P2X7 MODULATORS

CROSS REFERENCE TO RELATED APPLICATIONS

This application claims priority to U.S. Application No. 61/786,260 filed on March 14, 2013.

FIELD OF THE INVENTION

The present invention is related to compounds having P2X7 modulating properties, pharmaceutical compositions comprising these compounds, chemical processes for preparing these compounds and their use in the treatment of diseases associated with P2X7 receptor activity in animals, in particular humans.

BACKGROUND OF THE INVENTION

The P2X7 receptor is a ligand-gated ion channel and is present on a variety of cell types, largely those known to be involved in the inflammatory and/ or immune process, specifically, macrophages and monocytes in the periphery and predominantly in glial cells (microglia and astrocytes) of the CNS. (Duan and Neary, *Glia* 2006, *54*, 738-746; Skaper et al., *FASEB J* 2009, *24*, 337-345; Surprenant and North, *Annu. Rev*. *Physiol*. 2009, *71*, 333-359). Activation of the P2X7 receptor by extracellular nucleotides, in particular adenosine triphosphate, leads to the release of proinflammatory cytokines IL-1β and IL-18 (Muller, et. Al. *Am. J. Respir. Cell Mol. Biol*. 2011, *44*, 456-464), giant cell formation (macrophages/ microglial cells), degranulation (mast cells) and L-selectin shedding (lymphocytes) (Ferrari et al., *J. Immunol*. 2006, *176*, 3877-3883; Surprenant and North, *Annu. Rev*. *Physiol*. 2009, *71*, 333-359). P2X7 receptors are also located on antigen-presenting cells (keratinocytes, salivary acinar cells (parotid cells)), hepatocytes, erythrocytes, erythroleukaemic cells, monocytes, fibroblasts, bone marrow cells, neurones, and renal mesangial cells.

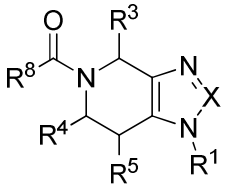
The importance of P2X7 in the nervous system arises primarily from experiments using P2X7 knock out mice. These mice demonstrate the role of P2X7 in the development and maintenance of pain as these mice were protected from the development of both adjuvant-induced inflammatory pain and partial nerve ligation induced neuropathic pain (Chessell et al., *Pain* 2005, *114*, 386-396). In

addition P2X7 knock out mice also exhibit an anti-depressant phenotype based on reduced immobility in forced swim and tail suspension tests (Basso et al., *Behav. Brain Res.* 2009, *198*, 83-90.). Moreover, the P2X7 pathway is linked to the release of the pro-inflammatory cytokine, IL-1β, which has been linked to precipitation of mood disorders in humans (Dantzer, *Immunol. Allergy Clin. North Am.* 2009, *29*, 247-264; Capuron and Miller, *Pharmacol. Ther*. 2011, *130*, 226-238). In addition, in murine models of Alzheimer's disease, P2X7 was upregulated around amyloid plaques indicating a role of this target in such pathology as well (Parvathenani et al., *J. Biol. Chem.* 2003, *278*, 13309-13317).

In view of the clinical importance of P2X7, the identification of compounds that modulate P2X7 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):

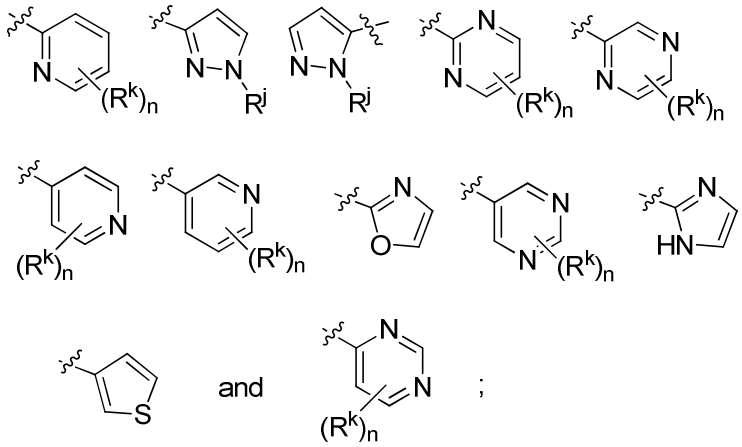


Formula (I)

wherein

R^1 is (a) phenyl, optionally substituted with zero to four groups independently selected from the group consisting of halo, C_1-C_4alkyl, alkoxy, perhaloalkyl and perhaloalkoxy; or

(b) heteroaryl, independently selected from the group consisting of:



wherein R^k is independently selected from the group consisting of H, halo, C_1-C_3alkyl, hydroxyl, perhaloalkyl and alkoxy;

R^j is independently selected from H or C_1-C_3alkyl wherein C_1-C_3alkyl is optionally substituted with from one to three halo substituents, one OH substituent or one alkoxy substituent; and

n is an integer from 0-3;

X is N or CR^2;

R^2 is H, perhaloalkyl or C_1-C_3 lower alkyl;

R^3 is H, perhaloalkyl, C_1-C_4 alkyl, alkalkoxy, CH_2R^i, -C(O)R^e or phenyl, wherein said phenyl is optionally substituted with zero to two groups independently selected from the group consisting of halo, C_1-C_3alkyl, alkoxy, perhaloalkyl and perhaloalkoxy;

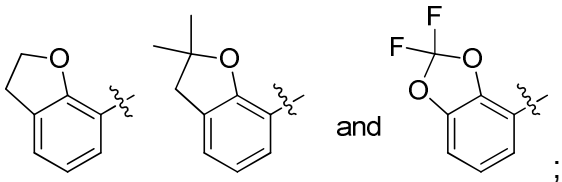
R^i is OH, NC_3H_6, $N(C_1$-C_3alkyl$)_2$ or halo;

R^e is OH, OC_1-C_3 alkyl, $N(C_1$-C_3alkyl$)_2$, or NC_3H_6;

R^4 and R^5 are independently H or C_1-C_3 alkyl;

R^8 is phenyl or pyridyl, optionally substituted with zero to four R^m substituents wherein R^m is independently selected from the group consisting of halo, C_1-C_3alkyl, hydroxy, alkoxy, perhaloalkyl and perhaloalkoxy; or

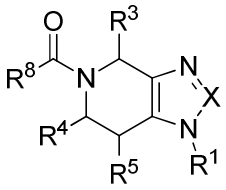
R^8 is independently selected from the group consisting of:



;

and pharmaceutically acceptable salts of compounds of Formula (I).

Another aspect of this invention concerns compounds of Formula (Ia):

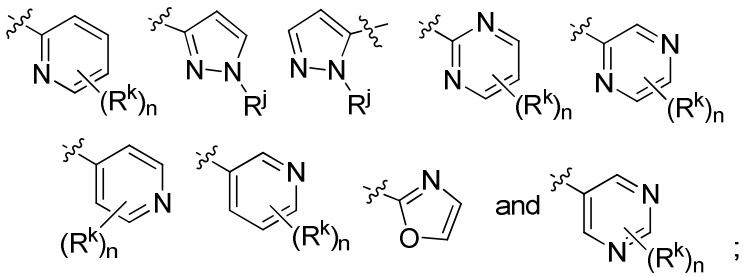


Formula (Ia)

wherein:

R^1 is (a) phenyl, optionally substituted with zero to four groups selected from: halo, C_1-C_4alkyl, alkoxy, perhaloalkyl and perhaloalkoxy; or

(b) heteroaryl, selected from the group consisting of:



;

wherein R^k is selected from: H, halo, C_1-C_3alkyl or alkoxy;

R^j is selected from H, C_1-C_3alkyl optionally substituted with halo, OH or alkoxy; and

n is an integer from 0-3;

X is N or CR^2;

R^2 is H, perhaloalkyl or C_1-C_3 lower alkyl;

R^3 is H, perhaloalkyl, C_1-C_4 alkyl, alkalkoxy , CH_2R^i, -C(O)R^e or phenyl, optionally substituted with zero to two groups selected from the group consisting of: halo, C_1-C_3alkyl, alkoxy, perhaloalkyl and perhaloalkoxy;

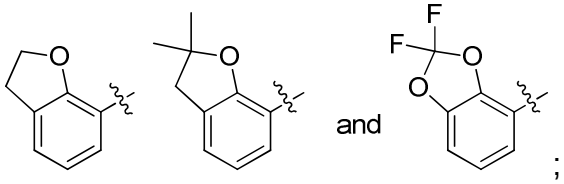
R^i is OH, OC_1-C_3 alkyl, NC_3H_6, $N(C_1$-$C_3alkyl)_2$ or halo;

R^e is OH, OC_1-C_3 alkyl, $N(C_1$-$C_3alkyl)_2$, NC_3H_6;

R^4 and R^5 are independently H or C_1-C_3 alkyl;

R^8 is phenyl or pyridyl, optionally substituted with zero to four R^m substituents wherein R^m is selected from the group consisting of: halo, C_1-C_3alkyl, alkoxy, perhaloalkyl and perhaloalkoxy; or

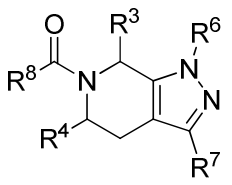
R^8 is selected from the group consisting of:



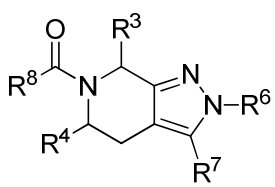
;

and pharmaceutically acceptable salts of compounds of Formula (Ia).

Another aspect of this invention concerns compounds of Formula (IIa and IIb):



Formula (IIa)



Formula (IIb)

wherein:

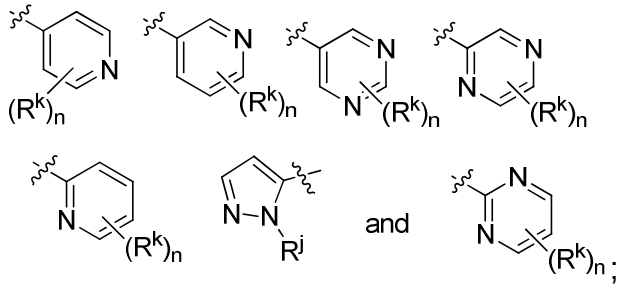
R^3, R^4 and R^6 are independently H or C_1-C_3 alkyl;

R^8 is phenyl or pyridyl, optionally substituted with zero to three R^m substituents

wherein R^m is independently selected from the group consisting of: halo, C_1-C_3alkyl and perhaloalkyl;

R^7 is (a) phenyl, optionally substituted with zero to two groups independently selected from the group consisting of halo and C_1-C_3alkyl; or

(b) heteroaryl, independently selected from the group consisting of:



wherein R^k is halo or C_1-C_3alkyl;

R^j is H or C_1-C_3alkyl; wherein C_1-C_3alkyl is optionally substituted with one halo substituent or one alkoxy substituent; and

n is an integer from 0-3; and

pharmaceutically acceptable salts of compounds of Formula (IIa and IIb).

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

In certain embodiments, the compounds of Formulas (I, Ia, IIa and IIb) are compounds selected from those species described or exemplified in the detailed description below.

In a further aspect, the invention relates to pharmaceutical compositions for treating a disease, disorder, or medical condition mediated by P2X7 receptor activity, comprising an effective amount of at least one compound selected from compounds of Formulas (I, Ia, IIa and IIb), pharmaceutically acceptable salts of compounds of Formulas (I, Ia, IIa and IIb), pharmaceutically acceptable prodrugs of compounds of Formulas (I, Ia, IIa and IIb), and pharmaceutically active metabolites of Formulas (I, Ia, IIa and IIb).

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 P2X7 receptor modulators. Thus, the invention is directed to a method for modulating P2X7 receptor activity, including when such receptor is in a subject, comprising exposing P2X7 receptor to an effective amount of at least one compound selected from compounds of Formulas (I, Ia, IIa and IIb), pharmaceutically acceptable salts of compounds of Formulas (I, Ia, IIa and IIb), pharmaceutically acceptable prodrugs of compounds of Formulas (I, Ia, IIa and IIb), and pharmaceutically active metabolites of compounds of Formulas (I, Ia, IIa and IIb).

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 P2X7 receptor activity, comprising administering to the subject in need of such treatment an effective amount of at least one compound selected from compounds of Formulas (I, Ia, IIa and IIb), pharmaceutically acceptable salts of compounds of Formulas (I, Ia, IIa and IIb), pharmaceutically acceptable prodrugs of compounds of Formulas (I, Ia, IIa and IIb), and pharmaceutically active metabolites of compounds of Formulas (I, Ia, IIa and IIb). Additional embodiments of methods of treatment are set forth in the detailed description.

In another aspect, 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.

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.

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

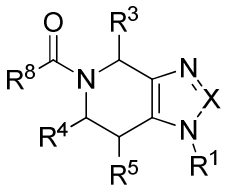
BRIEF DESCRIPTION OF THE FIGURES

Figure 1. Powder X-Ray Diffraction Pattern for (R)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone (Examples 158 and 344)

Figure 2. Powder X-Ray Diffraction Pattern for (S)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone (Example 228)

DETAILED DESCRIPTION OF THE INVENTION

A compound of Formula (I):

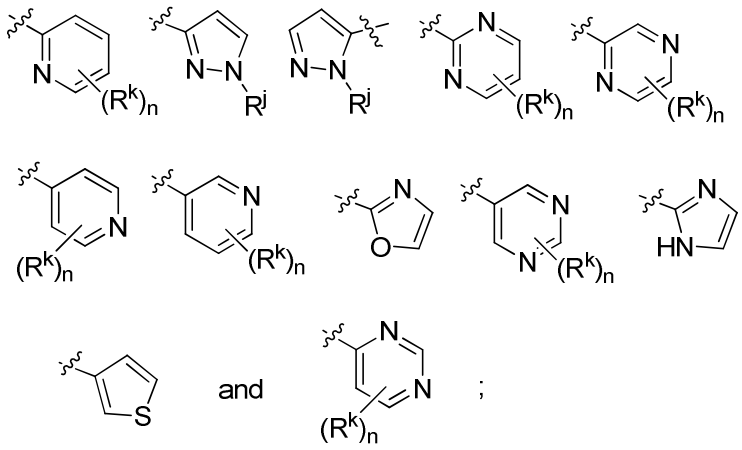


Formula (I)

wherein

R^1 is (a) phenyl, optionally substituted with zero to four groups independently selected from the group consisting of halo, C_1-C_4alkyl, alkoxy, perhaloalkyl and perhaloalkoxy; or

(b) heteroaryl, independently selected from the group consisting of:



wherein R^k is independently selected from the group consisting of H, halo, C_1-C_3alkyl, hydroxyl, perhaloalkyl and alkoxy;

R^j is independently selected from H or C_1-C_3alkyl wherein C_1-C_3alkyl is optionally substituted with from one to three halo substituents, one OH substituent or one alkoxy substituent; and

n is an integer from 0-3;

X is N or CR^2;

R^2 is H, perhaloalkyl or C_1-C_3 lower alkyl;

R^3 is H, perhaloalkyl, C_1-C_4 alkyl, alkalkoxy, CH_2R^i, $-C(O)R^e$ or phenyl, wherein said phenyl is optionally substituted with zero to two groups independently selected from the group consisting of halo, C_1-C_3alkyl, alkoxy, perhaloalkyl and perhaloalkoxy;

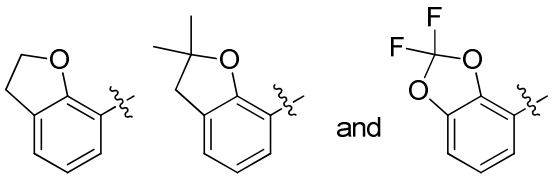
R^i is OH, NC_3H_6, $N(C_1\text{-}C_3alkyl)_2$ or halo;

R^e is OH, $OC_1\text{-}C_3$ alkyl, $N(C_1\text{-}C_3alkyl)_2$, or NC_3H_6;

R^4 and R^5 are independently H or $C_1\text{-}C_3$ alkyl;

R^8 is phenyl or pyridyl, optionally substituted with zero to four R^m substituents wherein R^m is independently selected from the group consisting of halo, $C_1\text{-}C_3$alkyl, hydroxy, alkoxy, perhaloalkyl and perhaloalkoxy; or

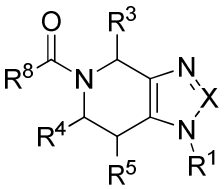
R^8 is independently selected from the group consisting of:



;

and pharmaceutically acceptable salts of compounds of Formula (I).

Another aspect of this invention concerns compounds of Formula (Ia):

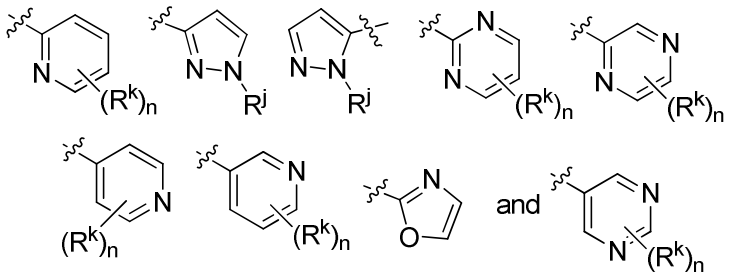


Formula (Ia)

wherein:

R^1 is (a) phenyl, optionally substituted with zero to four groups selected from the group consisting of: halo, $C_1\text{-}C_4$alkyl, alkoxy, perhaloalkyl and perhaloalkoxy; and

(b) heteroaryl, selected from the group consisting of:



wherein R^k is selected from: H, halo, $C_1\text{-}C_3$alkyl or alkoxy;

R^j is selected from H, $C_1\text{-}C_3$alkyl; wherein $C_1\text{-}C_3$alkyl is optionally substituted with halo, OH or alkoxy; and

n is an integer from 0-3;

X is N or CR^2;

R^2 is H, perhaloalkyl or C_1-C_3 lower alkyl;

R^3 is H, perhaloalkyl, C_1-C_4 alkyl, alkalkoxy , CH_2R^i, -C(O)R^e or phenyl; wherein phenyl is optionally substituted with zero to two groups selected from the group consisting of: halo, C_1-C_3alkyl, alkoxy, perhaloalkyl and perhaloalkoxy;

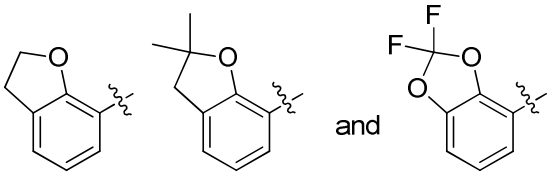
R^i is OH, OC_1-C_3 alkyl, NC_3H_6, $N(C_1$-C_3alkyl$)_2$ or halo;

R^e is OH, OC_1-C_3 alkyl, $N(C_1$-C_3alkyl$)_2$, NC_3H_6;

R^4 and R^5 are independently H or C_1-C_3 alkyl; and

R^8 is phenyl or pyridyl, optionally substituted with zero to four R^m substituents wherein R^m is selected from the group consisting of: halo, C_1-C_3alkyl, alkoxy, perhaloalkyl and perhaloalkoxy; or

R^8 is selected from the group consisting of:



; and

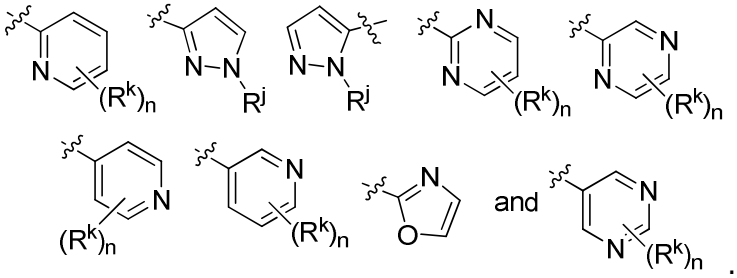
pharmaceutically acceptable salts of compounds of Formula (Ia).

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^1 is phenyl, optionally substituted with zero to four groups selected from: halo, C_1-C_3alkyl, alkoxy, perhaloalkyl or perhaloalkoxy.

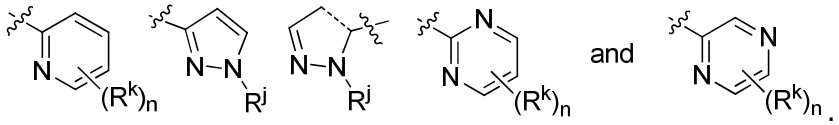
An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^1 is phenyl, optionally substituted with one to three groups selected from: halo, C_1-C_3alkyl, alkoxy, perhaloalkyl or perhaloalkoxy.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^1 is phenyl, optionally substituted with one to two groups selected from: halo or perhaloalkyl.

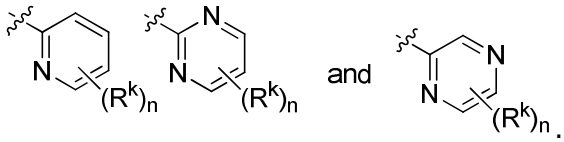
An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^1 is heteroaryl, selected from the group consisting of:



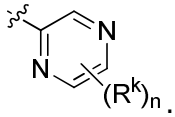
An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^1 is heteroaryl, selected from the group consisting of:



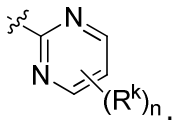
An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^1 is heteroaryl, selected from the group consisting of:



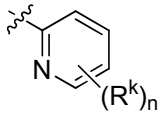
An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^1 is:



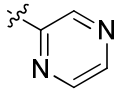
An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^1 is



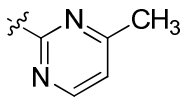
An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^1 is



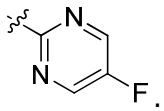
An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^1 is:



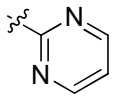
An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^1 is:



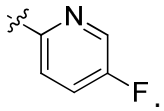
An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^1 is:



An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^1 is:



An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^1 is:



An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, X is N.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, X is CR^2.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, X is CR^2 and R^2 is H, perhaloalkyl or C_1-C_3 lower alkyl.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, X is CR^2 and R^2 is H or C_1-C_3 lower alkyl.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, X is CR^2 and R^2 is H.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^3 is phenyl, optionally substituted with halo, C_1-C_3alkyl, alkoxy, perhaloalkyl or perhaloalkoxy.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^3 is phenyl, optionally substituted with halo, C_1-C_3alkyl, alkoxy or perhaloalkyl.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^3 is phenyl, optionally substituted with halo.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^3 is H, perhaloalkyl or C_1-C_4 alkyl.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^3 is H or C_1-C_4 alkyl.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^3 is H.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^3 is C_1-C_4 alkyl.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^3 is C_1-C_3 alkyl.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^3 is C_1-C_2 alkyl.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^3 is CH_3.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^4 and R^5 are H.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^4 and R^5 are C_1-C_3 alkyl.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^4 is H and R^5 is C_1-C_3 alkyl.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^4 is C_1-C_3 alkyl and R^5 is H.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^4 and R^5 are CH_3.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^4 is H and R^5 is CH_3.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^4 is CH_3 and R^5 is H.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^8 is phenyl optionally substituted with zero to four R^m substituents wherein R^m is selected from the group consisting of: halo, C_1-C_3alkyl, alkoxy, perhaloalkyl and perhaloalkoxy.

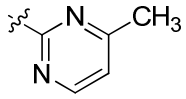
An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^8 is phenyl optionally substituted with two to four R^m substituents wherein R^m is selected from the group consisting of: halo, C_1-C_3alkyl, alkoxy, perhaloalkyl and perhaloalkoxy.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^8 is phenyl and R^m is selected from the group consisting of: halo, C_1-C_3alkyl and perhaloalkyl.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^8 is phenyl and R^m is halo in the ortho position and R^m is perhaloalkyl in the meta position.

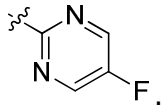
An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^8 is phenyl and R^m is Cl in the ortho position and R^m is CF_3 in the meta position.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, X is N, R^3 is CH_3, R^4 and R^5 are H, R^8 is phenyl, R^m is Cl in the ortho position, R^m is CF_3 in the meta position and R^1 is:



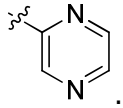
.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, X is N, R^3 is CH_3, R^4 and R^5 are H, R^8 is phenyl, R^m is Cl in the ortho position, R^m is CF_3 in the meta position and R^1 is:



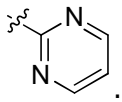
.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, X is N, R^3 is CH_3, R^4 and R^5 are H, R^8 is phenyl, R^m is Cl in the ortho position, R^m is CF_3 in the meta position and R^1 is:

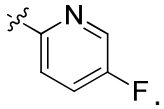


.

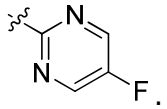
An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, X is N, R^3 is CH_3, R^4 and R^5 are H, R^8 is phenyl, R^m is Cl in the ortho position, R^m is CF_3 in the meta position and R^1 is:



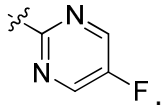
An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, X is CR^2, R^3 is CH_3, R^2, R^4 and R^5 are H, R^8 is phenyl, R^m is Cl in the ortho position, R^m is CF_3 in the meta position and R^1 is:



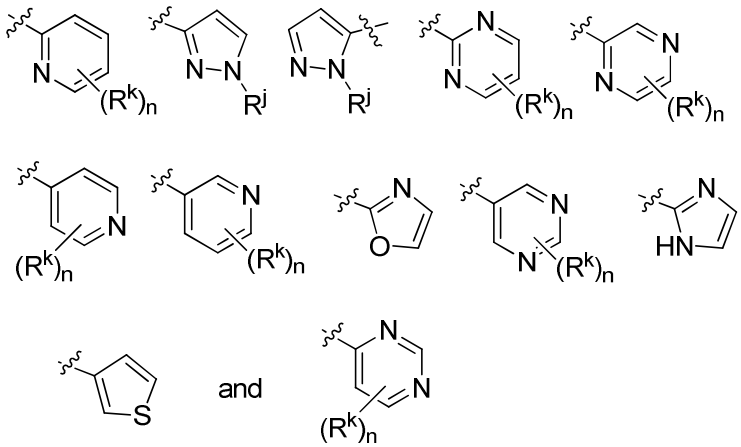
An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, X is N, R^3 and R^4 are H, R^5 is CH_3, R^8 is phenyl, R^m is Cl in the ortho position, R^m is CF_3 in the meta position and R^1 is:



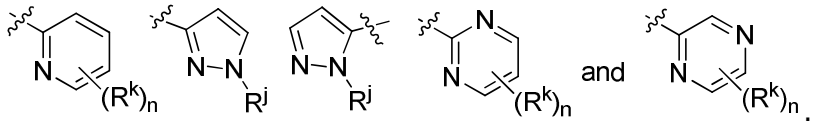
An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, X is N, R^3 and R^4 are H, R^5 is CH_3, R^8 is 4-pyridyl, R^m is Cl in the ortho position, R^m is CF_3 in the meta position and R^1 is:



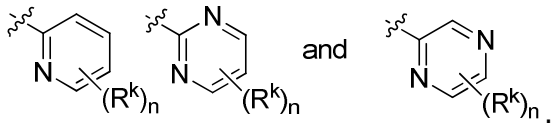
An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^1 is heteroaryl, independently selected from the group consisting of:



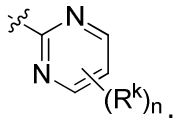
An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^1 is heteroaryl, independently selected from the group consisting of:



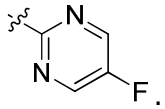
An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^1 is heteroaryl, independently selected from the group consisting of:



An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^1 is



An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^1 is



An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^8 is phenyl.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^8 is phenyl, R^m is Cl in the ortho position, and R^m is CF_3 in the meta position.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^8 is pyridyl, optionally substituted with zero to four R^m substituents wherein R^m is independently selected from the group consisting of halo, C_1-C_3alkyl, hydroxy, alkoxy, perhaloalkyl and perhaloalkoxy.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^8 is 2-pyridyl, 3-pyridyl or 4-pyridyl optionally substituted with one to three R^m substituents wherein R^m is independently selected from the group consisting of halo, C_1-C_3alkyl, perhaloalkyl and perhaloalkoxy.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^8 is 4-pyridyl optionally substituted with one to three R^m substituents wherein R^m is independently selected from the group consisting of: halo, perhaloalkyl and perhaloalkoxy.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, X is N.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, X is CR^2 and R^2 is H.

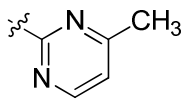
An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^3 is CH_3.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^4 and R^5 are CH_3.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^4 is H and R^5 is CH_3.

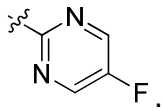
An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, R^4 is CH_3 and R^5 is H.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, X is N, R^3 is CH_3, R^4 and R^5 are H, R^8 is phenyl, R^m is Cl in the ortho position, R^m is CF_3 in the meta position and R^1 is:



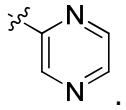
.

An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, X is N, R^3 is CH_3, R^4 and R^5 are H, R^8 is phenyl, R^m is Cl in the ortho position, R^m is CF_3 in the meta position and R^1 is:

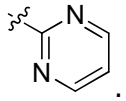


.

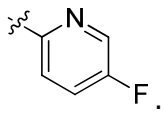
An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, X is N, R^3 is CH_3, R^4 and R^5 are H, R^8 is phenyl, R^m is Cl in the ortho position, R^m is CF_3 in the meta position and R^1 is:



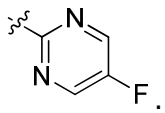
An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, X is N, R^3 is CH_3, R^4 and R^5 are H, R^8 is phenyl, R^m is Cl in the ortho position, R^m is CF_3 in the meta position and R^1 is:



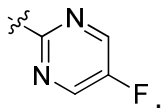
An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, X is CR^2, R^3 is CH_3, R^4 and R^5 are H, R^8 is phenyl, R^m is Cl in the ortho position, R^m is CF_3 in the meta position and R^1 is:



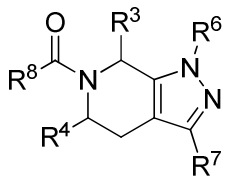
An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, X is N, R^3 and R^5 are H, R^4 is CH_3, R^8 is phenyl, R^m is F in the ortho position, R^m is CF_3 in the meta position and R^1 is:



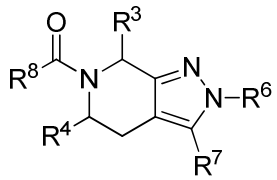
An additional embodiment of the invention is a compound of Formula (I) or Formula (Ia) wherein, X is N, R^3 and R^5 are H, R^4 is CH_3, R^8 is 4-pyridyl, R^m is F in the ortho position, R^m is CF_3 in the meta position and R^1 is:



Another aspect of the invention is compounds of Formula IIa or IIb:



Formula (IIa)



Formula (IIb)

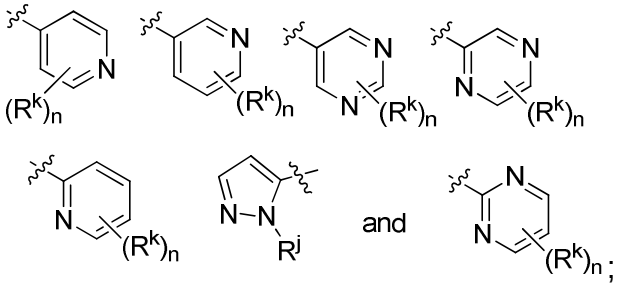
wherein:

R^3, R^4 and R^6 are independently H or C_1-C_3 alkyl;

R^8 is phenyl or pyridyl, optionally substituted with zero to three R^m substituents wherein R^m is independently selected from the group consisting of: halo, C_1-C_3alkyl and perhaloalkyl;

R^7 is (a) phenyl, optionally substituted with zero to two groups independently selected from the group consisting of halo and C_1-C_3alkyl; or

(b) heteroaryl, independently selected from the group consisting of:



wherein R^k is halo or C_1-C_3alkyl;

R^j is H or C_1-C_3alkyl; wherein C_1-C_3alkyl is optionally substituted with one halo substituent or one alkoxy substituent; and

n is an integer from 0-3; and

pharmaceutically acceptable salts of compounds of Formula (IIa and IIb).

An additional embodiment of the invention are compounds of Formula IIa and IIb wherein, R^8 is phenyl optionally substituted with two to four R^m substituents wherein R^m is selected from the group consisting of: halo, C_1-C_3alkyl, alkoxy, perhaloalkyl and perhaloalkoxy.

An additional embodiment of the invention are compounds of Formula IIa and IIb wherein, R^8 is phenyl and R^m is selected from the group consisting of: halo, C_1-C_3alkyl and perhaloalkyl.

An additional embodiment of the invention are compounds of Formula IIa and IIb wherein, R^8 is phenyl, R^m is halo in the ortho position and R^m is perhaloalkyl in the meta position.

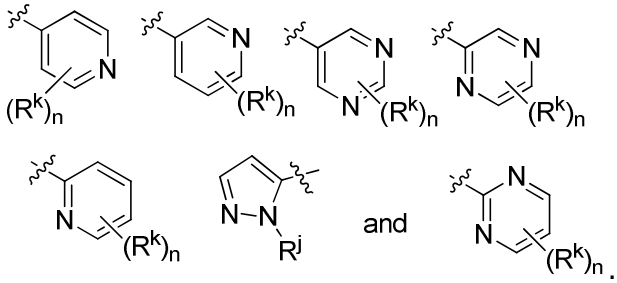
An additional embodiment of the invention are compounds of Formula IIa and IIb wherein, R^8 is phenyl, R^m is Cl in the ortho position and R^m is CF_3 in the meta position.

An additional embodiment of the invention are compounds of Formula IIa and IIb wherein, R^3 is H and R^4 is CH_3.

An additional embodiment of the invention are compounds of Formula IIa and IIb wherein, R^3 is CH_3 and R^4 is H.

An additional embodiment of the invention are compounds of Formula IIa and IIb wherein, R^7 is (a) phenyl, optionally substituted with zero to two groups selected from: halo or C_1-C_3alkyl,

An additional embodiment of the invention are compounds of Formula IIa and IIb wherein, R^7 is heteroaryl, selected from the group consisting of:



An additional embodiment of the invention are compounds of Formula IIa and IIb

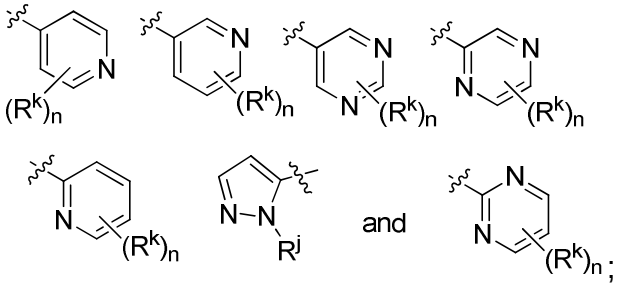
wherein:

R^3, R^4 and R^6 are independently H or C_1-C_3 alkyl;

R^8 is phenyl or pyridyl, optionally substituted with zero to three R^m substituents wherein R^m is independently selected from the group consisting of: halo, C_1-C_3alkyl and perhaloalkyl;

R^7 is (a) phenyl, optionally substituted with zero to two groups independently selected from the group consisting of halo and C_1-C_3alkyl; or

(b) heteroaryl, independently selected from the group consisting of:



wherein R^k is halo or C_1-C_3alkyl;

R^j is H or C_1-C_3alkyl; wherein C_1-C_3alkyl is optionally substituted with one halo substituent or one alkoxy substituent; and

n is an integer from 0-3; and

pharmaceutically acceptable salts of compounds of Formula (IIa and IIb).

An additional embodiment of the invention are compounds of Formula IIa and IIb wherein, R^8 is phenyl optionally substituted with two to three R^m substituents independently selected from the group consisting of halo, C_1-C_3alkyl and perhaloalkyl.

An additional embodiment of the invention are compounds of Formula IIa and IIb wherein, R^8 is phenyl optionally substituted with two to three R^m substituents independently selected from the group consisting of halo and perhaloalkyl.

An additional embodiment of the invention are compounds of Formula IIa and IIb wherein, R^8 is phenyl, substituted with two R^m groups, wherein R^m is halo in the ortho position and R^m is perhaloalkyl in the meta position.

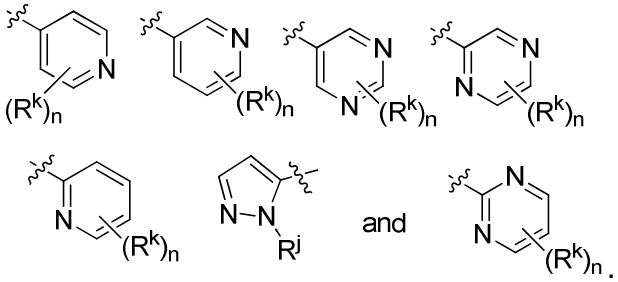
An additional embodiment of the invention are compounds of Formula IIa and IIb wherein, R^8 is phenyl, substituted with two R^m groups, wherein R^m is Cl in the ortho position and R^m is CF_3 in the meta position.

An additional embodiment of the invention are compounds of Formula IIa and IIb wherein, R^3 is H and R^4 is CH_3.

An additional embodiment of the invention are compounds of Formula IIa and IIb wherein, R^3 is CH_3 and R^4 is H.

An additional embodiment of the invention are compounds of Formula IIa and IIb wherein, R^7 is phenyl, optionally substituted with zero to two groups independently selected from the group consisting of halo and C_1-C_3alkyl.

An additional embodiment of the invention are compounds of Formula IIa and IIb wherein, R^7 is heteroaryl, independently selected from the group consisting of:



An additional embodiment of the invention is a compound selected from the group consisting of those presented in Table 1:

Table 1. Compounds of Formulas (I, Ia, IIa or IIb)

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-phenyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-Dichlorophenyl)(1-phenyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-Dichlorophenyl)(1-(pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(1-(1H-Pyrazol-5-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-chloro-3-(trifluoromethyl)phenyl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(pyrazin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(3,5-difluorophenyl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(3-(pyridin-2-yl)-6,7-dihydro-3H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-Dichlorophenyl)(3-(pyridin-2-yl)-6,7-dihydro-3H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(3-(pyrazin-2-yl)-6,7-dihydro-3H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-phenyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-phenyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(4-ethyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(4-isopropyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-fluorophenyl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Fluoro-3-(trifluoromethyl)phenyl)(1-(4-fluorophenyl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(3-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrimidin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

Ethyl 5-(2-chloro-3-(trifluoromethyl)benzoyl)-1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxylate;

Ethyl 5-(2,3-dichlorobenzoyl)-1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxylate;

Ethyl 5-(2-chloro-3-(trifluoromethyl)benzoyl)-1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxylate;

Ethyl 5-(2,3-dichlorobenzoyl)-1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxylate;

Ethyl 5-{[2-chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxylate;

Ethyl 5-[(2,3-dichlorophenyl)carbonyl]-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxylate;

(5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-4-yl)methanol;

1-(5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-4-yl)-N,N-dimethylmethanamine;

(2-Chloro-3-(trifluoromethyl)phenyl)(4-(fluoromethyl)-1-(pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxylic acid;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-N,N-dimethyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxamide;

4-(Azetidin-1-ylcarbonyl)-5-{[2-chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

(5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-4-yl)methyl 2-chloro-3-(trifluoromethyl)benzoate;

(2-Chloro-3-(trifluoromethyl)phenyl)(2-methyl-1-phenyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-phenyl-2-(trifluoromethyl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-(trifluoromethyl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

(R*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(4S*)-5-{[2-Fluoro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

(4R*)-5-{[2-Fluoro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

(4S*)-5-{[2-Fluoro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

(4R*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

(4S*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

(4R*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(4-fluorophenyl)-4-methyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

(4S*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(4-fluorophenyl)-4-methyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4,5,6,7-tetrahydro-3H-imidazo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-phenyl-4,5-dihydro-1H-imidazo[4,5-c]pyridine;

5-[(2,2-Difluoro-1,3-benzodioxol-4-yl)carbonyl]-1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

5-(2,3-Dihydro-1-benzofuran-7-ylcarbonyl)-1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

5-[(2,2-Dimethyl-2,3-dihydro-1-benzofuran-7-yl)carbonyl]-1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4,4-dimethyl-1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyrazin-2-yl-4,5-dihydro-1H-imidazo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-ethyl-1-pyrazin-2-yl-4,5-dihydro-1H-imidazo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrazin-2-yl-4,5-dihydro-1H-imidazo[4,5-c]pyridine;

5-{[2-Fluoro-3-(trifluoromethyl)phenyl]carbonyl}-1-phenyl-2-(trifluoromethyl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

5-[(2,3-Dichlorophenyl)carbonyl]-1-phenyl-2-(trifluoromethyl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

5-{[2-Fluoro-3-(trifluoromethyl)phenyl]carbonyl}-1-(1H-pyrazol-5-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

5-[(2,3-Dichlorophenyl)carbonyl]-1-(1H-pyrazol-5-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-phenyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-[(2,3-Dichlorophenyl)carbonyl]-1-phenyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(5-fluoropyrimidin-2-yl)-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

{[2-Fluoro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-[(2,3-Dichlorophenyl)carbonyl]-1-pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(1H-pyrazol-5-yl)-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Fluoro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-[(2,3-Dichlorophenyl)carbonyl]-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(5-fluoropyridin-2-yl)-4-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrazin-2-yl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(4R*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(4S*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-phenyl-1-pyrazin-2-yl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-phenyl-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-phenyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrimidin-2-yl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(4-fluorophenyl)-4-methyl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(3-fluoropyridin-2-yl)-4-methyl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(4-fluorophenyl)-4-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(3-fluoropyridin-2-yl)-4-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-(1H-pyrazol-3-yl)-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-(1H-pyrazol-3-yl)-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(4S*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(4R*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyrazin-2-yl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyridin-2-yl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-2-methyl-3-pyridin-2-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-pyridin-2-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine-TFA salt;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-(5-fluoropyridin-2-yl)-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-(5-fluoropyridin-3-yl)-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-pyridin-3-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-pyrazin-2-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-pyrimidin-2-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

(2-Chloro-3-(trifluoromethyl)phenyl)(3-phenyl-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

6-[(2,3-Dichlorophenyl)carbonyl]-3-phenyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine;

6-[(2,3-Dichlorophenyl)carbonyl]-1-methyl-3-phenyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine and 6-[(2,3-dichlorophenyl)carbonyl]-2-methyl-3-phenyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine (1:1);

6-[(2,3-Dichlorophenyl)carbonyl]-2-methyl-3-phenyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-[(2,3-Dichlorophenyl)carbonyl]-1-methyl-3-phenyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine;

6-[(2,3-Dichloropyridin-4-yl)carbonyl]-3-phenyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-(4-fluorophenyl)-2-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-(4-fluorophenyl)-1-methyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-2-methyl-3-pyridin-3-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-methyl-3-pyridin-3-yl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine;

6-[(2,3-Dichlorophenyl)carbonyl]-3-(4-fluorophenyl)-1-methyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-(4-fluorophenyl)-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-[(2,3-Dichlorophenyl)carbonyl]-2-methyl-3-pyridin-3-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-[(2,3-Dichlorophenyl)carbonyl]-2-methyl-3-pyridin-3-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-2-methyl-3-pyrimidin-5-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-[(2,3-Dichlorophenyl)carbonyl]-3-(4-fluorophenyl)-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-[(2,3-Dichlorophenyl)carbonyl]-3-pyridin-4-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine;

(2-Chloro-4-fluorophenyl)(1-(pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-(*S**)-6-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-(*R**)-6-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine;

5-[(2,3-Dichlorophenyl)carbonyl]-6-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine;

5-[(2,3-Dichloro-4-fluorophenyl)carbonyl]-6-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(3-fluoropyridin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(2-Fluoro-3-(trifluoromethyl)phenyl)(1-(pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Fluoro-3-(trifluoromethyl)phenyl)(1-(2-methoxyphenyl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(2-methoxyphenyl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(2-(2-fluoroethoxy)phenyl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(1-methyl-1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(1-methyl-1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(4-Chloro-2-fluorophenyl)(1-(pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-Dichloro-4-fluorophenyl)(1-(pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-fluoropyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(3,4-Difluoro-2-methylphenyl)(1-(pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo-[4,5-c]pyridin-5(4H)-yl)methanone;

(*R**)-(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(*S**)-(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(6-fluoropyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-methoxypyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(6-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-dichloro-4-fluorophenyl)(4-methyl-1-(pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-dichloro-4-fluorophenyl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2,3-Dichloro-4-fluorophenyl)(4-methyl-1-(pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2,3-Dichloro-4-fluorophenyl)(4-methyl-1-(pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2,3-Dichloro-4-fluorophenyl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2,3-Dichloro-4-fluorophenyl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(5-methoxypyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(6-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(6-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-methoxypyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-methoxypyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-methoxypyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(6-methyl-1-(1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2-methyl-3-(trifluoromethyl)phenyl)methanone;

(S*)-(4-chloro-2-fluorophenyl)(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(4-chloro-2-fluorophenyl)(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(*S**)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(*R*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(1-(3,5-dimethylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-dichlorophenyl)(1-(3,5-dimethylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-Dichlorophenyl)(1-(3-fluoropyridin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(1-(2-fluoroethyl)-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(1-methyl-1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(6R*)-5-[(2,3-Dichlorophenyl)carbonyl]-1-(3-fluoropyridin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6S*)-5-[(2,3-Dichlorophenyl)carbonyl]-1-(3-fluoropyridin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6R*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(3-fluoropyridin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6S*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(3-fluoropyridin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(R*)-(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(1-methyl-1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(1-methyl-1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(1-(2-fluoroethyl)-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(1-(2-fluoroethyl)-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

5-[(2,3-Dichlorophenyl)carbonyl]-1-(4-fluoropyridin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(2,3-Dichlorophenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-fluoro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-fluoropyridin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrimidin-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-fluoro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-dichlorophenyl)(1-(4,6-dimethylpyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-dichlorophenyl)(4-methyl-1-(6-methylpyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(4,6-dimethylpyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(4,6-dimethylpyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(2-ethyl-4-methyl-1-phenyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(3-methyl-2-(trifluoromethyl)pyridin-4-yl)methanone;

(R*)-(4-methyl-1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2-methyl-3-(trifluoromethyl)phenyl)methanone;

(2-fluoro-3-(trifluoromethyl)phenyl)(6-methyl-1-(1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-fluoro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2,3-Dichlorophenyl)(4-methyl-1-(pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2,3-Dichlorophenyl)(4-methyl-1-(pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(6R*)-5-[(2,3-Dichlorophenyl)carbonyl]-1-(4-fluoropyridin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6S*)-5-[(2,3-Dichlorophenyl)carbonyl]-1-(4-fluoropyridin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(S*)-(4-methyl-1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2-methyl-3-(trifluoromethyl)phenyl)methanone;

(6R*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(4-fluoropyridin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6S*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(4-fluoropyridin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6R*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6S*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-[(2,3-Dichlorophenyl)carbonyl]-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6R*)-5-[(2,3-Dichlorophenyl)carbonyl]-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6S*)-5-[(2,3-Dichlorophenyl)carbonyl]-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

