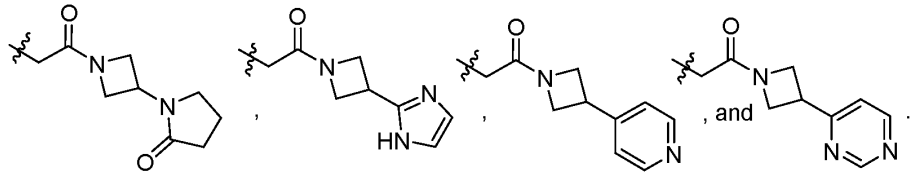
15. The compound of embodiment 1, wherein R^2 is selected from the group consisting of:



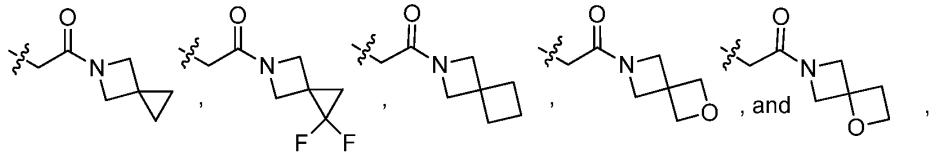
16. The compound of embodiment 1, wherein R^2 is selected from the group consisting of:



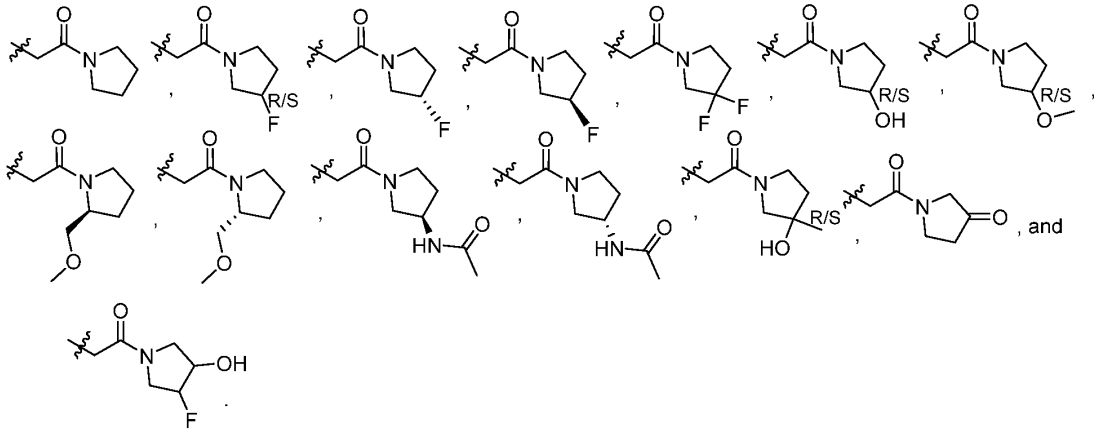
17. The compound of embodiment 1, wherein R^2 is selected from the group consisting of:



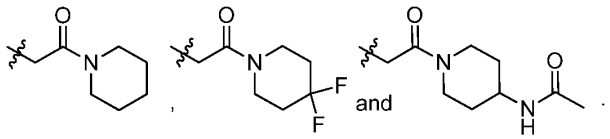
18. The compound of embodiment 1, wherein R^2 is selected from the group consisting of:



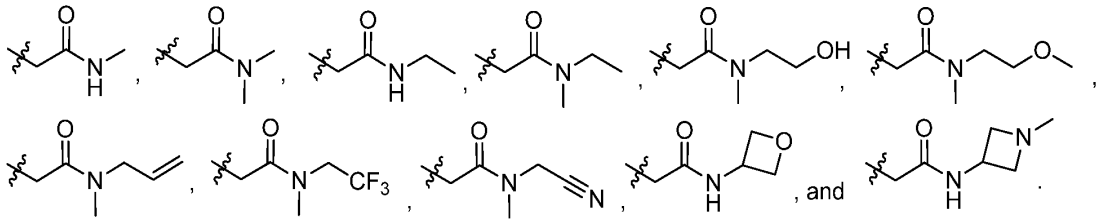
19. The compound of embodiment 1, wherein R^2 is selected from the group consisting of:



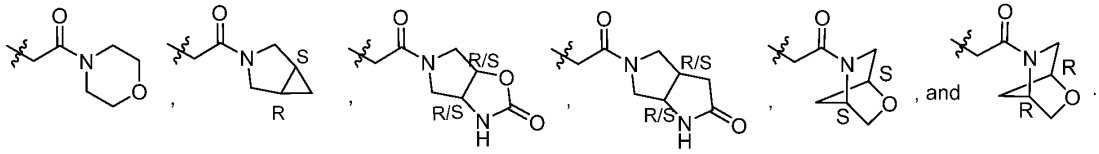
20. The compound of embodiment 1, wherein R^2 is selected from the group consisting of:



21. The compound of embodiment 1, wherein R^2 is selected from the group consisting of:



22. The compound of embodiment 1, wherein R^2 is selected from the group consisting of:



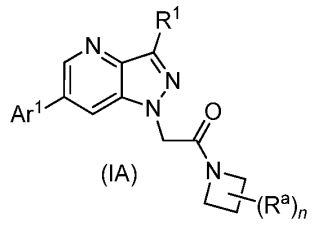
23. The compound of embodiment 1, wherein n is 1.

24. The compound of embodiment 1, wherein n is 2.

25. The compound of embodiment 1, wherein m is 1.

26. The compound of embodiment 1, wherein m is 2.

27. The compound of embodiment 1, having the structure of Formula (IA):



(IA)

wherein

R^1 is H, F, 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, OC_{1-6}perhaloalkyl, CN, and C_{3-6}cycloalkyl;

(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}alkyl, OC_{1-6}perhaloalkyl, and $(C=O)CH_3$; and

(c) thienyl independently substituted with one or two members selected from: halo, C_{1-6}alkyl, and C_{1-6}perhaloalkyl; and pyridine substituted with CF_3;

R^a is each independently selected from the group consisting of: H, halo, OH, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}haloalkenyl, C_{2-6}alkynyl, CH_2OH, $CH(OH)(CH_3)$, CH_2OCH_3, OC_{1-6}haloalkyl, OC_{1-6}alkyl, $NH(CH_3)$, $NHCO_2CH_3$, $NHC(=O)CH_3$, $NHC(=O)CF_3$, NHC(=O)cyclopropyl, $N(CH_3)C(=O)CH_3$, $C(=O)N(CH_3)_2$, $C(=O)CH_3$, CN, $NHSO_2CH_3$, SO_2CH_3, 1H-imidazol-2-yl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrimidin-4-yl, and pyrrolidine-2-one; or two R^a members combine to form a C_{3-6}cycloalkyl or heterocycloalkyl, wherein the C_{3-6}cycloalkyl and heterocycloalkyl is optionally substituted one or two F members; and

n is 1 or 2;

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

28. The compound of embodiment 27, wherein

R^1 is H, F, or CH_3;

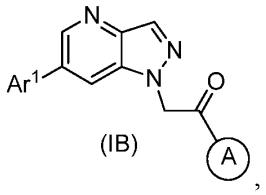
Ar^1 is phenyl substituted with two or three members each independently selected from the group consisting of: halo, C_{1-4}alkyl, C_{1-4}perhaloalkyl, OC_{1-4}alkyl, and OC_{1-4}perhaloalkyl;

R^a is each independently selected from the group consisting of: H, Cl, F, OH, CH_3, CH_2CH_3, CH_2F, CHF_2, CF_3, $=CH_2$, $CH=CH_2$, $CH=CH(CH_3)$, CH=CH(F), CH=CF(F), $C^{\equiv}CH$, CH_2OH, $CH(OH)(CH_3)$, CH_2OCH_3, $OCHF_2$, OCF_3, OCH_3, OCH_2CH_3, $NH(CH_3)$, $NHCO_2CH_3$, $NHC(=O)CH_3$, $NHC(=O)CF_3$, NHC(=O)cyclopropyl, $N(CH_3)C(=O)CH_3$, $C(=O)CH_3$, CN, $NHSO_2CH_3$, 1H-imidazol-2-yl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrimidin-4-yl, and pyrrolidine-2-one; or two R^a members combine to form a cyclopropyl, cyclobutyl, or oxetanyl; wherein the cyclopropyl is optionally substituted one or two F members;

and n is 1 or 2.

29. The compound of embodiment 27, wherein R^1 is H.

30. The compound of embodiment 1, having the structure of Formula (IB):



(IB),

wherein

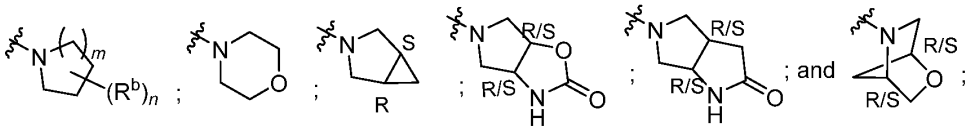
Ar^1 is selected from the group consisting of:

(a) phenyl substituted with one member selected from the group consisting of: halo, and C_{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

(c) thienyl independently substituted with one or two members selected from: halo, C_{1-6}alkyl, and C_{1-6}perhaloalkyl; and pyridine substituted with CF_3;

Ring (A) is selected from the group consisting of:



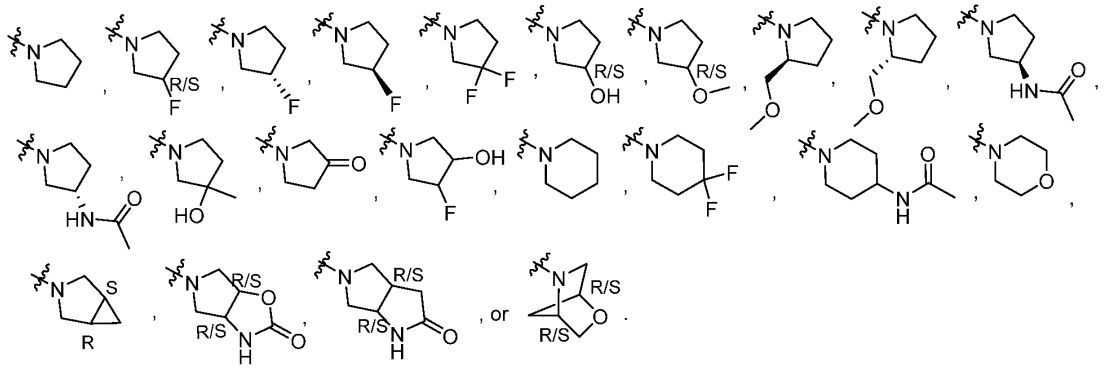
R^b is each independently selected from the group consisting of: H, OH, F, OCH_3, CH_2OCH_3, and $NHC(=O)CH_3$; or two R^b members come together to form =O;

n is 1 or 2; and

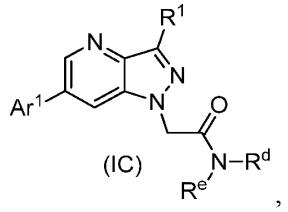
m is 1 or 2;

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

31. The compound of embodiment 30, wherein Ring (A) is



32. The compound of embodiment 1, having the structure of Formula (IC):



(IC)

wherein

R^1 is H, F, 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, and C_{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

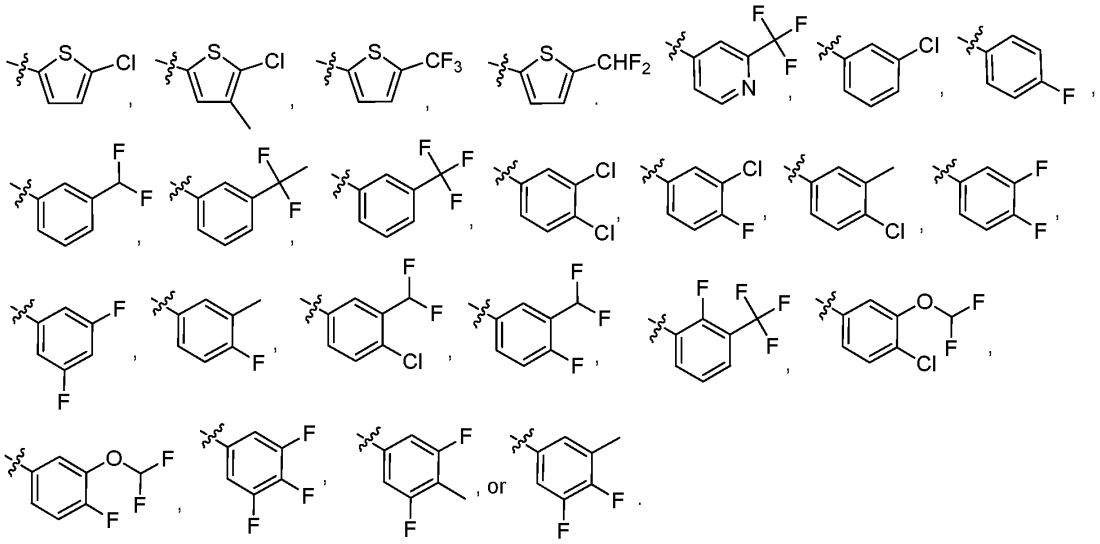
(c) thienyl independently substituted with one or two members selected from: halo, C_{1-6}alkyl, and C_{1-6}perhaloalkyl; and pyridine substituted with CF_3;

R^d is selected from the group consisting of: C_{1-6}alkyl; $CH_2CH{=}CH_2$; C_{1-6}haloalkyl; $CH_2CH_2OCH_3$; CH_2CH_2OH; CH_2CN; NH_2; $NH\text{-}C(=O)CH_3$; cyclopropyl; cyclobutyl; 3-bicyclo[1.1.1]pentanyl; 3,3-difluorocyclobutyl; 1-methylazetidin-3-yl; and oxetan-3-yl; and

R^e is H or CH_3;

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

33. The compound of embodiment 32, wherein Ar^1 is



34. A compound selected from the group consisting of:

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-hydroxy-3-(trifluoromethyl)azetidin-1-yl]ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methyleneazetidin-1-yl)ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-(methylamino)azetidin-1-yl]ethanone;

N-[1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]azetidin-3-yl]-N-methyl-acetamide;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

2-[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

N,N-Dimethyl-2-[6-[6-(trifluoromethyl)-2-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;

2-[6-[4-Chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

2-[6-[4-Chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

N,N-Dimethyl-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-morpholino-ethanone;

1-Morpholino-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

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

N-(1-Methylazetidin-3-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;

1-(3-Fluoroazetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(3,3-Difluoroazetidin-1-yl)-2-[6-(2,4-difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(Azetidin-1-yl)-2-[6-(5-chloro-2-thienyl)-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(Azetidin-1-yl)-2-[6-[5-(difluoromethyl)-2-thienyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(Azetidin-1-yl)-2-[3-fluoro-6-[5-(trifluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(Azetidin-1-yl)-2-[6-(4-fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(Azetidin-1-yl)-2-[6-(3-chlorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
1-(Azetidin-1-yl)-2-[6-[3-(fluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
1-(Azetidin-1-yl)-2-[6-[3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
1-(Azetidin-1-yl)-2-[6-[3-(1,1-difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
1-(Azetidin-1-yl)-2-[6-[3-(1,1-difluoroethyl)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]ethanone;
1-(Azetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
1-(Azetidin-1-yl)-2-[3-methyl-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
1-(Azetidin-1-yl)-2-[6-(3,4-dichlorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
1-(Azetidin-1-yl)-2-[6-(2,3-dichlorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
1-(Azetidin-1-yl)-2-[6-(3-chloro-2-fluoro-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
1-(Azetidin-1-yl)-2-[6-(3,4-difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
1-(Azetidin-1-yl)-2-[6-[2-fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
1-(Azetidin-1-yl)-2-[6-[3-(1,1-difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
1-(Azetidin-1-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
1-(Azetidin-1-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]ethanone;
1-(Azetidin-1-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]-3-methyl-pyrazolo[4,3-b]pyridin-1-yl]ethanone;
1-(Azetidin-1-yl)-2-[6-(4-chloro-3-methylphenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
1-(Azetidin-1-yl)-2-[6-(4-chloro-3-methylphenyl)-3-methyl-pyrazolo[4,3-b]pyridin-1-yl]ethanone;
1-(Azetidin-1-yl)-2-[6-(2-fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;
1-(Azetidin-1-yl)-2-[6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(Azetidin-1-yl)-2-[6-[3-(difluoromethoxy)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(Azetidin-1-yl)-2-[6-[4-chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(Azetidin-1-yl)-2-[6-[4-chloro-3-(difluoromethoxy)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(Azetidin-1-yl)-2-[6-(4-fluoro-2-methoxy-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;

2-[6-(3-Acetyl-4-fluoro-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(azetidin-1-yl)ethanone;

1-(Azetidin-1-yl)-2-[6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(Azetidin-1-yl)-2-[6-[2-(trifluoromethyl)-4-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