1-(5-Fluoropyrimidin-2-yl)-6-methyl-5-{[2-methyl-3-(trifluoromethyl)phenyl]carbonyl}-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6R*)-1-(5-Fluoropyrimidin-2-yl)-6-methyl-5-{[2-methyl-3-(trifluoromethyl)phenyl]carbonyl}-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6S*)-1-(5-Fluoropyrimidin-2-yl)-6-methyl-5-{[2-methyl-3-(trifluoromethyl)phenyl]carbonyl}-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(2-chloro-3-(trifluoromethyl)phenyl)(6-methyl-1-(1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(6R*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6S*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-[(2,3-Dichloro-4-fluorophenyl)carbonyl]-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6R*)-5-[(2,3-Dichloro-4-fluorophenyl)carbonyl]-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6S*)-5-[(2,3-Dichloro-4-fluorophenyl)carbonyl]-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-[(2,4-Dichloro-3-fluorophenyl)carbonyl]-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6R*)-5-[(2,4-Dichloro-3-fluorophenyl)carbonyl]-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6S*)-5-[(2,4-Dichloro-3-fluorophenyl)carbonyl]-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6R)-1-(5-Fluoropyrimidin-2-yl)-5-{[2-fluoro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6S)-1-(5-Fluoropyrimidin-2-yl)-5-{[2-fluoro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6R*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-1-pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6S*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-1-pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(R*)-(2-chloro-3-(trifluoromethyl)phenyl)(3-(5-fluoropyrimidin-2-yl)-7-methyl-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(S*)-(2-chloro-3-(trifluoromethyl)phenyl)(3-(5-fluoropyrimidin-2-yl)-7-methyl-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,3-dichlorophenyl)(4-methyl-1-(4-methylpyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-dichlorophenyl)(1-(4,6-dimethylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-fluoro-5-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-dichlorophenyl)(4-methyl-1-(6-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(4*R**)-(2-Chloro-3-(trifluoromethyl)phenyl)((4R)-4-methyl-1-(6-methyl-1,6-dihydropyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(4*R*)-(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(4-methylpyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrimidin-5-yl)-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-dichlorophenyl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-fluorophenyl)-4,7-dimethyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(5-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(4,6-dimethyl-1-phenyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(4,7-dimethyl-1-phenyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-Dichlorophenyl)(1-(4-fluorophenyl)-4,6-dimethyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-fluorophenyl)-4,6-dimethyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-Dichlorophenyl)(7-methyl-1-phenyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(7-methyl-1-phenyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-fluorophenyl)-7-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-Dichlorophenyl)(1-(4-fluorophenyl)-7-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(1-(2-methoxyethyl)-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(1-(2-methoxyethyl)-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(oxazol-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-methylpyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(4-methylpyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4,6-dimethylpyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(3-ethylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(5-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-4-fluorophenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,4-dichlorophenyl)(1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(3-ethoxypyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(3-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(3-methoxypyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-dichloro-4-fluorophenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-fluoro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-methyl-3-(trifluoromethyl)phenyl)methanone;

(2-fluorophenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(4-(tert-butyl)phenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(1,5-dimethyl-3-(1-methyl-1H-pyrazol-5-yl)-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(5-methyl-3-(1H-pyrazol-5-yl)-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,4-dichlorophenyl)(5-methyl-3-(1H-pyrazol-5-yl)-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2-fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(4-methylpyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(4-chloro-2-fluorophenyl)(1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(4-chloro-2-fluorophenyl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(4-chloro-2-fluorophenyl)(4-methyl-1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-methyl-3-(trifluoromethyl)phenyl)(1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,4-dichlorophenyl)(1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2-methyl-3-(trifluoromethyl)phenyl)methanone;

(2,4-dichlorophenyl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(4-chloro-2-fluorophenyl)(1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-methyl-3-(trifluoromethyl)phenyl)(1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(4-methyl-1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2-methyl-3-(trifluoromethyl)phenyl)methanone;

(2,4-dichlorophenyl)(4-methyl-1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)((4R,6R)-1-(4-fluorophenyl)-4,6-dimethyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)((4S,6S)-1-(4-fluorophenyl)-4,6-dimethyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

2-chloro-3-(trifluoromethyl)phenyl)((4S,6R)-1-(4-fluorophenyl)-4,6-dimethyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)((4R,6S)-1-(4-fluorophenyl)-4,6-dimethyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(2-chloro-3-(trifluoromethyl)phenyl)(6-methyl-1-phenyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-3-phenyl-6,7-dihydro-3H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(6-methyl-1-phenyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(3-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(3-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(3-propoxypyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(4-ethylpyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(1-(3-ethylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(3-(trifluoromethyl)phenyl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)((4R,6R)-4,6-dimethyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)((4S,6R)-4,6-dimethyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

2-chloro-3-(trifluoromethyl)phenyl)(4,6-dimethyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(1-(4,6-dimethylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(5-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(3-(5-fluoropyrimidin-2-yl)-7-methyl-2-((2-(trimethylsilyl)ethoxy)methyl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(S)-(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(3-(trifluoromethyl)phenyl)methanone;

(R*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(3-fluoro-5-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(7-methyl-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)((4S,6R)-4,6-dimethyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)((4R,6S)-4,6-dimethyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-fluoro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(1-(5-fluoropyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-methyl-3-(trifluoromethyl)phenyl)methanone;

(2,4-dichlorophenyl)(1-(5-fluoropyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-fluoro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(3-ethoxypyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(3-ethoxypyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(1-(2-hydroxyethyl)-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)((4S,6S)-4,6-dimethyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)((4R,6R)-4,6-dimethyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(3-phenyl-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)(2-(trifluoromethyl)pyridin-3-yl)methanone;

(2-chloro-4-fluorophenyl)(3-phenyl-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,6-dichlorophenyl)(3-phenyl-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2-chloro-6-fluorophenyl)(3-phenyl-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,3-dichlorophenyl)(3-(4-fluorophenyl)-2-methyl-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(2-methyl-3-(pyridin-4-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,3-dichlorophenyl)(2-methyl-3-(pyridin-4-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,3-dichlorophenyl)(2-methyl-3-(pyrimidin-5-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,3-dichlorophenyl)(3-(pyrimidin-5-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,3-dichlorophenyl)(2-methyl-1-phenyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-dichlorophenyl)(2-ethyl-1-phenyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrimidin-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrimidin-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-dichlorophenyl)(4-methyl-1-(5-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(3-chloro-4-(trifluoromethyl)pyridin-2-yl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(4-chloro-5-(trifluoromethyl)pyridin-3-yl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(3-chloro-4-(trifluoromethyl)pyridin-2-yl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(4-chloro-5-(trifluoromethyl)pyridin-3-yl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone; and

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

(*R**)-(6-methyl-1-(1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2-methyl-3-(trifluoromethyl)phenyl)methanone;

(*S**)-(6-methyl-1-(1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2-methyl-3-(trifluoromethyl)phenyl)methanone;

(*R**)-(2-fluoro-3-(trifluoromethyl)phenyl)(6-methyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(*S**)-(2-fluoro-3-(trifluoromethyl)phenyl)(6-methyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(*R**)-(2-chloro-3-(trifluoromethyl)phenyl)(6-methyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(*S**)-(2-chloro-3-(trifluoromethyl)phenyl)(6-methyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-5-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-chloro-5-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-chloro-5-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(3-chloro-5-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(3-chloro-5-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(3-chloro-5-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(4-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(4-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(4-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-fluoro-3-(trifluoromethoxy)phenyl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-fluoro-3-(trifluoromethoxy)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(3-(trifluoromethoxy)phenyl)methanone;

(R*)-(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(3-(trifluoromethoxy)phenyl)methanone;

(S*)-(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(3-(trifluoromethoxy)phenyl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-(trifluoromethyl)pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-(trifluoromethyl)pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-(trifluoromethyl)pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(1-(1H-imidazol-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2,3-dichlorophenyl)methanone;

(2-fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(3-chloro-2-methylphenyl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2,3-dichlorophenyl)(4-methyl-1-(6-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2,3-dichlorophenyl)(4-methyl-1-(6-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2,3-dichlorophenyl)(4-methyl-1-(4-methylpyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2,3-dichlorophenyl)(4-methyl-1-(4-methylpyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(1-(1H-imidazol-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2-chloro-3-(trifluoromethyl)phenyl)methanone;

(R*)-(2,3-dichlorophenyl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2,3-dichlorophenyl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-methylpyrimidin-4-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(6-methylpyrimidin-4-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(2-methylpyrimidin-4-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(2-methylpyrimidin-4-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(2-methylpyrimidin-4-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(2-methylpyrimidin-4-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-methylpyrimidin-4-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(6-methylpyrimidin-4-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(1-ethyl-1H-pyrazol-3-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(1-ethyl-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(1-ethyl-1H-pyrazol-5-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(1-ethyl-1H-pyrazol-5-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(1-(1-ethyl-1H-pyrazol-3-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)methanone;

(S)-(1-(1-ethyl-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)methanone;

(S)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(1-(1-ethyl-1H-pyrazol-3-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(1-(1-ethyl-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(1-isopropyl-1H-pyrazol-3-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(1-isopropyl-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(2-fluoro-3-(trifluoromethyl)phenyl)(1-(1-isopropyl-1H-pyrazol-3-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(2-fluoro-3-(trifluoromethyl)phenyl)(1-(1-isopropyl-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(1-(1-isopropyl-1H-pyrazol-3-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(1-(1-isopropyl-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(1-(1-isopropyl-1H-pyrazol-3-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(1-(1-isopropyl-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(2-chloro-3-(trifluoromethyl)phenyl)(6-methyl-1-(thiophen-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(thiophen-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(6-methyl-1-(1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(6-methyl-1-(1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2-hydroxy-3-(trifluoromethyl)phenyl)methanone;

(S)-(2-fluoro-3-(trifluoromethoxy)phenyl)(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(2-fluoro-3-(trifluoromethyl)phenyl)(1-(5-hydroxypyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-hydroxypyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(3-(5-fluoropyridin-2-yl)-7-methyl-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,3-dichlorophenyl)(7-methyl-3-(pyrimidin-2-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(7-methyl-3-(pyridin-2-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,3-dichlorophenyl)(7-methyl-3-(pyrazin-2-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(3-(4-fluorophenyl)-7-methyl-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,3-dichlorophenyl)(3-(4-fluorophenyl)-7-methyl-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,3-dichlorophenyl)(7-methyl-3-(1-methyl-1H-pyrazol-5-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(7-methyl-3-(1-methyl-1H-pyrazol-5-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone; and

(2-chloro-3-(trifluoromethyl)phenyl)(7-methyl-3-(pyrazin-2-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone.

An additional embodiment of the invention is a compound selected from the group presented in Table 1A.

Table 1A. Compounds of Formulas (I, Ia, IIa or IIb)

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-phenyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-Dichlorophenyl)(1-phenyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-Dichlorophenyl)(1-(pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(1-(1H-Pyrazol-5-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-chloro-3-(trifluoromethyl)phenyl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(pyrazin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(3,5-difluorophenyl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(3-(pyridin-2-yl)-6,7-dihydro-3H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-Dichlorophenyl)(3-(pyridin-2-yl)-6,7-dihydro-3H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(3-(pyrazin-2-yl)-6,7-dihydro-3H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-phenyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-phenyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(4-ethyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(4-isopropyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-fluorophenyl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Fluoro-3-(trifluoromethyl)phenyl)(1-(4-fluorophenyl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(3-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrimidin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

Ethyl 5-(2-chloro-3-(trifluoromethyl)benzoyl)-1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxylate;

Ethyl 5-(2,3-dichlorobenzoyl)-1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxylate;

Ethyl 5-(2-chloro-3-(trifluoromethyl)benzoyl)-1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxylate;

Ethyl 5-(2,3-dichlorobenzoyl)-1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxylate;

Ethyl 5-{[2-chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxylate;

Ethyl 5-[(2,3-dichlorophenyl)carbonyl]-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxylate;

(5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-4-yl)methanol;

1-(5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-4-yl)-N,N-dimethylmethanamine;

(2-Chloro-3-(trifluoromethyl)phenyl)(4-(fluoromethyl)-1-(pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxylic acid;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-N,N-dimethyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxamide;

4-(Azetidin-1-ylcarbonyl)-5-{[2-chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

(5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-4-yl)methyl 2-chloro-3-(trifluoromethyl)benzoate;

(2-Chloro-3-(trifluoromethyl)phenyl)(2-methyl-1-phenyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-phenyl-2-(trifluoromethyl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-(trifluoromethyl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

(R*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(4S*)-5-{[2-Fluoro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

(4R*)-5-{[2-Fluoro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

(4S*)-5-{[2-Fluoro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

(4R*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

(4S*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

(4R*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(4-fluorophenyl)-4-methyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

(4S*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(4-fluorophenyl)-4-methyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4,5,6,7-tetrahydro-3H-imidazo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-phenyl-4,5-dihydro-1H-imidazo[4,5-c]pyridine;

5-[(2,2-Difluoro-1,3-benzodioxol-4-yl)carbonyl]-1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

5-(2,3-Dihydro-1-benzofuran-7-ylcarbonyl)-1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

5-[(2,2-Dimethyl-2,3-dihydro-1-benzofuran-7-yl)carbonyl]-1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4,4-dimethyl-1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyrazin-2-yl-4,5-dihydro-1H-imidazo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-ethyl-1-pyrazin-2-yl-4,5-dihydro-1H-imidazo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrazin-2-yl-4,5-dihydro-1H-imidazo[4,5-c]pyridine;

5-{[2-Fluoro-3-(trifluoromethyl)phenyl]carbonyl}-1-phenyl-2-(trifluoromethyl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

5-[(2,3-Dichlorophenyl)carbonyl]-1-phenyl-2-(trifluoromethyl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

5-{[2-Fluoro-3-(trifluoromethyl)phenyl]carbonyl}-1-(1H-pyrazol-5-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

5-[(2,3-Dichlorophenyl)carbonyl]-1-(1H-pyrazol-5-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-phenyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-[(2,3-Dichlorophenyl)carbonyl]-1-phenyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(5-fluoropyrimidin-2-yl)-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

{[2-Fluoro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-[(2,3-Dichlorophenyl)carbonyl]-1-pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(1H-pyrazol-5-yl)-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Fluoro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-[(2,3-Dichlorophenyl)carbonyl]-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(5-fluoropyridin-2-yl)-4-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrazin-2-yl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(4R*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(4S*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-phenyl-1-pyrazin-2-yl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-phenyl-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-phenyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrimidin-2-yl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(4-fluorophenyl)-4-methyl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(3-fluoropyridin-2-yl)-4-methyl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(4-fluorophenyl)-4-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(3-fluoropyridin-2-yl)-4-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-(1H-pyrazol-3-yl)-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-(1H-pyrazol-3-yl)-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(4S*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(4R*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyrazin-2-yl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyridin-2-yl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-2-methyl-3-pyridin-2-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-pyridin-2-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine-TFA salt;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-(5-fluoropyridin-2-yl)-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-(5-fluoropyridin-3-yl)-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-pyridin-3-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-pyrazin-2-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-pyrimidin-2-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

(2-Chloro-3-(trifluoromethyl)phenyl)(3-phenyl-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

6-[(2,3-Dichlorophenyl)carbonyl]-3-phenyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine;

6-[(2,3-Dichlorophenyl)carbonyl]-1-methyl-3-phenyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine and 6-[(2,3-dichlorophenyl)carbonyl]-2-methyl-3-phenyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine (1:1);

6-[(2,3-Dichlorophenyl)carbonyl]-2-methyl-3-phenyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-[(2,3-Dichlorophenyl)carbonyl]-1-methyl-3-phenyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine;

6-[(2,3-Dichloropyridin-4-yl)carbonyl]-3-phenyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-(4-fluorophenyl)-2-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-(4-fluorophenyl)-1-methyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-2-methyl-3-pyridin-3-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-methyl-3-pyridin-3-yl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine;

6-[(2,3-Dichlorophenyl)carbonyl]-3-(4-fluorophenyl)-1-methyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-(4-fluorophenyl)-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-[(2,3-Dichlorophenyl)carbonyl]-2-methyl-3-pyridin-3-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-[(2,3-Dichlorophenyl)carbonyl]-2-methyl-3-pyridin-3-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-2-methyl-3-pyrimidin-5-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-[(2,3-Dichlorophenyl)carbonyl]-3-(4-fluorophenyl)-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-[(2,3-Dichlorophenyl)carbonyl]-3-pyridin-4-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine;

(2-Chloro-4-fluorophenyl)(1-(pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-(*S**)-6-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-(*R**)-6-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine;

5-[(2,3-Dichlorophenyl)carbonyl]-6-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine;

5-[(2,3-Dichloro-4-fluorophenyl)carbonyl]-6-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(3-fluoropyridin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(2-Fluoro-3-(trifluoromethyl)phenyl)(1-(pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Fluoro-3-(trifluoromethyl)phenyl)(1-(2-methoxyphenyl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(2-methoxyphenyl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(2-(2-fluoroethoxy)phenyl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(1-methyl-1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(1-methyl-1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(4-Chloro-2-fluorophenyl)(1-(pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-Dichloro-4-fluorophenyl)(1-(pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-fluoropyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(3,4-Difluoro-2-methylphenyl)(1-(pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo-[4,5-c]pyridin-5(4H)-yl)methanone;

(*R**)-(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(*S**)-(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(6-fluoropyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-methoxypyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(6-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-dichloro-4-fluorophenyl)(4-methyl-1-(pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-dichloro-4-fluorophenyl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2,3-Dichloro-4-fluorophenyl)(4-methyl-1-(pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2,3-Dichloro-4-fluorophenyl)(4-methyl-1-(pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2,3-Dichloro-4-fluorophenyl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2,3-Dichloro-4-fluorophenyl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(5-methoxypyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(6-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(6-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-methoxypyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-methoxypyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-methoxypyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(6-methyl-1-(1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2-methyl-3-(trifluoromethyl)phenyl)methanone;

(S*)-(4-chloro-2-fluorophenyl)(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(4-chloro-2-fluorophenyl)(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(*S**)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(*R*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(1-(3,5-dimethylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-dichlorophenyl)(1-(3,5-dimethylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-Dichlorophenyl)(1-(3-fluoropyridin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(1-(2-fluoroethyl)-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(1-methyl-1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(6R*)-5-[(2,3-Dichlorophenyl)carbonyl]-1-(3-fluoropyridin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6S*)-5-[(2,3-Dichlorophenyl)carbonyl]-1-(3-fluoropyridin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6R*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(3-fluoropyridin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6S*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(3-fluoropyridin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(R*)-(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(1-methyl-1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(1-methyl-1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(1-(2-fluoroethyl)-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(1-(2-fluoroethyl)-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

5-[(2,3-Dichlorophenyl)carbonyl]-1-(4-fluoropyridin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(2,3-Dichlorophenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-fluoro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-fluoropyridin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrimidin-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-fluoro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-dichlorophenyl)(1-(4,6-dimethylpyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-dichlorophenyl)(4-methyl-1-(6-methylpyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(4,6-dimethylpyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(4,6-dimethylpyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(2-ethyl-4-methyl-1-phenyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(3-methyl-2-(trifluoromethyl)pyridin-4-yl)methanone;

(R*)-(4-methyl-1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2-methyl-3-(trifluoromethyl)phenyl)methanone;

(2-fluoro-3-(trifluoromethyl)phenyl)(6-methyl-1-(1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-fluoro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2,3-Dichlorophenyl)(4-methyl-1-(pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2,3-Dichlorophenyl)(4-methyl-1-(pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(6R*)-5-[(2,3-Dichlorophenyl)carbonyl]-1-(4-fluoropyridin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6S*)-5-[(2,3-Dichlorophenyl)carbonyl]-1-(4-fluoropyridin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(S*)-(4-methyl-1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2-methyl-3-(trifluoromethyl)phenyl)methanone;

(6R*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(4-fluoropyridin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6S*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(4-fluoropyridin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6R*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6S*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-[(2,3-Dichlorophenyl)carbonyl]-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6R*)-5-[(2,3-Dichlorophenyl)carbonyl]-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6S*)-5-[(2,3-Dichlorophenyl)carbonyl]-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

1-(5-Fluoropyrimidin-2-yl)-6-methyl-5-{[2-methyl-3-(trifluoromethyl)phenyl]carbonyl}-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6R*)-1-(5-Fluoropyrimidin-2-yl)-6-methyl-5-{[2-methyl-3-(trifluoromethyl)phenyl]carbonyl}-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6S*)-1-(5-Fluoropyrimidin-2-yl)-6-methyl-5-{[2-methyl-3-(trifluoromethyl)phenyl]carbonyl}-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(2-chloro-3-(trifluoromethyl)phenyl)(6-methyl-1-(1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(6R*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6S*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-[(2,3-Dichloro-4-fluorophenyl)carbonyl]-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6R*)-5-[(2,3-Dichloro-4-fluorophenyl)carbonyl]-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6S*)-5-[(2,3-Dichloro-4-fluorophenyl)carbonyl]-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

5-[(2,4-Dichloro-3-fluorophenyl)carbonyl]-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6R*)-5-[(2,4-Dichloro-3-fluorophenyl)carbonyl]-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6S*)-5-[(2,4-Dichloro-3-fluorophenyl)carbonyl]-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6R)-1-(5-Fluoropyrimidin-2-yl)-5-{[2-fluoro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6S)-1-(5-Fluoropyrimidin-2-yl)-5-{[2-fluoro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6R*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-1-pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(6S*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-1-pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine;

(R*)-(2-chloro-3-(trifluoromethyl)phenyl)(3-(5-fluoropyrimidin-2-yl)-7-methyl-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(S*)-(2-chloro-3-(trifluoromethyl)phenyl)(3-(5-fluoropyrimidin-2-yl)-7-methyl-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,3-dichlorophenyl)(4-methyl-1-(4-methylpyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-dichlorophenyl)(1-(4,6-dimethylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-fluoro-5-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-dichlorophenyl)(4-methyl-1-(6-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(4*R**)-(2-Chloro-3-(trifluoromethyl)phenyl)((4R)-4-methyl-1-(6-methyl-1,6-dihydropyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(4*R*)-(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(4-methylpyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrimidin-5-yl)-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-dichlorophenyl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-fluorophenyl)-4,7-dimethyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(5-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(4,6-dimethyl-1-phenyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(4,7-dimethyl-1-phenyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-Dichlorophenyl)(1-(4-fluorophenyl)-4,6-dimethyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-fluorophenyl)-4,6-dimethyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-Dichlorophenyl)(7-methyl-1-phenyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(7-methyl-1-phenyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-fluorophenyl)-7-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-Dichlorophenyl)(1-(4-fluorophenyl)-7-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(1-(2-methoxyethyl)-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(1-(2-methoxyethyl)-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(oxazol-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-methylpyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(4-methylpyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4,6-dimethylpyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(3-ethylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(5-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-4-fluorophenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,4-dichlorophenyl)(1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(3-ethoxypyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(3-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(3-methoxypyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-dichloro-4-fluorophenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-fluoro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-methyl-3-(trifluoromethyl)phenyl)methanone;

(2-fluorophenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(4-(tert-butyl)phenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(1,5-dimethyl-3-(1-methyl-1H-pyrazol-5-yl)-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(5-methyl-3-(1H-pyrazol-5-yl)-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,4-dichlorophenyl)(5-methyl-3-(1H-pyrazol-5-yl)-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2-fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(4-methylpyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(4-chloro-2-fluorophenyl)(1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(4-chloro-2-fluorophenyl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(4-chloro-2-fluorophenyl)(4-methyl-1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-methyl-3-(trifluoromethyl)phenyl)(1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,4-dichlorophenyl)(1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2-methyl-3-(trifluoromethyl)phenyl)methanone;

(2,4-dichlorophenyl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(4-chloro-2-fluorophenyl)(1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-methyl-3-(trifluoromethyl)phenyl)(1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(4-methyl-1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2-methyl-3-(trifluoromethyl)phenyl)methanone;

(2,4-dichlorophenyl)(4-methyl-1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)((4R,6R)-1-(4-fluorophenyl)-4,6-dimethyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)((4S,6S)-1-(4-fluorophenyl)-4,6-dimethyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

2-chloro-3-(trifluoromethyl)phenyl)((4S,6R)-1-(4-fluorophenyl)-4,6-dimethyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)((4R,6S)-1-(4-fluorophenyl)-4,6-dimethyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(2-chloro-3-(trifluoromethyl)phenyl)(6-methyl-1-phenyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-3-phenyl-6,7-dihydro-3H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(6-methyl-1-phenyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(3-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(3-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(3-propoxypyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(4-ethylpyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(1-(3-ethylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(3-(trifluoromethyl)phenyl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)((4R,6R)-4,6-dimethyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)((4S,6R)-4,6-dimethyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

2-chloro-3-(trifluoromethyl)phenyl)(4,6-dimethyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(1-(4,6-dimethylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(5-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(3-(5-fluoropyrimidin-2-yl)-7-methyl-2-((2-(trimethylsilyl)ethoxy)methyl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(S)-(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(3-(trifluoromethyl)phenyl)methanone;

(R*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(3-fluoro-5-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(7-methyl-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)((4S,6R)-4,6-dimethyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)((4R,6S)-4,6-dimethyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-fluoro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(1-(5-fluoropyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-methyl-3-(trifluoromethyl)phenyl)methanone;

(2,4-dichlorophenyl)(1-(5-fluoropyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-fluoro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(3-ethoxypyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(3-ethoxypyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(1-(2-hydroxyethyl)-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)((4S,6S)-4,6-dimethyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)((4R,6R)-4,6-dimethyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(3-phenyl-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)(2-(trifluoromethyl)pyridin-3-yl)methanone;

(2-chloro-4-fluorophenyl)(3-phenyl-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,6-dichlorophenyl)(3-phenyl-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2-chloro-6-fluorophenyl)(3-phenyl-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,3-dichlorophenyl)(3-(4-fluorophenyl)-2-methyl-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(2-methyl-3-(pyridin-4-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,3-dichlorophenyl)(2-methyl-3-(pyridin-4-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,3-dichlorophenyl)(2-methyl-3-(pyrimidin-5-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,3-dichlorophenyl)(3-(pyrimidin-5-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,3-dichlorophenyl)(2-methyl-1-phenyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-dichlorophenyl)(2-ethyl-1-phenyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrimidin-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrimidin-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2,3-dichlorophenyl)(4-methyl-1-(5-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(3-chloro-4-(trifluoromethyl)pyridin-2-yl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(4-chloro-5-(trifluoromethyl)pyridin-3-yl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(3-chloro-4-(trifluoromethyl)pyridin-2-yl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(4-chloro-5-(trifluoromethyl)pyridin-3-yl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone; and

(2-Chloro-3-(trifluoromethyl)phenyl)(1-(pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

An additional embodiment of the invention is a compound selected from the group presented in Table 1B.

Table 1B. Selected Compounds of Formulas (I, Ia, IIa or IIb)

(*R**)-(6-methyl-1-(1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2-methyl-3-(trifluoromethyl)phenyl)methanone;

(*S**)-(6-methyl-1-(1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2-methyl-3-(trifluoromethyl)phenyl)methanone;

(*R**)-(2-fluoro-3-(trifluoromethyl)phenyl)(6-methyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(*S**)-(2-fluoro-3-(trifluoromethyl)phenyl)(6-methyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(*R**)-(2-chloro-3-(trifluoromethyl)phenyl)(6-methyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(*S**)-(2-chloro-3-(trifluoromethyl)phenyl)(6-methyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-5-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-chloro-5-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-chloro-5-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(3-chloro-5-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(3-chloro-5-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(3-chloro-5-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(4-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(4-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(4-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-fluoro-3-(trifluoromethoxy)phenyl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-fluoro-3-(trifluoromethoxy)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(3-(trifluoromethoxy)phenyl)methanone;

(R*)-(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(3-(trifluoromethoxy)phenyl)methanone;

(S*)-(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(3-(trifluoromethoxy)phenyl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-(trifluoromethyl)pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-(trifluoromethyl)pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-(trifluoromethyl)pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(1-(1H-imidazol-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2,3-dichlorophenyl)methanone;

(2-fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2-fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2-fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(3-chloro-2-methylphenyl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2,3-dichlorophenyl)(4-methyl-1-(6-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2,3-dichlorophenyl)(4-methyl-1-(6-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(R*)-(2,3-dichlorophenyl)(4-methyl-1-(4-methylpyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2,3-dichlorophenyl)(4-methyl-1-(4-methylpyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(1-(1H-imidazol-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2-chloro-3-(trifluoromethyl)phenyl)methanone;

(R*)-(2,3-dichlorophenyl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(2,3-dichlorophenyl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-methylpyrimidin-4-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(6-methylpyrimidin-4-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(2-methylpyrimidin-4-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(2-methylpyrimidin-4-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(2-methylpyrimidin-4-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(2-methylpyrimidin-4-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-methylpyrimidin-4-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(6-methylpyrimidin-4-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(1-ethyl-1H-pyrazol-3-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(1-ethyl-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(1-ethyl-1H-pyrazol-5-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(1-ethyl-1H-pyrazol-5-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(1-(1-ethyl-1H-pyrazol-3-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)methanone;

(S)-(1-(1-ethyl-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)methanone;

(S)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(1-(1-ethyl-1H-pyrazol-3-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(1-(1-ethyl-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(1-isopropyl-1H-pyrazol-3-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(1-isopropyl-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(2-fluoro-3-(trifluoromethyl)phenyl)(1-(1-isopropyl-1H-pyrazol-3-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(2-fluoro-3-(trifluoromethyl)phenyl)(1-(1-isopropyl-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(1-(1-isopropyl-1H-pyrazol-3-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(1-(1-isopropyl-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(1-(1-isopropyl-1H-pyrazol-3-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(1-(1-isopropyl-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(2-chloro-3-(trifluoromethyl)phenyl)(6-methyl-1-(thiophen-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(thiophen-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(6-methyl-1-(1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(6-methyl-1-(1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S*)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2-hydroxy-3-(trifluoromethyl)phenyl)methanone;

(S)-(2-fluoro-3-(trifluoromethoxy)phenyl)(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(2-fluoro-3-(trifluoromethyl)phenyl)(1-(5-hydroxypyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(S)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-hydroxypyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(3-(5-fluoropyridin-2-yl)-7-methyl-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,3-dichlorophenyl)(7-methyl-3-(pyrimidin-2-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(7-methyl-3-(pyridin-2-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,3-dichlorophenyl)(7-methyl-3-(pyrazin-2-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(3-(4-fluorophenyl)-7-methyl-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,3-dichlorophenyl)(3-(4-fluorophenyl)-7-methyl-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,3-dichlorophenyl)(7-methyl-3-(1-methyl-1H-pyrazol-5-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(7-methyl-3-(1-methyl-1H-pyrazol-5-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone; and

(2-chloro-3-(trifluoromethyl)phenyl)(7-methyl-3-(pyrazin-2-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone.

An additional embodiment of the invention is a compound selected from the group presented in Table 1C.

Table 1C. Selected Compounds of Formulas (IIa or IIb)

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-2-methyl-3-pyridin-2-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-pyridin-2-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine-TFA salt;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-(5-fluoropyridin-2-yl)-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-(5-fluoropyridin-3-yl)-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-pyridin-3-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-pyrazin-2-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-pyrimidin-2-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

(2-Chloro-3-(trifluoromethyl)phenyl)(3-phenyl-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

6-[(2,3-Dichlorophenyl)carbonyl]-3-phenyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine;

6-[(2,3-Dichlorophenyl)carbonyl]-1-methyl-3-phenyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine : 6-[(2,3-dichlorophenyl)carbonyl]-2-methyl-3-phenyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine (1:1);

6-[(2,3-Dichlorophenyl)carbonyl]-2-methyl-3-phenyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-[(2,3-Dichlorophenyl)carbonyl]-1-methyl-3-phenyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine;

6-[(2,3-Dichloropyridin-4-yl)carbonyl]-3-phenyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-(4-fluorophenyl)-2-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-(4-fluorophenyl)-1-methyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-2-methyl-3-pyridin-3-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-methyl-3-pyridin-3-yl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine;

6-[(2,3-Dichlorophenyl)carbonyl]-3-(4-fluorophenyl)-1-methyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-(4-fluorophenyl)-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-[(2,3-Dichlorophenyl)carbonyl]-2-methyl-3-pyridin-3-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-[(2,3-Dichlorophenyl)carbonyl]-2-methyl-3-pyridin-3-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-2-methyl-3-pyrimidin-5-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-[(2,3-Dichlorophenyl)carbonyl]-3-(4-fluorophenyl)-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

6-[(2,3-Dichlorophenyl)carbonyl]-3-pyridin-4-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine;

(R*)-(2-chloro-3-(trifluoromethyl)phenyl)(3-(5-fluoropyrimidin-2-yl)-7-methyl-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(S*)-(2-chloro-3-(trifluoromethyl)phenyl)(3-(5-fluoropyrimidin-2-yl)-7-methyl-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(1,5-dimethyl-3-(1-methyl-1H-pyrazol-5-yl)-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(5-methyl-3-(1H-pyrazol-5-yl)-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,4-dichlorophenyl)(5-methyl-3-(1H-pyrazol-5-yl)-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(3-(5-fluoropyrimidin-2-yl)-7-methyl-2-((2-(trimethylsilyl)ethoxy)methyl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(7-methyl-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2-chloro-4-fluorophenyl)(3-phenyl-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,6-dichlorophenyl)(3-phenyl-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2-chloro-6-fluorophenyl)(3-phenyl-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,3-dichlorophenyl)(3-(4-fluorophenyl)-2-methyl-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(2-methyl-3-(pyridin-4-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,3-dichlorophenyl)(2-methyl-3-(pyridin-4-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,3-dichlorophenyl)(2-methyl-3-(pyrimidin-5-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,3-dichlorophenyl)(3-(pyrimidin-5-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(3-(5-fluoropyridin-2-yl)-7-methyl-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,3-dichlorophenyl)(7-methyl-3-(pyrimidin-2-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(7-methyl-3-(pyridin-2-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,3-dichlorophenyl)(7-methyl-3-(pyrazin-2-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(3-(4-fluorophenyl)-7-methyl-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2,3-dichlorophenyl)(3-(4-fluorophenyl)-7-methyl-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

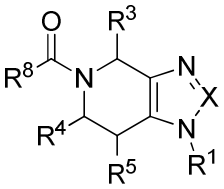
(2,3-dichlorophenyl)(7-methyl-3-(1-methyl-1H-pyrazol-5-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone;

(2-chloro-3-(trifluoromethyl)phenyl)(7-methyl-3-(1-methyl-1H-pyrazol-5-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone; and

(2-chloro-3-(trifluoromethyl)phenyl)(7-methyl-3-(pyrazin-2-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone.

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

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

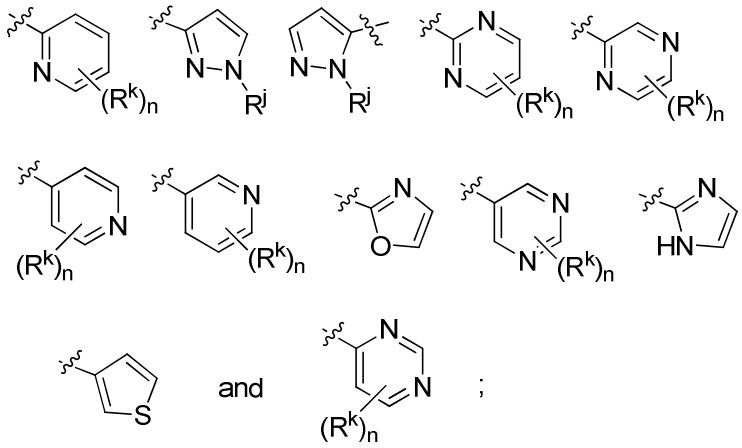


Formula (I)

wherein

R^1 is (a) phenyl, optionally substituted with zero to four groups independently selected from the group consisting of halo, C_1-C_4alkyl, alkoxy, perhaloalkyl and perhaloalkoxy; or

(b) heteroaryl, independently selected from the group consisting of:



wherein R^k is independently selected from the group consisting of H, halo, C_1-C_3alkyl, hydroxyl, perhaloalkyl and alkoxy;

R^j is independently selected from H or C_1-C_3alkyl wherein C_1-C_3alkyl is optionally substituted with from one to three halo substituents, one OH substituent or one alkoxy substituent; and

n is an integer from 0-3;

X is N or CR^2;

R^2 is H, perhaloalkyl or C_1-C_3 lower alkyl;

R^3 is H, perhaloalkyl, C_1-C_4 alkyl, alkalkoxy, CH_2R^i, -$C(O)R^e$ or phenyl, wherein said phenyl is optionally substituted with zero to two groups independently selected from the group consisting of halo, C_1-C_3alkyl, alkoxy, perhaloalkyl and perhaloalkoxy;

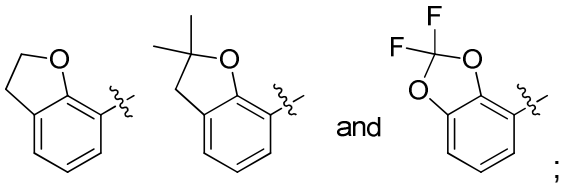
R^i is OH, NC_3H_6, $N(C_1$-C_3alkyl$)_2$ or halo;

R^e is OH, OC_1-C_3 alkyl, $N(C_1$-C_3alkyl$)_2$, or NC_3H_6;

R^4 and R^5 are independently H or C_1-C_3 alkyl;

R^8 is phenyl or pyridyl, optionally substituted with zero to four R^m substituents wherein R^m is independently selected from the group consisting of halo, C_1-C_3alkyl, hydroxy, alkoxy, perhaloalkyl and perhaloalkoxy; or

R^8 is independently selected from the group consisting of:



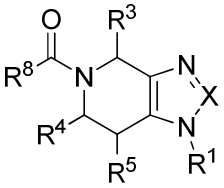
;

and pharmaceutically acceptable salts of compounds of Formula (I);and

(b) at least one pharmaceutically acceptable excipient.

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

(a) an effective amount of at least one compound selected from compounds Formula Ia:

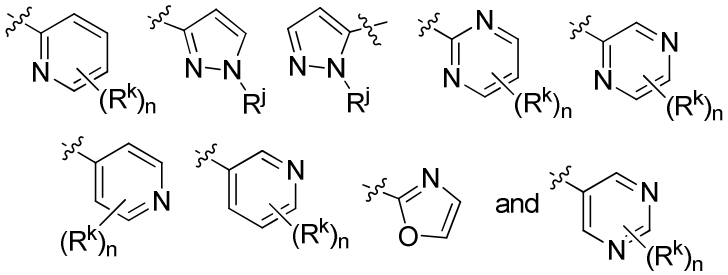


Formula (Ia)

wherein;

R^1 is (a) phenyl, optionally substituted with zero to four groups selected from the group consisting of: halo, C_1-C_4alkyl, alkoxy, perhaloalkyl and perhaloalkoxy; and

(b) heteroaryl, selected from the group consisting of:



wherein R^k is selected from the group consisting of: H, halo, C_1-C_3alkyl and alkoxy;

R^j is selected from the group consisting of: H, C_1-C_3alkyl optionally substituted with halo, OH and alkoxy; and

n is an integer from 0-3;

X is N or CR^2;

R^2 is H, perhaloalkyl or C_1-C_3 lower alkyl;

R^3 is H, perhaloalkyl, C_1-C_4 alkyl, alkalkoxy , CH_2R^i, -C(O)R^e or phenyl, optionally substituted with zero to two groups selected from:

halo, C_1-C_3alkyl, alkoxy, perhaloalkyl and perhaloalkoxy;

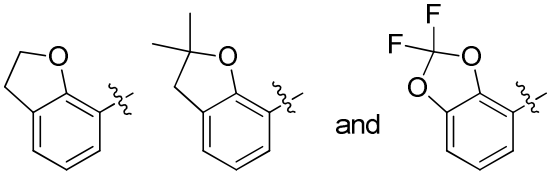
R^i is OH, OC_1-C_3 alkyl, NC_3H_6, $N(C_1$-C_3alkyl$)_2$ or halo;

R^e is OH, OC_1-C_3 alkyl, $N(C_1$-C_3alkyl$)_2$, NC_3H_6;

R^4 and R^5 are independently H or C_1-C_3 alkyl; and

R^8 is phenyl or pyridyl, optionally substituted with zero to four R^m substituents wherein R^m is selected from the group consisting of: halo, C_1-C_3alkyl, alkoxy, perhaloalkyl and perhaloalkoxy; or

R^8 is selected from the group consisting of:



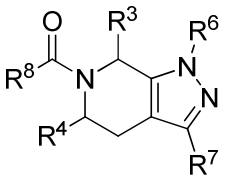
; and

pharmaceutically acceptable salts of compounds of Formula (Ia); and

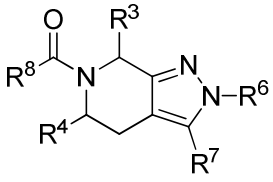
(b) at least one pharmaceutically acceptable excipient.

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 (IIa and IIb):



Formula (IIa)



Formula (IIb)

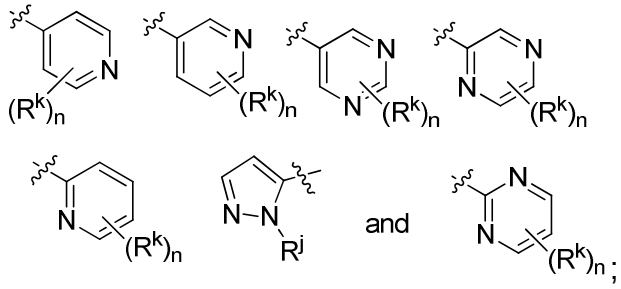
wherein:

R^3, R^4 and R^6 are independently H or C_1-C_3 alkyl;

R^8 is phenyl or pyridyl, optionally substituted with zero to three R^m substituents wherein R^m is independently selected from the group consisting of: halo, C_1-C_3alkyl and perhaloalkyl;

R^7 is (a) phenyl, optionally substituted with zero to two groups independently selected from the group consisting of halo and C_1-C_3alkyl; or

(b) heteroaryl, independently selected from the group consisting of:



wherein R^k is halo or C_1-C_3alkyl;

R^j is H or C_1-C_3alkyl; wherein C_1-C_3alkyl is optionally substituted with one halo substituent or one alkoxy substituent; and

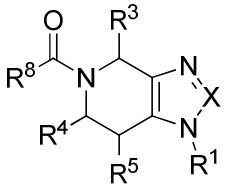
n is an integer from 0-3; and

pharmaceutically acceptable salts of compounds of Formula (IIa and IIb); 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 in Tables 1, 1A and 1B and at least one pharmaceutically acceptable excipient.

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 P2X7 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):

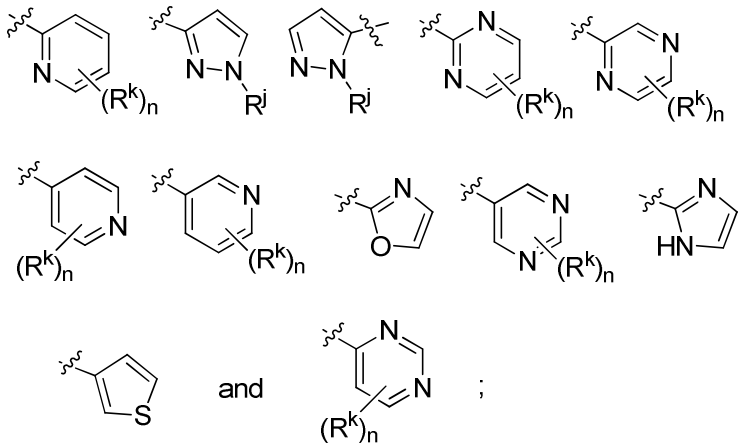


Formula (I)

wherein

R^1 is (a) phenyl, optionally substituted with zero to four groups independently selected from the group consisting of halo, C_1-C_4alkyl, alkoxy, perhaloalkyl and perhaloalkoxy; or

(b) heteroaryl, independently selected from the group consisting of:



wherein R^k is independently selected from the group consisting of H, halo, C_1-C_3alkyl, hydroxyl, perhaloalkyl and alkoxy;

R^j is independently selected from H or C_1-C_3alkyl wherein C_1-C_3alkyl is optionally substituted with from one to three halo substituents, one OH substituent or one alkoxy substituent; and

n is an integer from 0-3;

X is N or CR^2;

R^2 is H, perhaloalkyl or C_1-C_3 lower alkyl;

R^3 is H, perhaloalkyl, C_1-C_4 alkyl, alkalkoxy, CH_2R^i, -$C(O)R^e$ or phenyl, wherein said phenyl is optionally substituted with zero to two groups independently selected from the group consisting of halo, C_1-C_3alkyl, alkoxy, perhaloalkyl and perhaloalkoxy;

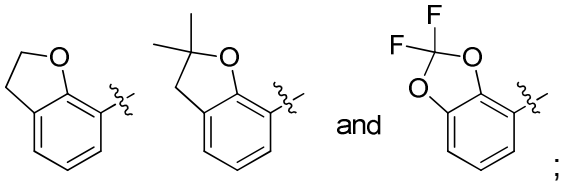
R^i is OH, NC_3H_6, $N(C_1$-C_3alkyl$)_2$ or halo;

R^e is OH, OC_1-C_3 alkyl, $N(C_1$-C_3alkyl$)_2$, or NC_3H_6;

R^4 and R^5 are independently H or C_1-C_3 alkyl;

R^8 is phenyl or pyridyl, optionally substituted with zero to four R^m substituents wherein R^m is independently selected from the group consisting of halo, C_1-C_3alkyl, hydroxy, alkoxy, perhaloalkyl and perhaloalkoxy; or

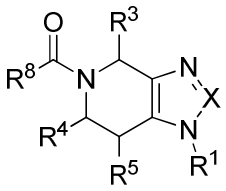
R^8 is independently selected from the group consisting of:



;

and pharmaceutically acceptable salts of compounds of Formula (I).