2-[6-(5-Chloro-2-thienyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

2-[6-(5-Chloro-2-thienyl)-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

2-[6-[5-(Difluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

2-[6-[5-(Difluoromethyl)-2-thienyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

1-(3-Fluoroazetidin-1-yl)-2-[6-[5-(trifluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(3-Fluoroazetidin-1-yl)-2-[3-fluoro-6-[5-(trifluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(3-Fluoroazetidin-1-yl)-2-[6-(3-fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(3-Fluoroazetidin-1-yl)-2-[6-(4-fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;

2-[6-(3-Chlorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

1-(3-Fluoroazetidin-1-yl)-2-[6-(m-tolyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(3-Fluoroazetidin-1-yl)-2-[6-[3-(fluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

2-[6-[3-(Difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

2-[6-[3-(1,1-Difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

2-[6-[3-(Difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

2-[6-(2,3-Difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

2-[6-(2,4-Difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

2-[6-(3,4-Difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

2-[6-(3,5-Difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

2-[6-(3-Chloro-2-fluoro-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

2-[6-(3-Chloro-4-fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

1-(3-Chloroazetidin-1-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

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

2-[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

2-[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

2-[6-[4-Chloro-3-(1,1-difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

2-[6-[4-Chloro-3-(1,1-difluoroethyl)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

2-[6-[4-Chloro-3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

2-[6-(4-Chloro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

1-(3-Fluoroazetidin-1-yl)-2-[6-(4-fluoro-2-methoxy-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;

2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

2-[6-[4-Chloro-3-(difluoromethoxy)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

2-[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

2-[6-(3,4-Difluoro-5-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

1-(3-Fluoroazetidin-1-yl)-2-[6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(3-Fluoroazetidin-1-yl)-2-[6-[2-(trifluoromethyl)-4-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(3-Methylazetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

(Racemic) 1-(2-Methylazetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methylazetidin-1-yl)ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methylazetidin-1-yl)ethanone;

(Racemic) 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(2-methylazetidin-1-yl)ethanone;

2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methylazetidin-1-yl)ethanone;

2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methylazetidin-1-yl)ethanone;

2-[6-[4-Chloro-3-(difluoromethoxy)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methylazetidin-1-yl)ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-ethynylazetidin-1-yl)ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-vinylazetidin-1-yl)ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-[(Z)-prop-1-enyl]azetidin-1-yl]ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-(fluoromethyl)azetidin-1-yl]ethanone;

1-[3-(Difluoromethyl)azetidin-1-yl]-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-[3-(Trifluoromethyl)azetidin-1-yl]-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-(trifluoromethyl)azetidin-1-yl]ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-[(Z)-2-fluorovinyl]azetidin-1-yl]ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-(2,2-difluorovinyl)azetidin-1-yl]ethanone;

1-(3-Methoxyazetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methoxyazetidin-1-yl)ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-ethoxyazetidin-1-yl)ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-(methoxymethyl)azetidin-1-yl]ethanone;

1-[3-(Methoxymethyl)azetidin-1-yl]-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

(Racemic) 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-(1-hydroxyethyl)azetidin-1-yl]ethanone;

1-[3-(Difluoromethoxy)azetidin-1-yl]-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-(trifluoromethoxy)azetidin-1-yl]ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-hydroxyazetidin-1-yl)ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-hydroxyazetidin-1-yl)ethanone;

1-(3-Hydroxyazetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-(hydroxymethyl)azetidin-1-yl]ethanone;

1-(3,3-Difluoroazetidin-1-yl)-2-[6-(4-methyl-2-thienyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(3,3-Difluoroazetidin-1-yl)-2-[6-(4-fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;

2-[6-(3-Chlorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3,3-difluoroazetidin-1-yl)ethanone;

1-(3,3-Difluoroazetidin-1-yl)-2-[6-(m-tolyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(3,3-Difluoroazetidin-1-yl)-2-[6-[3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(3,3-Difluoroazetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

3-[1-[2-(3,3-Difluoroazetidin-1-yl)-2-oxo-ethyl]pyrazolo[4,3-b]pyridin-6-yl]benzonitrile;

1-(3,3-Difluoroazetidin-1-yl)-2-[6-[6-(trifluoromethyl)-2-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(3,3-Difluoroazetidin-1-yl)-2-[6-[2-(trifluoromethyl)-4-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(3,3-Difluoroazetidin-1-yl)-2-[6-[5-(trifluoromethyl)-3-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(3,3-Difluoroazetidin-1-yl)-2-[6-(3,4-difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(3,3-Difluoroazetidin-1-yl)-2-[6-(3,5-difluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;

2-[6-(3-Chloro-4-fluoro-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3,3-difluoroazetidin-1-yl)ethanone;

2-[6-(3-Chloro-2-fluoro-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-(3,3-difluoroazetidin-1-yl)ethanone;

1-(3,3-Difluoroazetidin-1-yl)-2-[6-(4-fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(3,3-Difluoroazetidin-1-yl)-2-[6-(4-fluoro-2-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(3,3-Difluoroazetidin-1-yl)-2-[6-(2-fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(3,3-Difluoroazetidin-1-yl)-2-[6-[2-fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(3,3-Difluoroazetidin-1-yl)-2-[6-[4-fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(3,3-Difluoroazetidin-1-yl)-2-[6-[2-fluoro-5-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(3,3-Difluoroazetidin-1-yl)-2-[6-[2-methyl-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(3,3-Difluoroazetidin-1-yl)-2-[6-(4-fluoro-2-methoxy-phenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(3,3-Difluoroazetidin-1-yl)-2-[6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(3,3-Dimethylazetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(3-Fluoro-3-methyl-azetidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3,3-dimethylazetidin-1-yl)ethanone;

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

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-ethyl-3-fluoro-azetidin-1-yl)ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-fluoro-3-(fluoromethyl)azetidin-1-yl]ethanone;

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

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-ethyl-3-hydroxy-azetidin-1-yl)ethanone;

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

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-fluoro-3-(hydroxymethyl)azetidin-1-yl]ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-fluoro-3-(methoxymethyl)azetidin-1-yl]ethanone;

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

1-[2-[6-[3-(Trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]azetidine-3-carbonitrile;

1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]azetidine-3-carbonitrile;

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

1-(3-Acetylazetidin-1-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

N-[1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]azetidin-3-yl]acetamide;

1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]-N,N-dimethyl-azetidine-3-carboxamide;

MethylN-[1-[2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]azetidin-3-yl]carbamate;

N-[1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]azetidin-3-yl]-2,2,2-trifluoro-acetamide;

N-[1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]azetidin-3-yl]cyclopropanecarboxamide;

N-[1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]azetidin-3-yl]methanesulfonamide;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methylsulfonylazetidin-1-yl)ethanone;

1-[1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]azetidin-3-yl]pyrrolidin-2-one;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-(1H-imidazol-2-yl)azetidin-1-yl]ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[3-(4-pyridyl)azetidin-1-yl]ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-pyrimidin-4-ylazetidin-1-yl)ethanone;

1-(5-Azaspiro[2.3]hexan-5-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(2,2-Difluoro-5-azaspiro[2.3]hexan-5-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(6-Azaspiro[3.3]heptan-6-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-oxa-6-azaspiro[3.3]heptan-6-yl)ethanone;

1-(6-Oxa-2-azaspiro[3.3]heptan-2-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

2-[6-(4-Fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-pyrrolidin-1-yl-ethanone;

1-Pyrrolidin-1-yl-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
2-[6-(3-Cyclopropylphenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-pyrrolidin-1-yl-ethanone;
2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-pyrrolidin-1-yl-ethanone;
2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-pyrrolidin-1-yl-ethanone;
2-[6-(3,5-Difluoro-4-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-pyrrolidin-1-yl-ethanone;
1-[(3R)-3-Fluoropyrrolidin-1-yl]-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
1-[(3S)-3-Fluoropyrrolidin-1-yl]-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;
(Racemic) (R,S)-2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoropyrrolidin-1-yl)ethanone;
(Racemic) (R,S)-2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoropyrrolidin-1-yl)ethanone;
2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[(3R)-3-fluoropyrrolidin-1-yl]ethanone;
2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[(3S)-3-fluoropyrrolidin-1-yl]ethanone;
(Racemic) (R,S)-2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-hydroxypyrrolidin-1-yl)ethanone;
(Racemic) (R,S)-2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-hydroxypyrrolidin-1-yl)ethanone;
(Racemic) 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-methoxypyrrolidin-1-yl)ethanone;
2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[(2R)-2-(methoxymethyl)pyrrolidin-1-yl]ethanone;
2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[(2S)-2-(methoxymethyl)pyrrolidin-1-yl]ethanone;

N-[(3S)-1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]pyrrolidin-3-yl]acetamide;

N-[(3R)-1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]pyrrolidin-3-yl]acetamide;

1-(3,3-Difluoropyrrolidin-1-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3,3-difluoropyrrolidin-1-yl)ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3,3-difluoropyrrolidin-1-yl)ethanone;

(Racemic) 2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-hydroxy-3-methyl-pyrrolidin-1-yl)ethanone;

(Racemic) Trans-2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoro-4-hydroxy-pyrrolidin-1-yl)ethanone;

1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]pyrrolidin-3-one;

1-[2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]pyrrolidin-3-one;

1-(1-Piperidyl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(4,4-Difluoro-1-piperidyl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

N-[1-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]-4-piperidyl]acetamide;

2-[6-(4-Fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-1-morpholino-ethanone;

1-[(1R,5S)-3-Azabicyclo[3.1.0]hexan-3-yl]-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[(1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl]ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-[(1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl]ethanone;

(Racemic) Cis-5-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]-3a,4,6,6a-tetrahydro-3H-pyrrolo[3,4-d]oxazol-2-one;

(Racemic) Cis-5-[2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetyl]-1,3,3a,4,6,6a-hexahydropyrrolo[2,3-c]pyrrol-2-one;

2-[6-[5-(Difluoromethyl)-2-thienyl]pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

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

2-[6-(5-Chloro-2-thienyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

2-[6-(5-Chloro-4-methyl-2-thienyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

2-[6-[3-(Difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

2-[6-[3-(Difluoromethyl)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

2-[3-Fluoro-6-(4-fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

2-[3-Fluoro-6-(3-fluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

2-[6-(3-Chlorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

N,N-Dimethyl-2-[6-[2-(trifluoromethyl)-4-pyridyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;

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

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N-ethyl-acetamide;

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

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

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

2-[6-[4-Chloro-3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

2-[6-[3-(1,1-Difluoroethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

2-[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-N-methyl-acetamide;

2-[3-Fluoro-6-(4-fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

2-[6-(4-Chloro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

2-[6-(3-Chloro-4-fluoro-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

2-[6-(3,4-Dichlorophenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

2-[6-(3,5-Difluorophenyl)-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

2-[6-(3,4-Difluorophenyl)-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

2-[6-[3-(1,1-Difluoroethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

2-[6-[3-(1,1-Difluoroethyl)phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

2-[6-[2-Fluoro-3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

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

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

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

N-(Cyanomethyl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N-methyl-acetamide;

N-Allyl-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N-methyl-acetamide;

N,N-Dimethyl-2-[6-(3,4,5-trifluorophenyl)pyrazolo[4,3-b]pyridin-1-yl]acetamide;
2-[6-(3,4-Difluoro-5-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
2-[6-(2,4-Difluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;
N-Cyclopropyl-N-methyl-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;
N-Cyclopropyl-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;
N-Cyclopropyl-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N-methyl-acetamide;
N-Cyclopropyl-2-[3-methyl-6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;
N-Cyclopropyl-2-[6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;
N-Cyclobutyl-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;
N-Cyclobutyl-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N-methyl-acetamide;
N-Cyclobutyl-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;
N-(3,3-Difluorocyclobutyl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;
N-(3,3-Difluorocyclobutyl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;
N-(3-Bicyclo[1.1.1]pentanyl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N-methyl-acetamide;
N-(Oxetan-3-yl)-2-[6-[3-(trifluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]acetamide;
2-(6-(3-(Difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-(pyridin-3-yl)azetidin-1-yl)ethan-1-one;
2-(6-(3-(Difluoromethyl)-4-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)-1-(3-(pyridin-2-yl)azetidin-1-yl)ethan-1-one;

Methyl (1-(2-(6-(3-(Difluoromethyl)-4-fluorophenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)acetyl)azetidin-3-yl)carbamate;

(S)-N-(1-(2-(6-(3-(Difluoromethyl)-4-fluorophenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)acetyl)pyrrolidin-3-yl)acetamide;

(R)-N-(1-(2-(6-(3-(Difluoromethyl)-4-fluorophenyl)-3-fluoro-1H-pyrazolo[4,3-b]pyridin-1-yl)acetyl)pyrrolidin-3-yl)acetamide; and

1-(3-(Fluoro-18F)azetidin-1-yl)-2-(6-(3-(trifluoromethyl)phenyl)-1H-pyrazolo[4,3-b]pyridin-1-yl)ethan-1-one;

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

35. A compound selected from the group consisting of:

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

2-[6-(4-Fluoro-3-methyl-phenyl)pyrazolo[4,3-b]pyridin-1-yl]-N,N-dimethyl-acetamide;

2-[6-[4-Chloro-3-(difluoromethoxy)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

1-(Azetidin-1-yl)-2-[6-[3-(difluoromethyl)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

1-(Azetidin-1-yl)-2-[6-[3-(difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]ethanone;

2-[6-[3-(Difluoromethyl)-4-fluoro-phenyl]-3-fluoro-pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

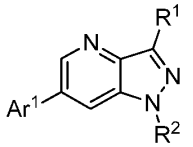
2-[6-[4-Chloro-3-(difluoromethyl)phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone;

2-[6-[3-(Difluoromethoxy)-4-fluoro-phenyl]pyrazolo[4,3-b]pyridin-1-yl]-1-(3-fluoroazetidin-1-yl)ethanone; and

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

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

36. 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;

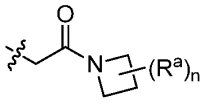
Ar^1 is selected from the group consisting of:

(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, OC_{1-6}perhaloalkyl, CN, and C_{3-6}cycloalkyl;

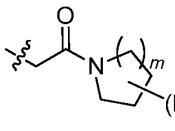
(b) phenyl substituted with two or three members each independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}perhaloalkyl, OC_{1-6}alkyl, OC_{1-6}perhaloalkyl, and $(C{=}O)CH_3$; and

(c) thienyl independently substituted with one or two members selected from: halo, C_{1-6}alkyl, and C_{1-6}perhaloalkyl; and pyridine substituted with CF_3;

R^2 is selected from the group consisting of:

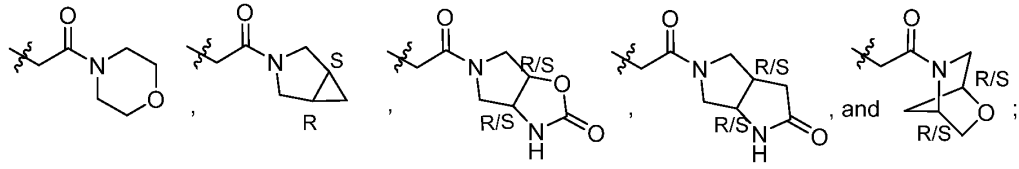
(d)  ; wherein

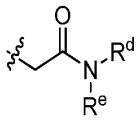
R^a is each independently selected from the group consisting of: H, halo, OH, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}haloalkenyl, C_{2-6}alkynyl, CH_2OH, $CH(OH)(CH_3)$, CH_2OCH_3, OC_{1-6}haloalkyl, OC_{1-6}alkyl, $NH(CH_3)$, $NHCO_2CH_3$, $NHC(=O)CH_3$, $NHC(=O)CF_3$, NHC(=O)cyclopropyl, $N(CH_3)C(=O)CH_3$, $C(=O)N(CH_3)_2$, $C(=O)CH_3$, CN, $NHSO_2CH_3$, SO_2CH_3, 1H-imidazol-2-yl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrimidin-4-yl, and pyrrolidine-2-one; or two R^a members combine to form a C_{3-6}cycloalkyl or heterocycloalkyl, wherein the cycloalkyl and heterocycloalkyl is optionally substituted one or two F members;

(e)  ; wherein

R^b is each independently selected from the group consisting of: H, OH, F, OCH_3, CH_2OCH_3, and $NHC(=O)CH_3$; or two R^b members come together to form =O;

(f)

 and

(g)  , wherein

R^d is selected from the group consisting of: C_{1-6}alkyl; C_{2-6}alkenyl C_{1-6}haloalkyl; $CH_2CH_2OCH_3$; CH_2CH_2OH; CH_2CN; NH_2; $NH\text{-}C(=O)CH_3$; C_{3-6}cycloalkyl; C_{3-6}cycloalkyl substituted with two F members; 1-methylazetidin-3-yl; and oxetan-3-yl;

R^e is H or CH_3;

n is 1 or 2; and

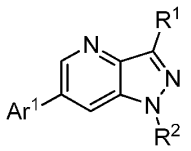
m is 1 or 2;

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

(B) at least one pharmaceutically acceptable excipient.