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 P2X7 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 (Ia):

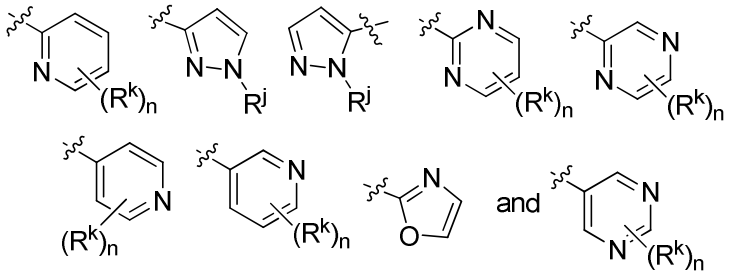


Formula (Ia)

wherein:

R^1 is (a) phenyl, optionally substituted with zero to four groups selected from the group consisting of: halo, C_1-C_4alkyl, alkoxy, perhaloalkyl and perhaloalkoxy; and

(b) heteroaryl, selected from the group consisting of:



wherein R^k is selected from the group consisting of: H, halo, C_1-C_3alkyl and alkoxy;

R^j is selected from the group consisting of: H, C_1-C_3alkyl optionally substituted with halo, OH and alkoxy; and

n is 0-3;

X is N or CR^2;

R^2 is H, perhaloalkyl or C_1-C_3 lower alkyl;

R^3 is H, perhaloalkyl, C_1-C_4 alkyl, alkalkoxy , CH_2R^i, -C(O)R^e or phenyl, optionally substituted with zero to two groups selected from the group consisting of: halo, C_1-C_3alkyl, alkoxy, perhaloalkyl and perhaloalkoxy;

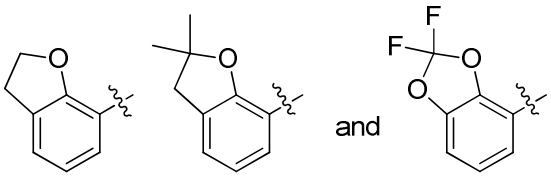
R^i is OH, OC_1-C_3 alkyl, NC_3H_6, $N(C_1$-C_3alkyl$)_2$ or halo;

R^e is OH, OC_1-C_3 alkyl, $N(C_1$-C_3alkyl$)_2$, or NC_3H_6;

R^4 and R^5 are independently H or C_1-C_3 alkyl; and

R^8 is phenyl or pyridyl, optionally substituted with zero to four R^m substituents wherein R^m is selected from the group consisting of: halo, C_1-C_3alkyl, alkoxy, perhaloalkyl and perhaloalkoxy; or

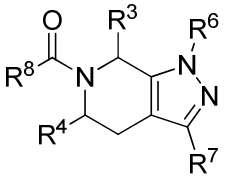
R^8 is selected from the group consisting of



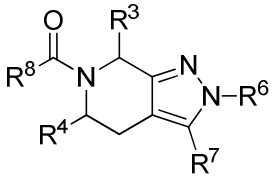
; and

pharmaceutically acceptable salts of compounds of Formula (Ia)

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 P2X7 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 (IIa and IIb):



Formula (IIa)



Formula (IIb)

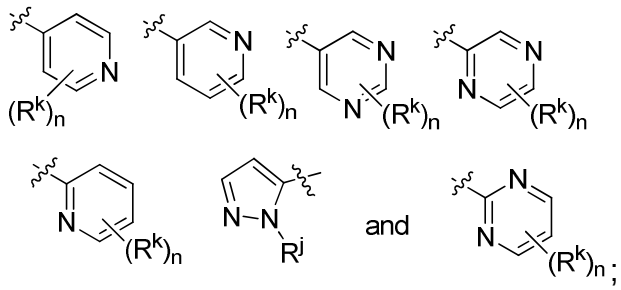
wherein:

R^3, R^4 and R^6 are independently H or C_1-C_3 alkyl;

R^8 is phenyl or pyridyl, optionally substituted with zero to three R^m substituents wherein R^m is independently selected from the group consisting of: halo, C_1-C_3alkyl and perhaloalkyl;

R^7 is (a) phenyl, optionally substituted with zero to two groups independently selected from the group consisting of halo and C_1-C_3alkyl; or

(b) heteroaryl, independently selected from the group consisting of:



wherein R^k is halo or C_1-C_3alkyl;

R^j is H or C_1-C_3alkyl; wherein C_1-C_3alkyl is optionally substituted with one halo substituent or one alkoxy substituent; and

n is an integer from 0-3; and

pharmaceutically acceptable salts of compounds of Formula (IIa and IIb).

In preferred embodiments of the inventive method, the disease, disorder, or medical condition is selected from: diseases of the autoimmune and inflammatory system such as: rheumatoid arthritis, osteoarthritis, psoriasis, septic shock, allergic dermatitis, asthma, allergic asthma, mild to severe asthma, steroid resistant asthma, idiopathic pulmonary fibrosis, allergic rhinitis, chronic obstructive pulmonary disease and airway hyper-responsiveness; diseases of the nervous and neuro-immune system such as acute and chronic pain states of neuropathic pain, inflammatory pain, spontaneous pain (opioid induced pain, diabetic neuropathy, postherpetic neuralgia, low back pain, chemotherapy-induced neuropathic pain, fibromyalgia) (Romagnoli, R, et. al., *Expert Opin. Ther. Targets*, 2008, 12(5), 647-661), and diseases involved with and without neuroinflammation of the CNS such as mood disorders (major depression, major depressive disorder, treatment resistant depression, bipolar disorder, anxious depression, anxiety) (Friedle, SA, et. al., *Recent Patents on CNS Drug Discovery*, 2010, 5, 35-45, Romagnoli, R, et. al., *Expert Opin. Ther. Targets*, 2008, 12(5), 647-661), cognition, sleep disorders, multiple sclerosis (Sharp AJ, et.al., J Neuroinflammation. 2008 Aug 8;5:33, Oyanguren-Desez O, et. al., *Cell Calcium*. 2011 Nov;50(5):468-72, Grygorowicz T, et. al., *Neurochem Int*. 2010 Dec;57(7):823-9), epileptic seizures (Engel T, et. al., *FASEB J*. 2012 Apr;26(4):1616-28, Kim JE, et. al. *Neurol Res.* 2009 Nov;31(9):982-8, Avignone E, et.al., *J Neurosci.* 2008 Sep 10;28(37):9133-44), Parkinson's disease (Marcellino D, et. al., *J Neural Transm.* 2010 Jun;117(6):681-7), schizophrenia, Alzheimer's disease (Diaz-Hernandez JI, et. al., *Neurobiol*

Aging. 2012 Aug;33(8):1816-28, Delarasse C, *J Biol Chem.* 2011 Jan 28;286(4):2596-606, Sanz JM, et. al., *J Immunol.* 2009 Apr 1;182(7):4378-85), Huntington's disease (Díaz-Hernández M, et. Al., *FASEB J.* 2009 Jun;23(6):1893-906), autism, spinal cord injury and cerebral ischemia/traumatic brain injury (Chu K, et. al., *J Neuroinflammation*. 2012 Apr 18;9:69, Arbeloa J, et. al, *Neurobiol Dis*. 2012 Mar;45(3):954-61).

P2X7 antagonism may also be beneficial in several stress-related disorders. In addition, P2X7 intervention may be beneficial in diseases of the cardiovascular, metabolic, gastrointestinal and urogenital systems such as diabetes (*Arterioscler Thromb Vasc Biol.* 2004 Jul;24(7):1240-5, *J Cell Physio*l. 2013 Jan;228(1):120-9), thrombosis (Furlan-Freguia C, et. al., *J Clin Invest.* 2011 Jul;121(7):2932-44) , irritable bowel syndrome, Crohn's disease, ischemic heart disease, hypertension (Ji X, et. al., *Am J Physiol Renal Physiol.* 2012 Oct;303(8):F1207-15), myocardial infarction, and lower urinary tract dysfunction such as incontinence. P2X7 antagonism may also present a novel therapeutic strategy for skeletal disorders, namely osteoporosis/osteopetrosis and may also modulate secretory function of exocrine glands. It is also hypothesized that blocking P2X7 may also be beneficial in glaucoma, interstitial cystitis (Martins JP, et. al., *Br J Pharmacol.* 2012 Jan;165(1):183-96) and lower urinary tract syndrome (*Br J Pharmacol.* 2012 Jan;165(1):183-96), IBD/IBS (*J Immunol.* 2011 Aug 1;187(3):1467-74. Epub 2011 Jun 22), Sleep, RA/OA, Cough/COPD/asthma, cardiovascular disease, GN, ureteric obstruction, diabetes mellitus, hypertension, sepsis, ischemia, Amyotrophic Lateral Sclerosis, Chaga's Disease, Chlamydia, Neuroblastoma, Tuberculosis, Polycystic Kidney Disease, and migraine.

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 P2X7 receptor activity, wherein the disease, disorder, or medical condition is selected from the group consisting of: rheumatoid arthritis, osteoarthritis, psoriasis, septic shock, allergic dermatitis, asthma, allergic asthma, mild to severe asthma, steroid resistant asthma, idiopathic pulmonary fibrosis, allergic rhinitis, chronic obstructive pulmonary disease and airway hyper-responsiveness; diseases of the nervous and neuro-immune system such as acute and chronic pain states of neuropathic pain, inflammatory pain, spontaneous pain (opioid induced pain, diabetic neuropathy, postherpetic neuralgia, low back pain, chemotherapy-induced

neuropathic pain, fibromyalgia); diseases involved with and without neuroinflammation of the central nervous system such as mood disorders (major depression, major depressive disorder, treatment resistant depression, bipolar disorder, anxious depression, anxiety), cognition, sleep disorders, multiple sclerosis, epileptic seizures, Parkinson's disease, schizophrenia, Alzheimer's disease, Huntington's disease, autism, spinal cord injury and cerebral ischemia/traumatic brain injury, stress-related disorders; diseases of the cardiovascular, metabolic, gastrointestinal and urogenital systems such as diabetes, diabetes mellitus, thrombosis, irritable bowel syndrome, irritable bowel syndrome, Crohn's disease, ischemic heart disease, ischaemia, hypertension, cardiovascular disease, myocardial infarction, and lower urinary tract dysfunction such as incontinence, lower urinary tract syndrome, Polycystic Kidney Disease, Glomerulonephritis**,** skeletal disorders, namely osteoporosis/osteopetrosis: and glaucoma, interstitial cystitis, cough, ureteric obstruction, sepsis, , Amyotrophic Lateral Sclerosis, Chaga's Disease, chlamydia, neuroblastoma, Tuberculosis, and migraine.

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 P2X7 receptor activity wherein the disease, disorder or medical condition is treatment resistant depression.

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

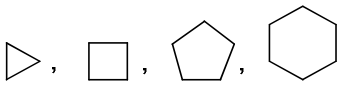
teachings provided herein would be considered equivalent to any one of the foregoing examples. The term C_1-C_3 alkyl as used here refers to a straight- or branched-chain alkyl group having from 1 to 3 carbon atoms in the chain. The term C_1-C_4 alkyl as used here refers to a straight- or branched-chain alkyl group having from 1 to 4 carbon atoms in the chain.

The term “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 “alkalkoxy” refers to the group alkyl-O-alkyl, where alkyl is defined above. Such groups include methylenemethoxy (-CH_2OCH_3) and ethylenemethoxy (-$CH_2CH_2OCH_3$).

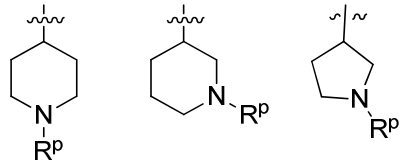
The terms “hydroxyl” and “hydroxy“ refer to an –OH group.

The term “cycloalkyl” refers to a saturated carbocycle having from 3 to 6 ring atoms per carbocycle. Illustrative examples of cycloalkyl groups include the following entities, in the form of properly bonded moieties:



The term “C_3-C_4 cycloalkyl” as used here refers to a saturated carbocycle having from 3 to 4 ring atoms.

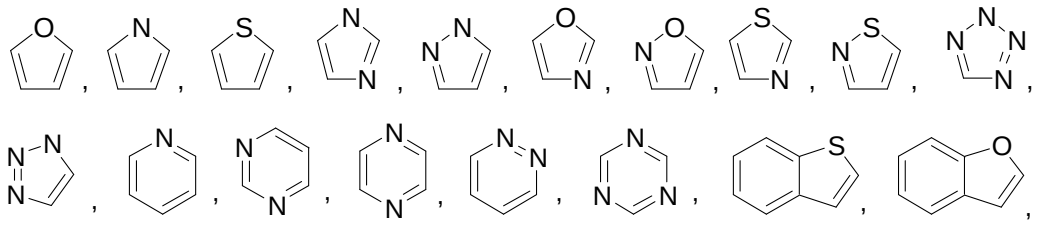
A “heterocycloalkyl” refers to a monocyclic ring structure that is saturated and has from 4 to 6 ring atoms per ring structure selected from carbon atoms and one nitrogen atom. Illustrative entities, in the form of properly bonded moieties, include:



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



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

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

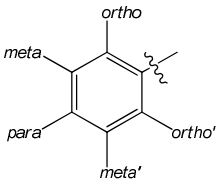
The term “halo” represents chloro, fluoro, bromo or iodo.

The term “perhaloalkyl” refers to a straight- or branched-chain alkyl group having from 1 to 4 carbon atoms in the chain optionally substituting hydrogens with halogens. Examples of perhaloalkyl groups include trifluoromethyl (CF_3), difluoromethyl (CF_2H), monofluoromethyl (CH_2F), pentafluoroethyl (CF_2CF_3), tetrafluoroethyl ($CHFCF_3$),monofluoroethyl (CH_2CH_2F), trifluoroethyl (CH_2CF_3), tetrafluorotrifluoromethylethyl (-$CF(CF_3)_2$), and groups that in light of the ordinary skill in the art and the teachings provided herein would be considered equivalent to any one of the foregoing examples.

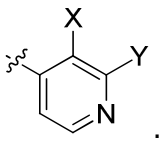
The term “perhaloalkoxy” refers to a straight- or branched-chain alkoxy group having from 1 to 4 carbon atoms in the chain optionally substituting hydrogens with halogens. Examples of perhaloalkoxy groups include trifluoromethoxy (OCF_3), difluoromethoxy (OCF_2H), monofluoromethoxy (OCH_2F), momofluoroethoxy (OCH_2CH_2F), pentafluoroethoxy (OCF_2CF_3), tetrafluoroethoxy ($OCHFCF_3$), trifluoroethoxy (OCH_2CF_3), tetrafluorotrifluoromethylethoxy (-$OCF(CF_3)_2$), and groups that in light of the ordinary skill in the art and the teachings provided herein would be considered equivalent to any one of the foregoing examples.

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

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



When referring to substituents on a pyridyl group, the terms “para”, “meta”, and “ortho” refer to the placement of a substituent relative to the point of attachment of the pyridyl ring. For example the structure below is described as 4-pyridyl with the X substituent in the ortho position and the Y substituent in the meta 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, 5^{th} 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.”

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 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.

Compounds of the invention may also exist as “rotamers,” that is, conformational isomers that occur when the rotation leading to different conformations is hindered, resulting a rotational energy barrier to be overcome to convert from one conformational isomer to another.

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 enatiopure 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, Ia, IIa and IIb) or pharmaceutically acceptable salts of compounds of Formula (I, Ia, IIa and IIb) 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 then the solvates are hydrates. In addition, certain crystalline forms of compounds of Formula (I, Ia, IIa and IIb) or pharmaceutically acceptable salts of compounds of Formula (I, Ia, IIa and IIb) may be obtained as co-crystals. In certain embodiments of the invention, compounds of Formula (I, Ia, IIa and IIb) were obtained in a crystalline form. In other embodiments, crystalline forms of compounds of Formula (I, Ia, IIa and IIb) were cubic in nature. In other embodiments, pharmaceutically acceptable salts of compounds of Formula (I, Ia, IIa and IIb) were obtained in a crystalline form. In still other embodiments, compounds of Formula (I, Ia, IIa and IIb) 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, Ia, IIa and IIb) convert in solution between one or more crystalline forms and/or polymorphic forms.

Reference to a compound herein stands for a reference to any one of: (a) the actually recited form of such compound, and (b) any of the forms of such compound in the medium in which the compound is being considered when named. For example, reference herein to a compound such as R-COOH, encompasses reference to any one of, for example, R-$COOH_{(s)}$, R-$COOH_{(sol)}$, and R-$COO^{-}_{(sol)}$. In this example, R-$COOH_{(s)}$ refers to the solid compound, as it could be for example in a tablet or some other solid pharmaceutical composition or preparation; R-$COOH_{(sol)}$ refers to the undissociated form of the compound in a solvent; and R-$COO^{-}_{(sol)}$ refers to the dissociated form of the compound in a solvent, such as the dissociated form of the compound in an aqueous environment,

whether such dissociated form derives from R-COOH, from a salt thereof, or from any other entity that yields $R\text{-}COO^-$ upon dissociation in the medium being considered. In another example, an expression such as “exposing an entity to compound of formula R-COOH” refers to the exposure of such entity to the form, or forms, of the compound R-COOH that exists, or exist, in the medium in which such exposure takes place. In still another example, an expression such as “reacting an entity with a compound of formula R-COOH” refers to the reacting of (a) such entity in the chemically relevant form, or forms, of such entity that exists, or exist, in the medium in which such reacting takes place, with (b) the chemically relevant form, or forms, of the compound R-COOH that exists, or exist, in the medium in which such reacting takes place. In this regard, if such entity is for example in an aqueous environment, it is understood that the compound R-COOH is in such same medium, and therefore the entity is being exposed to species such as $R\text{-}COOH_{(aq)}$ and/or $R\text{-}COO^-_{(aq)}$, where the subscript “(aq)” stands for “aqueous” according to its conventional meaning in chemistry and biochemistry. A carboxylic acid functional group has been chosen in these nomenclature examples; this choice is not intended, however, as a limitation but it is merely an illustration. It is understood that analogous examples can be provided in terms of other functional groups, including but not limited to hydroxyl, basic nitrogen members, such as those in amines, and any other group that interacts or transforms according to known manners in the medium that contains the compound. Such interactions and transformations include, but are not limited to, dissociation, association, tautomerism, solvolysis, including hydrolysis, solvation, including hydration, protonation, and deprotonation. No further examples in this regard are provided herein because these interactions and transformations in a given medium are known by any one of ordinary skill in the art.

In another example, a zwitterionic compound is encompassed herein by referring to a compound that is known to form a zwitterion, even if it is not explicitly named in its zwitterionic form. Terms such as zwitterion, zwitterions, and their synonyms zwitterionic compound(s) are standard IUPAC-endorsed names that are well known and part of standard sets of defined scientific names. In this regard, the name zwitterion is assigned the name identification CHEBI:27369 by the Chemical Entities of Biological Interest (ChEBI) dictionary of molecular entities. As generally well known, a zwitterion or zwitterionic compound is a neutral compound

that has formal unit charges of opposite sign. Sometimes these compounds are referred to by the term “inner salts”. Other sources refer to these compounds as “dipolar ions”, although the latter term is regarded by still other sources as a misnomer. As a specific example, aminoethanoic acid (the amino acid glycine) has the formula H_2NCH_2COOH, and it exists in some media (in this case in neutral media) in the form of the zwitterion $^{+}H_3NCH_2COO^{-}$. Zwitterions, zwitterionic compounds, inner salts and dipolar ions in the known and well established meanings of these terms are within the scope of this invention, as would in any case be so appreciated by those of ordinary skill in the art. Because there is no need to name each and every embodiment that would be recognized by those of ordinary skill in the art, no structures of the zwitterionic compounds that are associated with the compounds of this invention are given explicitly herein. They are, however, part of the embodiments of this invention. No further examples in this regard are provided herein because the interactions and transformations in a given medium that lead to the various forms of a given compound are known by any one of ordinary skill in the art.

Any formula given herein is also intended to represent unlabeled forms as well as isotopically labeled forms of the compounds. Isotopically labeled compounds have structures depicted by the formulas given herein except that one or more atoms are replaced by an atom having a selected atomic mass or mass number. Examples of isotopes that can be incorporated into compounds of the invention include isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorus, fluorine, and chlorine, 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 ^{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. In particular, an ^{18}F or ^{11}C labeled compound may be particularly preferred for PET or SPECT studies. Further, substitution with heavier isotopes such as deuterium (i.e., ^{2}H) may afford certain therapeutic advantages resulting from greater metabolic stability, for example increased *in vivo* half-life or reduced dosage requirements. Isotopically labeled compounds of this invention and prodrugs thereof can generally be prepared by carrying out the procedures disclosed in the schemes or

in the examples and preparations described below by substituting a readily available isotopically labeled reagent for a non-isotopically labeled reagent.

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

According to the foregoing interpretive considerations on assignments and nomenclature, it is understood that explicit reference herein to a set implies, where chemically meaningful and unless indicated otherwise, independent reference to embodiments of such set, and reference to each and every one of the possible embodiments of subsets of the set referred to explicitly.

The invention includes also pharmaceutically acceptable salts of the compounds of Formula (I, Ia, IIa and IIb), 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. Pharmcopoeia 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, Ia, IIa and IIb) 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,

IIa or IIb) 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, Ia, IIa and IIb) 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.

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.

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, Ia, IIa and IIb), 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, IIa or IIb)). 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, IIa or IIb). 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, Ia, IIa and IIb) 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, Ia, IIa and IIb), 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, IIa or IIb) 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, Ia, IIa and IIb) and their pharmaceutically acceptable salts, pharmaceutically acceptable prodrugs, and pharmaceutically active metabolites of the present invention are useful as modulators of the P2X7 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 P2X7 receptor expression or activity, and “activators” are compounds that increase, activate, facilitate, sensitize, or up-regulate P2X7 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 P2X7 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 P2X7 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 P2X7 receptor activity, such as: rheumatoid arthritis, osteoarthritis, psoriasis, septic shock, allergic dermatitis, asthma, allergic asthma, mild to severe asthma, steroid resistant asthma, idiopathic pulmonary fibrosis, allergic rhinitis, chronic obstructive pulmonary disease (COPD) and airway hyper-responsiveness; diseases of the nervous and neuro-immune system such as acute and chronic pain states of neuropathic pain, inflammatory pain, spontaneous pain (opioid induced pain, diabetic neuropathy, postherpetic neuralgia, low back pain, chemotherapy-induced neuropathic pain, fibromyalgia); diseases involved with and without neuroinflammation of the CNS such as mood

disorders (major depression, major depressive disorder, treatment resistant depression, bipolar disorder, anxious depression, anxiety), cognition, sleep disorders, multiple sclerosis, epileptic seizures, Parkinson's disease, schizophrenia, Alzheimer's disease, Huntington's disease, autism, spinal cord injury and cerebral ischemia/traumatic brain injury, stress-related disorders; diseases of the cardiovascular, metabolic, gastrointestinal and urogenital systems such as diabetes, diabetes mellitus, thrombosis, irritable bowel syndrome, IBD, Crohn's disease, ischemic heart disease, ischaemia, hypertension, cardiovascular disease, myocardial infarction, and lower urinary tract dysfunction such as incontinence, lower urinary tract syndrome, Polycystic Kidney Disease, Glomerulonephritis**, (**GN); skeletal disorders, namely osteoporosis/osteopetrosis: and glaucoma, interstitial cystitis, cough, ureteric obstruction, sepsis, , Amyotrophic Lateral Sclerosis, Chaga's Disease, chlamydia, neuroblastoma, Tuberculosis, and migraine.

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 coadministered separately with an active agent of compounds of Tables 1, 1A or 1B 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 P2X7 activity, such as another P2X7 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.

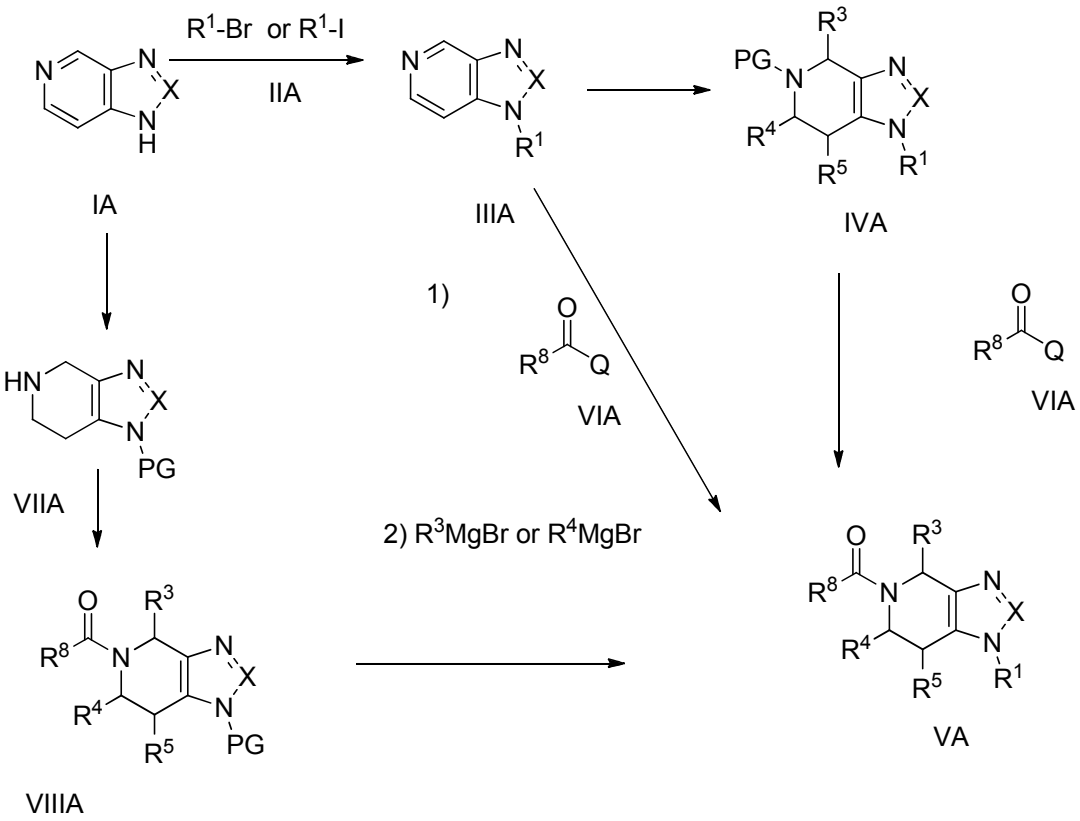
Compounds of the invention may alternatively be administered in methods of this invention by inhalation, via the nasal or oral routes, e.g., in a spray formulation also containing a suitable carrier.

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 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, IIa and IIb). 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.

Scheme 1



The group PG represents a protecting group. One skilled in the art will select the appropriate protecting group compatible with the desired reactions. The protecting groups may be removed at a convenient subsequent stage using methods known from the art. Alternatively, it may be necessary 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. Such compounds, precursors, or prodrugs are

also within the scope of the invention. Examples of preferred protecting groups include; carbamates, benzyl and substituted benzyl groups. Especially preferred protecting groups are; tert-butyloxycarbonyl, 2,2,2-trichloroethoxycarbonyl, alpha-chloroethoxycarbonyl, benzyl, 4-nitrobenzyl and diphenylmethyl.

Heterocycle IA is converted to compound IIIA through coupling with aryl halide IIA using copper oxide, 8-hydroxyquiniolone or 4,7dimeththoxy[1,10]-phenanthroline, $CsCO_3$ in a solvent such as DMSO or butryonitrile. This reaction is heated overnight at 110 °C or heated in a microwave reactor for 1 hour at 140 °C.

Compound IIIA is converted to amine IVA where PG = H by initial treatment with an alkylating agent such as benzyl bromide in a solvent such as DCM or DMF, followed by reduction with a reducing agent such as $NaBH_4$ in a solvent such as MeOH, EtOH or isopropanol. Final treatment with chloroethylchloroformate provides amine IVA where PG = H.

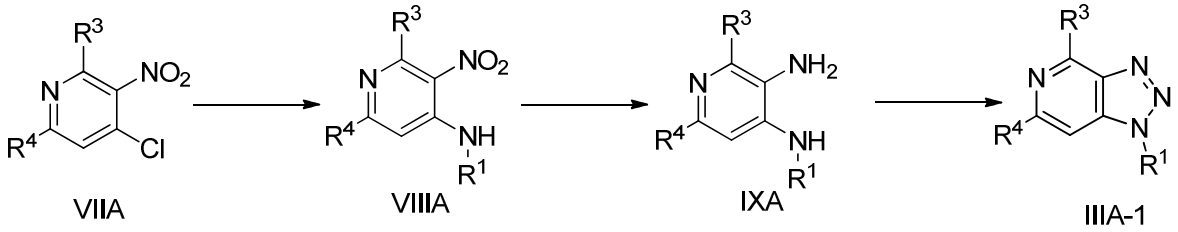
Compound IIIA is also converted to compound VA by initial treatment with acid chloride VIA, where Q = Cl in a solvent such as DCM or DMF. Subsequent treatment with a Grignard reagent such as R^3MgBr or R^4MgBr followed by reduction with hydrogen gas and a metal catalyst such as Pd/C or Pt/C provides VA. . If however one does not perform this final reduction, the partially reduced compound, the 4,5-dihydro-[4,5,c]pyridine (compound not shown) is obtained.

Compound IIIA is also converted to compound IVA by passing a solution of IIIA through a PtO_2 catalyst cartridge on a H-Cube hydrogenation apparatus at 70 bar and at 1 mL/min.

Compound IVA, where PG = H is converted to compound VA by treatment with compound VIA, where Q = OH using amide coupling conditions such as HATU, DIPEA in a solvent such as DCM or DMF.

One of ordinary skill in the art will also realize that when R^1 is a 3-pyrazolo or a 5-pyrazolo group, the N1 nitrogen may be unsubstituted, substituted or may be protected with a protecting group. This nitrogen may be subjected to standard conditions to convert it from one of the above mentioned states to another.

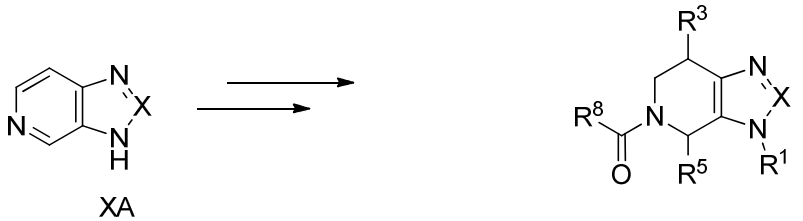
Scheme 2



Alternatively IIIA, for example IIIA-1 as shown in Scheme 2, is prepared through a series of steps commencing with the addition of $Pd(OAc)_2$ to BINAP in toluene, followed by the addition of the following reagents: a chloro-nitropyridine (VIIA), an amino compound such as an aminopyridine (R^1-NH_2) and a base such as K_2CO_3, NaH or NaOtBu in a solvent such as toluene, THF or DMSO. Heating for approximately 2 hours at 110° C in a sealed vessel provides compound VIIIA.

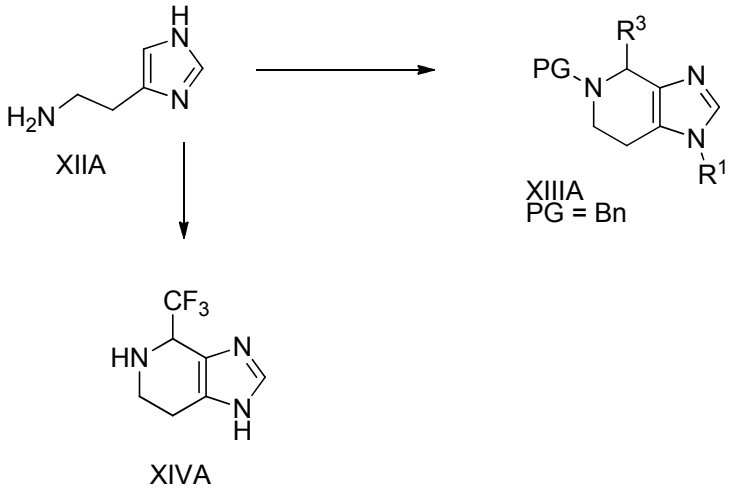
Reduction of VIIIA using catalytic hydrogenation conditions of hydrogen gas and a metal catalyst such as 10% Pd/C in a solvent such as MeOH or EtOH provides diamine compound IXA. Alternatively this reduction is carried out using Zn in HOAC or using a combination of Pd/C in a solvent such as NH_3 in MeOH. Triazole IIIA-1 is then formed by treatment of diamine IXA in THF and HOAc with t-butylnitrite or isoamyl nitrite at 100° C for 90 minutes.

Scheme 3



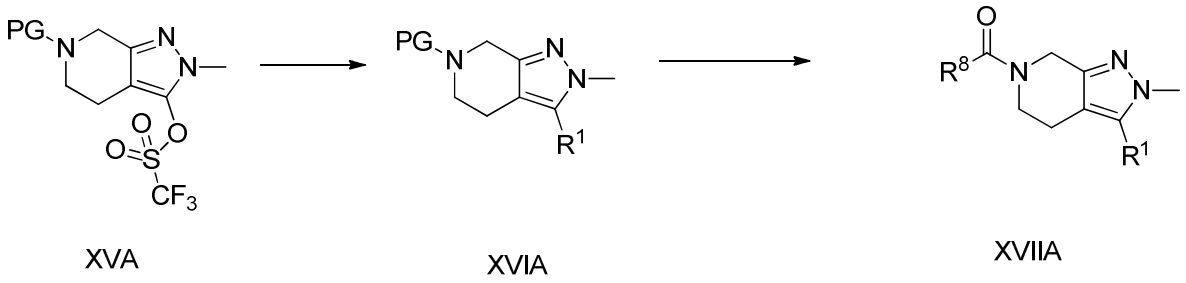
Through a series of steps analogous to those shown in Scheme I, compound XA is converted to analog XIA.

Scheme 4



Compound XIIIA is prepared by treatment of a mixture of compound XIIA, histamine, and benzaldehyde in a solvent such as MeOH or EtOH , with a reducing agent such as $NaBH_4$ to provide *N*-benzyl-2-(1H-imidazol-5-yl)ethanamine (compound not shown). To this compound in water at 0 °C, is added KOH followed by acetaldehyde. After approximately six hours at 80 °C followed by treatment with acid, compound XIIIA , PG = Bn, is isolated. Trifluoromethyl derivative XIVA is also prepared from compound XIIA. To a solution of compound XIIA in a solvent such as water at a temperature of about 0 °C, is added a base such as KOH along with trifluoroacetaldehyde. After heating at a temperature of approximately 80 °C for approximately 6 hours and acidification, compound XIVA is isolated.

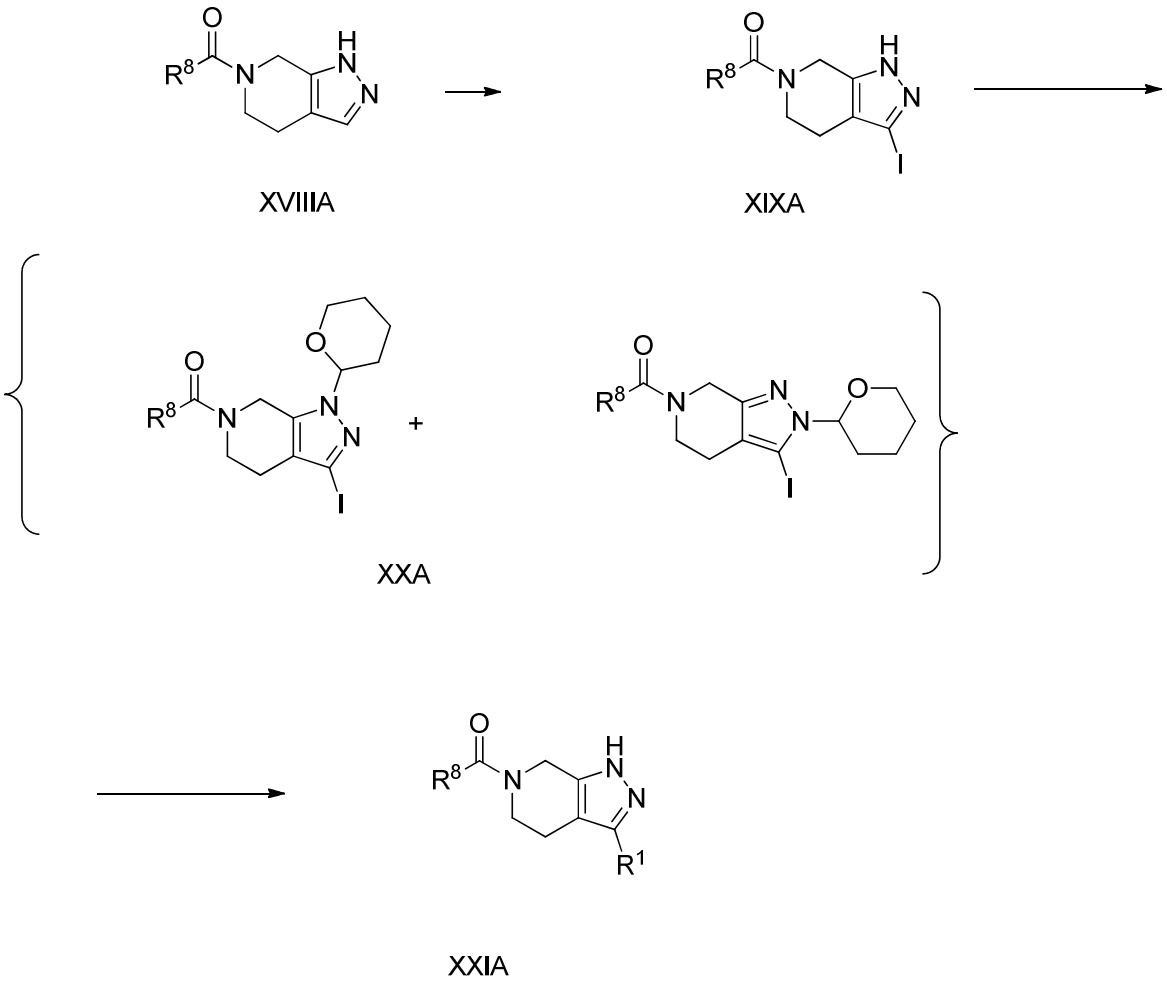
Scheme 5



Compound XVA is prepared from 1-*tert*-butyl 4-ethyl 3-oxopiperidine-1,4-dicarboxylate upon the addition of methyl hydrazine in EtOH. Heating to approximately 80 °C overnight followed by treatment with and diisopropylethylamine and N-phenyltrifluoromethanesulfonate in DCM provides compound XVA where PG = BOC. This compound is then converted to compound XVIA by addition of the appropriate boronic acid pinacol ester, cesium carbonate, copper chloride, palladium acetate and

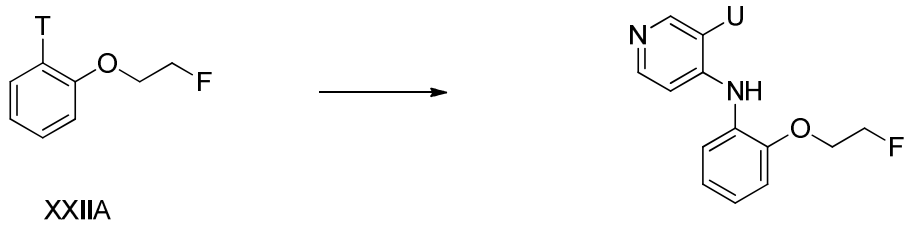
1,1' bis(diphenylphosphino)ferrocene in DMF. Compound XVIA is then converted to pyrazole compound XVIIA through standard removal of the nitrogen protecting group (PG) and coupling to compound VIA as described in Scheme 1.

Scheme 6



Compound XVIIIA is prepared from commercially available 4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine and compound VIA as described in Scheme 1. This compound is then converted to iodo compound XIXA upon treatment with *N*-iodosuccinimide in DMF. This pyrazole is then protected as its THP ether upon treatment with 3,4-dihydropyran and *para*-toluenesulfonic acid. The THP ethers, are represented here as a compound XXA, a mixture of regioisomers and are transformed into compound XXIA using the same conditions described in Scheme 5 for the conversion of XVA to XVIA, followed by THP deprotection using TFA in DCM.

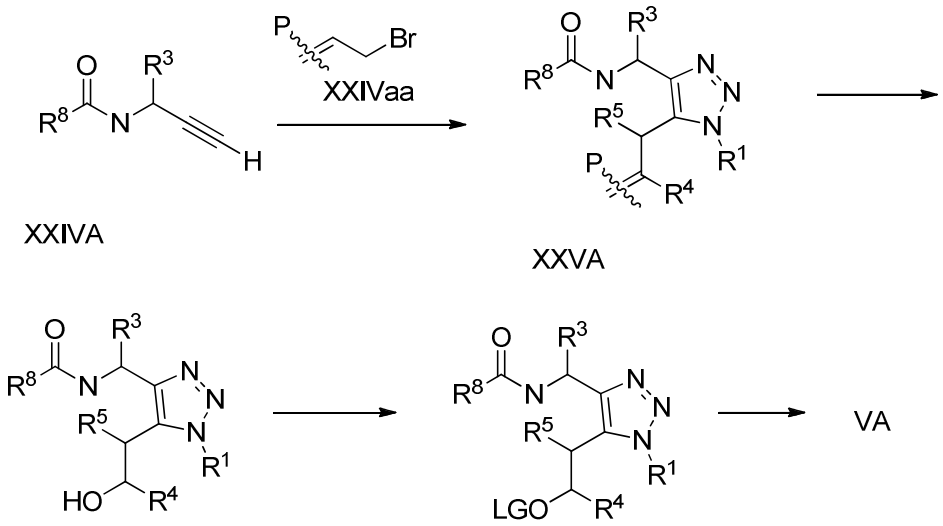
Scheme 7



XXIIA XXIIIA

Compound XXIIA, where T = Br is prepared via the reaction of 2-bromophenol and a base such as NaH in a solvent such as THF, followed by treatment with 1-bromo-2-fluoroethane. This compound is then converted to 2-(2-fluoroethoxy)aniline, compound XXIIA, where T = NH_2, by treatment of the bromo compound, XXIIA, T = Br, with benzophenone imine, NaOtBu, BINAP, $Pd_2(dba)_3$, in a solvent such as toluene at 120 C for approximately 3 hours. This compound is then converted to compound XXIIIA, where U = NO_2, using conditions analogous to those described in Scheme 2 for the conversion of VIIA to VIIIA. Subsequently XXIIIA, where U = NO_2 is converted to XXIIIA, where U = NH_2 as described in Scheme 2 for the conversion of VIIIA to IXA.

Scheme 8



Compound XXIVA is made from the reaction of but-2-yn-2-amine and compound VIA where Q is Cl in the presence of a base such as TEA and in a solvent such as THF. Alternatively compound VIA, where Q is OH is used employing the conditions described in Scheme I for the conversion of compound IVA, where PG is H, to compound VA.

Compound XXVA is prepared by the reaction of compound XXIVA, an azide source such as 2-azido-5-fluoropyrimidine, tetrazolo[1,5-a]pyrimidine, phenylazide, an alkyl azide, an aromatic azide, a heteroaromatic azide, an alkylating agent (XXIVaa, where P represents substitution of the olefin) with specific examples such as such allyl bromide, allyl iodidie, (E)-1-bromobut-2-ene, 3-bromo-2-methylprop-1-ene, 1-bromo-3-methylbut-2-ene, (E)-(3-bromoprop-1-en-1-yl)benzene, ethyl 2-(bromomethyl)acrylate, or 3-bromocyclohex-1-ene, a base such as Cs_2CO_3, TEA or Hunig's base, a copper (I) salt, such as $(CuOTf)_2$, CuI or CuBr, used in either stochiometeric amounts or sub-stochiometric amounts, at a temperature between -78 °C and rt, in a solvent such as THF, DCM, 2-Me-THF, CH_3CN, EtOAc or DMF.

Compound XXVIA is prepared via an ozonolysis of compound XXVA in a solvent such as MeOH, CH_2Cl_2, or THF at a temperature of about -78 °C, followed by reduction with a reducing agent such as $NaBH_4$, Pd/C and H_2, Zn/H_2O, borane-THF and borane-pyridine

Compound XXVIIA is prepared by conversion of the hydroxyl group of compound XXVIA to a leaving group (designated LG), by treatment with an agent such as a sulfonyl chloride such as tosyl chloride or mesyl chloride, in an organic solvent, such as THF, DCM, 2-Me-THF, CH_3CN, EtOAc or DMF, in the presence of a base such as TEA, Hunig's base or pyridine, with an acylation catalyst such as diemethylaminopyridine.

Compound XXVIIA is then converted to compound VA upon treatment with a base such as NaH in a solvent such as THF, with heating to a temperature of about 60 °C for approximately 3 hours.

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 Discover instrument. Hydrogenations on the H-cube were run by passing solvent containing reactant through a catalyst cartridge on an H-Cube hydrogenation apparatus at a pressure of 15 to 100 bar and a flow rate of 1 to 30 ml/min.

Normal-phase silica gel column chromatography (sgc) was performed on silica gel (SiO_2) using prepackaged cartridges, eluting with 2 M NH_3/MeOH in CH_2Cl_2 unless otherwise indicated.

Preparative reverse-phase high performance liquid chromatography (HPLC) was performed on a Agilent HPLC with an Xterra Prep RP_{18} (5 μm, 30 x 100 mm, or 50 X 150 mm) column, and a gradient of 10 to 99% acetonitrile/water (20 mM NH_4OH) over 12 to 18 min, and a flow rate of 30 or 80 mL/min, unless otherwise indicated.

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 between at 100-150 bar with a flow rate ranging from 40-60 mL/min. The columns used were heated to 35-40 °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. The format of the ^1H NMR data below is: chemical shift in ppm downfield of the tetramethylsilane reference (multiplicity, coupling constant J in Hz, integration).

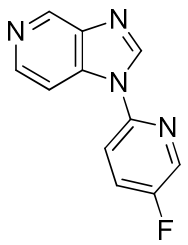
Chemical names were generated using ChemDraw Ultra 6.0.2 (CambridgeSoft Corp., Cambridge, MA) or ACD/Name Version 9 (Advanced Chemistry Development, Toronto, Ontario, Canada).

Abbreviations and acronyms used herein include the following:

Term	**Acronym/Abbreviation**
High-pressure liquid chromatography	HPLC
Diisopropylethylamine	DIPEA, Hunig's base
Tetrahydrofuran	THF
tert-Butylcarbamoyl	boc
Dichloromethane	DCM
Dichlorethane	DCE
Trifluoroacetic acid	TFA
Acetic Acid	HOAc
N,*N*-Dimethylformamide	DMF

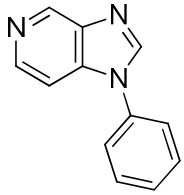
Methanol	MeOH
Ethanol	EtOH
Acetonitrile	ACN, MeCN
Ethyl Acetate	EtOAc, or EA
Triethylamine	TEA
2-(1H-9-Azobenzotriazole-1-yl)-1,1,3,3-tetramethylaminium hexafluorophosphate	HATU
Benzotriazol-1-yloxytris(dimethylamino)-phosphonium hexafluorophosphate	BOP
Acetic acid	HOAc
2-methyltetrahydrofuran	2-Me-THF
Methyl magnesium bromide	MeMgBr
Ethyl magnesium bromide	EtMgBr
Isopropyl magnesium bromide	i-PrMgBr
Dimethyl sulfoxide	DMSO
Supercritical Fluid Chromatography	SFC
Diethyl 1,4-dihydro-2,6-dimethyl-3,5-pyridinecarboxylate	Hantzsch Ester
Tetrahydropyran	THP
2,2'-bis(diphenylphosphino)-1,1'-binaphthyl	BINAP
Sodium tert-butoxide	NaOtBu
Tris(dibenzylideneacetone(dipalladium (0)	$Pd_2(dba)_3$
4,5-bis(diphenylphosphino)-9,9-dimethylxanthene	Xantphos

Intermediate 1: 1-(5-Fluoropyridin-2-yl)-1H-imidazo[4,5-c]pyridine.