37. A pharmaceutical composition comprising an effective amount of at least one compound of embodiment 34 and at least one pharmaceutically acceptable excipient.

38. 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;

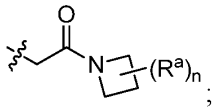
Ar^1 is selected from the group consisting of:

(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, OC_{1-6}perhaloalkyl, CN, and C_{3-6}cycloalkyl;

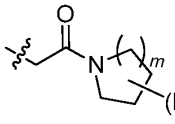
(b) phenyl substituted with two or three members each independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}perhaloalkyl, OC_{1-6}alkyl, OC_{1-6}perhaloalkyl, and $(C=O)CH_3$; and

(c) thienyl independently substituted with one or two members selected from: halo, C_{1-6}alkyl, and C_{1-6}perhaloalkyl; and pyridine substituted with CF_3;

R^2 is selected from the group consisting of:

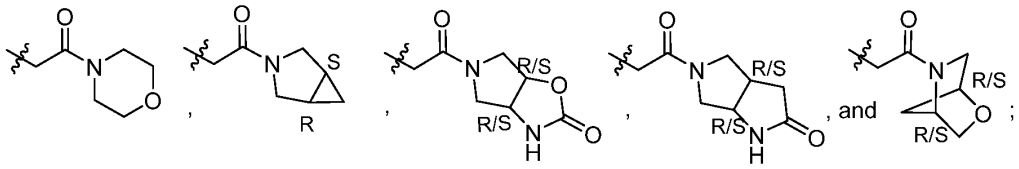
(d)  ; wherein

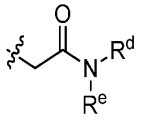
R^a is each independently selected from the group consisting of: H, halo, OH, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}haloalkenyl, C_{2-6}alkynyl, CH_2OH, $CH(OH)(CH_3)$, CH_2OCH_3, OC_{1-6}haloalkyl, OC_{1-6}alkyl, $NH(CH_3)$, $NHCO_2CH_3$, $NHC(=O)CH_3$, $NHC(=O)CF_3$, NHC(=O)cyclopropyl, $N(CH_3)C(=O)CH_3$, $C(=O)N(CH_3)_2$, $C(=O)CH_3$, CN, $NHSO_2CH_3$, SO_2CH_3, 1H-imidazol-2-yl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrimidin-4-yl, and pyrrolidine-2-one; or two R^a members combine to form a C_{3-6}cycloalkyl or heterocycloalkyl, wherein the cycloalkyl and heterocycloalkyl is optionally substituted one or two F members;

(e)  ; wherein

R^b is each independently selected from the group consisting of: H, OH, F, OCH_3, CH_2OCH_3, and $NHC(=O)CH_3$; or two R^b members come together to form =O;

(f)

 and

(g)  , wherein

R^d is selected from the group consisting of: C_{1-6}alkyl; C_{2-6}alkenyl C_{1-6}haloalkyl; $CH_2CH_2OCH_3$; CH_2CH_2OH; CH_2CN; NH_2; $NH\text{-}C(=O)CH_3$; C_{3-6}cycloalkyl; C_{3-6}cycloalkyl substituted with two F members; 1-methylazetidin-3-yl; and oxetan-3-yl;

R^e is H or CH_3;

n is 1 or 2; and

m is 1 or 2;

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

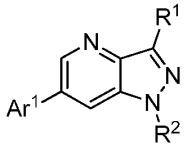
39. The method of embodiment 38, wherein the disorder, disease or condition mediated by the GluN2B receptor is selected from the group consisting of: bipolar disorder, major depressive disorder, treatment-resistant depression, post-partum depression, seasonal affective disorder, Alzheimer's disease, 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.

40. The method of embodiment 38, 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 the specific embodiments 1-58 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;

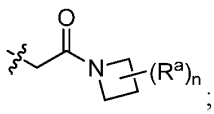
Ar^1 is selected from the group consisting of:

(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, OC_{1-6}perhaloalkyl, CN, and C_{3-6}cycloalkyl;

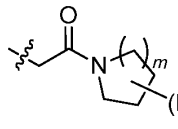
(b) phenyl substituted with two or three members each independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}perhaloalkyl, OC_{1-6}alkyl, OC_{1-6}perhaloalkyl, and $(C=O)CH_3$; and

(c) thienyl substituted with one or two members independently selected from: halo, C_{1-6}alkyl, and C_{1-6}perhaloalkyl; and pyridine substituted with CF_3;

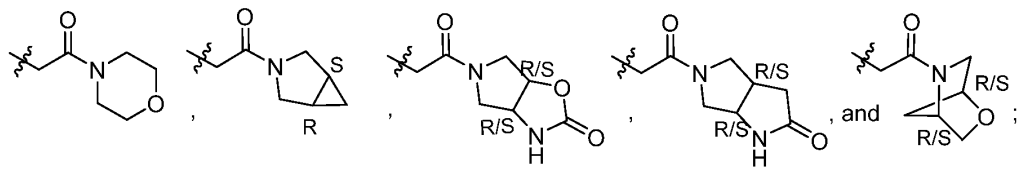
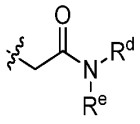
R^2 is selected from the group consisting of:

(d)  ; wherein

R^a is each independently selected from the group consisting of: H, halo, OH, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}haloalkenyl, C_{2-6}alkynyl, CH_2OH, $CH(OH)(CH_3)$, CH_2OCH_3, OC_{1-6}haloalkyl, OC_{1-6}alkyl, $NH(CH_3)$, $NHCO_2CH_3$, $NHC(=O)CH_3$, $NHC(=O)CF_3$, NHC(=O)cyclopropyl, $N(CH_3)C(=O)CH_3$, $C(=O)N(CH_3)_2$, $C(=O)CH_3$, CN, $NHSO_2CH_3$, SO_2CH_3, 1H-imidazol-2-yl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrimidin-4-yl, and pyrrolidine-2-one; or two R^a members combine to form a C_{3-6}cycloalkyl or heterocycloalkyl, wherein the cycloalkyl and heterocycloalkyl is optionally substituted one or two F members;

(e)  ; wherein

R^b is each independently selected from the group consisting of: H, OH, F, OCH_3, CH_2OCH_3, and $NHC(=O)CH_3$; or two R^b members come together to form =O;

(f)  and  ;

(g) , wherein

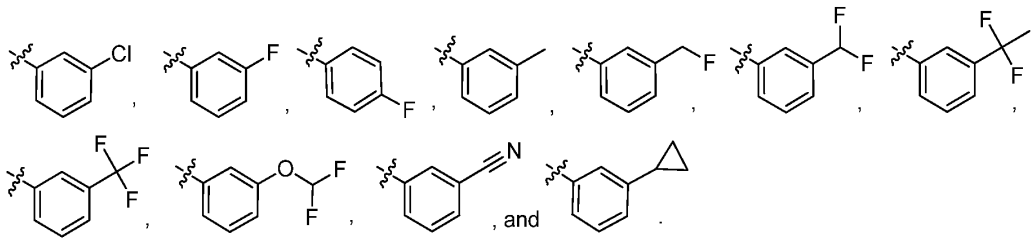
R^d is selected from the group consisting of: C_{1-6}alkyl; C_{2-6}alkenyl; C_{1-6}haloalkyl; $CH_2CH_2OCH_3$; CH_2CH_2OH; CH_2CN; NH_2; NH-C(=O)CH_3; C_{3-6}cycloalkyl; C_{3-6}cycloalkyl substituted with two F members; 1-methylazetidin-3-yl; and oxetan-3-yl;

R^e is H or CH_3;

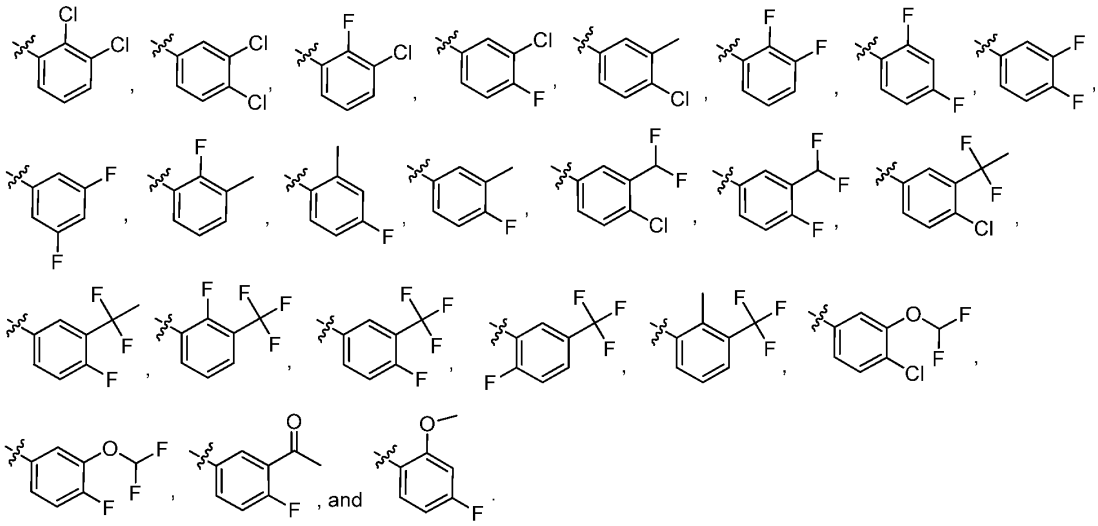
n is 1 or 2; and

m is 1 or 2.

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 phenyl substituted with one member selected from the group consisting of: Cl, F, CH_3, OCH_3, CH_2F, CHF_2, CF_3, CHF_2CH_3, $OCHF_2$, CN, and cyclopropyl.
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 selected from the group consisting of:

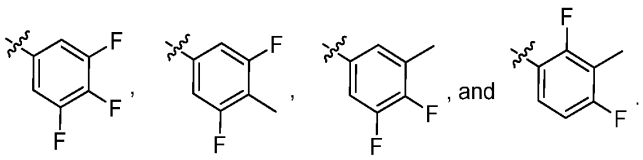


7. The compound of any one of embodiments 1 to 4, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein Ar^1 is phenyl substituted with two members each independently selected from the group consisting of: Cl, F, CH_3, CHF_2, CF_3, CHF_2CH_3, OCH_3, $OCHF_2$, and $(C=O)CH_3$.
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 selected from the group consisting of:



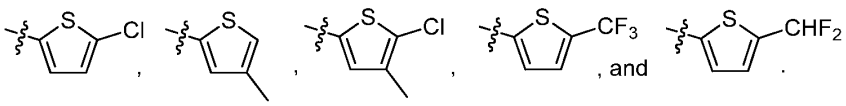
9. The compound of any one of embodiments 1 to 4, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein Ar^1 is phenyl substituted with three members each independently selected from the group consisting of: halo, and CH_3.

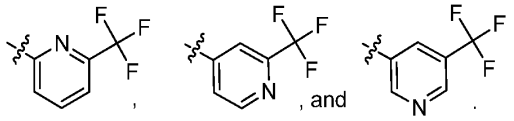
10. The compound of any one of embodiments 1 to 4, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein Ar^1 is selected from the group consisting of:

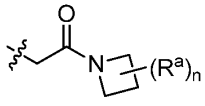


11. The compound of any one of embodiments 1 to 4, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein Ar^1 is thienyl substituted with one or two members independently selected from: Cl, CH_3, CF_3 and CHF_2.

12. 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 selected from the group consisting of:



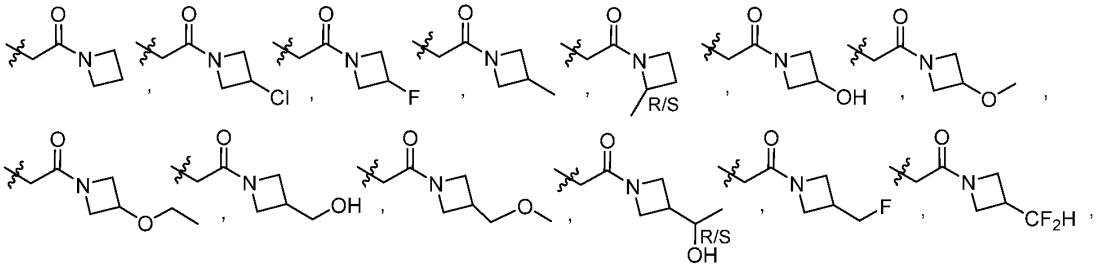
13. The compound of any one of embodiments 1 to 4, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein Ar^1 is selected from the group consisting of: 

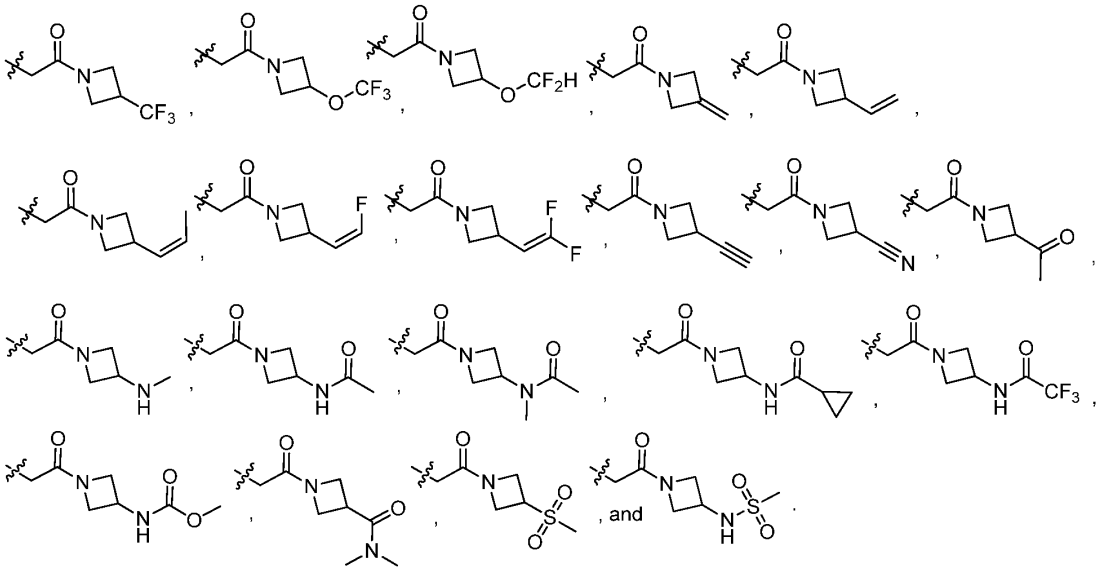
14. The compound of any one of embodiments 1 to 13, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^2 is ; wherein

R^a is each independently selected from the group consisting of: H, Cl, F, OH, CH_3, CH_2CH_3, CH_2F, CHF_2, CF_3, $=CH_2$, $CH=CH_2$, $CH=CH(CH_3)$, CH=CH(F), CH=CF(F), $C^{=}CH$, CH_2OH, $CH(OH)(CH_3)$, CH_2OCH_3, $OCHF_2$, OCF_3, OCH_3, OCH_2CH_3, $NH(CH_3)$, $NHCO_2CH_3$, $NHC(=O)CH_3$, $NHC(=O)CF_3$, NHC(=O)cyclopropyl, $N(CH_3)C(=O)CH_3$, $C(=O)N(CH_3)_2$, $C(=O)CH_3$, CN, $NHSO_2CH_3$, SO_2CH_3, 1H-imidazol-2-yl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrimidin-4-yl, and pyrrolidine-2-one; or two R^a members combine to form a cyclopropyl, cyclobutyl, or oxetanyl; wherein the cyclopropyl is optionally substituted one or two F members;

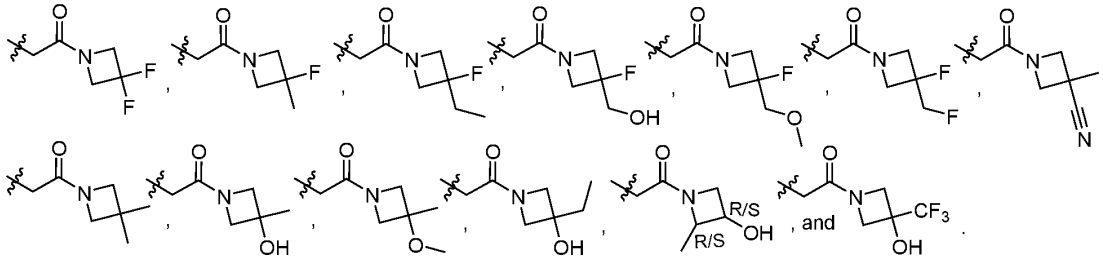
and n is 1 or 2.