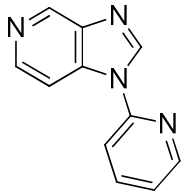
A solution of 5-azabenzimidazole (1.00 g, 8.40 mmol), 2-bromo-5-fluoropyridine (1.48 g, 8.40 mmol), copper (I) oxide (0.13 g, 0.84 mmol), 8-hydroxyquinoline (0.24 g, 1.68 mmol), and Cs_2CO_3 (5.47 g, 16.8 mmol) in DMSO (4 mL) was irradiated in a microwave apparatus for 1 hour at 140 °C. The reaction was diluted with H_2O (100 mL) and extracted with EtOAc (75 mL x 3). The organic layers were combined, dried (Na_2SO_4), and concentrated. Chromatography of the resulting residue (SiO_2; MeOH (NH_3):DCM) gave the title compound (0.45 g, 25%). MS (ESI): mass calculated for $C_{11}H_7FN_4$, 214.07; m/z found 215.1 $[M+H]^+$.

Intermediate 2: 1-Phenyl-1H-imidazo[4,5-c]pyridine.



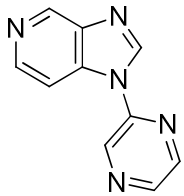
Intermediate 2 was prepared in a manner analogous to Intermediate 1, substituting 2-bromobenzene for 2-bromo-5-fluoropyridine. MS (ESI): mass calculated for $C_{12}H_9N_3$, 197.07; m/z found 198.1 $[M+H]^+$.

Intermediate 3: 1-(Pyridin-2-yl)-1H-imidazo[4,5-c]pyridine.



Intermediate 3 was prepared in a manner analogous to Intermediate 1, substituting 2-bromopyridine for 2-bromo-5-fluoropyridine. MS (ESI): mass calculated for $C_{11}H_8N_4$, 196.07; m/z found 197.1 $[M+H]^+$.

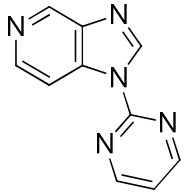
Intermediate 4: 1-(Pyrazin-2-yl)-1H-imidazo[4,5-c]pyridine.



Intermediate 4 was prepared in a manner analogous to Intermediate 1, substituting 2-bromopyrazine for 2-bromo-5-fluoropyridine. MS (ESI): mass calculated for $C_{10}H_7N_5$,

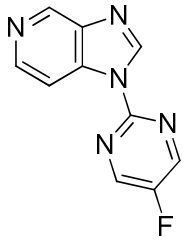
198.07; m/z found 199.1 $[M+H]^+$.

Intermediate 5: 1-(Pyrimidin-2-yl)-1H-imidazo[4,5-c]pyridine.



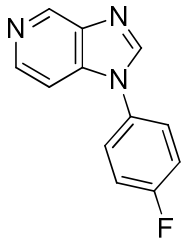
Intermediate 5 was prepared in a manner analogous to Intermediate 1, substituting 2-bromopyrimidine for 2-bromo-5-fluoropyridine. MS (ESI): mass calculated for $C_{10}H_7N_5$, 198.07; m/z found 199.1 $[M+H]^+$.

Intermediate 6: 1-(5-Fluoropyrimidin-2-yl)-1H-imidazo[4,5-c]pyridine.



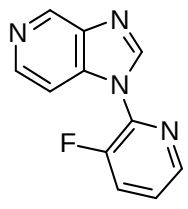
Intermediate 6 was prepared in a manner analogous to Intermediate 1, substituting 2-bromo-5-fluoropyrimidine for 2-bromo-5-fluoropyridine. MS (ESI): mass calculated for $C_{10}H_6FN_5$, 215.06; m/z found 216.1 $[M+H]^+$.

Intermediate 7: 1-(4-Fluorophenyl)-1H-imidazo[4,5-c]pyridine.



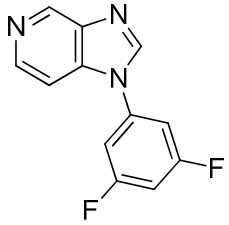
Intermediate 7 was prepared in a manner analogous to Intermediate 1, substituting 1-bromo-4-fluorobenzene for 2-bromo-5-fluoropyridine. MS (ESI): mass calculated for $C_{12}H_8FN_3$, 213.07; m/z found 214.1 $[M+H]^+$.

Intermediate 8: 1-(3-Fluoropyridin-2-yl)-1H-imidazo[4,5-c]pyridine.



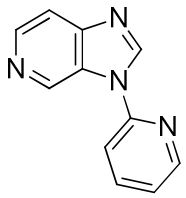
Intermediate 8 was prepared in a manner analogous to Intermediate 1, substituting 2-bromo-3-fluoropyridine for 2-bromo-5-fluoropyridine. MS (ESI): mass calculated for $C_{11}H_7FN_4$, 214.07; m/z found 215.1 $[M+H]^+$.

Intermediate 9: 1-(3,5-Difluorophenyl)-1H-imidazo[4,5-c]pyridine.



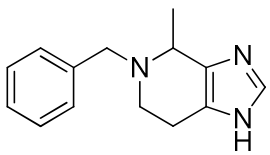
Intermediate 9 was prepared in a manner analogous to Intermediate 1, substituting bromo-3,5-difluorobenzene for 2-bromo-5-fluoropyridine. MS (ESI): mass calculated for $C_{11}H_7FN_3$, 231.06; m/z found 232.1 $[M+H]^+$.

Intermediate 10: 3-(Pyridin-2-yl)-3H-imidazo[4,5-c]pyridine.



Intermediate 10 was prepared in a manner analogous to Intermediate 1, substituting 2-bromopyridine for 2-bromo-5-fluoropyridine. MS (ESI): mass calculated for $C_{11}H_8N_4$, 196.07; m/z found 197.1 $[M+H]^+$.

Intermediate 11: 5-Benzyl-4-methyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine.

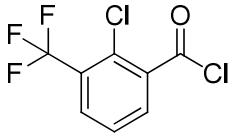


Step A. *N*-Benzyl-2-(1H-imidazol-5-yl)ethanamine. A solution of histamine (free base) (1.00 g, 9.0 mmol) and benzaldehyde (0.91 mL, 9.0 mmol) in MeOH (25 mL) was stirred at rt for 30 min. To this solution was slowly added $NaBH_4$ (0.21 g, 5.4 mmol). The reaction was let stir for 3 h, quenched with a minimal amount of H_2O and concentrated. The residue

was dissolved in EtOH and filtered through Celite©. The solvent was concentrated to give the title product (1.50 g, 83%). MS (ESI): mass calculated for $C_{12}H_{15}N_3$, 201.1; m/z found 202.2 $[M+H]^+$.

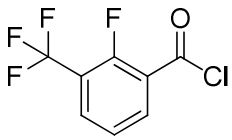
Step B. 5-Benzyl-4-methyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine. A suspension of *N*-benzyl-2-(1H-imidazol-5-yl)ethanamine (0.20 g, 1.0 mmol) in H_2O (5 mL) was cooled in an ice bath. To this suspension was added solid KOH (85%) (0.112 g, 2.0 mmol) followed by acetaldehyde (0.11 mL, 2.0 mmol). The reaction was allowed to warm to rt and heated to 80 °C. After 6 h, the reaction was cooled to rt, acidified using 6N HCl, and concentrated. The resulting residue was dissolved in hot EtOH and filtered through Celite©. The solvent was evaporated to give the title product as the HCl salt. The salt was then treated with 3N NaOH and extracted with EtOAc (50 mL x 3). The organic layers were combined, dried (Na_2SO_4), and concentrated. Chromatography of the resulting residue (SiO_2; MeOH (NH_3):DCM) gave the title compound (0.09 g, 40%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (s, 1H), 7.37 (t, J = 9.2 Hz, 2H), 7.32 (t, J = 7.5 Hz, 2H), 7.28 – 7.23 (m, 1H), 3.94 (d, J = 13.6 Hz, 1H), 3.81 – 3.68 (m, 1H), 3.59 (t, J = 19.1 Hz, 1H), 3.12 – 2.99 (m, 1H), 2.74 – 2.47 (m, 3H), 1.44 (d, J = 6.5 Hz, 3H). MS (ESI): mass calculated for $C_{14}H_{17}N_3$, 227.1; m/z found 228.2 $[M+H]^+$.

Intermediate 12: 2-Chloro-3-(trifluoromethyl)benzoyl chloride.



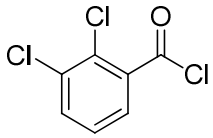
To a suspension of 2-chloro-3-(trifluoromethyl)benzoic acid (15 g, 67 mmol) and catalytic DMF (0.06 mL, 0.67 mmol) in DCM (150 mL) was added oxalyl chloride (6.8 mL, 80 mmol) dropwise. The reaction was let stir (vigorous bubbling) for 4 h and concentrated to an oily solid which became solid after overnight drying on high vacuum.

Intermediate 13: 2-Fluoro-3-(trifluoromethyl)benzoyl chloride.



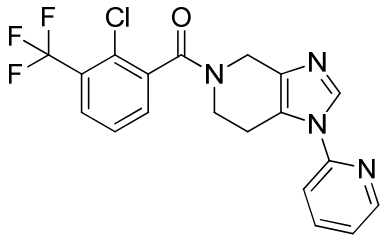
Intermediate 13 was prepared in a similar manner as Intermediate 12 substituting 2-fluoro-3-(trifluoromethyl)benzoic acid for 2-chloro-3-(trifluoromethyl)benzoic acid.

Intermediate 14: 2,3-Dichlorobenzoyl chloride.



Intermediate 14 was prepared in a similar manner as Intermediate 12 substituting 2,3-dichlorobenzoic acid for 2-chloro-3-(trifluoromethyl)benzoic acid.

Example 1. (2-Chloro-3-(trifluoromethyl)phenyl)(1-(pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone.



Step A. 5-Benzyl-1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine.

To a solution of Intermediate 3 (0.20 g, 1.02 mmol) in DCM (25 mL) was added benzyl bromide (0.12 g, 1.02 mmol). The reaction was let stir for 4 h then concentrated. The resulting solid was dissolved in MeOH (10 mL) and $NaBH_4$ (0.05 g, 1.4 mmol) was added slowly. After 5 h, the reaction was quenched with a small amount of water and concentrated. Chromatography of the resulting residue (SiO_2; MeOH (NH_3):DCM) gave the title compound (0.20 mg, 68%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.76 – 8.66 (m, 1H), 8.55 – 8.39 (m, 2H), 8.14 – 8.03 (m, 1H), 7.32 (ddt, J = 22.0, 11.6, 7.5 Hz, 6H), 3.89 (s, 1H), 3.78 (d, J = 5.4 Hz, 2H), 3.63 (s, 1H), 2.99 (t, J = 5.5 Hz, 1H), 2.83 (tt, J = 26.6, 5.6 Hz, 3H). MS (ESI): mass calculated for $C_{18}H_{18}N_4$, 290.2; m/z found 291.2 $[M+H]^+$.

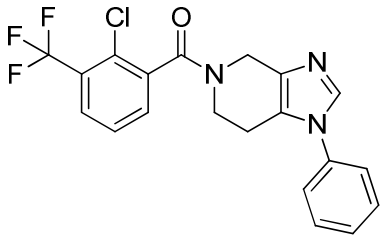
Step B. 1-(Pyridin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine.

To a solution of 5-benzyl-1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine (0.13 g, 0.45 mmol) in DCE (5 mL) was added 1-chloroethyl chloroformate (0.10 mL , 0.90 mmoL). The reaction was allowed to stir for 15 min then heated at reflux for 4 h. The reaction was let cool, concentrated, dissolved in MeOH and heated again at 60 °C for 1 h. The reaction was concentrated and the product was used in the next step without further purification (0.075 g, 83%). MS (ESI): mass calculated for $C_{11}H_{12}N_4$, 200.1; m/z found 201.2 $[M+H]^+$.

Step C. (2-Chloro-3-(trifluoromethyl)phenyl)(1-(pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone.

A solution of 1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine (0.050 g, 0.25 mmol), 2-chloro-3-trifluoromethyl benzoic acid (0.056 g, 0.25 mmol), HATU (0.10 g, 0.26 mmol, and DIPEA (0.09 mL, 0.50 mmol) in DMF (2 mL) was stirred for 30 min. The reaction was diluted with EtOAc (15 mL) and washed with H_2O (3 x 10 mL). The organic layers were combined, dried (Na_2SO_4), and concentrated. Chromatography of the resulting residue (SiO_2; MeOH (NH_3):DCM) gave the title compound (22 mg, 22%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (dd, J = 4.9, 1.8 Hz, 1H), 8.02 (d, J = 18.1 Hz, 1H), 7.92 – 7.71 (m, 2H), 7.58 – 7.40 (m, 2H), 7.37 – 7.28 (m, 2H), 5.12 – 4.78 (m, 1H), 4.51 – 4.19 (m, 2H), 3.97 (ddd, J = 13.4, 12.7, 9.9 Hz, 1H), 3.61 – 3.45 (m, 1H), 3.27 – 2.82 (m, 2H). MS (ESI): mass calculated for $C_{19}H_{14}ClF_3N_4O$, 406.1; m/z found 407.1 $[M+H]^+$.

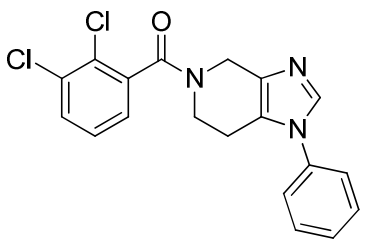
Example 2. (2-Chloro-3-(trifluoromethyl)phenyl)(1-phenyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone.



Example 2 was made in a manner analogous with Example 1 substituting Intermediate 2 for Intermediate 3 in Step A.

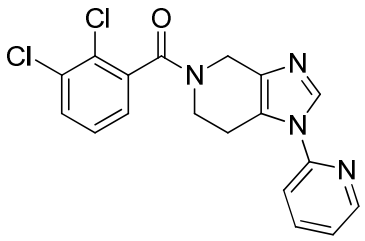
MS (ESI): mass calcd. for $C_{20}H_{15}ClF_3N_3O$, 405.1; m/z found, 406.3 $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.74 (m, 1H), 7.68 (s, 0.4H), 7.60 (s, 0.6H), 7.56 – 7.39 (m, 5H), 7.34 – 7.28 (m, 2H), 4.99 – 4.90 (m, 1H) , 4.45 – 4.27 (m, 2H), 3.93 (ddd, J = 12.8, 7.2, 5.2 Hz, 1H), 3.60 – 3.45 (m, 1H), 2.76-2.55 (m, 1H).

Example 3. (2,3-Dichlorophenyl)(1-phenyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone.



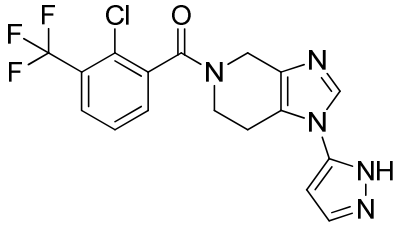
Example 3 was made in a manner analogous with Example 1 substituting 2,3-dichlorobenzoic acid for 2-chloro-3-trifluoromethyl benzoic acid in Step C and substituting Intermediate 2 for Intermediate 3 in Step A.
MS (ESI): mass calcd. for $C_{19}H_{15}Cl_2N_3O$, 371.1; m/z found, 372.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 (s, 0.4H), 7.60 (s, 0.6H), 7.56 – 7.39 (m, 4H), 7.33 – 7.20 (m, 4H), 4.96 – 4.90 (m, 1H) , 4.46 – 4.20 (m, 2H), 4.03 – 3.92 (m, 1H), 3.60 – 3.43 (m, 1H), 2.67 (ddd, J = 20.9, 15.5, 6.8 Hz, 1H).

Example 4. (2,3-Dichlorophenyl)(1-(pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone.



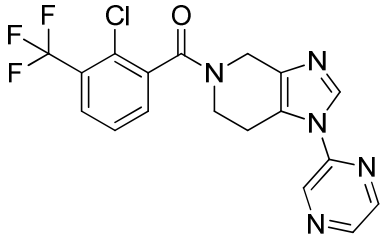
Example 4 was made in a manner analogous with Example 1 substituting 2,3-dichlorobenzoic acid for 2-chloro-3-trifluoromethyl benzoic acid in Step C. MS (ESI): mass calculated for $C_{18}H_{14}Cl_2N_4O$, 406.1; m/z found 407.1 [M+H]+.

Example 5. (1-(1H-Pyrazol-5-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-chloro-3-(trifluoromethyl)phenyl)methanone.



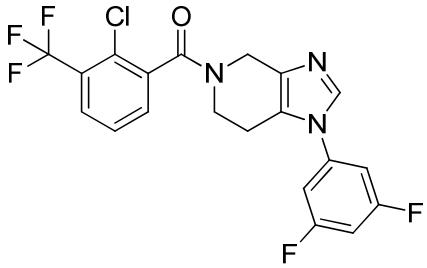
Example 5 was made in a manner analogous to Example 1 substituting 1-(1*H*-pyrazol-5-yl)-1*H*-imidazo[4,5-c]pyridine for Intermediate 3 in Example 1 Step A.
MS (ESI): mass calcd. for $C_{17}H_{13}ClF_3N_5O$, 395.0; m/z found, 396.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 11.98 – 11.66 (m, 1H), 7.91 (s, 1H), 7.81 (s, 1H), 7.76 (ddd, J = 7.8, 3.8, 1.7 Hz, 1H), 7.62 – 7.55 (m, 1H), 7.55 – 7.41 (m, 3H), 6.28 (dd, J = 9.6, 2.5 Hz, 1H), 5.09 – 4.78 (m, 1H), 4.46 – 4.24 (m, 2H), 4.03 (ddd, J = 12.7, 6.9, 5.3 Hz, 1H), 3.62 – 3.50 (m, 1H), 3.17 – 3.02 (m, 2H), 2.98 – 2.76 (m, 1H).

Example 6. (2-Chloro-3-(trifluoromethyl)phenyl)(1-(pyrazin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone.



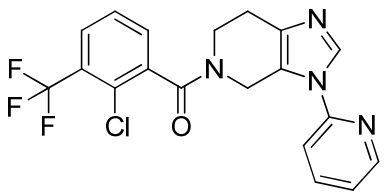
Example 6 was made in a manner analogous to Example 1 substituting Intermediate 4 for Intermediate 3 in Step A. MS (ESI): mass calcd. for $C_{18}H_{13}ClF_3N_5O$, 407.1; m/z found, 408.2 $[M+H]^+$.

Example 7. (2-Chloro-3-(trifluoromethyl)phenyl)(1-(3,5-difluorophenyl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone.



Example 7 was made in a manner analogous to Example 1 substituting Intermediate 9 for Intermediate 3 in Step A. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 – 7.75 (m, 1H), 7.52 – 7.46 (m, 4H), 6.96 – 6.90 (m, 2H), 4.885.07 – 4.71 (m, 3H), 3.58 3.59 – 3.57(m, 3H). MS (ESI): mass calculated for $C_{20}H_{13}ClF_5N_3O$, 441.07; m/z found 442.2 [M+H]+.

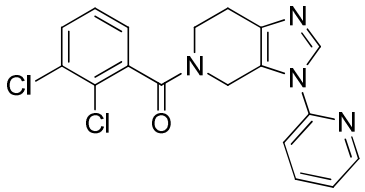
Example 8. (2-Chloro-3-(trifluoromethyl)phenyl)(3-(pyridin-2-yl)-6,7-dihydro-3H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone.



Example 8 was made in a manner analogous to Example 1 substituting Intermediate 10 for Intermediate 3 in Step A. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.54 (dd, J = 4.8, 1.0 Hz, 1H),

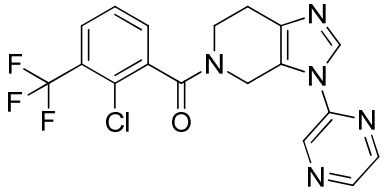
8.04 – 7.74 (m, 3H), 7.53 – 7.26 (m, 4H), 5.53 – 5.01 (m, 2H), 3.67 – 3.48 (m, 2H), 3.00 – 2.61 (m, 2H). MS (ESI): mass calculated for $C_{19}H_{14}ClF_3N_4O$, 406.08; m/z found 407.1 [M+H]+.

Example 9. (2,3-Dichlorophenyl)(3-(pyridin-2-yl)-6,7-dihydro-3H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone.



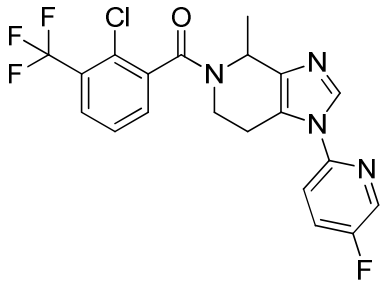
Example 9 was made in a manner analogous to Example 1 substituting 2,3-dichlorobenzoic acid for 2-chloro-3-trifluoromethyl benzoic acid in Step C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.59 – 8.49 (m, 1H), 8.05 – 7.84 (m, 2H), 7.57 – 7.18 (m, 5H), 5.41 – 5.05 (m, 2H), 3.67 – 3.53 (m, 2H), 2.99 – 2.64 (m, 2H). MS (ESI): mass calculated for $C_{18}H_{14}Cl_2N_4O$, 372.05; m/z found 373.1 [M+H]+.

Example 10. (2-Chloro-3-(trifluoromethyl)phenyl)(3-(pyrazin-2-yl)-6,7-dihydro-3H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone.



Example 10 was made in a manner analogous to Example 1 substituting Intermediate 10 for Intermediate 3 in Step A.
MS (ESI): mass calcd. for $C_{18}H_{13}ClF_3N_5O$, 407.1; m/z found, 408.2 $[M+H]^+$.

Example 11. (2-Chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone.



Step A. (2-Chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone.

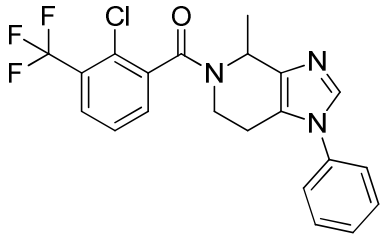
To a solution of Intermediate 1 (0.70 g, 3.27 mmol) in THF (20 mL) was added Intermediate 12 (0.87 g, 3.60 mmol) dropwise. The reaction was allowed to stir for 1 h then cooled to – 78 °C. To the cooled solution was added 3M MeMgBr in Et_2O (1.31 mL, 3.92 mmoL) and the reaction was let come to room temperature. The mixture was then quenched with 1N NaOH (50 mL) and extracted with EtOAc (3 x 30 mL). The organic layers were combined, dried (Na_2SO_4), and concentrated. Chromatography of the resulting residue (SiO_2; MeOH (NH_3):DCM) gave the title compound (770 mg, 54%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 – 8.34 (m, 1H), 7.92 – 7.73 (m, 2H), 7.70 – 7.33 (m, 4H), 6.08 (dtd, J = 19.7, 11.7, 8.0 Hz, 3H), 1.54 (t, J = 7.0 Hz, 3H). MS (ESI): mass calculated for $C_{20}H_{13}ClF_4N_4O$, 436.07; m/z found 437.1 $[M+H]^+$.

Step B. (2-Chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone.

To a solution of (2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone (0.80 g, 1.83 mmol) in degassed EtOH (25 mL) was added 10% palladium on carbon (0.20 g, 0.19 mmol). The reaction was placed under an atmosphere of hydrogen and let stir for 48 h. The reaction was diluted with DCM and filtered through a pad of Celite ©. The solvent was concentrated and chromatography of the resulting residue (SiO_2; MeOH (NH_3):DCM) gave the title compound (500 mg, 62%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.45 – 8.30 (m, 1H), 7.94 (dd, J = 18.2, 10.7 Hz, 1H), 7.76 (d, J = 5.7 Hz, 1H), 7.67 – 7.43 (m, 3H), 7.43 – 7.30 (m, 1H), 5.81 (dd, J = 13.3, 6.7 Hz, 1H), 5.07 (d, J = 5.6 Hz, 1H), 4.52 (d, J = 6.7 Hz, 1H), 3.61 – 3.31 (m, 1H), 3.08 – 2.69 (m, 1H), 1.63 - 145 (m, 3H). MS (ESI): mass calculated for $C_{20}H_{15}ClF_4N_4O$, 438.08; m/z found 439.1 $[M+H]^+$.

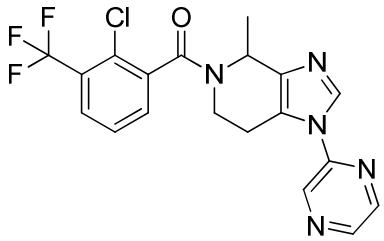
Example 12. (2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-phenyl-6,7-dihydro-1H-

imidazo[4,5-c]pyridin-5(4H)-yl)methanone.



Example 12 was prepared in an analogous way as Example 11 substituting Intermediate 2 for Intermediate 1 in Step A. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (dd, J = 5.1, 2.0 Hz, 1H), 7.65 (d, J = 15.1 Hz, 1H), 7.59 – 7.39 (m, 5H), 7.35 – 7.28 (m, 2H), 5.83 (dd, J = 13.5, 6.7 Hz, 1H), 5.07 (dd, J = 12.3, 10.6 Hz, 1H), 4.19 – 3.99 (m, 1H), 3.61 – 2.93 (m, 1H), 2.75 – 2.35 (m, 1H), 1.99 – 1.90 (m , 3H). MS (ESI): mass calculated for $C_{21}H_{17}ClF_3N_3O$, 419.08; m/z found 420.1 $[M+H]^+$.

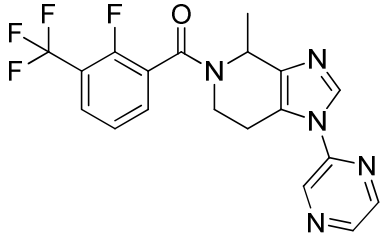
Example 13. (2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-phenyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone.



Example 13 was prepared in an analogous way as Example 11 substituting Intermediate 4 for Intermediate 1 in Step A.

MS (ESI): mass calcd. for $C_{19}H_{15}ClF_3N_5O$, 421.1; m/z found, 422.1 $[M+H]^+$.

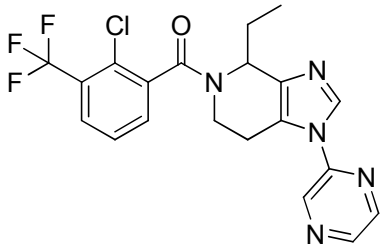
Example 14. (2-Fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone.



Example 14 was prepared in an analogous way as Example 11 substituting Intermediate 13 for Intermediate 12 in Step A. MS (ESI): mass calculated for $C_{19}H_{15}F_4N_5O$, 405.12; m/z

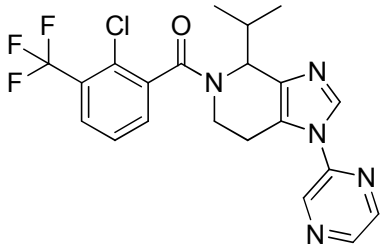
found 406.1 $[M+H]^+$.

Example 15. (2-Chloro-3-(trifluoromethyl)phenyl)(4-ethyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone.



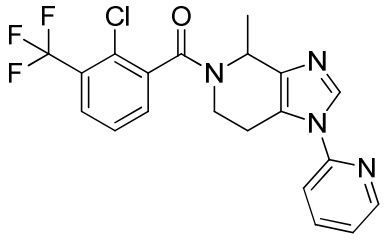
Example 15 was prepared in an analogous way as Example 11 substituting EtMgBr for MeMgBr and substituting Intermediate 4 for Intermediate 1 in Step A. MS (ESI): mass calculated for $C_{20}H_{17}ClF_3N_5O$, 435.11; m/z found 436.1 $[M+H]^+$.

Example 16. (2-Chloro-3-(trifluoromethyl)phenyl)(4-isopropyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone.



Example 16 was prepared in an analogous way as Example 11 substituting *i*PrMgBr for MeMgBr and Intermediate 14 for Intermediate 1 in Step A. MS (ESI): mass calculated for $C_{21}H_{19}ClF_3N_5O$, 449.11; m/z found 450.1 $[M+H]^+$.

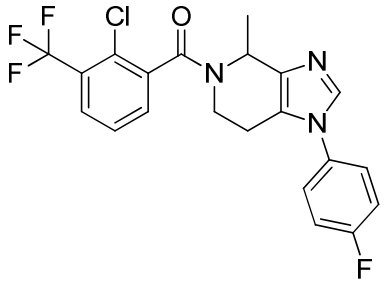
Example 17. (2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone.



Example 17 was prepared in an analogous way as Example 11 substituting Intermediate 3 for Intermediate 1 in Step A. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.58 – 8.44 (m, 1H), 7.99 (dt, J = 10.8, 8.7 Hz, 1H), 7.93 – 7.80 (m, 1H), 7.80 – 7.72 (m, 1H), 7.59 – 7.43 (m, 2H), 7.41 –

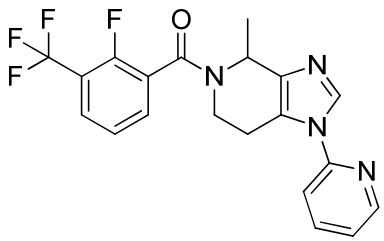
7.24 (m, 2H), 5.91 – 5.72 (m, 1H), 5.20 – 4.58 (m, 1H), 3.63 – 3.29 (m, 1H), 3.29 – 2.76 (m, 2H), 1.74 – 1.60 (m, 3H). MS (ESI): mass calculated for $C_{20}H_{16}ClF_3N_4O$, 420.1; m/z found 421.1 $[M+H]^+$.

Example 18. (2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-fluorophenyl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone.



Example 18 was prepared in an analogous way as Example 11 substituting Intermediate 7 for Intermediate 1 in Step A. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 – 7.73 (m, 1H), 7.62 (d, J = 1.3 Hz, 1H), 7.58 – 7.35 (m, 2H), 7.33 – 7.25 (m, 2H), 7.25 – 7.15 (m, 2H), 5.94 – 5.47 (m, 1H), 5.07 – 4.59 (m, 1H), 4.10 – 3.73 (m, 1H), 3.59 – 2.81 (m, 1H), 2.74 – 2.23 (m, 1H), 1.69 – 1.50 (m, 3H). MS (ESI): mass calculated for $C_{21}H_{16}ClF_4N_3O$, 437.1; m/z found 438.1 $[M+H]^+$.

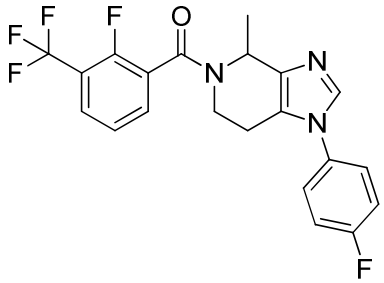
Example 19. (2-Fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone.



Example 19 was prepared in an analogous way as Example 11 substituting Intermediate 3 for Intermediate 1 and Intermediate 13 for Intermediate 12 in Step A. ^{1}H NMR (500 MH, $CDCl_3$) δ 8.53 (dd, J = 12.7, 11.7 Hz, 1H), 8.03 – 7.99 (m, 1H) , 7.92 – 7.80 (m, 1H), 7.70 – 7.60 (m, 2H), 7.40 – 7.27 (m, 3H), 5.78 (s, 1H), 5.10 – 4.56 (m, 1H), 3.75 – 3.31 (m, 1H), 3.31 – 2.76 (m, 2H), 1.83 – 1.38 (m, 3H). MS (ESI): mass calculated for $C_{20}H_{16}F_4N_4O$, 404.13; m/z found 405.2 $[M+H]^+$.

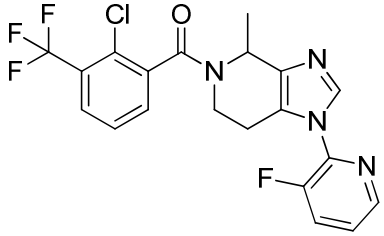
Example 20. (2-Fluoro-3-(trifluoromethyl)phenyl)(1-(4-fluorophenyl)-4-methyl-6,7-

dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone.



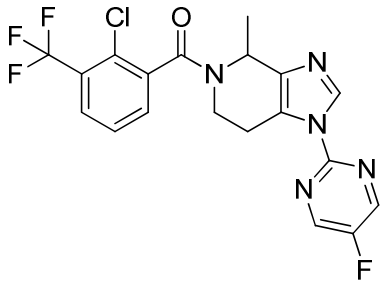
Example 20 was prepared in manner analogous to that described in Example 11 substituting Intermediate 7 for Intermediate 1 and Intermediate 13 for Intermediate 12 in Step A. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 – 7.66 (m, 1H) , 7.60 – 7.55 (m, 2H), 7.39 – 7.25 (m, 3H), 7.25 – 7.14 (m, 2H), 5.73 (br s, 1H), 5.16 – 4.53 (m, 1H), 3.48 (d, J = 7.7 Hz, 1H), 2.99 – 2.89 (m, 1H), 2.67 – 2.09 (m, 1H), 1.65 – 1.50 (m, 3H). MS (ESI): mass calculated for $C_{21}H_{16}F_5N_3O$, 421.12; m/z found 422.2 $[M+H]^+$.

Example 21. (2-Chloro-3-(trifluoromethyl)phenyl)(1-(3-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone.



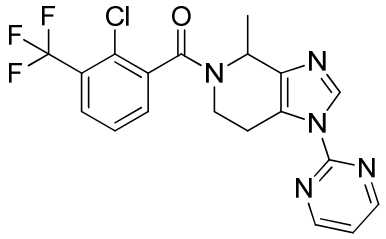
Example 21 was prepared in a manner analogous to that as described for Example 11 substituting Intermediate 8 for Intermediate 1 in Step A. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.43 – 8.28 (m, 1H), 7.96 – 7.92 (m, 1H) , 7.81 – 7.61 (m, 2H), 7.59 – 7.29 (m, 3H), 5.82 (dt, J = 12.9, 6.5 Hz, 1H), 5.06 (dd, J = 13.5, 6.7 Hz, 1H), 4.76 – 4.37 (m, 1H), 3.63 – 2.62 (m, 2H), 1.86 – 1.55 (m, 3H). MS (ESI): mass calculated for $C_{20}H_{15}ClF_4N_4O$, 438.09; m/z found 439.2 $[M+H]^+$.

Example 22. (2-Chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone.



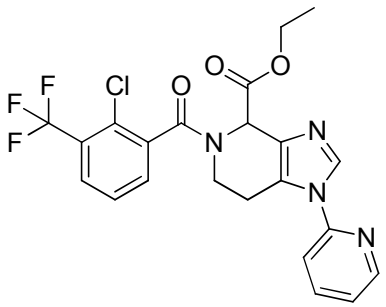
Example 22 was prepared in manner analogous to that described in Example 11 substituting Intermediate 6 for Intermediate 1 in Step A. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.61 – 8.38 (m, 3H), 7.82 – 7.70 (m, 1H), 7.58 – 7.32 (m, 2H), 5.90 – 5.60 (m, 1H), 5.19 – 4.54 (m, 1H), 3.66 – 2.82 (m, 3H), 1.81 – 1.29 (m, 3H). MS (ESI): mass calculated for $C_{19}H_{14}ClF_4N_5O$, 439.12; m/z found 440.2 $[M+H]^+$.

Example 23. (2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrimidin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone.



Example 23 was prepared in manner analogous to that described in Example 11 substituting Intermediate 5 for Intermediate 1 in Step A. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.75 – 8.49 (m, 3H), 7.76 (dt, J = 9.6, 4.8 Hz, 1H), 7.59 – 7.42 (m, 2H), 7.21 (ddd, J = 17.7, 8.0, 4.8 Hz, 1H), 5.91 – 5.67 (m, 1H), 5.16 – 4.55 (m, 1H), 3.60 – 2.87 (m, 3H), 1.72 – 1.56 (m, 3H). MS (ESI): mass calculated for $C_{19}H_{15}ClF_3N_5O$, 421.09; m/z found 422.2 $[M+H]^+$.

Example 24. Ethyl 5-(2-chloro-3-(trifluoromethyl)benzoyl)-1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxylate.



Step A. 5-*tert*-Butyl 4-ethyl 6,7-dihydro-1H-imidazo[4,5-c]pyridine-4,5(4H)-dicarboxylate. To a solution of ethyl 4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxylate dihydrochloride. (1.00 g, 3.73 mmol) and Et_3N (1.04 mL, 7.46 mmol) in DCM (100 mL) was added di-*tert*-butyl dicarbonate (0.90 g, 4.11 mmol). The reaction was let stir for 4 h and concentrated. Chromatography of the resulting residue (SiO_2; MeOH (NH_3):DCM) gave the title compound (0.80 mg, 72%). MS (ESI): mass calculated for $C_{14}H_{21}N_3O_4$, 295.2; m/z found 296.2 $[M+H]^+$.

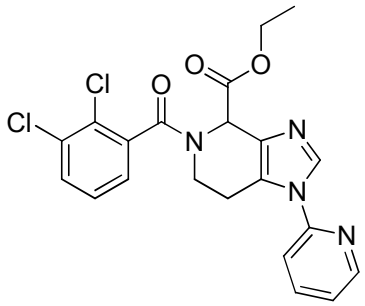
Step B. 5-*tert*-Butyl 4-ethyl 1-(pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridine-4,5(4H)-dicarboxylate. A solution of 5-tert-butyl 4-ethyl 6,7-dihydro-1H-imidazo[4,5-c]pyridine-4,5(4H)-dicarboxylate (0.50 g, 1.69 mmol), 2-bromo-pyridine (0.27 g, 1.69 mmol), copper (I) oxide (0.03 g, 0.17 mmol), 8-hydroxyquinoline (0.05 g, 0.34 mmol), and Cs_2CO_3 (1.10 g, 3.39 mmol) in DMSO (2 mL) was irradiated in a microwave apparatus for 1 hour at 140 °C. The reaction was diluted with H_2O (100 mL) and extracted with EtOAc (75 mL x 3). The organic layers were combined, dried (Na_2SO_4), and concentrated. Chromatography of the resulting residue (SiO_2; MeOH (NH_3):DCM) gave the title compound (0.25 g, 40%). MS (ESI): mass calculated for $C_{19}H_{24}N_4O_4$, 372.2; m/z found 273.2 $[M+H\text{-}BOC]^+$.

Step C. Ethyl 1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxylate. To a solution of 5-*tert*-butyl 4-ethyl 1-(pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridine-4,5(4H)-dicarboxylate (0.20 g, 0.54 mmol) in DCM (25 mL) was added 1N HCl in ether (1.08 mL, 1.08 mmol). The reaction was let stir for 14 h and concentrated to give the desired product as the HCl salt (0.12 g, 72%). MS (ESI): mass calculated for $C_{14}H_{16}N_4O_2$, 272.1; m/z found 273.2 $[M+H]^+$.

Step D. Ethyl 5-(2-chloro-3-(trifluoromethyl)benzoyl)-1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxylate. A mixture of ethyl 1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxylate hydrochloride (0.050 g, 0.18 mmol), 2-chloro-3-trifluoromethyl benzoic acid (0.045 g, 0.20 mmol), HATU (0.077 g, 0.20 mmol), and DIPEA (0.035 mL, 0.20 mmol) in DMF (2 mL) was stirred for 30 min. The reaction was diluted with EtOAc (15 mL) and washed with H_2O (3 x 10 mL). The organic layers were combined, dried (Na_2SO_4), and concentrated. Chromatography of the resulting residue (SiO_2; MeOH (NH_3):DCM) gave the title compound (26 mg, 30%). ^1H NMR (500

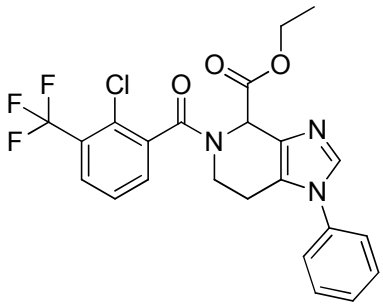
MHz, $CDCl_3$) δ 8.58 – 8.45 (m, 1H), 8.10 – 7.98 (m, 1H), 7.94 – 7.82 (m, 1H), 7.82 – 7.72 (m, 1H), 7.63 (dd, J = 7.6, 1.3 Hz, 1H), 7.55 – 7.28 (m, 3H), 6.23 (dd, J = 12.3, 6.3 Hz, 1H), 5.25 – 5.00 (m, 1H), 4.48 – 4.06 (m, 2H), 4.01 – 3.60 (m, 3H), 3.50 – 2.85 (m, 3H). MS (ESI): mass calculated for $C_{22}H_{18}ClF_3N_4O_3$, 478.1; m/z found 479.2 $[M+H]^+$.

Example 25. Ethyl 5-(2,3-dichlorobenzoyl)-1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxylate.



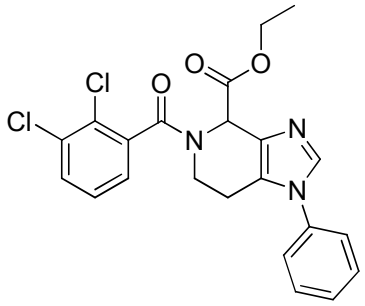
Example 25 was prepared in manner analogous to that described in Example 24 substituting 2,3-dichlorobenzoic acid for 2-chloro-3-trifluoromethyl benzoic acid in Step D. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.58 – 8.46 (m, 1H), 8.03 – 7.82 (m, 3H), 7.61 – 7.43 (m, 1H), 7.43 – 7.18 (m, 3H), 6.24 – 6.12 (m, 1H), 5.23 – 4.99 (m, 1H), 4.44 – 4.03 (m, 1H), 4.00 – 3.67 (m, 2H), 3.51 – 3.00 (m, 2H) 1.35 – 1.25 (m, 3H). MS (ESI): mass calculated for $C_{21}H_{18}Cl_2N_4O$, 444.1; m/z found 445.2 $[M+H]^+$.

Example 26. Ethyl 5-(2-chloro-3-(trifluoromethyl)benzoyl)-1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxylate.



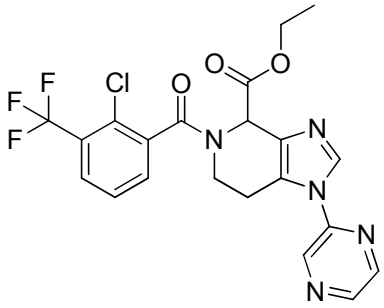
Example 26 was prepared in manner analogous to that described in Example 24 substituting bromobenzene for 2-bromo-pyridine in Step B. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (t, J = 7.4 Hz, 1H), 7.70 (s, 1H), 7.62 (dd, J = 11.1, 3.1 Hz, 1H), 7.57 – 7.38 (m, 4H), 7.37 – 7.27 (m, 2H), 6.23 (s, 1H), 5.26 – 4.97 (m, 1H), 4.50 – 3.38 (m, 2H), 3.10 – 2.90 (m, 1H), 2.77 – 2.42 (m, 2H), 1.38 (ddd, J = 18.6, 13.6, 6.4 Hz, 3H). MS (ESI): mass calculated for $C_{23}H_{19}ClF_3N_3O_3$, 477.1; m/z found 478.2 $[M+H]^+$.

Example 27. Ethyl 5-(2,3-dichlorobenzoyl)-1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxylate.



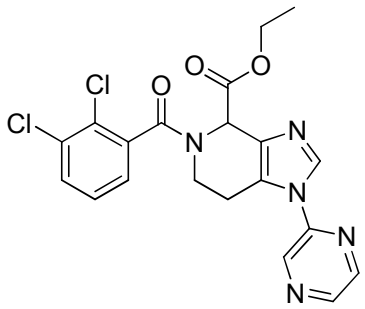
Example 27 was prepared in manner analogous to that described in Example 24 substituting bromobenzene for 2-bromo-pyridine in Step B and 2,3-dichlorobenzoic acid for 2-chloro-3-trifluoromethylbenzoic acid in Step D. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 – 7.63 (m, 1H) , 7.56 – 7.38 (m, 4H), 7.38 – 7.24 (m, 4H), 5.37 – 4.99 (m, 1H), 4.47 – 3.60 (m, 3H), 3.07 – 2.41 (m, 2H), 2.11 – 1.13 (m, 4H).MS (ESI): mass calculated for $C_{22}H_{19}Cl_2N_3O_3$, 443.1; m/z found 444.1 $[M+H]^+$.

Example 28: Ethyl 5-{[2-chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxylate.



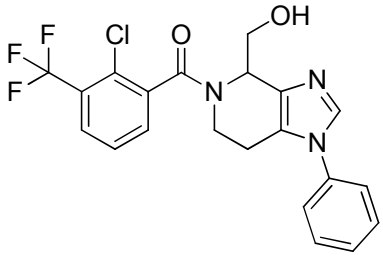
Example 28 was prepared in manner analogous to that described in Example 24 substituting 2-bromopyrazine for 2-bromo-pyridine in Step B. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.83 – 8.42 (m, 2H), 8.24 – 8.00 (m, 1H), 7.84 – 7.36 (m, 3H), 6.49 – 6.17 (m, 1H), 4.48 – 3.47 (m, 4H), 3.52 – 2.66 (m, 2H), 1.86 – 1.13 (m, 4H). MS (ESI): mass calculated for $C_{21}H_{17}ClF_3N_5O_3$, 479.1; m/z found 480.1 $[M+H]^+$.

Example 29. Ethyl 5-[(2,3-dichlorophenyl)carbonyl]-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxylate.



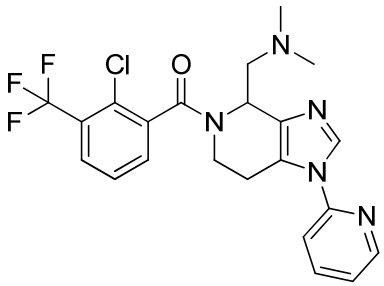
Example 29 was prepared in manner analogous to that described in Example 24 substituting 2-bromopyrazine for 2-bromo-pyridine in Step B and 2,3-dichlorobenzoic acid for 2-chloro-3-trifluoromethylbenzoic acid in Step D. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.84 – 8.42 (m, 2H), 8.18 – 8.02 (m, 1H), 7.84 – 7.39 (m, 3H), 6.44 – 6.16 (m, 1H), 4.51 – 3.60 (m, 4H), 3.55 – 2.69 (m, 2H), 1.89 – 1.18 (m, 4H). MS (ESI): mass calculated for $C_{20}H_{17}Cl_2N_5O_3$, 445.1; m/z found 446.1 $[M+H]^+$.

Example 30. (5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-4-yl)methanol.



To a solution of Example 26 (0.10 g, 0.21 mmol) in THF (10 mL) at -78 °C was added lithium borohydride (0.02 g, 1.08 mmol). After 14 h the reaction was quenched with 1 N NaOH and extracted with DCM (3 x 25 mL). The organic layers were combined, dried (Na_2SO_4), and concentrated. Chromatography of the resulting residue (SiO_2; MeOH (NH_3):DCM) gave the title compound (0.07 g, 76%). MS (ESI): mass calculated for $C_{21}H_{17}ClF_3N_3O_2$, 435.1; m/z found 436.1 $[M+H]^+$.

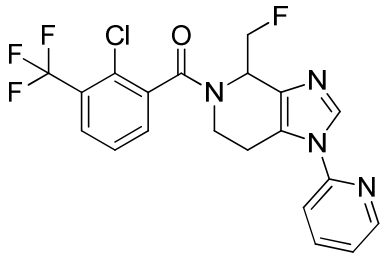
Example 31. 1-(5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-4-yl)-N,N-dimethylmethanamine.



Step A. (5-(2-chloro-3-(trifluoromethyl)benzoyl)-1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-4-yl)methyl sulfochloridate. A solution of (2-chloro-3-(trifluoromethyl)phenyl)(4-(hydroxymethyl)-1-(pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone- 0.10 g, 0.23 mmol), methane sulfonyl chloride (0.27 mg, 0.23 mmol), and Et_3N (0.32 mL, 0.23 mmol) in DCM (10 mL) was stirred for 1 h. The reaction was diluted with H_2O and extracted with DCM (3 x 10 mL). The organic layers were combined, dried (Na_2SO_4), and concentrated. Chromatography of the resulting residue (SiO_2; MeOH (NH_3):DCM) gave the title compound (0.04 g, 30%). MS (ESI): mass calculated for $C_{21}H_{18}ClF_3N_4O_4S$, 514.1; m/z found 515.1 $[M+H]^+$.

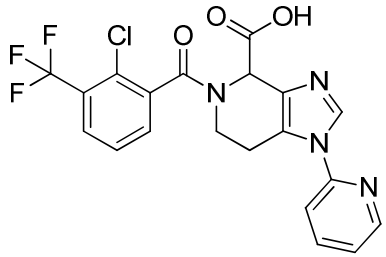
Step B. 1-(5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-4-yl)-N,N-dimethylmethanamine. A solution of (5-(2-chloro-3-(trifluoromethyl)benzoyl)-1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-4-yl)methyl sulfochloridate (0.05 g, 0.097 mmol), dimethylamine hydrochloride (0.016 g, 0.19 mmol), and Na_2CO_3 (0.021 g, 0.19 mmol) in CH_3CN was irradiated in a microwave at 100 °C for 1 h. The reaction was allowed to cool and concentrated. Chromatography of the resulting residue (SiO_2; MeOH (NH_3):DCM) gave the title compound (0.02 g, 44%). ^1H NMR (500 MHz, $CDCl_3$) δ 8.54 – 8.51 (m, 1H) , 8.10 – 7.62 (m, 4H), 7.58 – 7.28 (m, 3H), 5.30 (s, 1H), 4.00 – 3.42 (m, 2H), 3.35 – 2.77 (m, 2H), 2.77 – 2.40 (m, 2H), 2.09 -2.03 (m, 6 H). MS (ESI): mass calculated for $C_{22}H_{21}ClF_3N_5O$, 463.1; m/z found, m/z found 464.2 $[M+H]^+$.

Example 32. (2-Chloro-3-(trifluoromethyl)phenyl)(4-(fluoromethyl)-1-(pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone.



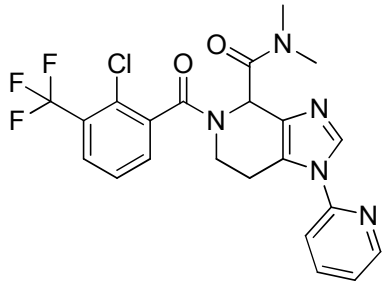
MS (ESI): mass calculated for $C_{20}H_{15}ClF_4N_4O$, 438.09; m/z found 439.1 $[M+H]^+$.

Example 33. 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxylic acid.



A solution of Example 24 (0.10 g, 0.21 mmol) and KOH (0.012 g, 0.21 mmol) in EtOH (5 mL) was heated at 80 °C. After 4 h, the reaction was concentrated to give the title product as the potassium salt (0.07g, 70%). MS (ESI): mass calculated for $C_{20}H_{14}ClF_3N_4O_3$, 450.07; m/z found, 451.1 $[M+H]^+$.

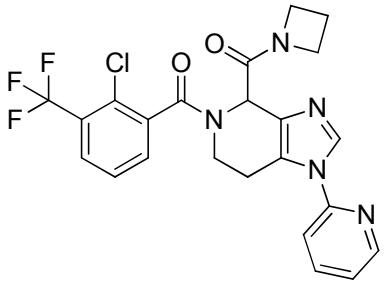
Example 34. 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-N,N-dimethyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxamide.



A solution of 5-{[2-chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxylic acid (0.05 g, 0.10 mmol), dimethylamine hydrochloride (0.01 g, 0.10 mmol), HATU (0.04 g, 0.11 mmol), and DIPEA (0.05 mL, 0.26 mmol) in DMF (2 mL) was stirred for 30 min. The reaction was diluted with EtOAc (15 mL) and washed with H_2O (3 x 10 mL). The organic layers were combined, dried (Na_2SO_4), and concentrated. Chromatography of the resulting residue (SiO_2; MeOH (NH_3):DCM) gave the title compound (26 mg, 53%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60 – 8.35 (m, 1H), 8.09 – 7.69 (m, 3H), 7.65 – 7.27 (m, 4H), 6.64 – 6.46 (m, 1H), 4.17 (tt, J = 19.0, 5.6 Hz, 1H), 3.72 – 3.53 (m, 3H), 3.33 – 2.85 (m, 6H). MS (ESI): mass calculated for $C_{22}H_{19}ClF_3N_5O_2$, 477.12; m/z found, 478.1 $[M+H]^+$.

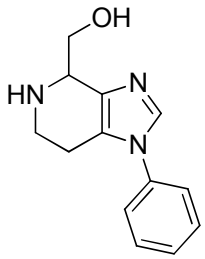
Example 35. 4-(Azetidin-1-ylcarbonyl)-5-{[2-chloro-3-(trifluoromethyl)phenyl]carbonyl}-

1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine.



Example 35 was prepared in a manner analogous to Example 34 substituting azetidine hydrochloride for dimethylamine hydrochloride. MS (ESI): mass calculated for $C_{23}H_{19}ClF_3N_5O_2$, 489.118; m/z found, 490. 2 $[M+H]^+$.

Intermediate 233. (1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-4-yl)methanol.



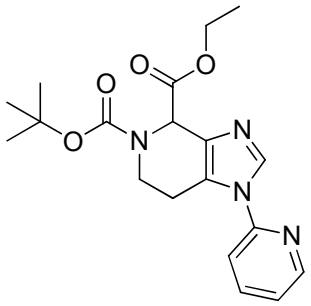
Step A. 5-*tert*-butyl 4-ethyl 1-phenyl-6,7-dihydro-1H-imidazo[4,5-c]pyridine-4,5(4H)-dicarboxylate. A solution of 5-tert-butyl 4-ethyl 6,7-dihydro-1H-imidazo[4,5-c]pyridine-4,5(4H)-dicarboxylate (0.65 g, 2.20 mmol), iodobenzene (0.45 g, 2.20 mmol), copper (I) oxide (0.03 g, 0.22 mmol), 8-hydroxyquinoline (0.06 g, 0.44 mmol), and Cs_2CO_3 (1.40 g, 4.40 mmol) in DMSO (2 mL) was irradiated in a microwave apparatus for 1 hour at 140 °C. The reaction was diluted with H_2O (100 mL) and extracted with EtOAc (75 mL x 3). The organic layers were combined, dried (Na_2SO_4), and concentrated. Chromatography of the resulting residue (SiO_2; MeOH (NH_3):DCM) gave the title compound (0.41 g, 50%). MS (ESI): mass calculated for $C_{20}H_{25}N_3O_4$, 371.2; m/z found 272.2 $[M+H\text{-}BOC]^+$.

Step B. ethyl 1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxylate. To a solution of 5-*tert*-butyl 4-ethyl 1-phenyl-6,7-dihydro-1H-imidazo[4,5-c]pyridine-4,5(4H)-dicarboxylate (0.40 g, 1.07 mmol) in DCM (25 mL) was added 1N HCl in ether (1.2 mL, 1.20 mmol). The reaction was allowed to stir for 14 h and concentrated to give the desired product as the HCl salt (0.320 g, 96%). MS (ESI): mass calculated for $C_{15}H_{17}N_3O_2$, 271.13; m/z found 272.2 $[M+H]^+$.

Step C. (1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-4-yl)methanol. To a solution of ethyl 1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-4-carboxylate

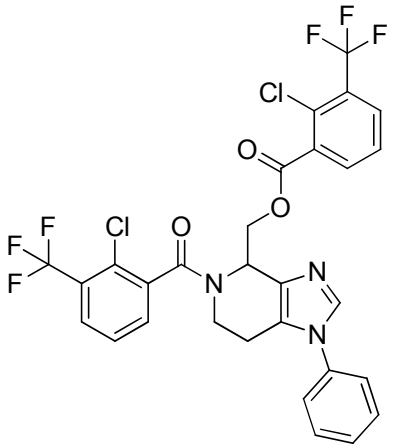
(0.10 g, 0.37 mmol) in THF (10 mL) at -78 °C was added $LiAlH_4$ (1M in THF) (1.1 mL, 1.10 mmol). After 14 h the reaction was quenched with 1 N NaOH, Rochelle's salt, and extracted with DCM (3 x 25 mL). The organic layers were combined, dried (Na_2SO_4), and concentrated. Chromatography of the resulting residue (SiO_2; MeOH (NH_3):DCM) gave the title compound (0.06 g, 71%). MS (ESI): mass calculated for $C_{13}H_{15}N_3O$, 229.12; m/z found 230.1 $[M+H]^+$.

Intermediate 504. 5-tert-butyl 4-ethyl 1-(pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridine-4,5(4H)-dicarboxylate.



Intermediate 504 was prepared in a similar manner as Intermediate 233 substituting 2-bromopyridine in Step A. MS (ESI): mass calculated for $C_{19}H_{24}N_4O_4$, 372.18; m/z found 373.2 $[M+H]^+$.

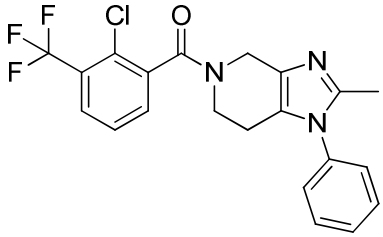
Example 36. (5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-4-yl)methyl 2-chloro-3-(trifluoromethyl)benzoate.



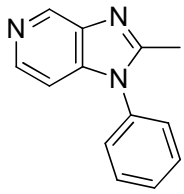
A solution of Intermediate 233. (0.050 g, 0.22 mmol), 2-chloro-3-trifluoromethyl benzoic acid (0.054 g, 0.24 mmol), HATU (0.091 g, 0.24 mmol), and DIPEA (0.04 mL, 0.24 mmol) in DMF (2 mL) was stirred for 30 min. The reaction was diluted with EtOAc (15 mL) and

washed with H_2O (3 x 10 mL). The organic layers were combined, dried (Na_2SO_4), and concentrated. Chromatography of the resulting residue (SiO_2; MeOH (NH_3):DCM) gave the title compound (30 mg, 21%). MS (ESI): mass calculated for $C_{29}H_{19}Cl_2F_6N_3O_3$, 641.07; m/z found, 642.1 $[M+H]^+$.

Example 37. (2-Chloro-3-(trifluoromethyl)phenyl)(2-methyl-1-phenyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone.

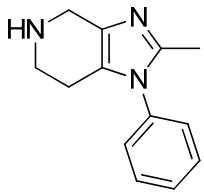


Step 1: 2-methyl-1-phenyl-1H-imidazo[4,5-c]pyridine



To a solution of N_4-phenylpyridine-3,4-diamine (8.08 g, 43.7 mmol) and p-toluenesulfonic acid (0.379 g, 2.2 mmol) was added trimethyl orthoformate (83 mL, 655 mmol). The solution was heated to 80 °C for 4h after which time it was cooled to rt and concentrated. Flash chromatography (1:1 petroleum ether: ethyl acetate) provided the product as a pale yellow solid (4.7 g, 75%).

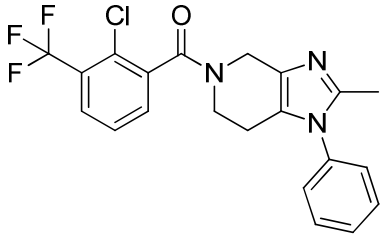
Step 2: 2-methyl-1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine



To a solution of 2-methyl-1-phenyl-1H-imidazo[4,5-c]pyridine (1.05 g, 5 mmol) in CH_2Cl_2 (5 mL) was added benzyl bromide (3.0 mL, 25 mmol). The solution stirred at rt for 4h after which time it was concentrated to dryness. The residue was dissolved in MeOH (10 mL) and to it 20% $Pd(OH)_2/C$ (0.24 g) was added. The reaction was stirred under an atmosphere of hydrogen for 3h at rt. The mixture was filtered and the filtrate was concentrated under

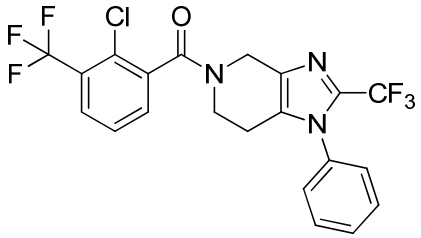
reduced pressure to a white solid (0.60 g, 56% over 2 steps).

Step 3: (2-Chloro-3-(trifluoromethyl)phenyl)(2-methyl-1-phenyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone.



To a solution of 2-methyl-1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine (114 mg, 0.51 mmol), 2-chloro-3-trifluoromethylcarboxylic acid (90 mg, 0.42 mmol) and HATU (319 mg, 0.84 mmol) in DCM (15 mL) was added NEt_3 (0.16 mL, 1.26 mmol). The mixture was stirred at rt overnight after which time the reaction was concentrated under reduced pressure and purified by basic HPLC to provide the product as a white solid (100 mg, 55%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.03-7.89 (m, 1H), 7.80-7.54 (m, 7H), 5.06-4.27 (m, 2H), 4.14-3.38 (m, 2H), 2.63-2.32 (m, 5H). MS (ESI): mass calculated for $C_{21}H_{17}ClF_3N_3O$, 419.10; m/z found, 420.0 $[M+H]^+$.

Example 38. (2-Chloro-3-(trifluoromethyl)phenyl)(1-phenyl-2-(trifluoromethyl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone.

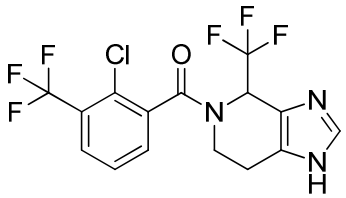


Step A: 1-phenyl-2-(trifluoromethyl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine 1-phenyl-2-(trifluoromethyl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine. The title compound was made in a manner analogous to Example 61 step 2 substituting 1-phenyl-2-(trifluoromethyl)-1H-imidazo[4,5-c]pyridine for 1-phenyl-1H-[1,2,3]triazolo[4,5-c]pyridine.

Step B: (2-Chloro-3-(trifluoromethyl)phenyl)(1-phenyl-2-(trifluoromethyl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone was made in manner analogous to Example 65 using 1-phenyl-2-(trifluoromethyl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine.. MS

(ESI): mass calcd. for $C_{21}H_{14}ClF_6N_3O$, 473.1; m/z found, 474.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 7.59 – 7.40 (ddd, J = 3.8, 2.6, 1.1 Hz, 3H), 7.32 – 7.27 (dd, J = 6.7, 3.0 Hz, 2H), 4.02 – 3.90 (t, J = 1.6 Hz, 2H), 3.18 – 3.06 (t, J = 5.7 Hz, 2H), 2.46 – 2.30 (ddt, J = 7.0, 5.6, 1.3 Hz, 2H).

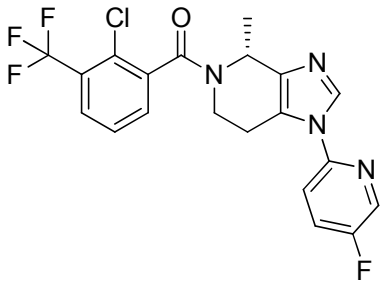
Example 39. 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-(trifluoromethyl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine.



Step A. 4-(trifluoromethyl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine hydrochloride. A suspension of histamine dihydrochloride (1.0 g, 5.3 mmol) in H_2O (20 mL) was cooled in an ice bath. To this suspension was added solid KOH (85%) (0.9 g, 16 mmol) followed by trifluoroacetaldehyde hydrate (0.5 g, 5.3 mmol). The reaction was allowed to warm to rt and heated to 80 °C. After 6 h, the reaction was cooled to rt, acidified using 6N HCl, and concentrated. The resulting residue was dissolved in hot EtOH and filtered through Celite©. The solvent was evaporated to give the product as the HCl salt. This was purified by dissolving in minimal water and loading on silica (SiO_2; MeOH (NH_3):DCM) to give the title compound (0.6 g, 45%).

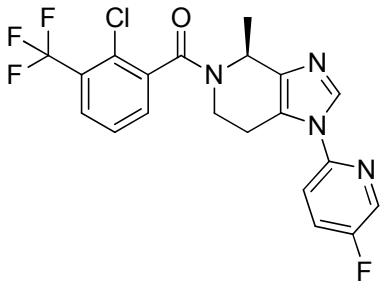
Step B. (2-Chloro-3-(trifluoromethyl)phenyl)(4-(trifluoromethyl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone. A solution of 4-(trifluoromethyl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine hydrochloride (0.10 g, 0.44 mmol), 2-chloro-3-trifluoromethyl benzoic acid (0.10 g, 0.44 mmol), HATU (0.18 g, 0.48 mmol, and DIPEA (0.19 mL, 1.1 mmol) in DMF (2 mL) was stirred for 30 min. The reaction was diluted with EtOAc (15 mL) and washed with H_2O (3 x 10 mL). The organic layers were combined, dried (Na_2SO_4), and concentrated. Chromatography of the resulting residue (SiO_2; MeOH (NH_3):DCM) gave the title compound (0.06 g, 34%). ^1H NMR (500 MHz, $CDCl_3$) δ 8.02 – 7.94 (m, 1H), 7.80 – 7.58 (m, 1H), 7.51 – 7.39 (m, 1H), 6.60 – 6.50 (m, 1H) , 4.42 (q, J = 7.6 Hz, 1H), 2.95 (s, 4H). MS (ESI): mass calculated for $C_{15}H_{10}ClF_6N_3O$, 397.042; m/z found 398.1 $[M+H]^+$.

Example 40. (R*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone.



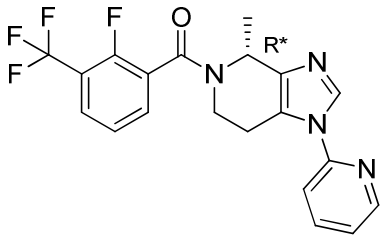
The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 11 performed using CHIRALCEL OD-H (5µm, 250x20mm) and a mobile phase of 70% CO_2, 30% EtOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALCEL OD-H (250x4.6mm) and a mobile phase of 70% CO_2, 30% EtOH over 7 minutes. (100% single enantiomer, 2.29 min retention time). MS (ESI): mass calculated for $C_{20}H_{15}ClF_4N_4O$, 438.1; m/z found, 439.3 $[M+H]^+$.

Example 41. (4S*)-5-{[2-Fluoro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine.



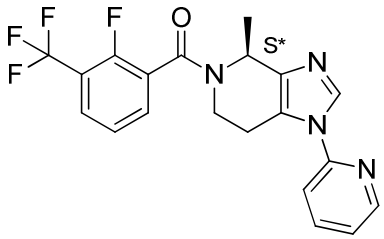
The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 11 performed using CHIRALCEL OD-H (5µm, 250x20mm) and a mobile phase of 70% CO_2, 30% EtOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALCEL OD-H (250x4.6mm) and a mobile phase of 70% CO_2, 30% EtOH over 7 minutes. (100% single enantiomer, 2.81 min retention time). MS (ESI): mass calculated for $C_{20}H_{15}ClF_4N_4O$, 438.1; m/z found, 439.3$[M+H]^+$.

Example 42. (4R*)-5-{[2-Fluoro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine.



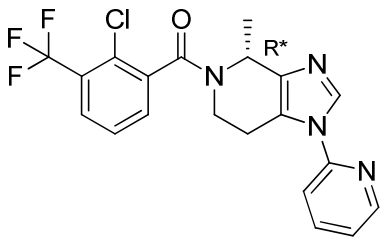
Example 42 was prepared in a manner analogous to example 40 using example 19 as starting material. Purification by LC Gilson prep system- stationary phase Lux 5um Amylose-2, 30mm x 250mm; mobile phase 20% EtOH + 0.2% TEA, 80% hexanes.^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60 – 8.45 (m, 1H), 7.99 (t, J = 17.2 Hz, 1H), 7.91 – 7.79 (m, 1H), 7.75 – 7.46 (m, 2H), 7.42 – 7.28 (m, 3H), 5.79 (s, 1H), 5.09 – 4.59 (m, 1H), 3.73 – 3.37 (m, 1H), 3.37 – 2.84 (m, 2H), 1.85 – 1.44 (m, 3H). MS (ESI): mass calculated for $C_{20}H_{16}F_4N_4O$, 404.1; m/z found, 405.2 $[M+H]^+$.

Example 43. (4S*)-5-{[2-Fluoro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine.



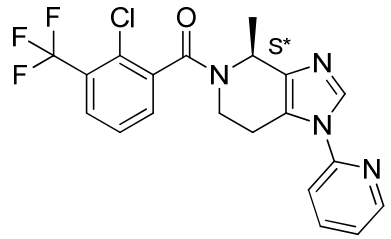
Example 43 was prepared in a manner analogous to example 40 using example 19 as starting material. Purification by LC Gilson prep system- stationary phase Lux 5um Amylose-2, 30mm x 250mm; mobile phase 20% EtOH + 0.2% TEA, 80% hexanes. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.59 – 8.46 (m, 1H), 8.03 – 7.99 (m, 1H), 7.93 – 7.81 (m, 1H), 7.74 – 7.48 (m, 2H), 7.42 – 7.28 (m, 3H), 5.78 (s, 1H), 5.14 – 4.53 (m, 1H), 3.76 – 3.34 (m, 1H), 3.31 – 2.82 (m, 2H), 1.68 – 1.33 (m, 3H). MS (ESI): mass calculated for $C_{20}H_{16}F_4N_4O$, 404.126; m/z found, 405.2 $[M+H]^+$.

Example 44. (4R*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine.



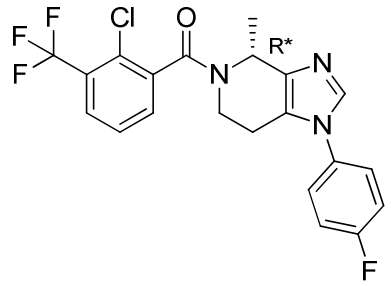
Example 44 was prepared in a manner analogous to example 40 using Example 17 as starting material. Purification by SFC JASCO prep system- stationary phase Chiralpak OD 5um, 21mm x 250mm; mobile phase 10% IPA + 0.2% IPamine, 90% CO_2. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.59 – 8.45 (m, 1H), 8.04 – 7.98 (m, 1H), 7.88 – 7.84 (m, 1H), 7.76 (dd, J = 6.3, 4.7 Hz, 1H), 7.58 – 7.28 (m, 4H), 5.86 – 5.79 (m, 1H), 4.58 (d, J = 6.5 Hz, 1H), 4.12 – 3.92 (m, 1H), 3.34 – 2.80 (m, 2H), 1.69 – 1.44 (m, 3H). (ESI): mass calculated for $C_{20}H_{16}ClF_3N_4O$, 420.10; m/z found, 421.1 $[M+H]^+$.

Example 45. (4S*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine.



Example 45 was prepared in a manner analogous to example 40 using Example 17 as starting material. Purification by SFC JASCO prep system- stationary phase Chiralpak OD 5um, 21mm x 250mm; mobile phase 10% IPA + 0.2% IPamine, 90% CO_2. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.59 – 8.45 (m, 1H), 8.03 – 7.98 (m 1H), 7.91 – 7.81 (m, 1H), 7.81 – 7.72 (m, 1H), 7.59 – 7.28 (m, 4H), 5.90 – 5.74 (m, 1H), 5.07 (dd, J = 11.3, 4.4 Hz, 1H), 4.78 – 4.45 (m, 1H), 4.03 (dt, J = 12.2, 6.1 Hz, 1H), 3.62 – 2.79 (m, 4H).MS (ESI): mass calculated for $C_{20}H_{16}ClF_3N_4O$, 420.10; m/z found, 421.1 $[M+H]^+$.

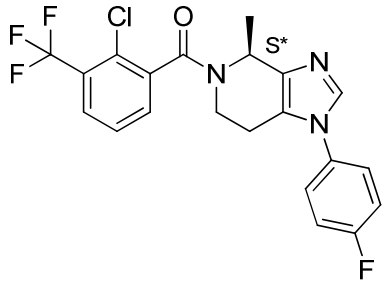
Example 46. (4R*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(4-fluorophenyl)-4-methyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine.



Example 46 was prepared in a manner analogous to Example 40 using Example 18 as starting material. Purification by LC Gilson prep system- stationary phase Chiralpak AD-H 5um, 21mm x 250mm; mobile phase 10% EtOH + 0.2% TEA, 90% hexanes. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (dd, J = 5.1, 3.2 Hz, 1H), 7.62 (s, 1H), 7.58 – 7.36 (m, 2H), 7.33 –

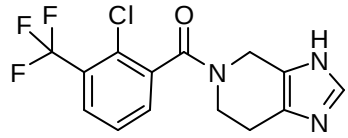
7.24 (m, 2H), 7.24 – 7.14 (m, 2H), 5.89 – 5.78 (m, 1H), 5.07 (dt, J = 12.3, 6.0 Hz, 1H), 4.77 – 4.39 (m, 1H), 3.62 – 2.86 (m, 1H), 2.77 – 2.28 (m, 1H), 1.80 – 1.10 (m, 3H). MS (ESI): mass calculated for $C_{21}H_{16}ClF_4N_3O$, 437.10; m/z found, 438.1 $[M+H]^+$.

Example 47. (4S)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(4-fluorophenyl)-4-methyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine.



Example 47 was prepared in a manner analogous to Example 40 using Example 18 as starting material. Purification by LC Gilson prep system- stationary phase Chiralpak AD-H 5um, 21mm x 250mm; mobile phase 10% EtOH + 0.2% TEA, 90% hexanes. MS (ESI): mass calculated for $C_{21}H_{16}ClF_4N_3O$, 437.10; m/z found, 438.1 $[M+H]^+$.

Example 48: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4,5,6,7-tetrahydro-3H-imidazo[4,5-c]pyridine.

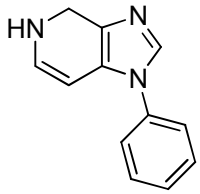


The title compound was prepared in a manner analogous to Example 1, Step C substituting 4,5,6,7-tetrahydro-3H-imidazo[4,5-c]pyrdine for 1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine . MS (ESI): mass calcd. for $C_{14}H_{11}ClF_3N_3O$, 329.0; m/z found, 330.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 7.79-7.73 (m, 1H), 7.57 (s, 0.5H), 7.53 –

7.39 (m, 2.5H), 5.02 – 4.71 (m, 1H), 4.39 – 4.19 (m, 1.5H), 3.99 (dt, J = 12.6, 6.0 Hz, 0.5H), 3.60 – 3.47 (m, 1H), 2.84 (td, J = 5.3, 2.6 Hz, 1H), 2.77 – 2.58 (m, 1H).

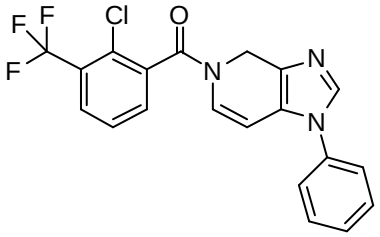
Example 49: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-phenyl-4,5-dihydro-1H-imidazo[4,5-c]pyridine.

Step A: 1-phenyl-4,5-dihydro-1H-imidazo[4,5-c]pyridine.



A solution of Intermediate 2 (196 mg, 1.00 mmol) in AcOH (25 ml) was passed through a Pt_2O catalyst cartridge on an H-Cube hydrogenation apparatus at a pressure of 80 bar and a flow rate of 1 ml/min at 100 ^oC. The reaction was looped through the apparatus for 5 h. The crude reaction mixture was concentrated and purified on 16 g SiO_2 column with 0-10% NH_3/MeOH CH_2Cl_2 to give the desired compound (35 mg, 17%). MS (ESI): mass calcd. for $C_{12}H_{11}N_3$, 197.1; m/z found, 198.2 $[M+H]^+$.

Step B: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-phenyl-4,5-dihydro-1H-imidazo[4,5-c]pyridine.

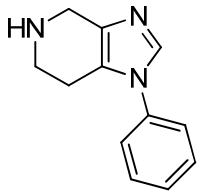


To a solution of the product of Example 49, Step A (5.5 mg, 0.028 mmol) in DCM (3 mL) was added TEA (11 μL, 0.084 mmol), 2-chloro-3-(trifluoromethyl)benzoic acid (7 mg, 0.031 mmol) and HATU (13 mg, 0.033 mmol). The reaction was stirred at room temperature overnight. The crude reaction mixture was concentrated and purified on 4 g SiO_2 column with 0-3% NH_3/MeOH CH_2Cl_2 to give the desired compound (9.9 mg, 87%). MS (ESI): mass calcd. for $C_{20}H_{13}ClF_3N_3O$, 403.1; m/z found, 404.3 $[M+H]^+$. ^1H NMR (400

MHz, $CDCl_3$) δ 9.06 (s, 1H), 8.09 (m 1H), 7.94-7.84 (m, 1H), 7.76 – 7.53 (m, 2H), 7.53 – 7.39 (m, 2H), 7.39 – 7.22 (m, 4H), 6.96-6.86 (m, 1H), 6.73 (s, 1H), 5.95 (q, J = 7.0 Hz, 1H), 5.54 (s, 1H), 3.22 (q, J = 7.3 Hz, 2H), 1.37 (t, J = 7.3 Hz, 3H).

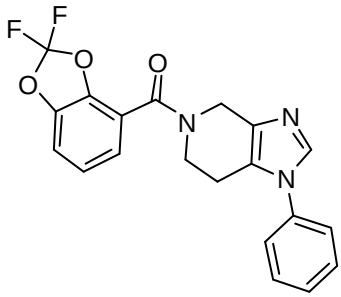
Example 50: 5-[(2,2-Difluoro-1,3-benzodioxol-4-yl)carbonyl]-1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine.

Step A: 1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine.



A solution of Intermediate 2 (111 mg, 0.569 mmol) in AcOH (15 ml) was passed through a Rh/C catalyst cartridge on an H-Cube hydrogenation apparatus at a pressure of 80 bar and a flow rate of 1 ml/min at 100 ^oC. The reaction was looped through the apparatus for 2 h. The crude reaction mixture was concentrated and purified on 12 g SiO_2 column with 0-10% NH_3/MeOH CH_2Cl_2 to give the desired compound (90 mg, 80%). MS (ESI): mass calcd. for $C_{12}H_{13}N_3$, 199.3; m/z found, 200.2 $[M+H]^+$.

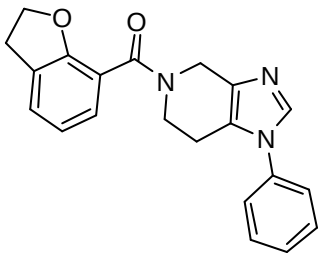
Step B: 5-[(2,2-Difluoro-1,3-benzodioxol-4-yl)carbonyl]-1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine.



To a solution of the product of Example 50, Step A (28 mg, 0.141 mmol) and TEA (23 μL, 0.169 mmol) in $CHCl_3$ (1 mL) cooled to 0 ^oC was added 2,2-difluoro-1,3-benzodioxole-4-

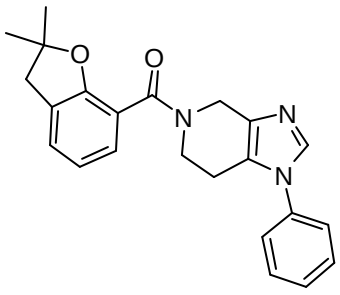
carbonyl chloride (34 mg, 0.155 mmol). The reaction was warmed to room temperature and stirred overnight. The crude reaction mixture purified on 12 g SiO_2 column with 0-4% NH_3/MeOH CH_2Cl_2 to give the desired compound (43 mg, 80%). MS (ESI): mass calcd. for $C_{20}H_{15}F_2N_3O_3$, 383.1; m/z found, 384.0 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.39 (m, 4H), 7.36 – 7.09 (m, 5H), 4.88 (s, 1H), 4.58 (t, J = 1.6 Hz, 2H), 4.08 (t, J = 5.9 Hz, 2H), 3.66 (t, J = 5.6 Hz, 1H), 2.86 – 2.74 (m, 3H).

Example 51: 5-(2,3-Dihydro-1-benzofuran-7-ylcarbonyl)-1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine.



The title compound was prepared in a manner analogous to Example 50 substituting 2,3-dihydro-1-benzofuran-7-carbonyl chloride for 2,2-difluoro-1,3-benzodioxole-4-carbonyl chloride . MS (ESI): mass calcd. for $C_{21}H_{19}N_3O_2$, 345.1; m/z found, 346.3 $[M+H]^+$.

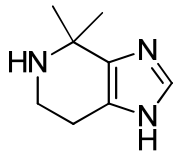
Example 52: 5-[(2,2-Dimethyl-2,3-dihydro-1-benzofuran-7-yl)carbonyl]-1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine.



The title compound was prepared in a manner analogous to Example 50 substituting 2,2-dimethyl-2,3-dihydro-1-benzofuran-7-carbonyl chloride for 2,2-difluoro-1,3-benzodioxole-4-carbonyl chloride . MS (ESI): mass calcd. for $C_{23}H_{23}N_3O_2$, 373.2; m/z found, 374.3 $[M+H]^+$.

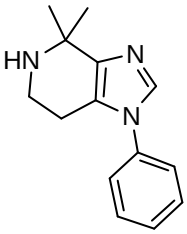
Example 53: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4,4-dimethyl-1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine.

Step A: 4,4-dimethyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine.



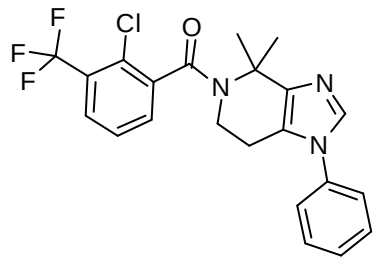
A solution of histamine (500 mg, 4.5 mmol) and acetone (3.3 mL, 45 mmol) in AcOH (3 mL) was heated at 100 ^{o}C overnight. The crude reaction mixture was concentrated and purified on 16 g SiO_2 column with 0-80% NH_3/MeOH CH_2Cl_2 to give the desired compound (543 mg, 80%). MS (ESI): mass calcd. for $C_8H_{13}N_3$, 151.1; m/z found, 152.2 $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (s, 1H), 3.16 (t, J = 5.7 Hz, 2H), 2.61 (t, J = 5.7 Hz, 2H), 1.43 (s, 6H).

Step B: 4,4-dimethyl-1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine



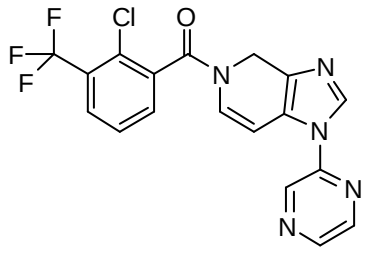
The title compound was prepared in a manner analogous to Intermediate 15, Step 1 substituting the product of Example 53, Step A for 1H-[1,2,3]-triazolo-[4,5-C]-pyridine. MS (ESI): mass calcd. for C $H_{17}N_3$, 227.1; m/z found, 228.1 $[M+H]^+$.

Step C: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4,4-dimethyl-1-phenyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine.



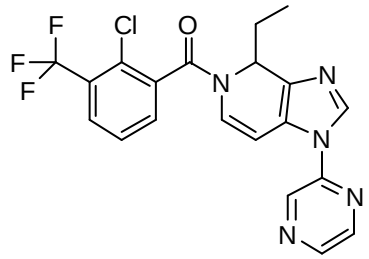
To a solution of the product of Example 53, Step B (59 mg, 0.26 mmol) in DCM (2 mL) was added Intermediate 12 (63 mg, 0.26 mmol) and K_2CO_3 (89 mg, 0.65 mmol). The resulting suspension was stirred at room temperature for 2 h. The crude reaction mixture was filtered and concentrated and then purified on 12 g SiO_2 column with 0-4% NH_3/MeOH CH_2Cl_2 to give the desired compound (55 mg, 48%). MS (ESI): mass calcd. for $C_{22}H_{19}ClF_3N_3O$, 433.1; m/z found, 434.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (dd, J = 7.8, 1.4 Hz, 1H), 7.67 (s, 1H), 7.54 – 7.37 (m, 5H), 7.30 (dd, J = 5.3, 3.3 Hz, 2H), 3.53-3.38 (m, 2H), 2.72 – 2.54 (m, 2H), 2.01 (d, J = 6.3 Hz, 6H).

Example 54: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyrazin-2-yl-4,5-dihydro-1H-imidazo[4,5-c]pyridine.



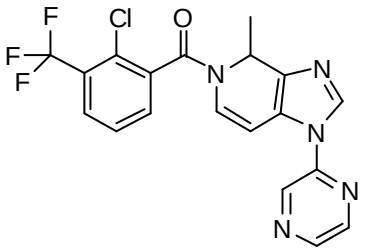
The title compound was prepared in a manner analogous to Example 11 substituting Intermediate 4 for 1-pyrazin-2-yl-1H-[1,2,3]triazolo[4,5-c]pyridine. MS (ESI): mass calcd. for $C_{18}H_{11}ClF_3N_5O$, 405.1; m/z found, 406.1 $[M+H]^+$.

Example 55: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-ethyl-1-pyrazin-2-yl-4,5-dihydro-1H-imidazo[4,5-c]pyridine.



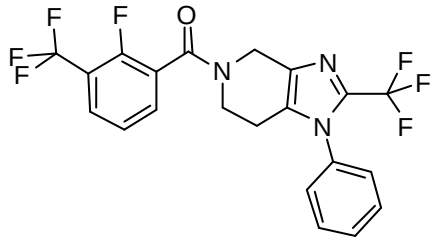
The title compound was prepared in a manner analogous to Example 11 substituting Intermediate 4 for 1-pyrazin-2-yl-1H-[1,2,3]triazolo[4,5-c]pyridine and EtMgBr for MeMgBr. MS (ESI): mass calcd. for $C_{20}H_{15}ClF_3N_5O$, 433.1; m/z found, 434.2 $[M+H]^+$.

Example 56: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrazin-2-yl-4,5-dihydro-1H-imidazo[4,5-c]pyridine.



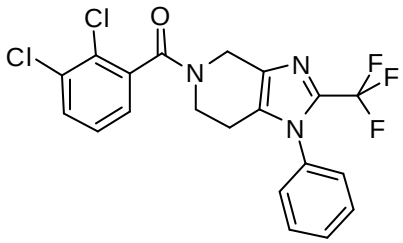
The title compound was prepared in a manner analogous to Example 11 substituting Intermediate 4 for 1-pyrazin-2-yl-1H-[1,2,3]triazolo[4,5-c]pyridine. MS (ESI): mass calcd. for $C_{19}H_{13}ClF_3N_5O$, 419.1; m/z found, 420.0 $[M+H]^+$.

Example 57: 5-{[2-Fluoro-3-(trifluoromethyl)phenyl]carbonyl}-1-phenyl-2-(trifluoromethyl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine.



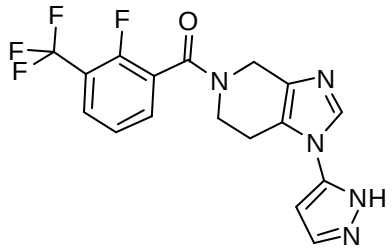
MS (ESI): mass calcd. for $C_{21}H_{14}F_7N_3O$, 457.1; m/z found, 458.1 $[M+H]^+$.

Example 58: 5-[(2,3-Dichlorophenyl)carbonyl]-1-phenyl-2-(trifluoromethyl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine.



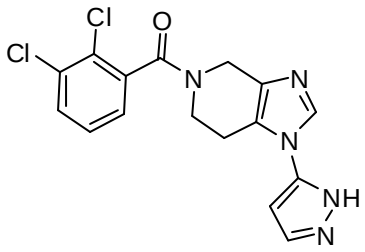
MS (ESI): mass calcd. for $C_{20}H_{14}Cl_2F_3N_3O$, 439.0; m/z found, 440.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.44 (m, 3H), 7.37 – 7.17 (m, 3H), 5.04 – 4.83 (m, 1H), 4.49 – 4.26 (m, 1H), 4.22 (dt, J = 13.1, 5.5 Hz, 1H), 3.99 (dt, J = 13.2, 6.0 Hz, 1H), 3.61 – 3.44 (m, 1H), 2.59 (td, J = 6.0, 1.6 Hz, 1H), 2.54 – 2.42 (m, 1H), 2.42 – 2.29 (m, 1H)

Example 59: 5-{[2-Fluoro-3-(trifluoromethyl)phenyl]carbonyl}-1-(1H-pyrazol-5-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine.



Example 59 was prepared in analogy to Example 5. MS (ESI): mass calcd. for $C_{17}H_{13}F_4N_5O$, 379.1; m/z found, 380.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 11.74 (s, 1H), 7.91 (s, 1H), 7.81 (s, 1H), 7.75 – 7.56 (m, 3H), 7.34 (dt, J = 10.9, 7.8 Hz, 1H), 6.30 (d, J = 2.4 Hz, 1H), 4.90 (s, 1H), 4.48 (s, 2H), 3.83 (s, 1H), 3.63 (s, 1H), 3.20 (q, J = 7.3 Hz, 1H), 3.06 (s, 1H), 2.90 (s, 1H), 1.34 (t, J = 7.3 Hz, 1H).

Example 60: 5-[(2,3-Dichlorophenyl)carbonyl]-1-(1H-pyrazol-5-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine.

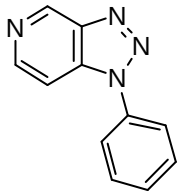


Example 60 was prepared in analogy to Example 5. . MS (ESI): mass calcd. for $C_{16}H_{13}Cl_2N_5O$, 361.0; m/z found, 362.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 12.18 – 11.79 (m, 1H), 7.98 – 7.85 (s, 0.4H), 7.88 – 7.76 (s, 0.6H), 7.62 – 7.53 (m, 1H), 7.54 – 7.47 (ddd, J = 7.9, 3.6, 1.7 Hz, 1H), 7.33 – 7.17 (m, 3H), 6.32 – 6.23 (dd, J = 10.6, 2.4 Hz, 1H),

5.05 – 4.78 (ddt, J = 68.4, 16.2, 1.7 Hz, 1H), 4.47 – 4.28 (m, 1H), 4.28 – 4.20 (m, 1H), 4.13 – 4.02 (dt, J = 12.5, 5.9 Hz, 1H), 3.60 – 3.49 (td, J = 6.2, 5.6, 3.8 Hz, 1H), 3.15 – 2.99 (dt, J = 7.5, 4.1 Hz, 1H), 2.97 – 2.73 (m, 1H).

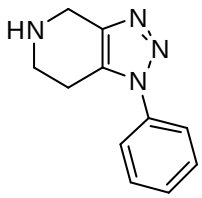
Example 61: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-phenyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.

Step 1 Intermediate 15 : 1-Phenyl-1H-[1,2,3]triazolo[4,5-c]pyridine.



A solution of 1H-[1,2,3]-triazolo-[4,5-C]-pyridine (200 mg, 1.7 mmol), iodobenzene (407 mg, 2.0 mmol), Cs_2CO_3, (1.08 g, 3.3 mmol), copper (I) oxide (17 mg, 0.12 mmol), 4,7-dimethoxy-[1,10]-phenanthroline (84 mg, 0.35 mmol), PEG 400 (0.3 ml) were combined in butyronitrile (3 ml) and heated to 110 °C overnight. The reaction was diluted with $CHCl_3$, filtered through Celite© and then concentrated and purified on 16 g SiO2 with 0-3.5% NH_3/MeOH in CH_2Cl_2 to give 52 mg (16%) of 1-phenyl-1H-[1,2,3]triazolo[4,5-c]pyridine. MS (ESI): mass calcd. for $C_{11}H_8N_4$, 196.1; m/z found, 197.1 $[M+H]^+$. ^{1}H NMR δ (400 MHz, $CDCl_3$) δ 9.58 (s, 1H), 8.66 (d, J = 5.8 Hz, 1H), 7.83 - 7.75 (m, 2H), 7.72 - 7.62 (m, 3H), 7.62 - 7.52 (m, 1H).

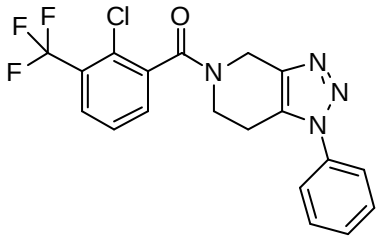
Step 2 Intermediate 16: 1-Phenyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



A solution of 1-phenyl-1H-[1,2,3]triazolo[4,5-c]pyridine (61 mg, 0.31 mmol) in MeOH (15 ml) was passed through a PtO_2 catalyst cartridge on an H-Cube hydrogenation apparatus at a pressure of 70 bar and a flow rate of 1 ml/min. The reaction was concentrated and the crude reaction mixture purified on 12 g SiO_2 column with 0-8% NH_3/MeOH CH_2Cl_2 to give

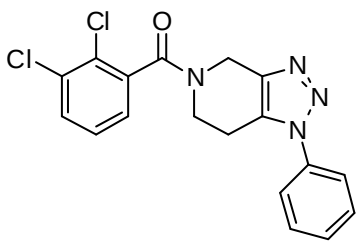
35 mg (56%) of 1-phenyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine. MS (ESI): mass calcd. for $C_{11}H_{12}N_4$, 200.2; m/z found, 201.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 7.99 (dt, J = 8.0, 1.1 Hz, 2H), 7.61 – 7.50 (m, 2H), 7.48 – 7.41 (m, 2H), 7.33 – 7.27 (m, 1H), 4.14 – 4.07 (m, 2H), 3.20 (t, J = 5.9 Hz, 2H), 2.88 (t, J = 5.9 Hz, 2H).