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^2 is selected from the group consisting of:

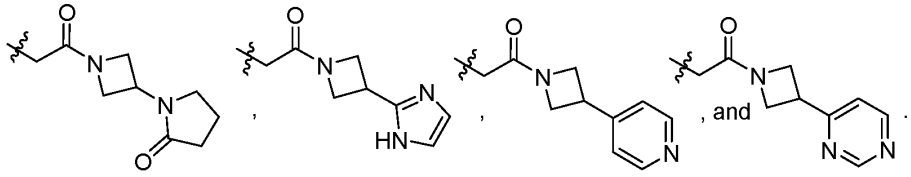




16. The compound of any one of embodiments 1 to 13, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^2 is selected from the group consisting of:

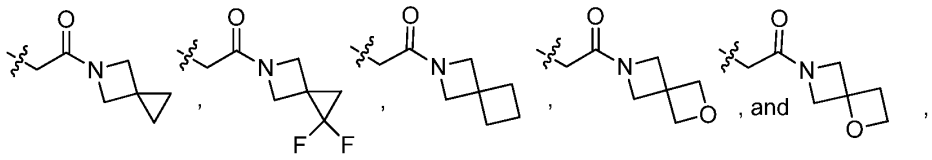


17. The compound of any one of embodiments 1 to 13, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^2 is selected from the group consisting of:

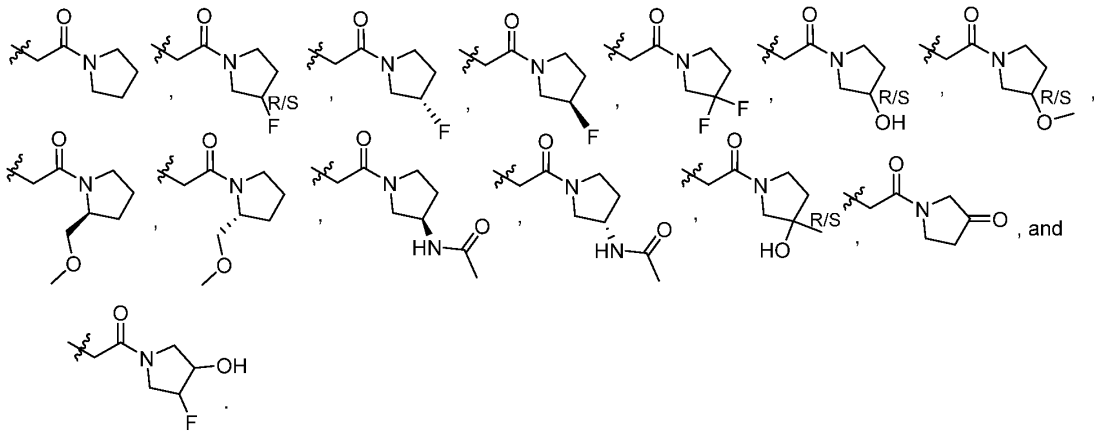


18. The compound of any one of embodiments 1 to 13, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^2 is selected from

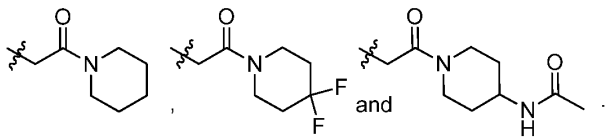
the group consisting of:



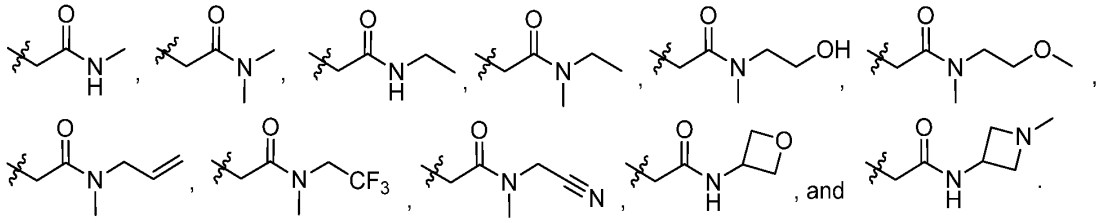
19. The compound of any one of embodiments 1 to 13, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^2 is selected from the group consisting of:



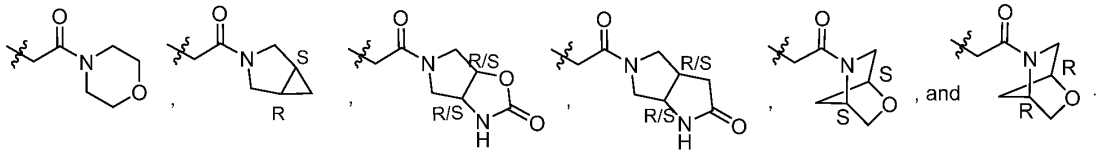
20. The compound of any one of embodiments 1 to 13, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^2 is selected from the group consisting of:



21. 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^2 is selected from the group consisting of:



22. 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^2 is selected from the group consisting of:



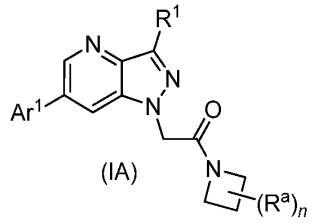
23. The compound of any one of embodiments 1 to 22, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein *n* is 1.

24. The compound of any one of embodiments 1 to 22, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein *n* is 2.

25. The compound of any one of embodiments 1 to 24, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein *m* is 1.

26. The compound of any one of embodiments 1 to 24, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein *m* is 2.

27. The compound of embodiment 1 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, having the structure of Formula (IA):



(IA)

wherein

R^1 is H, F, 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, OC_{1-6}perhaloalkyl, CN, and C_{3-6}cycloalkyl;

(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}alkyl, OC_{1-6}perhaloalkyl, and $(C=O)CH_3$; and

(c) thienyl substituted with one or two members independently selected from: halo, C_{1-6}alkyl, and C_{1-6}perhaloalkyl; and pyridine substituted with CF_3;

R^a is each independently selected from the group consisting of: H, halo, OH, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}haloalkenyl, C_{2-6}alkynyl, CH_2OH, $CH(OH)(CH_3)$, CH_2OCH_3, OC_{1-6}haloalkyl, OC_{1-6}alkyl, $NH(CH_3)$, $NHCO_2CH_3$, $NHC(=O)CH_3$, $NHC(=O)CF_3$, NHC(=O)cyclopropyl, $N(CH_3)C(=O)CH_3$, $C(=O)N(CH_3)_2$, $C(=O)CH_3$, CN, $NHSO_2CH_3$, SO_2CH_3, 1H-imidazol-2-yl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrimidin-4-yl, and pyrrolidine-2-one; or two R^a members combine to form a C_{3-6}cycloalkyl or heterocycloalkyl, wherein the C_{3-6}cycloalkyl and heterocycloalkyl is optionally substituted one or two F members; and

n is 1 or 2.

28. The compound of embodiment 27 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein

R^1 is H, F, or CH_3;

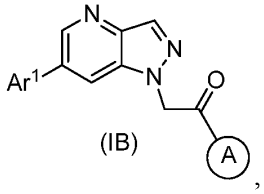
Ar^1 is phenyl substituted with two or three members each independently selected from the group consisting of: halo, C_{1-4}alkyl, C_{1-4}perhaloalkyl, OC_{1-4}alkyl, and OC_{1-4}perhaloalkyl;

R^a is each independently selected from the group consisting of: H, Cl, F, OH, CH_3, CH_2CH_3, CH_2F, CHF_2, CF_3, $=CH_2$, $CH=CH_2$, $CH=CH(CH_3)$, CH=CH(F), CH=CF(F), $C^{=}CH$, CH_2OH, $CH(OH)(CH_3)$, CH_2OCH_3, $OCHF_2$, OCF_3, OCH_3, OCH_2CH_3, $NH(CH_3)$, $NHCO_2CH_3$, $NHC(=O)CH_3$, $NHC(=O)CF_3$, NHC(=O)cyclopropyl, $N(CH_3)C(=O)CH_3$, $C(=O)CH_3$, CN, $NHSO_2CH_3$, 1H-imidazol-2-yl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrimidin-4-yl, and pyrrolidine-2-one; or two R^a members combine to form a cyclopropyl, cyclobutyl, or oxetanyl; wherein the cyclopropyl is optionally substituted one or two F members;

and n is 1 or 2.