Step 3 Example 61: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-phenyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



A solution of 1-phenyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine (17 mg, 0.085 mmol) and 2-chloro-3-(triflouromethyl) benzoic acid (21 mg, 0.093 mmol) in DCM (8 mL) was treated with Et_3N (35 μL, 0.25 mmol) followed by HATU (38 mg, 0.1 mmol). The reaction was stirred overnight, then concentrated to minimum volume and purified on 16 g SiO_2 with 0-3.5% NH_3 in MeOH / CH_2Cl_2 to give 32 mg (91%) of 5-{[2-chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-phenyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine. MS (ESI): mass calcd. for $C_{19}H_{14}ClF_3N_4O$, 406.1; m/z found, 407.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 7.84 – 7.75 (m, 1H), 7.62 – 7.43 (m, 7H), 5.11 (q, J = 16.5 Hz, 1H), 4.64 – 4.45 (m, 1H), 4.32 (dt, J = 13.2, 5.4 Hz, 0.5H), 4.05 – 3.95 (m, 0.5H), 3.65 – 3.48 (m, 1H), 3.04 (t, J = 5.9 Hz, 1H), 3.01 – 2.76 (m, 1H).

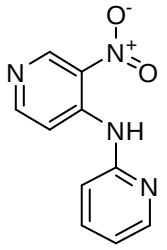
Example 62: 5-[(2,3-Dichlorophenyl)carbonyl]-1-phenyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



A solution of 1-phenyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine (17 mg, 0.085 mmol) and 2,3-dichlorobenzoic acid (18 mg, 0.093 mmol) in DCM (8 ml) was treated with Et_3N (35 μL, 0.25 mmol) followed by HATU (38 mg, 0.1 mmol). The reaction was stirred overnight, then concentrated to minimum volume and purified on 16 g SiO_2 with 0-3.5% NH_3 in MeOH / CH_2Cl_2 to give 24 mg (75%) of 5-[(2,3-dichlorophenyl)carbonyl]-1-phenyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine. MS (ESI): mass calcd. for $C_{18}H_{14}Cl_2N_4O$, 372.0; m/z found, 373.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 7.63 – 7.42 (m, 5H), 7.38 – 7.17 (m, 2H), 5.23 – 4.88 (m, 1H), 4.54 (q, J = 15.7 Hz, 1H), 4.23 (dt, J = 13.2, 5.5 Hz, 1.0H), 4.10 – 4.00 (m, 1.0H), 3.65 – 3.48 (m, 1H), 3.03 (t, J = 5.7 Hz, 1H), 3.00 – 2.74 (m, 1H).

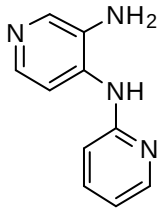
Example 63: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.

Step 1 Intermediate 17: N-(3-Nitropyridin-4-yl)pyridin-2-amine.



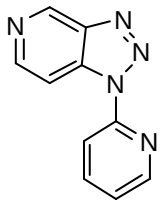
$Pd(OAc)_2$ (9.5 mg, 0.042 mmol) and BINAP (26 mg, 0.042 mmol) were combined in toluene (1 ml) and stirred at rt for 10 minutes. This mixture was then added to a sealed vessel which contained 4-chloro-3-nitropyridine (172 mg 1.0 mmol), 2-aminopyridine (100 mg, 1.0 mmol), and K_2CO_3 (160 mg, 1.2 mmol) in toluene (2 ml). The reaction was heated to 110 °C for 2 h. The reaction was filtered while hot and the filter cake washed with EtOAc. The combined filtrates were concentrated and purified on 16 g SiO_2 with 0-40% EtOAc / hexanes. MS (ESI): mass calcd. for $C_{10}H_8N_4O_2$, 216.0; m/z found, 217.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 10.39 (s, 1H), 9.35 (s, 1H), 8.81 (d, J = 6.2 Hz, 1H), 8.50 (d, J = 6.1 Hz, 1H), 8.44 (dd, J = 5.0, 1.2 Hz, 1H), 7.74 (ddd, J = 8.2, 7.4, 1.9 Hz, 1H), 7.09 (ddd, J = 7.4, 5.0, 0.9 Hz, 1H), 7.02 (t, J = 7.8 Hz, 1H).

Step 2 Intermediate 18: N-4-Pyridin-2-ylpyridine-3,4-diamine.



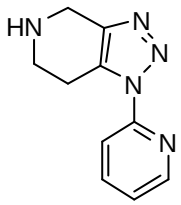
A solution of N-(3-Nitropyridin-4-yl)pyridin-2-amine (195 mg, 0.9 mmol) in EtOH (15 ml) was treated with 10% Pd/C (10 mg) and and then put under an atmosphere of H_2 and stirred for 4 h. The reaction was filtered through Celite© and concentrated to pale yellow solid. MS (ESI): mass calcd. for $C_{10}H_{10}N_4$, 186.1; m/z found, 187.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 8.28 (ddd, J = 5.0, 1.9, 0.9 Hz, 1H), 8.15 (s, 1H), 8.06 (d, J = 5.4 Hz, 1H), 7.58 (ddd, J = 8.3, 7.3, 1.9 Hz, 1H), 7.54 (d, J = 5.4 Hz, 1H), 6.90 – 6.81 (m, 2H), 6.58 (s, 1H), 3.52 (s, 2H).

Step 3 Intermediate 19: 1-Pyridin-2-yl-1H-[1,2,3]-triazolo[4,5-c]pyridine.



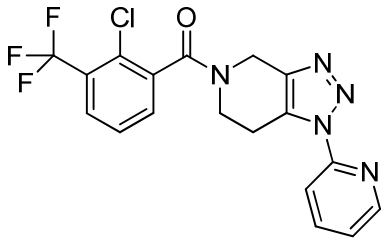
N-4-Pyridin-2-ylpyridine-3,4-diamine (100 mg, 0.54 mmol) in THF (5 ml) and HOAc (0.034 ml, 0.59 mmol) was treated with *t*-butyl nitrite (0.11 ml, 0.81 mmol) and heated to 100 °C for 90 min. The reaction was cooled to 23 °C and a solid precipitated. The reaction mixture was warmed to dissolve the solid, filtered and the filtrate was partially concentrated. A solid was isolated (55 mg, 52%) then filtrate concentrated to provide a additional crop of product (57 mg, 54%). MS (ESI): mass calcd. for $C_{10}H_7N_5$, 197.1; m/z found, 198.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 9.55 (d, J = 1.0 Hz, 1H), 8.70 (d, J = 5.8 Hz, 1H), 8.65 (ddd, J = 4.9, 1.8, 0.8 Hz, 1H), 8.55 (dd, J = 5.8, 1.2 Hz, 1H), 8.33 (dt, J = 8.3, 0.9 Hz, 1H), 8.00 (ddd, J = 8.3, 7.5, 1.9 Hz, 1H), 7.39 (ddd, J = 7.4, 4.9, 1.0 Hz, 1H).

Step 4 Intermediate 20: 1-(Pyridin-2-yl)-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



1-Pyridin-2-yl-1H-[1,2,3]-triazolo[4,5-c]pyridine (23 mg, 0.12 mmol) in HOAc (14 mL) was hydrogenated at 50 bar using Rh/C as catalyst on the H-cube apparatus with a flow rate of 1 ml/min and looped with product recycling for 2 hrs. Reaction was concentrated then partially purified on 12 g SiO_2 with 0-10% NH_3 MeOH/ CH_2Cl_2. Used without further purification in next reaction. MS (ESI): mass calcd. for $C_{10}H_{11}N_5$, 201.2; m/z found, 202.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 8.49 (ddd, J = 4.9, 2.0, 0.9 Hz, 1H), 8.18 – 8.10 (m, 1H), 7.90 (ddd, J = 8.3, 7.4, 1.9 Hz, 1H), 7.36 – 7.27 (m, 1H), 4.12 (t, J = 1.4 Hz, 2H), 3.31 – 3.12 (m, 4H).

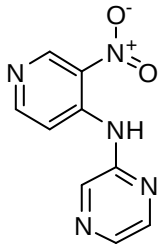
Step 5 Example 63: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



A solution of 1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine (13 mg, 0.065 mmol) in THF (1 mL) was treated with 2-chloro-3-(trifluoromethyl)benzoyl chloride (19 mg, 0.078 mmol) followed by Et_3N (0.013 mL, 0.097 mmol). After 5 min the reaction was diluted with CH_2Cl_2 and the organic portion washed with $NaHCO_3$. The organic portion was then dried over Na_2SO_4, concentrated and purified on 4 g SiO_2 to yield 20 mg (75%) of : 5-{[2-Chloro-3-(trifluoromethyl) phenyl]carbonyl}-1-pyridin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine. MS (ESI): mass calcd. for $C_{18}H_{13}ClF_3N_5O$, 407.1; m/z found, 408.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.49 (dddd, J = 32.1, 4.9, 1.8, 0.8 Hz, 1H), 8.17 (ddt, J = 17.3, 8.3, 1.0 Hz, 1H), 7.93 (ddt, J = 8.4, 7.5, 1.7 Hz, 1H), 7.79 (ddd, J = 6.6, 4.4, 2.2 Hz, 1H), 7.57 – 7.42 (m, 2H), 7.35 (dddd, J = 12.3, 7.5, 4.9, 1.0 Hz, 1H), 5.25 – 4.96 (m, 1H), 4.35 (dt, J = 13.3, 5.4 Hz, 1H), 4.11 – 3.95 (m, 1H), 3.61 – 3.53 (m, 1H), 3.51 – 3.44 (m, 1H), 3.36 (s, 1H).

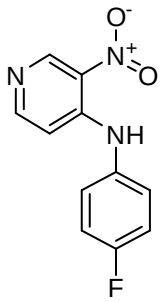
Intermediates 21-30 were made in manner analogous to Intermediate 17 substituting the appropriate aryl or heteroaryl amine for N-(3-Nitropyridin-4-yl)pyridin-2-amine and the appropriate halo-nitro pyridine for 4-chloro-3-nitropyridine in the synthesis of Intermediate 17.

Intermediate 21: N-(3-Nitropyridin-4-yl)pyrazin-2-amine.



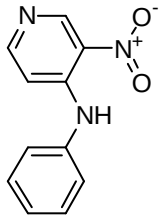
MS (ESI): mass calcd. for $C_9H_7N_5O_2$, 217.1; m/z found, 218.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 10.57 (s, 1H), 9.40 (s, 1H), 8.84 (d, J = 6.1 Hz, 1H), 8.59 (d, J = 6.1 Hz, 1H), 8.45 (d, J = 1.3 Hz, 1H), 8.38 – 8.30 (m, 2H).

Intermediate 22: N-(4-Fluorophenyl)-3-nitropyridin-4-amine.



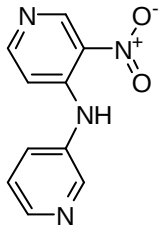
MS (ESI): mass calcd. for $C_{11}H_8FN_3O_2$, 233.0; m/z found, M/Z = 234.1 $[M+H]^+$, ^1H NMR (400 MHz, DMSO- d_6): 9.79 (s, 1H), 9.08 (s, 1H), 8.22 (d, J = 6.1 Hz, 1H), 7.50-7.23 (m, 4H), 6.77 (d, J = 6.1 Hz, 1H).

Intermediate 23: 3-Nitro-N-phenylpyridin-4-amine.



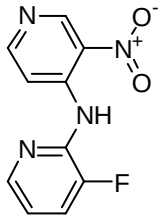
MS (ESI): mass calcd. for $C_{11}H_9N_3O_2$, 215.1; m/z found, M/Z = 216.1 $[M+H]^+$, ^1H NMR (400 MHz, $CDCl_3$): δ 9.66 (s, 1H), 9.26 (s, 1H), 8.23 (d, J = 6.1 Hz, 1H), 7.48 (t, J = 7.6 Hz, 2H), 7.34 (t, J = 7.4 Hz, 1H), 7.28 (d, J = 7.7 Hz, 2H), 6.93 (d, J = 6.2 Hz, 1H).

Intermediate 24: N-(3-Nitropyridin-4-yl)pyridin-3-amine.



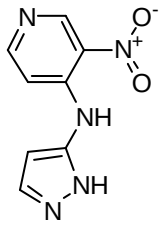
MS (ESI): mass calcd. for $C_{10}H_8N_4O_2$, 216.1; m/z found, M/Z = 217.1 $[M+H]^+$, ^1H NMR (400 MHz, DMSO- d_6): δ 9.87 (s, 1H), 9.11 (s, 1H), 8.58 (d, J = 2.5 Hz, 1H), 8.51 (dd, J = 4.7, 1.3 Hz, 1H), 8.26 (d, J = 6.1 Hz, 1H), 7.82 (d, J = 8.4 Hz, 1H), 7.50 (dd, J = 8.1, 4.7 Hz, 1H), 6.86 (d, J = 6.1 Hz, 1H)

Intermediate 25: 3-Fluoro-N-(3-nitropyridin-4-yl)pyridin-2-amine.



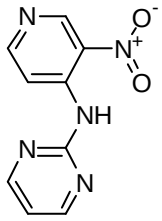
MS (ESI): mass calcd. for $C_{10}H_7FN_4O_2$, 234.1; m/z found, M/Z = 235.1 $[M+H]^+$, ^1H NMR (400 MHz, $CDCl_3$): δ 10.78 (s, 1H), 9.40 (s, 1H), 9.09 (d, J = 6.1 Hz, 1H), 8.57 (d, J = 6.2 Hz, 1H), 8.22 (d, J = 4.4 Hz, 1H), 7.51 (t, J = 9.2 Hz, 1H), 7.10 (dd, J = 8.1, 3.6 Hz, 1H).

Intermediate 26: 3-Nitro-N-1H-pyrazol-5-ylpyridin-4-amine.



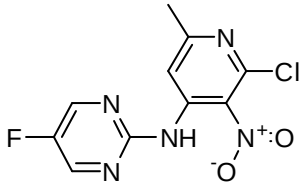
MS (ESI): mass calcd. for $C_8H_7N_5O_2$, 205.1; m/z found, M/Z = 206.1 $[M+H]^+$, ^1H NMR (400 MHz, DMSO-d_6): δ 12.74 (s, 1H), 9.88 (s, 1H), 9.10 (s, 1H), 8.37-8.35 (m, 1H), 7.80 (d, J = 6.3 Hz, 2H), 6.31 (s, 1H).

Intermediate 27: N-(3-Nitropyridin-4-yl)pyrimidin-2-amine.



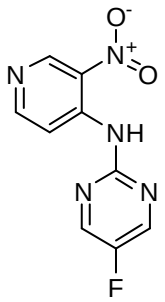
MS (ESI): mass calcd. for $C_9H_7N_5O_2$, 217.1; m/z found, M/Z = 218.1 $[M+H]^+$, ^1H NMR (400 MHz, CD_3OD): δ 9.65-9.62 (m, 2H), 8.84 (d, J = 4.9 Hz, 2H), 8.73-8.67 (m, 1H), 7.39 (t, J = 4.9 Hz, 1H).

Intermediate 28: N-(2-Chloro-6-methyl-3-nitropyridin-4-yl)-5-fluoropyrimidin-2-amine.



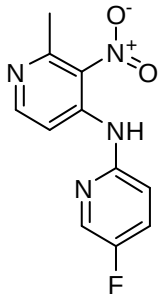
MS (ESI): mass calcd. for $C_{10}H_7ClFN_5O_2$, 283.1; m/z found, M/Z = 284.1 $[M+H]^+$, ^1H NMR (400 MHz, DMSO-d_6): δ 10.47 (s, 1H), 8.69 (s, 2H), 7.83 (s, 1H), 2.46 (s, 3H).

Intermediate 29: 5-Fluoro-N-(3-nitropyridin-4-yl)pyrimidin-2-amine.



MS (ESI): mass calcd. for $C_9H_6FN_5O_2$, 235.1; m/z found, 236.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 10.84 – 10.79 (s, 1H), 9.44 – 9.35 (s, 1H), 9.00 – 8.92 (d, J = 6.1 Hz, 1H), 8.65 – 8.58 (dd, J = 6.1, 0.7 Hz, 1H), 8.55 – 8.47 (s, 2H).

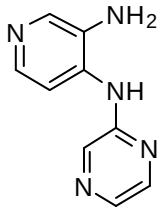
Intermediate 30: 5-Fluoro-N-(2-methyl-3-nitropyridin-4-yl)pyridin-2-amine.



MS (ESI): mass calcd. for $C_{11}H_9FN_4O_2$, 248.071; m/z found, 249.1 $[M+H]^+$.

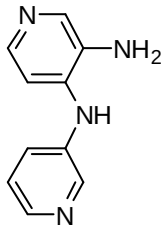
Intemediates 32-39 were made in a manner analogous to Intermediate 18 substituting Intermediates 21-30 for N-(3-Nitropyridin-4-yl)pyridin-2-amine in the synthesis of Intermediate 18.

Intermediate 32: N-4-Pyrazin-2-ylpyridine-3,4-diamine.



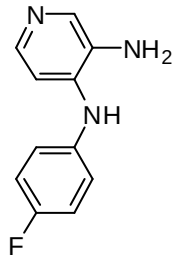
MS (ESI): mass calcd. for $C_9H_9N_5$, 187.1; m/z found, 188.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, J = 1.4 Hz, 1H), 8.20 (t, J = 2.1 Hz, 2H), 8.13 (d, J = 5.4 Hz, 1H), 8.11 (d, J = 2.7 Hz, 1H), 7.73 (d, J = 5.4 Hz, 1H), 6.75 (s, 1H).

Intermediate 33: N-4-Pyridin-3-ylpyridine-3,4-diamine.



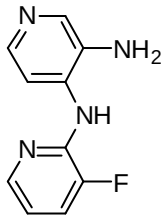
MS (ESI): mass calcd. for $C_{10}H_{10}N_4$, 186.1; m/z found, M/Z = 187.1 $[M+H]^+$, ^1H NMR (400 MHz, DMSO- d_6): δ 8.34 (d, J = 2.5 Hz, 1H), 8.11 (dd, J = 4.6, 1.2 Hz, 1H), 7.92 (s, 1H), 7.71 (s, 1H), 7.65 (d, J = 5.3 Hz, 1H), 7.45-7.41 (m, 1H), 7.27 (dd, J = 8.2, 4.6 Hz, 1H), 6.90 (d, J = 5.3 Hz, 1H), 4.94 (s, 2H).

Intermediate 34: N-4-(4-Fluorophenyl)pyridine-3,4-diamine.



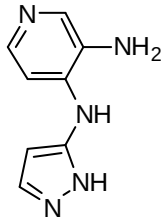
MS (ESI): mass calcd. for $C_{11}H_{10}FN_3$, 203.1; m/z found, M/Z = 204.1 $[M+H]^+$, ^1H NMR (400 MHz, DMSO- d_6): δ 7.85 (s, 1H), 7.60 (d, J = 5.3 Hz, 1H), 7.44 (s, 1H), 7.19-7.05 (m, 4H), 6.78 (d, J = 5.3 Hz, 1H), 4.83 (s, 2H).

Intermediate 35: N-4-(3-Fluoropyridin-2-yl)pyridine-3,4-diamine.



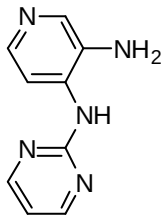
MS (ESI): mass calcd. for $C_{10}H_9FN_4$, 204.1; m/z found, M/Z = 205.2 $[M+H]^+$, ^1H NMR (400 MHz, CD_3OD): δ 8.08-7.96 (m, 2H), 7.83 (q, J = 5.5 Hz, 2H), 7.49 (ddd, J = 11.2, 8.0, 1.4 Hz, 1H), 6.89 (ddd, J = 8.3, 4.9, 3.6 Hz, 1H).

Intermediate 36: N-4-1H-Pyrazol-5-ylpyridine-3,4-diamine.



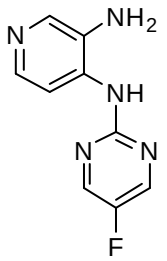
MS (ESI): mass calcd. for $C_8H_9N_5$, 175.1; m/z found, M/Z = 176.2 $[M+H]^+$, ^1H NMR (400 MHz, DMSO- d_6): δ 12.41 (s, 1H), 8.63 (s, 1H), 7.81-7.63 (m, 4H), 6.10 (s, 1H), 5.45 (s, 2H).

Intermediate 37: N-4-Pyrimidin-2-ylpyridine-3,4-diamine.



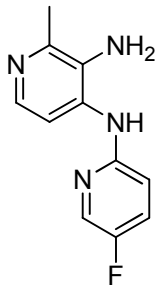
MS (ESI): mass calcd. for $C_9H_9N_5$, 187.1; m/z found, M/Z = 188.2 $[M+H]^+$, ^1H NMR (400 MHz, DMSO- d_6): δ 8.76 (s, 1H), 8.50 (d, J = 4.8 Hz, 2H), 7.96 (s, 1H), 7.85 (d, J = 5.4 Hz, 1H), 7.73 (d, J = 5.3 Hz, 1H), 6.90 (t, J = 4.8 Hz, 1H), 5.15 (s, 2H).

Intermediate 38: N-4-(5-Fluoropyrimidin-2-yl)pyridine-3,4-diamine.



MS (ESI): mass calcd. for $C_9H_8FN_5$, 205.1; m/z found, 206.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, J = 0.6 Hz, 2H), 8.21 – 8.12 (m, 2H), 8.01(d, J = 5.5 Hz, 1H), 7.40 (s, 1H), 3.43 – 3.38 (s, 2H).

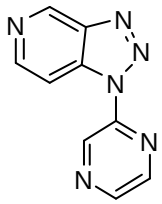
Intermediate 39: N-4-(5-Fluoropyridin-2-yl)-2-methylpyridine-3,4-diamine.



MS (ESI): mass calcd. for $C_{11}H_{11}FN_4$, 218.1; m/z found, 219.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 5.4 Hz, 1H), 7.38 – 7.24 (m, 3H), 6.80 – 6.72 (m, 1H), 6.48 (s, 1H), 3.54 – 3.47 (m, 2H), 2.49 (s, 3H).

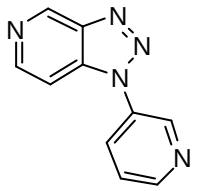
Intermediates 40-47 were made in a manner analogous to Intermediate 19 substituting Intermediates 32-39 for *N*-4-Pyridin-2-ylpyridine-3,4-diamine in the synthesis of Intermediate 19.

Intermediate 40: 1-Pyrazin-2-yl-1H-[1,2,3]triazolo[4,5-c]pyridine.



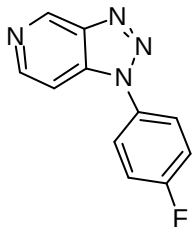
MS (ESI): mass calcd. for $C_9H_6N_6$, 198.1; m/z found, 199.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 9.70 (d, J = 1.2 Hz, 1H), 9.59 (d, J = 1.1 Hz, 1H), 8.75 (d, J = 5.8 Hz, 1H), 8.71 (d, J = 2.5 Hz, 1H), 8.62 (dd, J = 2.6, 1.5 Hz, 1H), 8.45 (dd, J = 5.8, 1.2 Hz, 1H).

Intermediate 41: 1-Pyridin-3-yl-1H-[1,2,3]triazolo[4,5-c]pyridine.



MS (ESI): mass calcd. for $C_{10}H_7N_5$, 197.1; m/z found, M/Z = 198.1 $[M+H]^+$, ^1H NMR (400 MHz, DMSO- d_6): δ 9.61 (s, 1H), 9.14 (d, J = 1.9 Hz, 1H), 8.80 (d, J = 4.7 Hz, 1H), 8.68 (d, J = 5.9 Hz, 1H), 8.43-8.31 (m, 1H), 8.06 (d, J = 5.9 Hz, 1H), 7.75 (dd, J = 8.2, 4.8 Hz, 1H).

Intermediate 42: 1-(4-Fluorophenyl)-1H-[1,2,3]triazolo[4,5-c]pyridine.

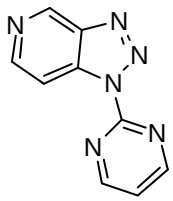


. MS (ESI): mass calcd. for $C_{11}H_7FN_4$, 214.1; m/z found, M/Z = 215.1 $[M+H]^+$, ^1H NMR (400 MHz, DMSO- d_6): 9.60 (s, 1H), 8.66 (d, J = 5.9 Hz, 1H), 7.98 (d, J = 4.8 Hz, 1H), 7.95 (d, J = 4.9 Hz, 2H), 7.56 (t, J = 8.8 Hz, 2H).

Intermediate 43: 1-(3-Fluoropyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine.

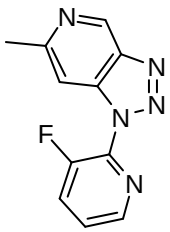
. MS (ESI): mass calcd. for $C_{10}H_6FN_5$, 215.1; m/z found, M/Z = 216.1 $[M+H]^+$, ^1H NMR (400 MHz, CD_3OD): δ 9.50 (d, J = 1.1 Hz, 1H), 8.63 (d, J = 5.9 Hz, 1H), 8.54 (dd, J = 3.6, 1.1 Hz, 1H), 8.13 (dd, J = 5.9, 1.0 Hz, 1H), 8.10-7.99 (m, 1H), 7.70-7.64 (m, 1H).

Intermediate 44: 1-Pyrimidin-2-yl-1H-[1,2,3]triazolo[4,5-c]pyridine.



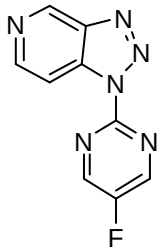
MS (ESI): mass calcd. for $C_9H_6N_6$, 198.1; m/z found, M/Z = 199.1 $[M+H]^+$, ^1H NMR (400 MHz, CD_3OD): δ 10.10 (s, 1H), 9.17-9.07 (m, 3H), 8.92 (d, J = 6.7 Hz, 1H), 7.74 (t, J = 4.9 Hz, 1H).

Intermediate 45: 1-(3-Fluoropyridin-2-yl)-6-methyl-1H-[1,2,3]triazolo[4,5-c]pyridine.



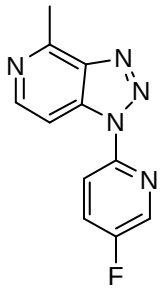
MS (ESI): mass calcd. for $C_{11}H_8FN_5$, 229.1; m/z found, M/Z = 230.2 $[M+H]^+$, ^1H NMR (400 MHz, DMSO- d_6): δ 9.48 (s, 1H), 8.59 (d, J = 4.6 Hz, 1H), 8.29-8.17 (m, 1H), 7.89 (s, 1H), 7.81-7.72 (m, 1H), 2.67 (s, 3H).

Intermediate 46: 1-(5-Fluoropyrimidin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine.



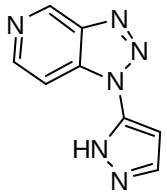
MS (ESI): mass calcd. for $C_9H_5FN_6$, 216.1; m/z found, 217.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 9.59 (d, J = 1.2 Hz, 1H), 8.85 (s, 2H), 8.78 (d, J = 5.8 Hz, 1H), 8.42 (dd, J = 5.8, 1.2 Hz, 1H).

Intermediate 47: 1-(5-Fluoropyridin-2-yl)-4-methyl-1H-[1,2,3]triazolo[4,5-c]pyridine.



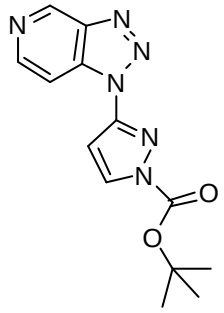
MS (ESI): mass calcd. for $C_{11}H_8FN_5$, 229.1; m/z found, 230.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.56 (d, J = 5.9 Hz, 1H), 8.49 (dd, J = 3.0, 0.6 Hz, 1H), 8.34 (ddd, J = 9.1, 3.8, 0.7 Hz, 1H), 8.27 (dd, J = 5.9, 0.8 Hz, 1H), 7.73 (ddd, J = 9.0, 7.4, 2.9 Hz, 1H), 3.10 (s, 3H).

Intermediate 48: 1-(1H-Pyrazol-5-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine.



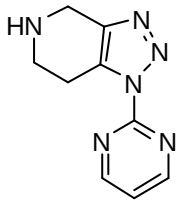
MS (ESI): mass calcd. for $C_8H_6N_6$, 186.1; m/z found, M/Z = 187.1 $[M+H]^+$, ^1H NMR (400 MHz, DMSO): δ 13.42 (s, 1H), 9.57 (s, 1H), 8.67 (d, J = 5.8 Hz, 1H), 8.12 (d, J = 5.8 Hz, 1H), 8.06 (d, J = 2.0 Hz, 1H), 6.88 (d, J = 1.8 Hz, 1H).

Intermediate 49: tert-Butyl 3-(1H-[1,2,3]triazolo[4,5-c]pyridin-1-yl)-1H-pyrazole-1-carboxylate.



A solution of 1-(1H-pyrazol-5-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine (1.3 g, 7.0 mmol) in DCM (40 ml) was treated with di-tert-butyl-dicarbonate (1.7 g, 7.7 mmol) and stirred overnight. The reaction mixture was concentrated and purified on 40 g SiO_2 with 0-70% EtOAc/hexanes. MS (ESI): mass calcd. for $C_{13}H_{14}N_6O_2$, 286.2; m/z found, 287.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 9.55 (d, J = 1.2 Hz, 1H), 8.74 (d, J = 5.8 Hz, 1H), 8.32 (dd, J = 5.8, 1.2 Hz, 1H), 8.24 (d, J = 2.9 Hz, 1H), 7.10 (d, J = 2.9 Hz, 1H), 1.72 (s, 9H).

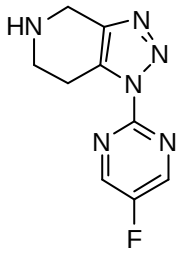
Intermediate 50: 1-Pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



The title compound was prepared in a manner analogous to Intermediate 20 substituting Intermediate 44 for 1-Pyridin-2-yl-1H-[1,2,3]-triazolo[4,5-c]pyridine and PtO_2 for Rh/C. MS (ESI): mass calcd. for $C_9H_{10}N_6$, 202.2; m/z found, 203.1 $[M+H]^+$. ^1H NMR (400 MHz,

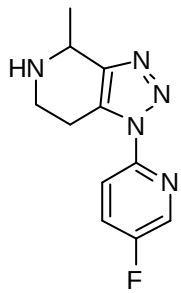
DMSO): δ 9.17 (s, 2H), 9.04 (d, J = 4.9 Hz, 2H), 7.72 (t, J = 4.9 Hz, 1H), 4.46 (t, J = 1.3 Hz, 2H), 3.49 (t, J = 6.0 Hz, 2H), 3.38 (s, 2H).

Intermediate 51: 1-(5-Fluoropyrimidin-2-yl)-4,5,6,7-tetrahydro-1H-[1,2,3]-triazolo[4,5-c]pyridine. -



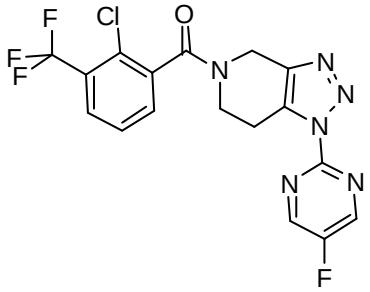
The title compound was prepared in a manner analogous to Intermediate 20 substituting Intermediate 46 for 1-Pyridin-2-yl-1H-[1,2,3]-triazolo[4,5-c]pyridine and PtO_2 for Rh/C. MS (ESI): mass calcd. for $C_9H_9N_6$, 220.2; m/z found, 221.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 8.73 (s, 2H), 4.13 (t, J = 1.4 Hz, 2H), 3.23 – 3.11 (m, 2H).

Intermediate 52: 1-(5-Fluoropyridin-2-yl)-4-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



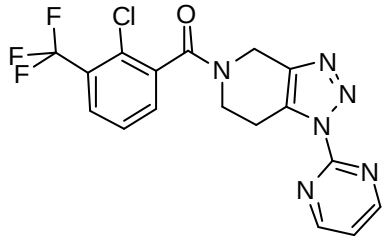
The title compound was prepared in a manner analogous to Intermediate 20 substituting Intermediate 47 for 1-Pyridin-2-yl-1H-[1,2,3]-triazolo[4,5-c]pyridine. MS (ESI): mass calcd. for $C_{11}H_{12}FN_5$, 233.2; m/z found, 234.1 $[M+H]^+$.

Example 64: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(5-fluoropyrimidin-2-yl)-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



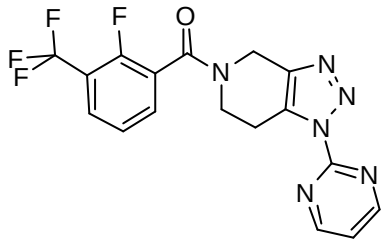
The title compound was prepared in a manner analogous to Example 63, Step 5 substituting Intermediate 51 for 1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine. MS (ESI): mass calcd. for $C_{17}H_{11}ClF_4N_6O$, 426.1; m/z found, 427.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, J = 15.8 Hz, 2H), 7.84 - 7.75 (m, 1H), 7.57 - 7.43 (m, 2H), 5.20 - 5.02 (m, 1H), 4.64 - 4.42 (m, 1H), 4.36 - 4.26 (m, 0.5H), 4.14 - 4.02 (m, 0.5H), 3.67 - 3.13 (m, 3H).

Example 65: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



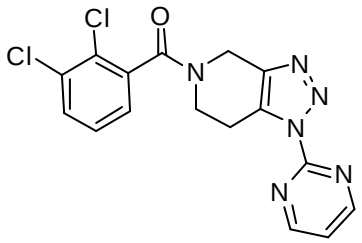
A solution of 1-pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine (97 mg, 0.48 mmol), 2-chloro-3-(trifluoromethyl)-benzoic acid (118 mg, 0.53 mmol) and Et_3N (0.1 ml, 0.72 mmol) in DMF (2.5 ml), was treated with HATU (219 mg, 0.58 mmol) and stirred for 3h. The reaction mixture was then concentrated and purified on silica gel with 0-4% NH_3 MeOH / CH_2Cl_2, followed by 50-100% EA/hexanes. MS (ESI): mass calcd. for $C_{17}H_{12}ClF_3N_6O$, 408.1; m/z found, 409.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.94 – 8.88 (d, J = 4.8 Hz, 1H), 8.88 – 8.82 (d, J = 4.8 Hz, 1H), 7.84 – 7.72 (m, 1H), 7.59 – 7.46 (m, 2H), 7.47 – 7.39 (dt, J = 11.5, 4.8 Hz, 1H), 5.24 – 5.01 (m, 1H), 4.65 – 4.46 (m, 1H), 4.38 – 4.26 (dt, J = 13.4, 5.5 Hz, 0.5H), 4.13 – 4.00 (ddd, J = 13.4, 6.9, 5.4 Hz, 0.5H), 3.68 – 3.50 (m, 1H), 3.50 – 3.43 (dt, J = 6.9, 4.8 Hz, 1H), 3.43 – 3.16 (m, 1H).

Example 66: 5-{[2-Fluoro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



The title compound was prepared in a manner analogous to Example 65 substituting 2-fluoro-3-(trifluoromethyl)-benzoic acid for 2-chloro-3-(trifluoromethyl)-benzoic acid. MS (ESI): mass calcd. for $C_{17}H_{12}F_4N_6O$, 392.1; m/z found, 393.1 $[M+H]^+$.

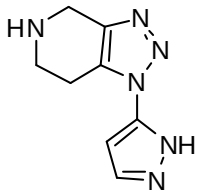
Example 67: 5-[(2,3-Dichlorophenyl)carbonyl]-1-pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



The title compound was prepared in a manner analogous to Example 65 substituting 2, 3 dichlorobenzoic acid for 2-chloro-3-(trifluoromethyl)-benzoic acid. MS (ESI): mass calcd. for $C_{16}H_{12}Cl_2N_6O$, 374.0; m/z found, 375.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.88 (dd, J = 15.2, 4.8 Hz, 1H), 7.54 (ddd, J = 8.0, 5.7, 1.6 Hz, 1H), 7.42 (dt, J = 10.9, 4.8 Hz, 1H), 7.36 – 7.17 (m, 3H), 5.20 – 5.01 (m, 1H), 4.63 – 4.44 (m, 1H), 4.27 – 4.03 (m, 1H), 3.68 – 3.51 (m, 1H), 3.50 – 3.12 (m, 1H), 3.42 – 3.16 (m, 1H).

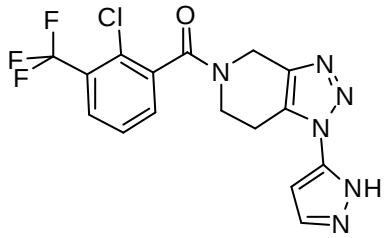
Example 68: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(1H-pyrazol-5-yl)-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.

Step A: 1-(1H-pyrazol-5-yl)-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



The title compound was prepared in a manner analogous to Intermediate 20 substituting Intermediate 48 for 1-Pyridin-2-yl-1H-[1,2,3]-triazolo[4,5-c]pyridine and PtO_2 for Rh/C. MS (ESI): mass calcd. for $C_8H_{10}N_6$, 190.1; m/z found, 191.1 $[M+H]^+$. ^1H NMR (400 MHz, MeOD) δ 7.79 (d, J = 2.5 Hz, 1H), 6.67 (d, J = 2.5 Hz, 1H), 3.98 (t, J = 1.2 Hz, 2H), 3.15 - 2.96 (m, 4H).

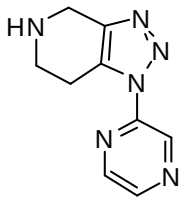
Step B: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(1H-pyrazol-5-yl)-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



The title compound was prepared in a manner analogous to Example 65 substituting the product of Example 68, Step A for 1-pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine. MS (ESI): mass calcd. for $C_{16}H_{12}ClF_3N_6O$, 396.1; m/z found, 397.1 $[M+H]^+$.

Example 69: 5-{[2-Fluoro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.

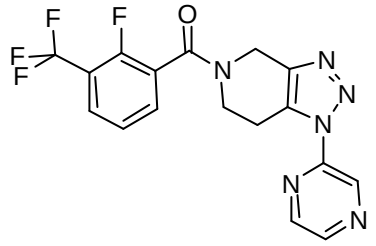
Step A: 1-(pyrazin-2-yl)-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



The title compound was prepared in a manner analogous to Intermediate 20 substituting Intermediate 40 for 1-Pyridin-2-yl-1H-[1,2,3]-triazolo[4,5-c]pyridine and PtO_2 for Rh/C. MS (ESI): mass calcd. for $C_9H_{10}N_6$, 202.1; m/z found, 203.1 [M+H]+. ^1H NMR (400 MHz,

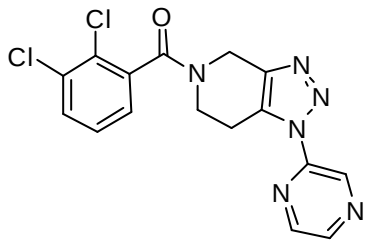
$CDCl_3$) δ 9.50 (d, J = 1.4 Hz, 1H), 8.62 (d, J = 2.5 Hz, 1H), 8.47 (dd, J = 2.6, 1.5 Hz, 1H), 4.13 (d, J = 1.4 Hz, 2H), 3.24 - 3.13 (m, 4H).

Step B: 5-{[2-Fluoro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



The title compound was prepared in a manner analogous to Example 65 substituting the product of Example 69, Step A for 1-pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine, 2-fluoro-3-(trifluoromethyl)benzoic acid for 2-chloro-3-(trifluoromethyl)-benzoic acid and DCM for DMF. MS (ESI): mass calcd. for $C_{17}H_{12}F_4N_6O$, 392.1; m/z found, 393.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 9.52 (dd, J = 15.7, 1.4 Hz, 1H), 8.66 (dd, J = 7.3, 2.5 Hz, 1H), 8.52-8.45(m, 1H), 7.80 – 7.71 (m, 1H), 7.72 – 7.58 (m, 1H), 7.38 (dt, J = 14.9, 7.7 Hz, 1H), 5.09 (s, 1H), 4.67 (s, 1H), 3.67 (s, 1H), 3.43 (t, J = 5.8 Hz, 1H), 3.33 (s, 1H), 1.88 – 1.71 (s, 1H)..

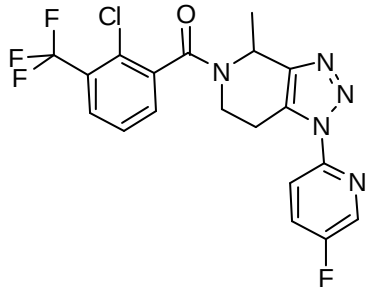
Example 70: 5-[(2,3-Dichlorophenyl)carbonyl]-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



The title compound was prepared in a manner analogous to Example 65 substituting 2,3-dichlorobenzoic acid for 2-chloro-3-(trifluoromethyl)-benzoic acid and DCM for DMF. MS (ESI): mass calcd. for $C_{16}H_{12}Cl_2N_6O$, 374.0; m/z found, 375.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 9.52 (ddd, J = 11.3, 1.4, 0.5 Hz, 1H), 8.66 (ddd, J = 10.9, 2.6, 0.5 Hz, 1H), 8.52-8.41 (m, 1H), 7.55 (ddd, J = 8.0, 3.1, 1.5 Hz, 1H), 7.38 – 7.17 (m, 2H), 5.19 – 5.01 (m,

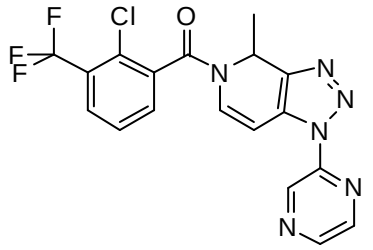
1H), 4.64 – 4.40 (m, 1H), 4.28 – 4.00 (m, 1H), 3.69 – 3.50 (m, 1H), 3.43 (d, J = 1.5 Hz, 1H).

Example 71: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(5-fluoropyridin-2-yl)-4-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



The title compound was prepared in a manner analogous to Example 63, Step 5 substituting Intermediate 52 for 1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine andDCM for THF. MS (ESI): mass calcd. for $C_{19}H_{14}ClF_4N_5O$, 439.1; m/z found, 440.1 $[M+H]^+$.

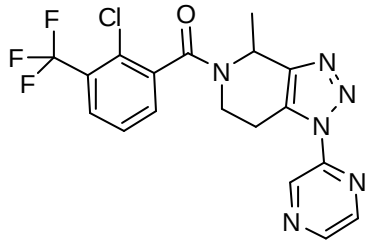
Example 72: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrazin-2-yl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



A suspension of 1-pyrazin-2-yl-1H-[1,2,3]triazolo[4,5-c]pyridine (100 mg, 0.5 mmol) in THF (2.5 mL) was treated with 2-chloro-3-(trifluoromethyl)benzoyl chloride (135 mg, 0.56 mmol) and the reaction stirred for 10 min at 23 °C. The reaction was cooled to -50 °C and treated with MeMgBr (3.0 M solution in Et_2O, 0.18 mL, 0.56 mmol), and reaction slowly warmed to 23 °C over 30 minutes. Saturated $NaHCO_3$ solution was added to the reaction mixture, which was then extracted with EtOAc and purified on 16 g SiO_2 with 0-50% ethyl acetate/hexanes to provide 174 mg (82%) of 5-{[2-chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrazin-2-yl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine. MS (ESI): mass calcd. for $C_{18}H_{12}ClF_3N_6O$, 420.1; m/z

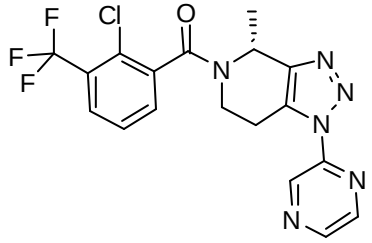
found, 421.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 9.64 – 9.45 (t, J = 1.8 Hz, 1H), 8.75 – 8.58 (d, J = 2.6 Hz, 1H), 8.51 – 8.38 (ddd, J = 6.8, 2.6, 1.5 Hz, 1H), 7.95 – 7.78 (dt, J = 4.5, 1.8 Hz, 1H), 7.70 – 7.38 (m, 2H), 6.69 – 6.54 (m, 1H), 6.44 – 6.22 (m, 2H), 1.70 – 1.50 (m, 4H).

Example 73: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



A suspension of the 5-{[2-chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrazin-2-yl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine (150 mg, 0.36 mmol) in MeOH (3.0 mL) and THF (1.0 mL) was treated with 10% Pd/C (30 mg), put under an atmosphere of H_2 and stirred overnight. The reaction was filtered through Celite© and purified on 12 g SiO_2 with 0-70% EA/ DCM. MS (ESI): mass calcd. for $C_{18}H_{14}ClF_3N_6O$, 422.1; m/z found, 423.1 $[M+H]^+$.

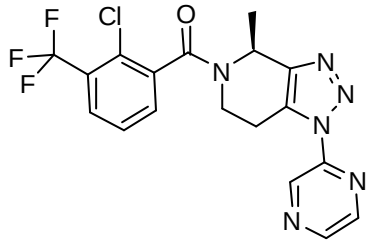
Example 74: (4R*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 73 performed using CHIRALPAK AD-H (5µm, 250x20mm) and a mobile phase of 75% CO_2, 25% EtOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD-H (250x4.6mm) and a mobile phase of 70% CO_2, 30% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single

enantiomer, 2.57 min retention time). MS (ESI): mass calcd. for $C_{18}H_{14}ClF_3N_6O$, 422.1; m/z found, 423.1 $[M+H]^+$.

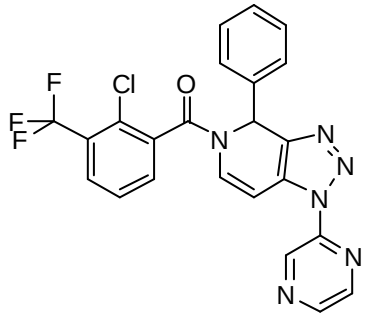
Example 75: (4S*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 73 performed using CHIRALPAK AD-H (5µm, 250x20mm) and a mobile phase of 75% CO_2, 25% EtOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD-H (250x4.6mm) and a mobile phase of 70% CO_2, 30% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 3.30 min retention time). MS (ESI): mass calcd. for $C_{18}H_{14}ClF_3N_6O$, 422.1; m/z found, 423.1 $[M+H]^+$.

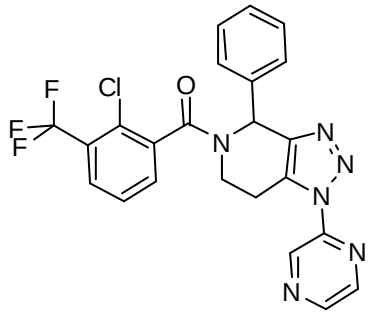
Examples 76-88 were made in a manner analogous to Example 72 & 73 substituting the appropriate Grignard reagent for MeMgBr.

Example 76: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-phenyl-1-pyrazin-2-yl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



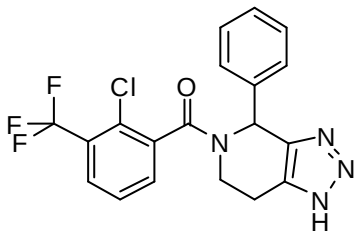
The title compound was prepared in a manner analogous to Example 72 substituting PhMgBr for MeMgBr. MS (ESI): mass calcd. for $C_{23}H_{14}ClF_3N_6O$, 482.1; m/z found, 483.1 $[M+H]^+$.

Example 77: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-phenyl-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



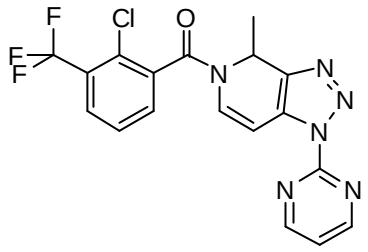
The title compound was prepared in a manner analogous to Example 73 substituting Example 76 for 5-{[2-chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrazin-2-yl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine. MS (ESI): mass calcd. for $C_{23}H_{16}ClF_3N_6O$, 484.1; m/z found, 485.2 $[M+H]^+$.

Example 78: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-phenyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



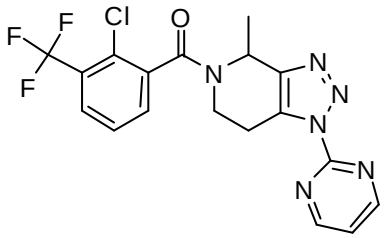
The title compound was obtained as a byproduct of the reaction carried out to generate Example 77. MS (ESI): mass calcd. for $C_{19}H_{14}ClF_3N_4O$, 406.1; m/z found, 407.1 $[M+H]^+$.

Example 79: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrimidin-2-yl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



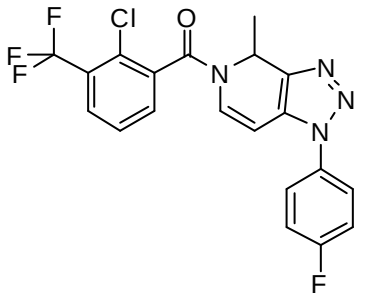
The title compound was prepared in a manner analogous to Example 72 substituting Intermediate 44 for 1-pyrazin-2-yl-1H-[1,2,3]triazolo[4,5-c]pyridine. MS (ESI): mass calcd. for $C_{18}H_{12}ClF_3N_6O$, 420.1; m/z found, 421.1 $[M+H]^+$.

Example 80: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



The title compound was prepared in a manner analogous to Example 73 substituting Example 79 for 5-{[2-chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrazin-2-yl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine. MS (ESI): mass calcd. for $C_{18}H_{14}ClF_3N_6O$, 422.1; m/z found, 423.1 $[M+H]^+$.

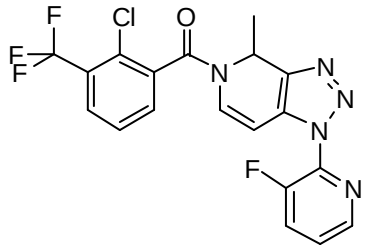
Example 81: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(4-fluorophenyl)-4-methyl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



The title compound was prepared in a manner analogous to Example 72 substituting Intermediate 42 for 1-pyrazin-2-yl-1H-[1,2,3]triazolo[4,5-c]pyridine. MS (ESI): mass

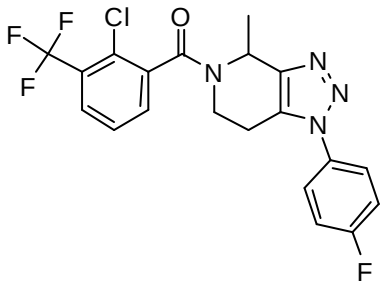
calcd. for $C_{20}H_{13}ClF_4N_4O$, 436.1; m/z found, 437.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 (ddd, J = 7.3, 4.6, 1.6 Hz, 1H), 7.69 – 7.41 (m, 3H), 7.32 – 7.19 (m, 3H), 6.39 – 6.20 (m, 2H), 5.79 – 5.70 (m, 1H), 1.67 – 1.54 (m, 3H).

Example 82: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(3-fluoropyridin-2-yl)-4-methyl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



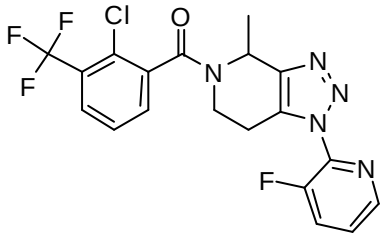
The title compound was prepared in a manner analogous to Example 72 substituting Intermediate 43 for 1-pyrazin-2-yl-1H-[1,2,3]triazolo[4,5-c]pyridine. MS (ESI): mass calcd. for $C_{19}H_{12}ClF_4N_5O$, 437.1; m/z found, 438.1 $[M+H]^+$.

Example 83: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(4-fluorophenyl)-4-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



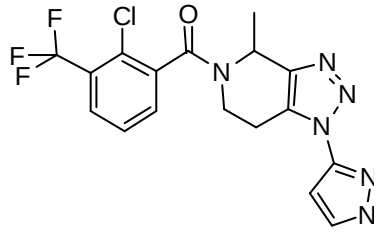
The title compound was prepared in a manner analogous to Example 73 substituting Example 81 for 5-{[2-chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrazin-2-yl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine. MS (ESI): mass calcd. for $C_{20}H_{15}ClF_4N_4O$, 438.1; m/z found, 439.1 $[M+H]^+$.

Example 84: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(3-fluoropyridin-2-yl)-4-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



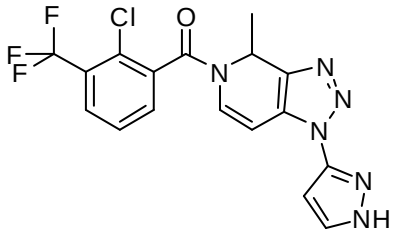
The title compound was prepared in a manner analogous to Example 73 substituting Example 82 for 5-{[2-chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrazin-2-yl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine. MS (ESI): mass calcd. for $C_{19}H_{14}ClF_4N_5O$, 439.0; m/z found, 440.1 $[M+H]^+$.

Example 85: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-(1H-pyrazol-3-yl)-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



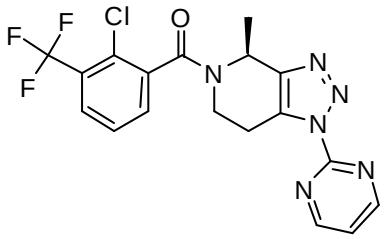
A solution of Intermediate 232 (480 mg, 0.94 mmol) in formic acid 4.0 ml) was treated with 6.0 N HCl (0.31 ml, 1.9 mmol) and stirred for 16 h. The following was performed three times: MeOH was added and rotovapped to the crude reaction mixture to give the desired product. The enantiomers were separated by chiral SFC on (CHIRALPAK AD-H 5µm 250x20mm). Mobile phase (70% CO_2, 30% EtOH) to give Examples 133 and 134. MS (ESI) mass calcd. $C_{22}H_{22}ClF_3N_6O_3$, 410.09; m/z found, 411.1 $[M+H]^+$. MS (ESI): mass calcd. for $C_{17}H_{14}ClF_3N_6O$, 410.1; m/z found, 411.1 $[M+H]^+$.

Example 86: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-(1H-pyrazol-3-yl)-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



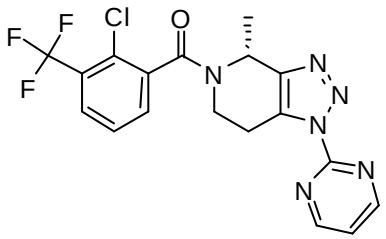
The title compound was prepared in a manner analogous to Example 61 step 3. . MS (ESI): mass calcd. for $C_{17}H_{12}ClF_3N_6O$, 408.1; m/z found, 409.1 $[M+H]^+$.

Example 87: (4S*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 80 performed using CHIRALPAK AD-H (5µm, 250x20mm) and a mobile phase of 70% CO_2, 30% EtOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) and a mobile phase of 70% CO_2, 30% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 2.85 min retention time. MS (ESI): mass calcd. for $C_{18}H_{14}ClF_3N_6O$, 422.1; m/z found, 422.8 $[M+H]^+$.

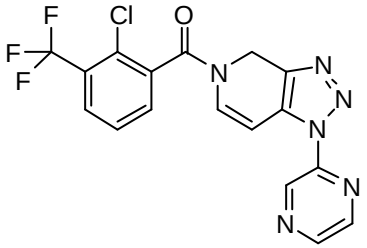
Example 88: (4R*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 80 performed using CHIRALPAK AD-H (5µm, 250x20mm) and a mobile phase of 70% CO_2, 30% EtOH. The enantiomeric purity was

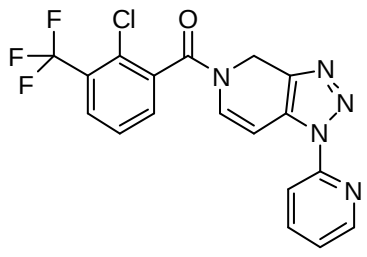
confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) and a mobile phase of 70% CO_2, 30% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 3.57 min retention time. MS (ESI): mass calcd. for $C_{18}H_{14}ClF_3N_6O$, 422.1; m/z found, 422.8 $[M+H]^+$.

Example 89: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyrazin-2-yl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



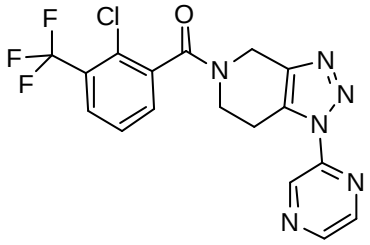
A solution of 1-pyrazin-2-yl-1H-[1,2,3]triazolo[4,5-c]pyridine (Intermediate 40) (50 mg, 0.25 mmol) in THF (2.0 mL) was treated with 2-chloro-3-(trifluoromethyl)benzoyl chloride (67 mg, 0.28 mmol) and stirred for 5 minutes. The reaction was treated with Hantzsch Ester (269 mg, 1.0 mmol) and heated to 80 °C in sealed tube for 90 min. Reaction was concentrated and purified on 16 g SiO_2 with 0-50% EtOAc/hexanes to yield 87 mg (85% yield) MS (ESI): mass calcd. for $C_{17}H_{10}ClF_3N_6O$, 406.1; m/z found, 407.1 $[M+H]^+$.

Example 90: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyridin-2-yl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



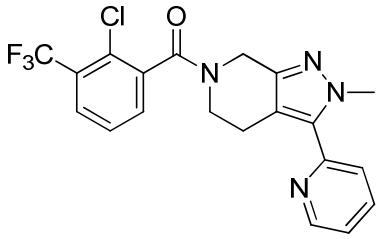
The title compound was prepared in a manner analogous to Example 89 substituting Intermediate 19 for Intermediate 40. MS (ESI): mass calcd. for $C_{18}H_{11}ClF_3N_5O$, 405.1; m/z found, 406.1 $[M+H]^+$.

Example 91: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.

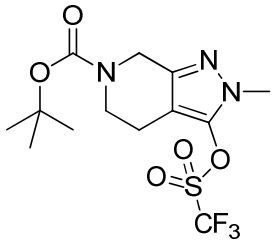


The title compound was prepared in a manner analogous to Example 73 substituting Example 89 for 5-{[2-chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrazin-2-yl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine. MS (ESI): mass calcd. for $C_{17}H_{12}ClF_3N_6O$, 408.1; m/z found, 409.1 $[M+H]^+$.

Example 92: 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-2-methyl-3-pyridin-2-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine.



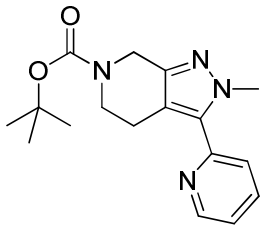
Intermediate 53: *tert*-Butyl 2-methyl-3-(((trifluoromethyl)sulfonyl)oxy)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridine-6(7H)-carboxylate



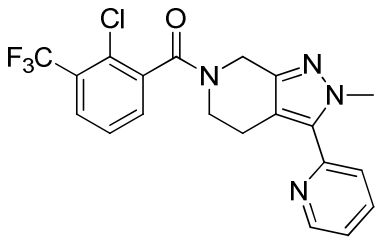
Step A: *tert*-Butyl 2-methyl-3-(((trifluoromethyl)sulfonyl)oxy)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridine-6(7H)-carboxylate. To a solution of 1-*tert*-butyl 4-ethyl 3-oxopiperidine-1,4-dicarboxylate (5.0 g, 18.4 mmol) in ethanol (10 mL) was added methylhydrazine (1.07 mL, 20.3 mmol). The solution was allowed to stir overnight at 80 ^oC under an atmosphere of nitrogen. The reaction was cooled to rt and concentrated in vacuo. The residue was dissolved in 40 mL CH_2Cl_2 and diisopropylethylamine (3.5 mL, 20.3 mmol) and N-phenyltrifluoromethanesulfonate (7.32 g, 20.3 mmol) were added. The

solution was allowed to stir overnight. The reaction was concentrated and the residue was purified by chromatography on silica gel (0-30% ethyl acetate/hexanes) to provide the desired product as a colorless oil (4.67 g, 79%). MS (ESI) mass calcd. $C_{13}H_{18}F_3N_3O_5S$, 385.1; m/z found, 386.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 4.53 - 4.45 (m, 2H), 3.77 (s, 2H), 3.69 (s, 1H), 3.66 - 3.57 (m, 2H), 2.60 - 2.54 (m, 2H), 1.49 (s, 3H), 1.48 (s, 6H).

Intermediate 54: *tert*-Butyl 2-methyl-3-(pyridin-2-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridine-6(7H)-carboxylate.

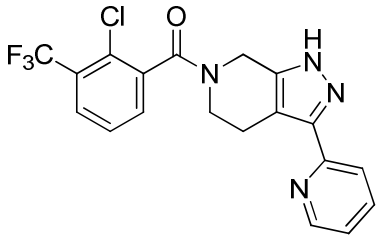


Step B: *tert*-Butyl 2-methyl-3-(pyridin-2-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridine-6(7H)-carboxylate. To a solution of *tert*-butyl 2-methyl-3-(((trifluoromethyl)sulfonyl)oxy)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridine-6(7H)-carboxylate (1.0 g, 2.60 mmol) in DMF (25 mL) was added pyridine-2-boronic acid pinacol ester (1.33 g, 6.49 mmol), cesium carbonate (3.42 g, 10.38 mmol), copper chloride (257 mg, 0.259 mmol), palladium acetate (29 mg, 0.130 mmol) and 1,1'-bis(diphenylphosphino)ferrocene (145 mg, 0.259 mmol). The reaction was stirred at 100 ^oC overnight under an atmosphere of N_2. The reaction was poured into ice water and extracted with CH_2Cl_2 three times. The combined organic layers were dried over anhydrous $MgSO_4$, filtered and evaporated. Chromatography on silica gel (0-100% ethyl acetate/hexanes) provided the desired product (145 mg, 17%). MS (ESI) mass calcd. $C_{17}H_{22}N_4O_2$, 314.2; m/z found, 315.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.73 - 8.70 (m, 0.5H), 7.80 - 7.76 (m, 0.5H), 7.40 -7.35 (m, 2H), 7.31 - 7.24 (m, 1H), 4.66 - 4.44 (m, 2H), 4.07 (s, 2H), 3.84 (s, 1H), 3.70 - 3.56 (m, 2H), 2.73-2.55 (m, 2H), 1.54 - 1.42 (m, 9H).



Step C: 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-2-methyl-3-pyridin-2-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine . To a solution of *tert*-butyl 2-methyl-3-(pyridin-2-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridine-6(7H)-carboxylate (135 mg, 0.429 mmol) in CH_2Cl_2 (5 mL) was added 4 M HCl in dioxane (0.43 mL, 1.72 mmol). The reaction was allowed to stir at rt for 1h, then 1 mL MeOH was added and the reaction was stirred overnight. The reaction was concentrated to a yellow gum. It was combined with 2-chloro-3-(trifluoromethyl)benzoic acid (155 mg, 0.690 mmol), BOP (305 mg, 0.690 mmol) and triethylamine (0.37 mL, 2.65 mmol). After stirring overnight at rt, the reaction was filtered and purified by HPLC (Agilent prep system, Waters XBridge C18 5μm 50x100 mm column, 5-99% MeOH/20 nM NH_4OH over 18 min at 80 mL/min). The desired product was isolated as a white solid (56 mg, 31%). MS (ESI) mass calcd. $C_{20}H_{16}ClF_3N_4O$, 420.1; m/z found, 421.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.75 - 8.69 (m, 1H), 7.85 - 7.72 (m, 2H), 7.54 - 7.34 (m, 3H), 7.31 - 7.25 (m, 1H), 5.09 (d, J = 16.6 Hz, 0.5H), 4.90 (d, J = 16.6 Hz, 0.5H), 4.46 (d, J = 15.8 Hz, 0.5H), 4.36 (d, J = 15.8 Hz, 0.5H), 4.24 (dt, J = 12.8, 5.4 Hz, 0.5H), 4.10 (s, 1H), 4.04 (s, 2H), 3.92 - 3.87 (m, 0.5H), 3.52-3.41 (m, 1H), 2.94 - 2.82 (m, 1H), 2.80-2.61 (m, 1H).

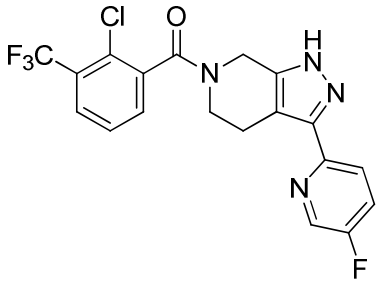
Example 93: 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-pyridin-2-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine-TFA salt



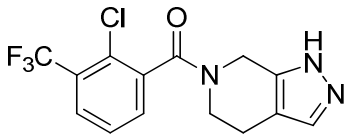
To a vial containing 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-2-methyl-3-pyridin-2-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine (17 mg, 0.040 mmol) was added pyridinium chloride (215 mg, 1.86 mmol). The vial was flushed with N_2 and heated to 170 ^oC for 30 min. To the reaction was added EtOAc and 1 M NaOH. The layers were separated and the water layer was extracted with EtOAc three times. The combined organic layers were concentrated in vacuo and the residue was purified by acidic HPLC. The product was isolated as orange oil (8 mg, 38%). MS (ESI) mass calcd. $C_{19}H_{14}ClF_3N_4O$, 406.1; m/z found, 407.1 $[M+H]^+$. ^1H NMR (500 MHz, MeOD) δ 8.70 - 8.66 (m, 1H), 8.41 - 8.34 (m, 1H), 8.05 (dd, J = 13.1, 8.2 Hz, 1H), 7.93 (td, J = 7.7, 1.8 Hz, 1H), 7.79 - 7.61 (m, 3H), 5.10

– 5.06 (m, 0.7H), 4.97 – 4.93 (m, 0.7H), 4.48 (s, 0.7H), 4.32 - 2.27 (m, 0.3H), 4.04 - 3.97 (m, 0.3H), 3.66 - 3.54 (m, 1.3H), 3.14-3.09 (m, 0.7H), 3.04 - 2.88 (m, 1.3H).

Example 94: 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-(5-fluoropyridin-2-yl)-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine.

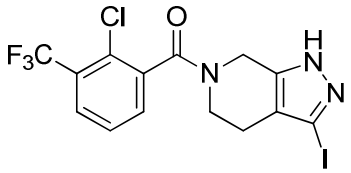


Intermediate 55: 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-(5-fluoropyridin-2-yl)-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine.



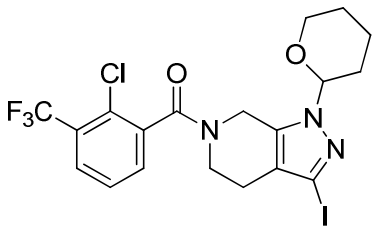
Step A: 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine. To a solution of 4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine (1.01 g, 5.15 mmol) in DMF (17 mL) was added 2-chloro-3-(trifluoromethyl)benzoic acid (2.31 g, 10.30 mmol), Hunig's base (3.55 mL, 20.60 mmol) and HATU (2.31 g, 10.30 mmol). The solution was allowed to stir for 30 min at rt then poured into ice water (300 mL). The resulting solid was collected by suction filtration and allowed to air dry. The solid was purified by chromatography on silica gel (0-100% ethyl acetate/hexanes). The product fractions were concentrated to a white solid which was dissolved in ethanol (20 mL) and 1M NaOH (20 mL) and stirred at 80 ^{o}C for 1h. Water (50 mL) and CH_2Cl_2 (50 mL) were added. The layers were separated and the water layer was extracted two times with CH_2Cl_2. The organic layers were combined, dried over anhydrous $MgSO_4$, filtered and concentrated to an oil (1.37g, 81%). MS (ESI) mass calcd. $C_{14}H_{11}ClF_3N_3O$, 329.1; m/z found, 330.1 $[M+H]^+$. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 - 7.73 (m, 1H), 7.52 - 7.41 (m, 2H), 7.37 (br s, 1H), 5.11 (d, J = 16.6 Hz, 0.5H), 4.85 (d, J = 16.6 Hz, 0.5H), 4.46 (d, J = 15.9 Hz, 0.5H), 4.36 (d, J = 15.9 Hz, 0.5H), 4.22 - 4.18 (m, 0.5H), 3.94 - 3.88 (m, 0.5H), 3.49-3.44 (m, 1H), 2.85 - 2.80 (m, 1H), 2.75-2.65 (m, 1H), 2.62 - 2.54 (m, 1H).

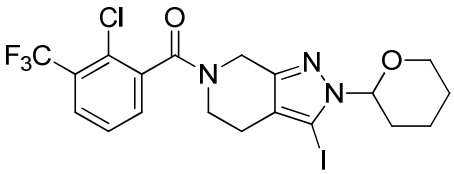
Intermediate 56: 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-iodo-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine.



Step B: 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-iodo-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine. To a solution of 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine (63 mg, 0.191 mmol) in DMF (1 mL) was added *N*-iodosuccinimide (47 mg, 0.210 mmol). The reaction was allowed to stir for 2 h at rt then poured into ice water (10 mL). The product was extracted with EtOAc three times. The organic layers were combined, dried over anhydrous $MgSO_4$, filtered and concentrated. Chromatography on silica gel (0-50% ethyl acetate/hexanes) provided the desired product (48 mg, 55%). MS (ESI) mass calcd. $C_{14}H_{10}ClF_3IN_3O$, 454.95; m/z found, 455.9 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.27 (br s, 1H), 7.81 - 7.74 (m, 1H), 7.52 - 7.43 (m, 2H), 5.13 (d, *J* = 16.7 Hz, 0.6H), 4.82 (d, *J* = 16.7 Hz, 0.6H), 4.47 (d, *J* = 16.0 Hz, 0.4H), 4.37 (d, *J* = 16.0 Hz, 0.4H), 4.27 - 4.19 (m, 0.4H), 3.95 – 3.85 (m, 0.4H), 3.45 – 3.50 (m, 1.2H), 2.62 – 2.66 (m, 0.8H), 2.51 (m, 0.6H), 2.46 - 2.37 (m, 0.6H).

Intermediate 57: 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-iodo-1-(tetrahydro-2H-pyran-2-yl)-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine



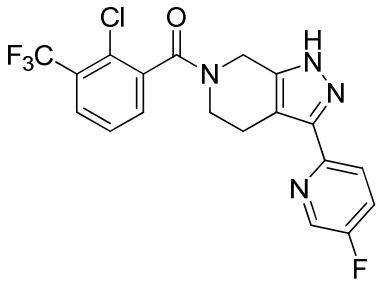


Step C: 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-iodo-1-(tetrahydro-2H-pyran-2-yl)-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine / 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-iodo-2-(tetrahydro-2H-pyran-2-yl)-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine.

To a solution of 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-iodo-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine (40 mg, 0.09 mmol) in dichloroethane (1 mL) was added 3,4-dihydropyran (24 mL, 0.26 mmol) and *para*-toluenesulfonic acid (2 mg, 0.009 mmol). After stirring for 4 h at rt the reaction was diluted with CH_2Cl_2 and washed with

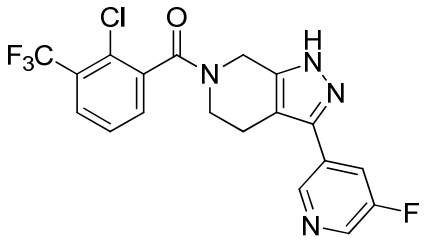
aqueous saturated sodium bicarbonate. The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated. Chromatography on silica gel (0-50% ethyl acetate/hexanes) provided the desired product as a mixture of regioisomers (45 mg, 95%). MS (ESI) mass calcd. $C_{19}H_{18}ClF_3IN_3O_2$, 539.0; m/z found, 540.0 $[M+H]^+$.

Example 94: 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-(5-fluoropyridin-2-yl)-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine.



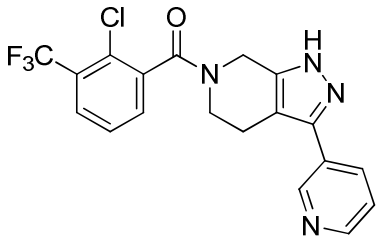
To a solution of 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-iodo-1-(tetrahydro-2H-pyran-2-yl)-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine (a mixture of regioisomers) (81 mg, 0.15 mmol) in DMF (1 mL) was added 5-fluoropyridine-2-boronic acid pinacol ester (84 mg, 0.38 mmol), cesium carbonate (198 mg, 0.600 mmol), copper chloride (15 mg, 0.15 mmol), palladium acetate (2 mg, 0.008 mmol) and 1,1'-bis(diphenylphosphino)ferrocene (8 mg, 0.150 mmol). The reaction was stirred at 85 ^oC overnight under an atmosphere of N_2. The reaction was diluted with water and aqueous sodium carbonate (5%) and extracted with EtOAc three times. The organic layers were combined, dried over anhydrous $MgSO_4$, filtered and concentrated. The residue was purified by HPLC (Agilent prep system, Waters XBridge, C18, 5µm, 30x100 mm column, 5-99% MeOH/20 nM NH_4OH over 18 min at 30 mL/min). The product fractions were concentrated in vacuo and then dissolved in CH_2Cl_2 (1 mL). (THP deprotection) To the solution, triethylsilane (0.011 mL, 0.0737 mmol) and TFA (0.236 mL, 0.059 mmol) were added. The reaction was stirred at rt for 1h then concentrated in vacuo. Chromatography on silica gel (0-100% ethyl acetate/hexanes) provided the desired product as a colorless oil (4 mg, 6%). MS (ESI) mass calcd. $C_{19}H_{13}ClF_4N_4O$, 424.1; m/z found, 425.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.50 - 8.47 (m, 1H), 7.81 - 7.74 (m, 1H), 7.56 - 7.42 (m, 4H), 5.13 (d, J = 16.5 Hz, 0.5H), 4.93 (d, J = 16.5 Hz, 0.5H), 4.51 (d, J = 15.8 Hz, 0.5H), 4.40 (d, J = 15.9 Hz, 0.5H), 4.34 - 4.25 (m, 0.5H), 4.07 - 3.98 (m, 0.5H), 3.61 - 3.49 (m, 1H), 3.08 - 3.03 (m, 1H), 3.01 - 2.94 (m, 0.5H), 2.88 - 2.78 (m, 0.5H).

Example 95: 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-(5-fluoropyridin-3-yl)-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine.



To a solution of 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-iodo-1-(tetrahydro-2H-pyran-2-yl)-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine (90 mg, 0.167 mmol) in 1,4-dioxane (1 mL) was added 5-fluoropyridine-3-boronic acid (70 mg, 0.50 mmol), potassium phosphate (106 mg, 0.50 mmol), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (18 mg, 0.025 mmol) and 1,1'-bis(diphenylphosphino)ferrocene (6 mg, 0.010 mmol). The reaction was stirred at 100 ^{o}C overnight under an atmosphere of N_2. The reaction was filtered through Celite© and the Celite© was washed with EtOAc. The solvent was concentrated and the residue was purified by HPLC (Agilent prep system, Waters XBridge, C18, 5µm, 30x100 mm column, 5-99% MeOH/20 mM NH_4OH over 18 min at 30 mL/min) followed by THP deprotection as described in Example 94 to provide the desired product (30 mg, 42%). MS (ESI) mass calcd. $C_{19}H_{13}ClF_4N_4O$, 424.1; m/z found, 425.1 $[M+H]^+$. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.73 - 8.64 (d, J = 6.1 Hz, 1H), 8.48 - 8.39 (m, 1H), 7.83 - 7.74 (m, 1H), 7.72 - 7.60 (m, 1H), 7.56 - 7.44 (m, 2H), 5.15 (d, J = 16.6 Hz, 0.7H), 4.88 (d, J = 16.6 Hz, 0.7H), 4.50 (d, J = 15.9 Hz, 0.3H), 4.39 (d, J = 15.9 Hz, 0.3H), 4.25 (dt, J = 12.8, 5.5 Hz, 0.3H), 4.04 - 3.95 (m, 0.3H), 3.54 (t, J = 5.7 Hz, 1.4H), 2.99 (t, J = 5.7 Hz, 0.7H), 2.92 - 2.73 (m, 1.3H).

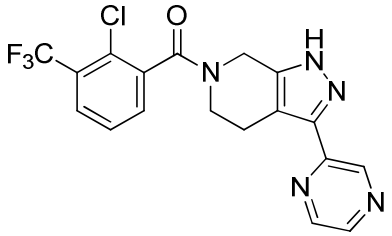
Example 96: 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-pyridin-3-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine.



This compound was prepared in a manner analogous to Example 95. MS (ESI) mass calcd. $C_{19}H_{14}ClF_3N_4O$, 406.1; m/z found 407.1 $[M+H]^+$. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.87 - 8.83 (m, 1H), 8.64 - 8.57 (m, 1H), 7.94 - 7.84 (m, 1H), 7.82 - 7.75 (m, 1H), 7.56 - 7.34 (m,

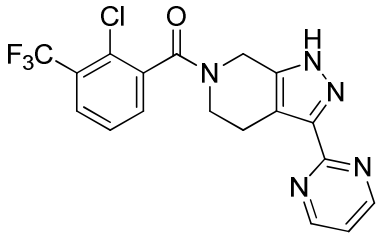
3H), 5.15 (d, J = 16.6 Hz, 0.6H), 4.89 (d, J = 16.6 Hz, 0.6H), 4.51 (d, J = 15.9 Hz, 0.4H), 4.40 (d, J = 15.9 Hz, 0.4H), 4.27 (dt, J = 13.0, 5.4 Hz, 0.4H), 4.01 - 3.91 (m, 0.4H), 3.53 (t, J = 5.8 Hz, 1.2H), 2.98 (t, J = 5.8 Hz, 0.8H), 2.91 - 2.71 (m, 1.2H).

Example 97: 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-pyrazin-2-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine .



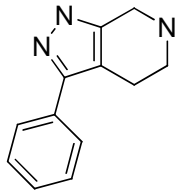
To a solution of 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-iodo-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine (Intermediate 57) (47 mg, 0.103 mmol) in 1,4-dioxane (1 mL) was added 2-tributylstannylpyrazine (0.041 mL, 0.124 mmol), lithium chloride (4 mg, 0.103 mmol) and tetrakis(triphenylphosphine)palladium(0) (119 mg, 0.103 mmol). The reaction was allowed to stir overnight at 110 ^{o}C and an additional 3h in a microwave reactor at 170 ^{o}C. The reaction was diluted with water and EtOAc and 50% potassium fluoride on Celite© (1g) was added. After stirring for 1h, the solution was filtered and the layers in the filtrate were separated. The organic layer was concentrated in vacuo and the residue was purified by HPLC (Agilent prep system, Waters XBridge, C18, 5μm, 30x100 mm column, 5-99% MeOH/20 mM NH_4OH over 18 min at 30 mL/min) to give the desired product. (3 mg, 8%). MS (ESI) mass calcd. $C_{18}H_{13}ClF_3N_5O$, 407.1; m/z found 408.1 $[M+H]^+$. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.88 (br s, 1H), 8.60-8.50 (m, 2H), 7.82 - 7.75 (m, 1H), 7.57 - 7.41 (m, 3H), 5.20 - 5.13 (m, 0.5H), 4.95 - 4.87 (m, 0.5H), 4.52 (d, J = 15.7 Hz, 0.5H), 4.41 (d, J = 15.8 Hz, 0.5H), 4.34 - 4.27 (m, 0.5H), 4.10 - 3.97 (m, 0.5H), 3.60 - 3.53 (m, 1H), 3.16 - 3.12 (m, 1H), 2.98 (m, 1H).

Example 98: 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-pyrimidin-2-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine



This compound was prepared in a manner analogous to Example 97 substituting copper iodide in place of lithium chloride. MS (ESI) mass calcd. $C_{18}H_{13}ClF_3N_5O$, 407.08; m/z found 408.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 11.13 (br s, 1H), 8.76 (dd, J = 14.9, 4.9 Hz, 2H), 7.77 (dd, J = 11.3, 8.1 Hz, 1H), 7.57 - 7.41 (m, 2H), 7.22 - 7.17 (m, 1H), 5.19 (d, J = 16.4 Hz, 0.5H), 4.90 (d, J = 15.7 Hz, 0.5H), 4.51 (d, J = 15.7 Hz, 0.5H), 4.41 (d, J = 15.8 Hz, 0.5H), 4.32 - 4.22 (m, 0.5H), 4.01 - 3.94 (m, 0.5H), 3.57 - 3.46 (m, 1H), 3.32 - 3.09 (m, 1.5H), 3.04 - 2.92 (m, 0.5H).

Intermediate 58: 3-phenyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine



Step A: *tert*-Butyl 3-oxo-2,3,4,5-tetrahydro-1H-pyrazolo[3,4-c]pyridine-6(7H)-carboxylate.

To a solution of 1-*tert*-butyl 4-ethyl 3-oxopiperidine-1,4-dicarboxylate (5.0 g, 18.43 mmol) in ethanol (10 mL) was added hydrazine monohydrate (1.04 g, 20.27 mmol) via syringe. The resulting solution was heated to 80 °C and stirred overnight. A white precipitate formed after stirring overnight. The reaction was cooled to rt and solvent was decanted from the reaction mixture, the solids were dried under vacuum to provide the desired product (3.8 g, 86%). MS (ESI) mass calcd. $C_{11}H_{17}N_3O_3$, 239.2; m/z found, 240.2 $[M+H]^+$. ^1H NMR (500 MHz, MeOD) δ 4.40 (s, 2H), 3.67 – 3.54 (m, 2H), 2.40 (t, J = 5.6 Hz, 2H), 1.48 (s, 9H).

Step B: *tert*-Butyl 3-(((trifluoromethyl)sulfonyl)oxy)-4,5-dihydro-1H-pyrazolo[3,4-c]pyridine-6(7H)-carboxylate.

tert-Butyl 3-oxo-2,3,4,5-tetrahydro-1H-pyrazolo[3,4-c]pyridine-6(7H)-carboxylate (3.8 g, 15.88 mmol) was dissolved in 60 mL of CH_2Cl_2 and diisopropylethylamine (6.0 mL, 34.93 mmol) and N-phenyltrifluoromethanesulfonate (6.3 g, 17.46 mmol) were added. The solution was allowed to stir at rt for 2 hours. The reaction was concentrated and the residue

was purified by chromatography on silica gel (0-30% ethyl acetate/hexanes) to provide the desired product (2.38 g, 40%). MS (ESI) mass calcd. $C_{12}H_{16}F_3N_3O_5S$, 371.3; m/z found, 372.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 4.56 (s, 2H), 3.66 (s, 2H), 2.59 (t, J = 5.5 Hz, 2H), 1.48 (d, J = 10.8 Hz, 9H).

Step C: *tert*-Butyl 3-(((trifluoromethyl)sulfonyl)oxy)-1-((2-(trimethylsilyl)ethoxy)methyl)-4,5-dihydro-1H-pyrazolo[3,4-c]pyridine-6(7H)-carboxylate.

tert-Butyl 3-(((trifluoromethyl)sulfonyl)oxy)-4,5-dihydro-1H-pyrazolo[3,4-c]pyridine-6(7H)-carboxylate (2.09 g, 5.63 mmol) was dissolved in THF (30 mL), and NaH (60%) (292.64 mg, 7.32 mmol) was added. The resulting solution was allowed to stir for 1 hour. 2-(Trimethylsilyl)ethoxymethyl chloride (1.32 mL, 7.32 mmol) was then added and the reaction mixture was stirred overnight at rt. The reaction was then cooled to 0 °C and quenched with NH_4Cl. Upon quenching a white precipitate formed and was re-dissolved with the addition of water. The reaction mixture was extracted with EtOAc, dried and concentrated. The residue was purified by chromatography on silica gel (0-20% ethyl acetate/hexanes) to provide the desired product (590 mg, 21%). The product was not UV active but stained in $KMnO_4$. MS (ESI) mass calcd. $C_{18}H_{30}F_3N_3O_6SSi$, 501.6; m/z found, 502.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 5.30 (s, 2H), 4.59 (s, 2H), 3.70 – 3.62 (m, 2H), 3.60 – 3.52 (m, 2H), 2.60 (t, J = 5.2 Hz, 2H), 1.51 (s, 9H), 0.94 – 0.87 (m, 11H).

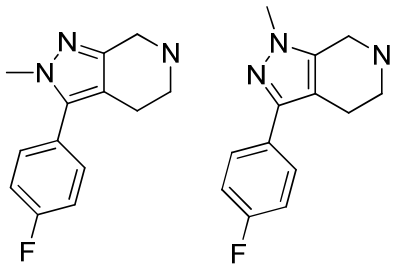
Step D: *tert*-Butyl 3-phenyl-1-((2-(trimethylsilyl)ethoxy)methyl)-4,5-dihydro-1H-pyrazolo[3,4-c]pyridine-6(7H)-carboxylate.

To a solution of *tert*-butyl 3-(((trifluoromethyl)sulfonyl)oxy)-1-((2-(trimethylsilyl)ethoxy)methyl)-4,5-dihydro-1H-pyrazolo[3,4-c]pyridine-6(7H)-carboxylate (440 mg, 0.88 mmol) in 1, 4-dioxane (9 mL) was added phenylboronic acid (331 mg, 2.63 mmol), potassium phosphate (559 mg, 2.63 mmol), 1,1'-bis(diphenylphosphino)ferrocene-dichloropalladium (II) (32 mg, 0.05 mmol) and 1,1'-bis(diphenylphosphino)ferrocene (10 mg, 0.02 mmol). The reaction was stirred at 160 ^oC for 1 hour in a microwave reactor. The reaction was cooled to rt and filtered through Celite© and rinsed with ethyl acetate. The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated. The residue was purified via chromatography on silica gel (0-25% ethyl acetate/hexanes) to provide the desired product (298 mg, 79%). MS (ESI) mass calcd. $C_{23}H_{35}N_3O_3Si$ 429.7; m/z found, 430.2 $[M+H]^+$.

Step E: 3-Phenyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine.

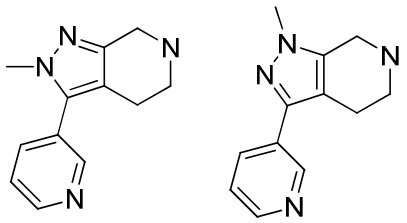
tert-Butyl 3-phenyl-1-((2-(trimethylsilyl)ethoxy)methyl)-4,5-dihydro-1H-pyrazolo[3,4-c]pyridine-6(7H)-carboxylate (298 mg, 0.69 mmol) was dissolved in DCM (8 mL) with TFA (0.5 mL, 6.98 mmol) and was allowed to stir under N_2 pressure at rt overnight. Solvent was removed and the residue partitioned between 2M Na_2CO_3 and DCM, then extracted with DCM three times. The combined organic layers were dried over Na_2SO_4 and concentrated. The resulting product was used as is in the next step.

Intermediate 59: 3-(4-Fluorophenyl)-2-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine HCl and 3-(4-fluorophenyl)-1-methyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine HCl.



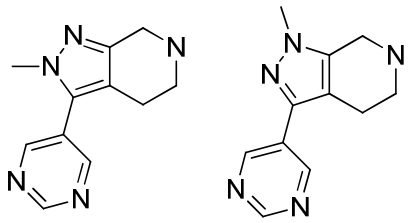
To a 1:1 mixture of *tert*-butyl 2-methyl-3-(((trifluoromethyl)sulfonyl)oxy)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridine-6(7H)-carboxylate and *tert*-butyl 3-methyl-3-(((trifluoromethyl)sulfonyl)oxy)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridine-6(7H)-carboxylate (1.0 g, 2.60 mmol) in 1, 4-dioxane (9 mL) was added 4-fluorophenylboronic acid (1.09 g, 7.79 mmol), potassium phosphate (1.65 g, 7.79 mmol), 1,1'-bis(diphenylphosphino)ferrocene-dichloropalladium (II) (287 mg, 0.4 mmol) and 1,1'-bis(diphenylphosphino)ferrocene (87 mg, 0.15 mmol). The reaction was stirred at 160 ^oC for 1 hour in a microwave reactor. The reaction was cooled to rt and filtered through Celite© and rinsed with ethyl acetate. The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated. The residue was purified via chromatography on silica gel (0-50% ethyl acetate/hexanes) to provide the desired product as a mixture of regio-isomers (520 mg, 60%). The product was then converted the analogous HCl salt with 4M HCl in dioxane. MS (ESI) mass calcd. $C_{18}H_{22}FN_3O_2$ 331.4; m/z found, 332.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.25 (m, 2H), 7.23 – 7.12 (m, 2H), 4.57 (s, 2H), 3.79 (s, 3H), 3.64 (s, 2H), 2.54 (s, 2H), 1.50 (d, J = 9.9 Hz, 9H).

Intermediate 60: 2-Methyl-3-(pyridin-3-yl)-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine HCl and 1-methyl-3-(pyridin-3-yl)-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine HCl.



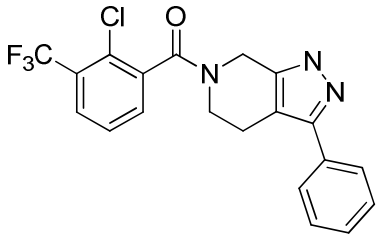
Prepared in manner analogous to that described for Intermediate 59 using pyridine-3-boronic acid to afford the desired product as a mixture of regio-isomers (417 mg, 98%) which was purified via chromatography on silica gel (0-30% ethyl acetate/hexanes). The product was then converted the analogous HCl salt with 4M HCl in dioxane. MS (ESI) mass calcd. $C_{17}H_{22}N_4O_2$ 314.4; m/z found, 315.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.66 (dd, J = 4.8, 1.7 Hz, 1H), 8.63 (dd, J = 2.2, 0.7 Hz, 1H), 7.70 – 7.62 (m, 1H), 7.47 – 7.39 (m, 1H), 4.63 - 4.53 (m, 2H), 3.85 – 3.80 (m, 3H), 3.70 - 3.65 (m, 2H), 2.71 - 2.65 (m, 2H), 1.52 – 1.48 (m, 9H).

Intermediate 61: 2-Methyl-3-(pyrimidin-5-yl)-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine HCl and 1-methyl-3-(pyrimidin-5-yl)-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine HCl.



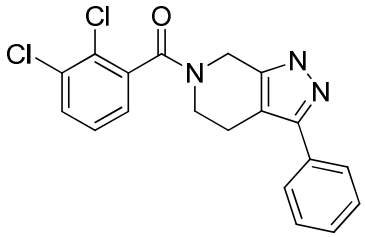
Prepared in manner analogous to that described for Intermediate 59 using pyrimidine-5-boronic acid to afford the desired product as a mixture of regio-isomers (407 mg, 99%) which was purified via chromatography on silica gel (0-30% 2M NH_3/methanol in DCM). The product was then converted the analogous HCl salt with 4M HCl in dioxane. MS (ESI) mass calcd. $C_{16}H_{21}N_5O_2$ 315.4; m/z found, 316.2 $[M+H]^+$.

Example 99: (2-Chloro-3-(trifluoromethyl)phenyl)(3-phenyl-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone.



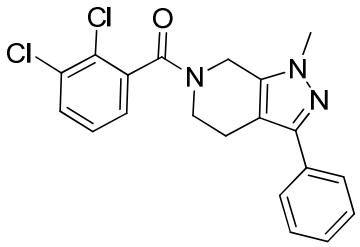
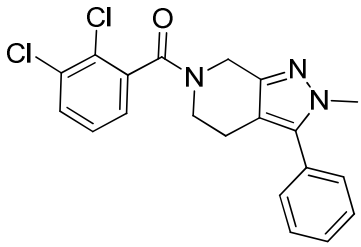
To a solution of Intermediate 58 (433 mg, 1.38 mmol) in DCM (5 mL) was added 2-chloro-3-(trifluoromethyl)benzoic acid (310.3 mg, 1.38 mmol), triethylamine (1.15 mL, 8.29 mmol) and BOP (611.03 mg, 1.38 mmol). The solution was allowed to stir overnight. Following dilution with water, the mixture was extracted with DCM three times. The combined organic layers were dried over Na_2SO_4 and conc. The resulting residue was purified by basic HPLC (0-99% acetonitrile). (356 mg, 56%). MS (ESI): mass calcd. for $C_{20}H_{15}ClF_3N_3O$, 405.81; m/z found, 406.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 7.76 (ddd, J = 12.1, 7.8, 1.4 Hz, 1H), 7.56 – 7.33 (m, 7H), 5.17 – 4.97 (m, 1H), 4.52 – 4.33 (m, 1H), 4.28 (dt, J = 12.9, 5.4 Hz, 1H), 3.99 – 3.83 (m, 1H), 3.54 – 3.41 (m, 1H), 2.97 (t, J = 5.8 Hz, 1H), 2.79 – 2.68 (m, 1H).

Example 100: 6-[(2,3-Dichlorophenyl)carbonyl]-3-phenyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine.