29. The compound of embodiment 27 or embodiment 28, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein R^1 is H.

30. The compound of embodiment 1 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, having the structure of Formula (IB):



(IB),

wherein

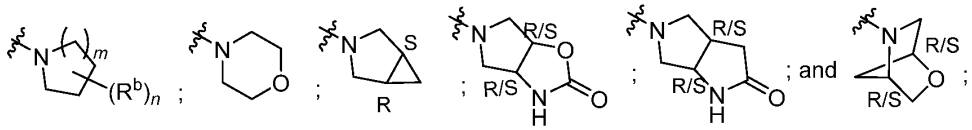
Ar^1 is selected from the group consisting of:

(a) phenyl substituted with one member selected from the group consisting of: halo, and C_{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

(c) thienyl independently substituted with one or two members selected from: halo, C_{1-6}alkyl, and C_{1-6}perhaloalkyl; and pyridine substituted with CF_3;

Ring (A) is selected from the group consisting of:



; and

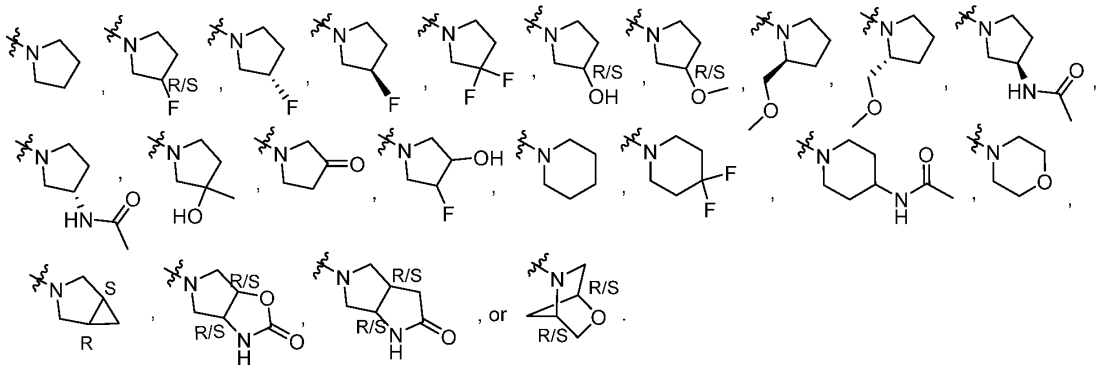
;

R^b is each independently selected from the group consisting of: H, OH, F, OCH_3, CH_2OCH_3, and $NHC(=O)CH_3$; or two R^b members come together to form =O;

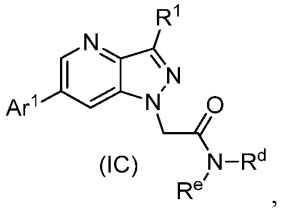
n is 1 or 2; and

m is 1 or 2.

31. The compound of embodiment 30 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein Ring (A) is



32. The compound of embodiment 1 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, having the structure of Formula (IC):



(IC)

wherein

R^1 is H, F, 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, and C_{1-6}perhaloalkyl;

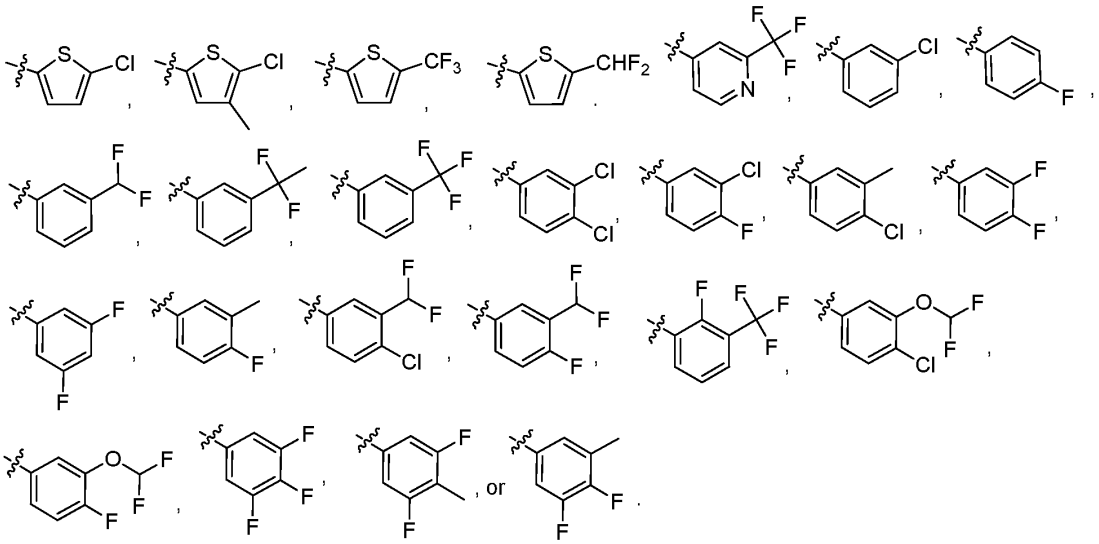
(b) phenyl substituted with two or three members each independently selected from the group consisting of: halo, C_{1-6}alkyl, C_{1-6}perhaloalkyl, OC_{1-6}perhaloalkyl; and

(c) thienyl independently substituted with one or two members selected from: halo, C_{1-6}alkyl, and C_{1-6}perhaloalkyl; and pyridine substituted with CF_3;

R^d is selected from the group consisting of: C_{1-6}alkyl; $CH_2CH{=}CH_2$; C_{1-6}haloalkyl; $CH_2CH_2OCH_3$; CH_2CH_2OH; CH_2CN; NH_2; NH-C(=O)CH_3; cyclopropyl; cyclobutyl; 3-bicyclo[1.1.1]pentanyl; 3,3-difluorocyclobutyl; 1-methylazetidin-3-yl; and oxetan-3-yl; and

R^e is H or CH_3.

33. The compound of embodiment 32 or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopic variant, or N-oxide thereof, wherein Ar^1 is



34. A compound selected from the compounds in Table 1 and pharmaceutically acceptable salts, solvates, stereoisomers, isotopic variants, and N-oxides thereof.

35. The compound of any one of embodiments 1 to 34, or a pharmaceutically acceptable salt or solvate thereof.

36. The compound of any one of embodiments 1 to 34, or a pharmaceutically acceptable salt or N-oxide thereof.

37. The compound of any one of embodiments 1 to 34, or a pharmaceutically acceptable salt thereof.

38. The compound of any one of embodiments 1 to 34.

39. A pharmaceutically acceptable salt of the compound of any one of embodiments 1 to 34.

40. A pharmaceutical composition comprising the compound of any one of embodiments 1 to 34, or a pharmaceutically acceptable salt, solvate, isotopic variant, or N-oxide thereof, and a pharmaceutically acceptable excipient.

41. A pharmaceutical composition comprising the compound of any one of embodiments 1 to 34, or a pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable excipient.

42. A pharmaceutical composition comprising the compound of any one of embodiments 1 to 34, or a pharmaceutically acceptable salt or N-oxide thereof, and a pharmaceutically acceptable excipient.
43. A pharmaceutical composition comprising the compound of any one of embodiments 1 to 34, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.
44. A pharmaceutical composition comprising the compound of any one of embodiments 1 to 34 and a pharmaceutically acceptable excipient.
45. A pharmaceutical composition comprising a pharmaceutically acceptable salt of the compound of any one of embodiments 1 to 34, and a pharmaceutically acceptable excipient.
46. A unit dosage form comprising a therapeutically effective amount of the pharmaceutical composition of any one of embodiments 40 to 45.
47. 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 34, or a pharmaceutically acceptable salt, solvate, isotopic variant, or N-oxide thereof.
48. 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 34, or a pharmaceutically acceptable salt, or solvate thereof.
49. 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 34, or a pharmaceutically acceptable salt or N-oxide thereof.
50. 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 34, or a pharmaceutically acceptable salt thereof.

51. 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 40 to 45 or the unit dosage form of embodiment 46.
52. The method of any one of embodiments 47 to 51, 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.
53. The method of embodiment 52, 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.
54. The method of embodiment 52, wherein the disease, disorder or medical condition mediated by GluN2B receptor activity comprises bipolar disorder.
55. The method of embodiment 52, wherein the disease, disorder or medical condition mediated by GluN2B receptor activity comprises a mood disorder.
56. The method of embodiment 52, wherein the disease, disorder or medical condition mediated by GluN2B receptor activity comprises treatment resistant depression.
57. The method of embodiment 52, wherein the disease, disorder or medical condition mediated by GluN2B receptor activity comprises major depressive disorder.
58. The method of embodiment 52, wherein the disease, disorder or medical condition mediated by GluN2B receptor activity comprises epilepsy.