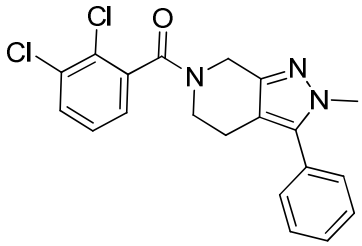
Prepared in manner analogous to that described for Example 99 using 2,3-dichlorobenzoic acid instead of 2-chloro-3-(trifluoromethyl)benzoic acid to afford the desired product. MS (ESI): mass calcd. for $C_{19}H_{15}Cl_2N_3O$, 372.26; m/z found, 373.2 $[M+H]^+$. ^1H NMR ($CDCl_3$): 7.59 – 7.55 – 7.20 (m, 8H), 5.17 – 4.86 (m, 1H), 4.55 – 4.34 (m, 1H), 4.26 – 3.89 (m, 1H), 3.56 – 3.45 (m, 1H), 3.03 – 2.93 (m, 1H), 2.91 – 2.68 (m, 2H).

Example 101: 6-[(2,3-Dichlorophenyl)carbonyl]-1-methyl-3-phenyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine - 6-[(2,3-dichlorophenyl)carbonyl]-2-methyl-3-phenyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine (1:1).

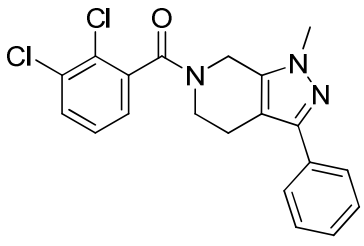
To a solution of 6-[(2,3-Dichlorophenyl)carbonyl]-3-phenyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine (35mg, 0.09 mmol) in DMF (0.5 mL) was added NaH (60%) (5 mg, 0.1 mmol). The reaction was allowed to stir at rt for 1 hr then iodomethane (0.005 mL, 0.09 mmol) was added. The reaction mixture was allowed to stir for 2 hours. After aqueous workup, the resulting mixture was extracted with ethyl acetate. The combined organic layers were dried and concentrated into a yellow residue which was purified via Basic HPLC (0-99% acetonitrile/water (NH_4OH)) to afford the desired product 924 mg, 33%). MS (ESI): mass calcd. for $C_{20}H_{17}C_{l2}N_3O$, 386.28; m/z found, 387.2 $[M+H]^+$.

Example 102: 6-[(2,3-Dichlorophenyl)carbonyl]-2-methyl-3-phenyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine.



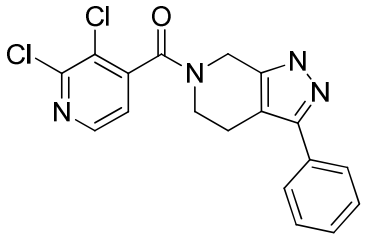
The desired product was obtained from SFC separation of Example 101. MS (ESI): mass calcd. for $C_{20}H_{17}Cl_2N_3O$, 386.28; m/z found, 387.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 7.52 – 7.20 (m, 8H), 5.14 – 4.76 (m, 1H), 4.57 – 4.19 (m, 1H), 4.19 – 3.86 (m, 1H), 3.84 – 2.78 (m, 3H), 3.46 – 3.40 (m, 1H), 2.72 (t, J = 5.8 Hz, 1H), 2.65 – 2.46 (m, 1H).

Example 103: 6-[(2,3-Dichlorophenyl)carbonyl]-1-methyl-3-phenyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine.



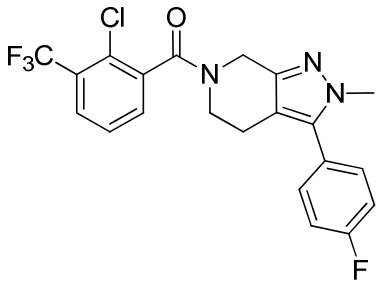
The desired product was obtained SFC separation of Example 101. MS (ESI): mass calcd. for $C_{20}H_{17}Cl_2N_3O$, 386.28; m/z found, 387.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 7.70 – 7.62 (m, 2H), 7.58 – 7.52 (m, 1H), 7.45 – 7.36 (m, 2H), 7.35 – 7.27 (m, 2H), 7.27 – 7.21 (m, 1H), 5.03 (d, J = 16.4 Hz, 1H), 4.80 (d, J = 16.4 Hz, 1H), 3.76 (s, 3H), 3.51 – 3.45 (m, 2H), 2.89 – 2.81 (m, 1H), 2.79 – 2.70 (m, 1H).

Example 104: 6-[(2,3-Dichloropyridin-4-yl)carbonyl]-3-phenyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine.



Prepared in an analogous manner to Example 99 using 2,3-dichloropyridine-4-carboxylic acid to afford the desired product MS (ESI): mass calcd. for $C_{18}H_{14}Cl_2N_4O$, 373.24; m/z found, 374.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.38 (dd, J = 18.2, 4.8 Hz, 1H), 7.52 – 7.36 (m, 5H), 7.24 – 7.19 (m, 1H), 5.01 – 4.95 (m, 1H), 4.46 – 4.37 (m, 1H), 4.23 – 3.90 (m, 1H), 3.57 – 3.39 (m, 1H), 2.97 (t, J = 5.8 Hz, 1H), 2.91 – 2.72 (m, 1H).

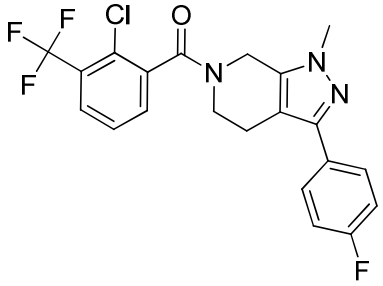
Example 105: 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-(4-fluorophenyl)-2-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine.



To a solution of Intermediate 59 (200 mg, 0.74 mmol) in DCM (5 mL) was added 2-chloro-3-(trifluoromethyl)benzoic acid (167 mg, 0.74 mmol), Triethylamine (0.62 mL, 4.48 mmol) and BOP (611.03 mg, 1.38 mmol). The solution was allowed to stir overnight. The reaction was then given an aqueous workup and extracted with DCM three times. The combined organic layers were dried over Na_2SO_4 and concentrated. The resulting mixture of regioisomers was purified by basic HPLC (0-99% acetonitrile) then by SFC to obtain the

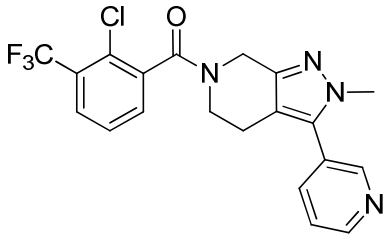
desired product (31 mg, 9%) MS (ESI): mass calcd. for $C_{21}H_{16}ClF_4N_3O$, 437.83; m/z found, 438.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, J = 7.8 Hz, 1H), 7.53 – 7.48 (m, 1H), 7.45 (dd, J = 14.5, 7.3 Hz, 1H), 7.35 – 7.27 (m, 2H), 7.22 – 7.13 (m, 2H), 5.01 – 4.95 (m, 1H), 4.45 – 4.38 (m, 1H), 4.27 – 3.84 (m, 1H), 3.78 (m, 3H), 3.50 – 3.37 (m, 1H), 2.74 – 2.66 (m, 1H), 2.62 – 2.43 (m, 1H).

Example 106: 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-(4-fluorophenyl)-1-methyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine.



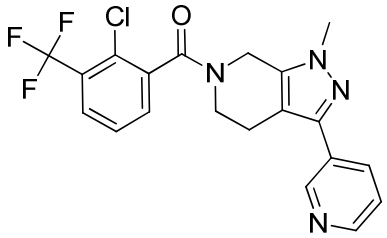
The desired product (2.6 mg, 1%) was obtained via SFC separation of Example 105. MS (ESI): mass calcd. for $C_{21}H_{16}ClF_4N_3O$, 437.83; m/z found, 438.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 7.80 (dd, J = 7.3, 2.0 Hz, 1H), 7.64 – 7.59 (m, 2H), 7.55 – 7.46 (m, 2H), 7.13 – 7.04 (m, 2H), 5.06 (d, J = 16.4 Hz, 1H), 4.80 (d, J = 16.4 Hz, 1H), 3.87 (s, 3H), 3.48 (t, J = 5.7 Hz, 2H), 2.95 – 2.67 (m, 2H).

Example 107: 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-2-methyl-3-pyridin-3-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine.



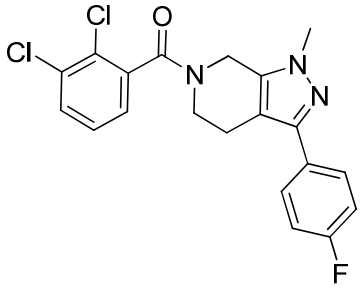
Prepared in an analogous manner to Example 105 using intermediate 60. The resulting mixture of regioisomers was purified by basic HPLC (0-99% acetonitrile), then by SFC to obtain the desired product (60.4 mg, 24%) MS (ESI): mass calcd. for $C_{20}H_{16}ClF_3N_4O$, 420.82; m/z found, 421.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.78 – 8.54 (m, 2H), 7.75 (t, J = 11.2 Hz, 1H), 7.68 (dd, J = 9.5, 7.9 Hz, 1H), 7.51 (d, J = 7.6 Hz, 1H), 7.45 (dt, J = 14.6, 7.4 Hz, 2H), 5.02 – 4.96 (m, 1H), 4.44 – 4.37 (m, 1H), 4.26 – 3.88 (m, 1H), 3.86 – 3.80 (m, 3H), 3.49 – 3.41 (m, 1H), 2.77 – 2.70 (m, 1H), 2.66 – 2.46 (m, 1H).

Example 108: 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-methyl-3-pyridin-3-yl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine.



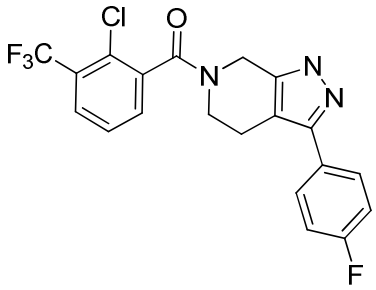
The desired product (33.6 mg, 13%) was obtained via SFC separation of Example 107. MS (ESI): mass calcd. for $C_{20}H_{16}ClF_3N_4O$, 420.82; m/z found, 421.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.93 – 8.87 (m, 1H), 8.55 (dd, J = 11.6, 4.4 Hz, 1H), 8.01 (dt, J = 8.0, 1.9 Hz, 1H), 7.80 (dt, J = 9.2, 4.5 Hz, 1H), 7.56 – 7.48 (m, 2H), 7.38 – 7.30 (m, 1H), 5.09 (d, J = 16.5 Hz, 1H), 4.80 (d, J = 16.5 Hz, 1H), 3.90 (s, 3H), 3.53 – 3.48 (m, 2H), 3.03 – 2.67 (m, 2H).

Example 109: 6-[(2,3-Dichlorophenyl)carbonyl]-3-(4-fluorophenyl)-1-methyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine.



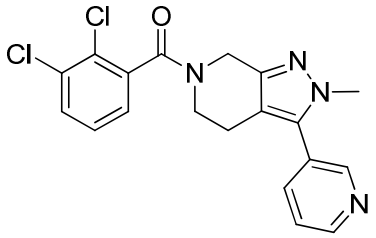
Prepared in an analogous manner to Example 99 using 2,3-dichlorobenzoic acid instead of 2-chloro-3-(trifluoromethyl)benzoic acid and Intermediate 59 instead of Intermediate 58 to afford the desired product. MS (ESI): mass calcd. for $C_{20}H_{16}Cl_2FN_3O$, 404.27; m/z found, 405.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 7.68 – 7.59 (m, 2H), 7.55 (dd, J = 8.0, 1.5 Hz, 1H), 7.31 (td, J = 7.8, 2.4 Hz, 1H), 7.25 – 7.22 (m, 1H), 7.13 – 7.05 (m, 2H), 5.01 (d, J = 16.4 Hz, 1H), 4.80 (d, J = 16.5 Hz, 1H), 3.86 (s, 3H), 3.48 (t, J = 5.7 Hz, 2H), 2.96 – 2.66 (m, 2H).

Example 110: 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-(4-fluorophenyl)-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine.



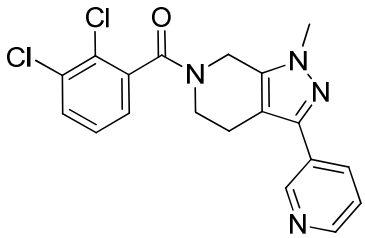
To a vial containing 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-3-(4-fluorophenyl)-2-methyl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine (50 mg, 0.11 mmol) was added pyridinium chloride (270 mg, 2.30 mmol). The vial was flushed with N_2 and heated to 170 ^{o}C for 30 min in a microwave reactor. To the reaction was added EtOAc and 1M NaOH. The layers were separated and the water layer was extracted with EtOAc three times. The combined organic layers were concentrated in vacuo and the residue was purified by HPLC (Gilson prep system, inertsil ODS-3, C18, 3µm 30x100mm column at 45 °C, gradient of 5-70% MeCN/water with 0.05% TFA over 7 min, flow rate of 80 mL/min). The product was isolated as orange oil (9 mg, 19%) MS (ESI): mass calcd. for $C_{20}H_{14}ClF_4N_3O$, 423.8; m/z found, 424.2 $[M+H]^+$. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 – 7.69 (m, 1H), 7.58 – 7.38 (m, 4H), 7.18 – 7.13 (m, 2H), 5.01 (m, 1H), 4.48 – 4.39 (m, 1H), 4.30 – 3.87 (m, 1H), 3.60 – 3.40 (m, 1H), 2.94 (t, J = 5.8 Hz, 1H), 2.86 – 2.65 (m, 1H).

Example 111: 6-[(2,3-Dichlorophenyl)carbonyl]-2-methyl-3-pyridin-3-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine.



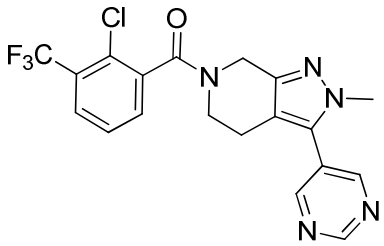
Prepared in an analogous manner to Example 107 using 2,3-dichlorobenzoic acid to afford the desired product (52.6 mg 22%) MS (ESI): mass calcd. for $C_{19}H_{16}Cl_2N_4O$, 387.27; m/z found, 388.2 $[M+H]^+$. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.67 (ddd, J = 11.6, 4.8, 1.5 Hz, 1H), 8.63 (dd, J = 11.8, 1.8 Hz, 1H), 7.67 (ddt, J = 9.6, 8.0, 1.9 Hz, 1H), 7.51 (dt, J = 7.9, 1.6 Hz, 1H), 7.44 (ddd, J = 12.8, 7.8, 4.9 Hz, 1H), 7.29 (dd, J = 11.0, 4.4 Hz, 1H), 7.24 (t, J = 7.6 Hz, 1H), 5.14 – 4.82 (m, 1H), 4.58 – 4.20 (m, 1H), 4.17 – 3.90 (m, 1H), 3.88 – 3.79 (m, 3H), 3.52 – 3.39 (m, 1H), 2.73 (t, J = 5.8 Hz, 1H), 2.66 – 2.46 (m, 1H).

Example 112: 6-[(2,3-Dichlorophenyl)carbonyl]-2-methyl-3-pyridin-3-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine.



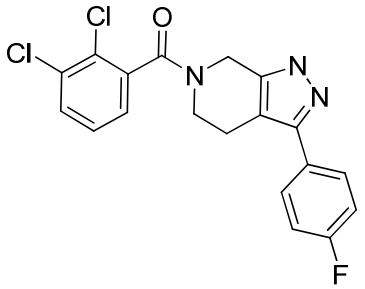
Prepared in an analogous manner to Example 107 using 2,3-dichlorobenzoic acid to afford the desired product (31.2 mg 13%) via SFC separation . MS (ESI): mass calcd. for $C_{19}H_{16}Cl_2N_4O$, 387.27; m/z found, 388.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.88 (s, 1H), 8.54 (s, 1H), 8.02 (d, J = 8.0 Hz, 1H), 7.58 – 7.53 (m, 1H), 7.37 – 7.29 (m, 2H), 7.26 – 7.22 (m, 1H), 5.05 (d, J = 16.5 Hz, 1H), 4.81 (d, J = 16.5 Hz, 1H), 3.89 (s, 3H), 3.55 – 3.49 (m, 3H), 2.99 – 2.70 (m, 2H).

Example 113: 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-2-methyl-3-pyrimidin-5-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine.



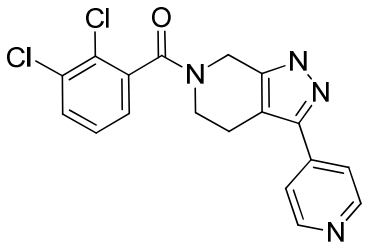
Step A: 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-2-methyl-3-pyrimidin-5-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine. Prepared in an analogous manner to Example 105 using intermediate 61. The resulting residue was purified by basic HPLC (0-99% acetonitrile) and then via SFC to obtain the desired product. MS (ESI): mass calcd. for $C_{19}H_{15}ClF_3N_5O$, 421.81; m/z found, 422.2 $[M+H]^+$.

Example 114: 6-[(2,3-Dichlorophenyl)carbonyl]-3-(4-fluorophenyl)-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine.



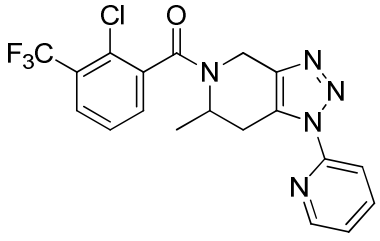
Prepared in an analogous manner to Example 110 using 6-[(2,3-Dichlorophenyl)carbonyl]-3-(4-fluorophenyl)-1-methyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine to afford the desired product (22.1 mg 10%) MS (ESI): mass calcd. for $C_{19}H_{14}Cl_2FN_3O$, 390.25; m/z found, 391.2$[M+H]^+$. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 – 7.42 (m, 3H), 7.33 – 7.21 (m, 2H), 7.18 – 7.08 (m, 2H), 5.15 – 4.77 (m, 1H), 4.58 – 4.33 (m 1H), 4.27 – 3.88 (m, 1H), 3.57 – 3.42 (m, 1H), 2.92 (t, J = 5.8 Hz, 1H), 2.86 – 2.64 (m, 1H).

Example 115: 6-[(2,3-Dichlorophenyl)carbonyl]-3-pyridin-4-yl-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-c]pyridine.

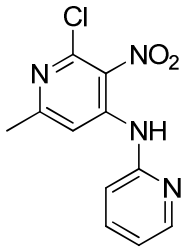


Prepared in an analogous manner to Example 110 using 6-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-methyl-3-pyridin-3-yl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine to afford the desired product (52.6 mg 22%) MS (ESI): mass calcd. for $C_{18}H_{14}Cl_2N_4O$, 373.24; m/z found, 374.2 $[M+H]^+$. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.67 (dd, J = 21.7, 5.3 Hz, 2H), 7.59 – 7.45 (m, 2H), 7.35 – 7.19 (m, 3H), 5.18 - 4.80 (m, 1H), 4.62 – 4.27 (m 1H), 4.23 – 3.96 (m, 1H), 3.60 – 3.49 (m, 1H), 3.05 – 2.98 (m, 1H), 2.95 – 2.75 (m, 1H).

Example 116: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine

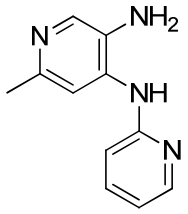


Intermediate 62: *N*-(2-Chloro-6-methyl-3-nitropyridin-4-yl)pyridin-2-amine



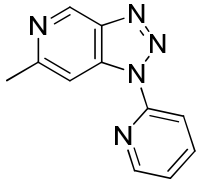
Step A: *N*-(2-Chloro-6-methyl-3-nitropyridin-4-yl)pyridin-2-amine. To a solution of 2-aminopyridine (361 mg, 3.72 mmol) in THF (30 mL) was added 60% sodium hydride (164 mg, 4.09 mmol). After stirring for 2 h at rt, 2,4-dichloro-6-methyl-3-nitropyridine (864 mg, 4.09 mmol) was added. After stirring 3.5h additional at rt, sat. NH_4Cl solution (30 mL) was added. The organic layer was separated and the water layer was extracted with CH_2Cl_2 two times. The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated. Chromatography on silica gel (0-30% ethyl acetate/hexanes) provided the desired product (366 mg, 37%). MS (ESI) mass calcd. $C_{11}H_9ClN_4O_2$, 264.04; m/z found, 265.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.51 (br s, 1H), 8.39 (ddd, J = 5.0, 1.9, 0.7, 1H), 8.32 (s, 1H), 7.71 (ddd, J = 8.2, 7.4, 1.9, 1H), 7.07 (ddd, J = 7.4, 5.0, 0.9, 1H), 6.93 (dt, J = 8.2, 0.8, 1H), 2.53 (s, 3H).

Intermediate 62b: 6-Methyl-N^4-(pyridin-2-yl)pyridine-3,4-diamine.



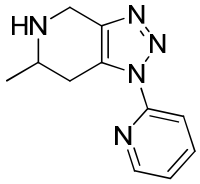
Step B: 6-Methyl-N^4-(pyridin-2-yl)pyridine-3,4-diamine. To a solution of *N*-(2-chloro-6-methyl-3-nitropyridin-4-yl)pyridin-2-amine (860 mg, 3.25 mmol) in methanol (30 mL) was added zinc powder (2.12 g, 32.49 mmol) and acetic acid (0.93 mL, 16.25 mmol). The reaction was heated to reflux and stirred for 2h after which time 4M HCl in dioxane was added (4.0 mL, 16.0 mmol). After stirring at reflux overnight, the zinc was filtered off and the filtrate was concentrated. The residue was dissolved in CH_2Cl_2 (100 mL) and IPA (10 mL) and 5% Na_2CO_3 (aq) was added until pH 11 was obtained. The organic layer was separated. Solid NaCl was added to the water layer to saturate it and then it was extracted with 20% IPA/CH_2Cl_2 three times. The organic layers were combined, dried over anhydrous $MgSO_4$, filtered and concentrated to an oil (550 mg, 85%). MS (ESI) mass calcd. $C_{11}H_{12}N_4$, 200.11; m/z found, 201.1 $[M+H]^+$.

Intermediate 63: 6-Methyl-1-(pyridin-2-yl)-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine.



Step C: 6-Methyl-1-(pyridin-2-yl)-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine. To a solution of 6-methyl-N^4-(pyridin-2-yl)pyridine-3,4-diamine (550 mg, 2.7 mmol) in THF (30 mL) was added acetic acid (0.17 mL, 6.49 mmol) and *tert*-butyl nitrite (0.54 mL, 4.12 mmol). The reaction was then heated to reflux and stirred overnight. The reaction was concentrated and the residue was purified by chromatography on silica gel (0-10% [2M NH_3 in MeOH]/CH_2Cl_2) to give the desired product as a yellow gum (408 mg, 70%). MS (ESI) mass calcd. $C_{11}H_9N_5$, 211.09; m/z found, 212.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 9.44 (d, J = 0.9, 1H), 8.67 - 8.62 (m, 1H), 8.37 (s, 1H), 8.31 - 8.23 m, 1H), 8.01 - 7.96 (m, 1H), 7.41 - 7.35 (m, 1H), 2.80 (s, 3H).

Intermediate 64: 6-Methyl-1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine.



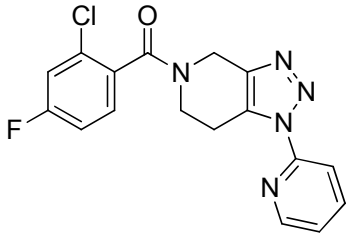
Step D: 6-Methyl-1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine. A solution of 6-methyl-1-(pyridin-2-yl)-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine (530 mg, 1.932 mmol) in acetic acid (100 mL) was passed through a Rh/C cartridge using an HCube® hydrogenation apparatus at 90 bar, 90 °C and 1 mL/min. The acetic acid was concentrated and to the residue was added 1N NaOH until pH 12 was obtained. The water layer was extracted with 20% IPA/CH_2Cl_2 three times. The organic layers were combined, dried over anhydrous $MgSO_4$, filtered and concentrated to a light brown solid (243 mg, 58%). MS (ESI) mass calcd. $C_{11}H_{13}N_5$, 215.12; m/z found, 216.1 $[M+H]^+$. ^1H NMR (600 MHz, MeOD) δ 8.57 (ddd, J = 4.9, 1.8, 0.9 Hz, 1H), 8.11 - 8.03 (m, 2H), 7.47 (ddd, J = 7.2, 4.9,

1.2 Hz, 1H), 4.13 - 3.97 (m, 2H), 3.35 – 3.40 (m, 1H), 3.09 - 3.02 (m, 1H), 2.86 - 2.79 (m, 1H), 1.34 (d, J = 6.4 Hz, 3H).

Step E : 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine

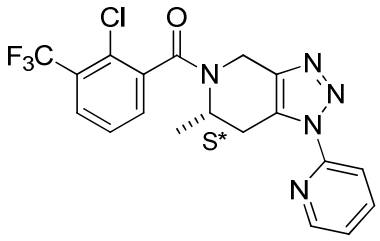
Step E was carried out from 6-methyl-1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine using the conditions described in Example 65. MS (ESI) mass calcd. $C_{19}H_{15}ClF_3N_5O$, 421.09; m/z found, 422.1 $[M+H]^+$.

Example 117: (2-Chloro-4-fluorophenyl)(1-(pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



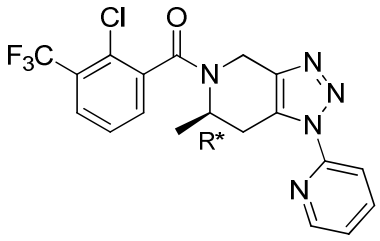
The title compound was prepared in a manner analogous to Example 61 substituting Intermediate 20 for 1-phenyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine and 2-chloro-4-fluorobenzoic acid for 2,3-dichlorobenzoic acid. MS (ESI) mass calcd. $C_{17}H_{13}ClFN_5O$, 357.1; m/z found, 358.0 $[M+H]^+$.

Example 118: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-(*S**)-6-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine



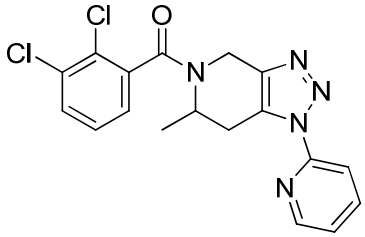
Example 118 and Example 119 were prepared by separation of the enantiomers of Example 116 using a (Chiralcel OD-H column). MS (ESI) mass calcd. $C_{19}H_{15}ClF_3N_5O$, 421.09; m/z found, 422.1 $[M+H]^+$.

Example 119: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-(*R**)-6-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine



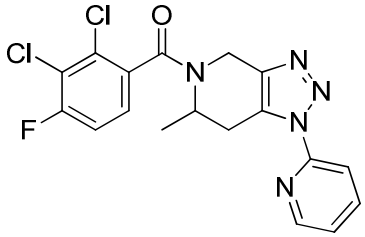
Example 118 and Example 119 were prepared by separation of the enantiomers of Example 117 using a (Chiralcel OD-H column). MS (ESI) mass calcd. $C_{19}H_{15}ClF_3N_5O$, 421.09; m/z found, 422.1 $[M+H]^+$

Example 120: 5-[(2,3-Dichlorophenyl)carbonyl]-6-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine



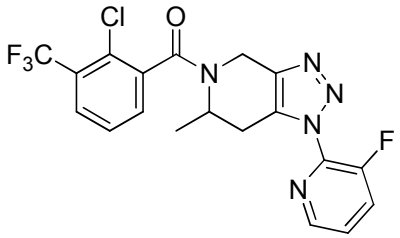
Example 120 was prepared from 6-methyl-1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine and 2,3 dichlorobenzoic acid using the conditions described in Example 65. MS (ESI) mass calcd. $C_{18}H_{15}Cl_2N_5O$, 387.07; m/z found, 388.1 $[M+H]^+$.

Example 121: 5-[(2,3-Dichloro-4-fluorophenyl)carbonyl]-6-methyl-1-pyridin-2-yl-4,5,6,7-tetrahydro-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine



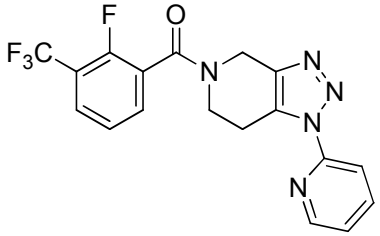
Example 121 was prepared from 6-methyl-1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine and 2,3-dichloro-4-fluorobenzoic acid using the conditions described in Example 65. MS (ESI) mass calcd. $C_{18}H_{14}Cl_2FN_5O$, 405.06; m/z found, 406.1 $[M+H]^+$.

Example 122: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(3-fluoropyridin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



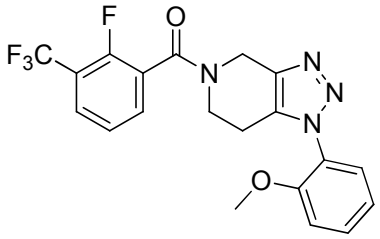
Example 122 was prepared via the route described for Example 116 beginning from 2-amino-3-fluoropyridine instead of 2-aminopyridine (in step A). Subsequent steps were carried out analogous to those described in steps B-D. MS (ESI) mass calcd. $C_{19}H_{14}ClF_4N_5O$, 439.08; m/z found, 440.1 $[M+H]^+$.

Example 123: (2-Fluoro-3-(trifluoromethyl)phenyl)(1-(pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



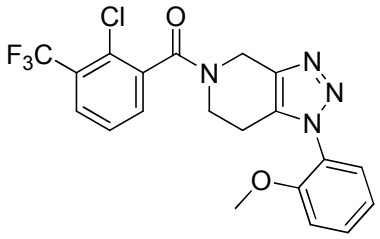
The title compound was prepared in a manner analogous to Example 61 substituting Intermediate 20 for 1-phenyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine and 2-fluoro-3-(trifluoromethyl)benzoic acid for 2-chloro-3-(trifluoromethyl)benzoic acid. MS (ESI) mass calcd. $C_{18}H_{13}F_4N_5O$, 391.1; m/z found, 392.1 $[M+H]^+$.

Example 124: (2-Fluoro-3-(trifluoromethyl)phenyl)(1-(2-methoxyphenyl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analgous to Example 61 substituting 2-fluoro-3-(trifluoromethyl)benzoic acid for 2-chloro-3-(trifluoromethyl)benzoic acid. The starting material was obtained following the procedure used to obtain Intermediate 20 where in Step 1, Intermediate 17 o-anisidine was substituted for 2-aminopyridine. MS (ESI) mass calcd. $C_{20}H_{16}F_4N_4O_2$, 420.1; m/z found, 421.2 $[M+H]^+$.

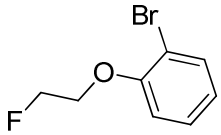
Example 125: (2-Chloro-3-(trifluoromethyl)phenyl)(1-(2-methoxyphenyl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analgous to Example 61. The starting material was obtained following the procedure used to obtain Intermediate 20 where in Step 1, Intermediate 17 o-anisidine was substituted for 2-aminopyridine. MS (ESI) mass calcd. $C_{20}H_{16}ClF_3N_4O_2$, 436.1; m/z found, 437.1 $[M+H]^+$.

Example 126: (2-Chloro-3-(trifluoromethyl)phenyl)(1-(2-(2-fluoroethoxy)phenyl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone

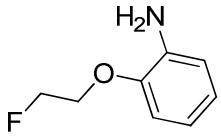
Step 1: 1-bromo-2-(2-fluoroethoxy)benzene.



To a solution of 2-bromophenol (1.0 g, 5.8 mmol) in THF (20 mL) was add NaH (60%) (462 mg, 11.6 mmol). The reaction mixture was stirred at room temperature for 10 min and then 1-bromo-2-fluoroethane (1.5 g, 11.6 mmol) was added and the mixture was irradiated in a microwave reactor at 130 °C for 40 min. The crude mixture was quenched with H_2O and the water layer was extracted with EtOAc. The combined organic layers were dried (Na_2SO_4), filtered and concentrated. The residue was purified by chromatography on silica

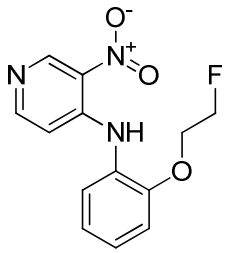
gel (0-20% DCM in Heptane) to provide the desired compound as a colorless oil (800 mg, 63%).

Step 2: 2-(2-fluoroethoxy)aniline



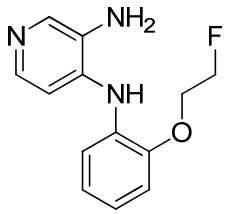
To a solution of the product of Example 126, Step 1 (800 mg, 3.65 ,mmol) in deoxygenated toluene (15 mL) was added NaOtBu (498 mg, 5.2 mmol), BINAP (364 mg, 0.58 mmol) $Pd_2(dba)_3$ (217 mg, 0.24 mmol) and benzophenone imine (0.8 mL, 4.7 mmol). The reaction mixture was heated at 120 °C for 3 h. The crude mixture was then washed with DCM and the aqueous layer was made basic with sat. $NaHCO_3$. The aqueous layer was extracted with DCM and the combined organic extracts were dried (Na_2SO_4), filtered and concentrated. The residue was purified by chromatography on silica gel (0-5% MeOH in DCM) to afford the title compound (566 mg, 90%). MS (ESI) mass calcd. $C_8H_{10}FNO$, 155.1; m/z found, 156.1 $[M+H]^+$.

Step 3: N-(2-(2-fluoroethoxy)phenyl)-3-nitropyridin-4-amine



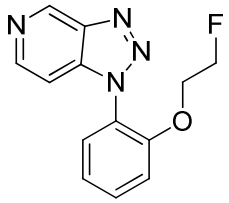
The title compound was prepared in a manner analogous to Intermediate 17, Step 1 substituting the product of Example 126, Step 2 for 2-aminopyridine. MS (ESI) mass calcd. $C_{13}H_{12}FN_3O_3$, 277.1; m/z found, 278.2 $[M+H]^+$.

Step 4: N^4-(2-(2-fluoroethoxy)phenyl)pyridine-3,4-diamine



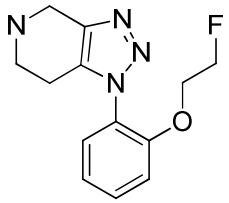
The title compound was prepared in a manner analogous to Intermediate 18, Step 2 substituting the product of Example 126, Step 3 for N-(3-Nitropyridin-4-yl)pyridin-2-amine. MS (ESI) mass calcd. $C_{13}H_{14}FN_3O$, 247.1; m/z found, 248.1 $[M+H]^+$.

Step 5: 1-(2-(2-fluoroethoxy)phenyl)-1H-[1,2,3]triazolo[4,5-c]pyridine



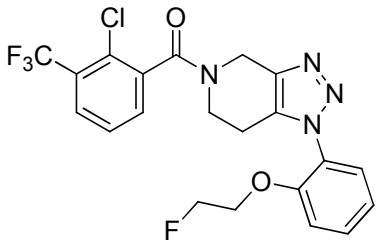
The title compound was prepared in a manner analogous to Intermediate 19, Step 3 substituting the product of Example 126, Step 4 for *N*-4-Pyridin-2-ylpyridine-3,4-diamine. MS (ESI) mass calcd. $C_{13}H_{11}FN_4O$, 258.1; m/z found, 259.2 $[M+H]^+$.

Step 6: 1-(2-(2-fluoroethoxy)phenyl)-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



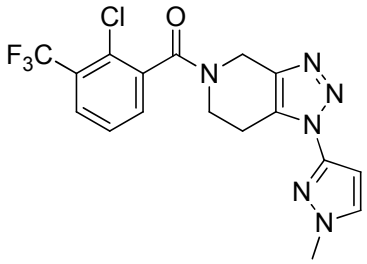
The title compound was prepared in a manner analogous to Intermediate 20, Step 4 substituting the product of Example 126, Step 5 for 1-Pyridin-2-yl-1H-[1,2,3]-triazolo[4,5-c]pyridine. MS (ESI) mass calcd. $C_{13}H_{15}FN_4O$, 262.1; m/z found, 263.2 $[M+H]^+$.

Step 7: (2-Chloro-3-(trifluoromethyl)phenyl)(1-(2-methoxyphenyl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone

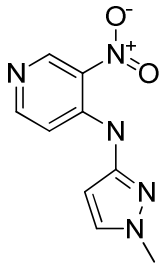


The title compound was prepared in a manner analogous to Example 61 substituting the product of Example 126, Step 6 for 1-phenyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine. MS (ESI) mass calcd. $C_{21}H_{17}ClF_4N_4O_2$, 468.1; m/z found, 469.2 $[M+H]^+$.

Example 127: (2-Chloro-3-(trifluoromethyl)phenyl)(1-(1-methyl-1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone

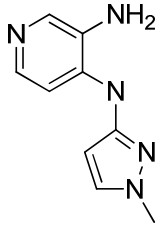


Step 1: N-(1-methyl-1H-pyrazol-3-yl)-3-nitropyridin-4-amine.



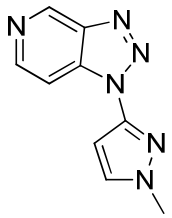
The title compound was prepared in a manner analogous to Intermediate 17, Step 1 substituting 1-methyl-1H-pyrazol-3-amine for 2-aminopyridine. MS (ESI) mass calcd. $C_9H_9N_5O_2$, 219.1; m/z found, 220.2 $[M+H]^+$.

Step 2: N^4-(1-methyl-1H-pyrazol-3-yl)pyridine-3,4-diamine



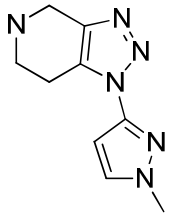
The title compound was prepared in a manner analogous to Intermediate 18, Step 2 substituting the product of Example 127, Step 1 for N-(3-Nitropyridin-4-yl)pyridin-2-amine. MS (ESI) mass calcd. $C_9H_{11}N_5$, 189.1; m/z found, 190.2 $[M+H]^+$.

Step 3: 1-(1-methyl-1H-pyrazol-3-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine



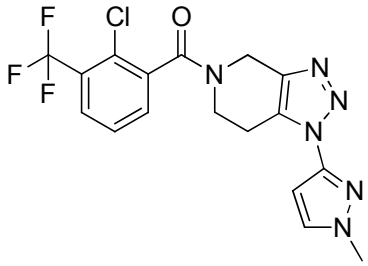
The title compound was prepared in a manner analogous to Intermediate 19, Step 3 substituting the product of Example 127, Step 2 for *N*-4-Pyridin-2-ylpyridine-3,4-diamine. MS (ESI) mass calcd. $C_9H_8N_6$, 200.1; m/z found, 201.2 $[M+H]^+$.

Step 4: 1-(1-methyl-1H-pyrazol-3-yl)-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



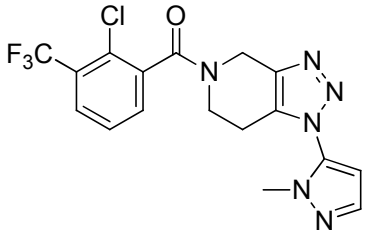
The title compound was prepared in a manner analogous to Intermediate 20, Step 4 substituting the product of Example 127, Step 3 for 1-Pyridin-2-yl-1H-[1,2,3]-triazolo[4,5-c]pyridine. MS (ESI) mass calcd. $C_9H_{12}N_6$, 204.1.1; m/z found, 205.2 $[M+H]^+$.

Step 5: (2-chloro-3-(trifluoromethyl)phenyl)(1-(1-methyl-1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



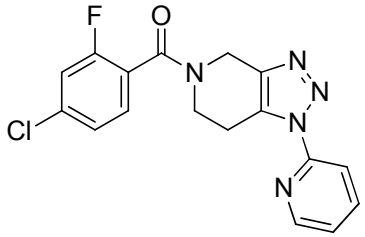
The title compound was prepared in a manner analogous to Example 61 substituting the product of Example 126, Step 4 for 1-phenyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine. MS (ESI) mass calcd. $C_{17}H_{14}ClF_3N_6O$, 410.1; m/z found, 411.2 $[M+H]^+$.

Example 128: (2-Chloro-3-(trifluoromethyl)phenyl)(1-(1-methyl-1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



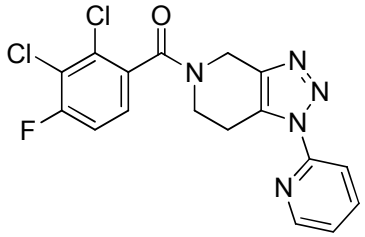
The title compound was prepared in a manner analogous to Example 127 substituting 1-methyl-1H-pyrazol-5-ylamine for 1-methyl-1H-pyrazol-3-amine in Example 127, Step 1. MS (ESI) mass calcd. $C_{17}H_{14}ClF_3N_6O$, 410.1; m/z found, 411.2 $[M+H]^+$.

Example 129: (4-Chloro-2-fluorophenyl)(1-(pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



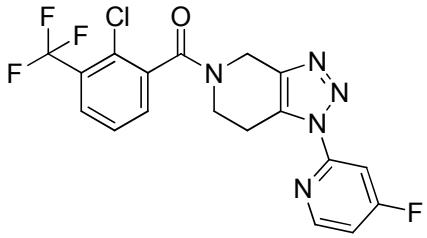
The title compound was prepared in a manner analogous to Example 61 substituting Intermediate 20 for 1-phenyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine and 4-chloro-2-fluorobenzoic acid for 2,3-dichlorobenzoic acid. MS (ESI) mass calcd. $C_{17}H_{13}ClFN_5O$, 357.1; m/z found, 358.2 $[M+H]^+$.

Example 130: (2,3-Dichloro-4-fluorophenyl)(1-(pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



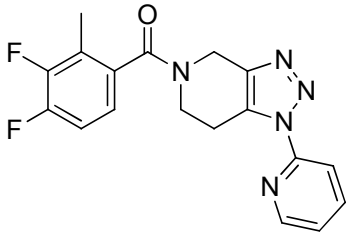
The title compound was prepared in a manner analogous to Example 61 substituting Intermediate 20 for 1-phenyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine and 2,3-dichloro-4-fluorobenzoic acid for 2,3-dichlorobenzoic acid. MS (ESI) mass calcd. $C_{17}H_{12}Cl_2FN_5O$, 391.0; m/z found, 392.2 $[M+H]^+$.

Example 131: (2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-fluoropyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



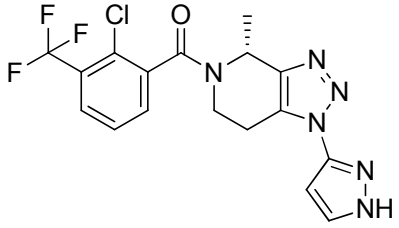
The title compound was prepared in a manner analogous to Example 127 substituting 4-fluoropyridin-2-amine for 1-methyl-1H-pyrazol-3-amine in Example 127, Step 1. MS (ESI) mass calcd. $C_{18}H_{12}ClF_4N_5O$, 425.1; m/z found, 426.2 $[M+H]^+$.

Example 132: (3,4-Difluoro-2-methylphenyl)(1-(pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo-[4,5-c]pyridin-5(4H)-yl)methanone



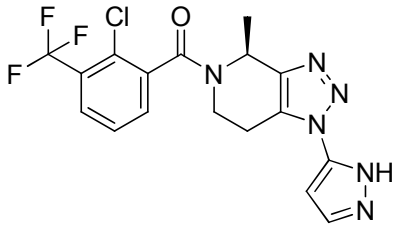
The title compound was prepared in a manner analogous to Example 61 substituting Intermediate 20 for 1-phenyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine and 3,4-difluoro-2-methylbenzoic acid for 2,3-dichlorobenzoic acid. MS (ESI) mass calcd. $C_{18}H_{15}F_2N_5O$, 355.1; m/z found, 356.2 $[M+H]^+$.

Example 133: (*R**)-(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



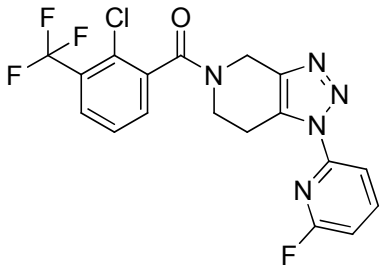
Example 85 was purified by chiral SFC on (Chiralpak AD-H 5µm 250x20mm) using a mobile phase of 70% CO_2 and 30% EtOH to obtain the title compound as a single enantiomer, absolute configuration unknown. MS (ESI) mass calcd. $C_{17}H_{14}ClF_3N_6O$, 410.09; m/z found, 411.1 $[M+H]^+$.

Example 134: (*S**)-(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



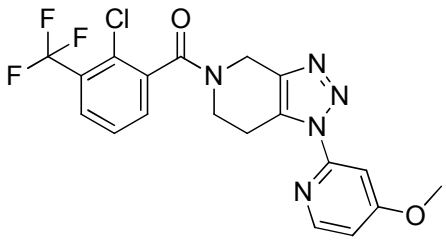
Example 85 was purified by chiral SFC on (Chiralpak AD-H 5µm 250x20mm) using a mobile phase of 70% CO_2 and 30% EtOH to obtain the title compound as a single enantiomer, absolute configuration unknown. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD-H (250x4.6mm) and a mobile phase of 70% CO_2, 30% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 1.99 min retention time). MS (ESI) mass calcd. $C_{17}H_{14}ClF_3N_6O$, 410.09; m/z found, 411.1 $[M+H]^+$.

Example 135: (2-Chloro-3-(trifluoromethyl)phenyl)(1-(6-fluoropyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example 127 substituting 6-fluoropyridin-2-amine for 1-methyl-1H-pyrazol-3-amine in Example 127, Step 1. MS (ESI) mass calcd. $C_{18}H_{12}ClF_4N_5O$, 425.1; m/z found, 426.1 $[M+H]^+$.

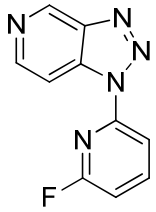
Example 136: (2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-methoxypyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example 127 substituting 2-amino-4-methoxypyridine for 1-methyl-1H-pyrazol-3-amine in Example 127, Step 1.

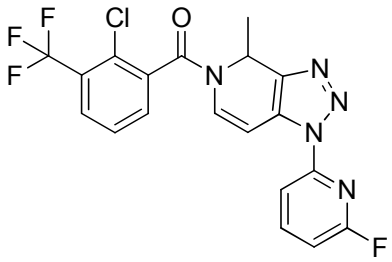
Example 137: (2-Chloro-3-(trifluoromethyl)phenyl)(1-(6-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone

Step 1: 1-(6-fluoropyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine



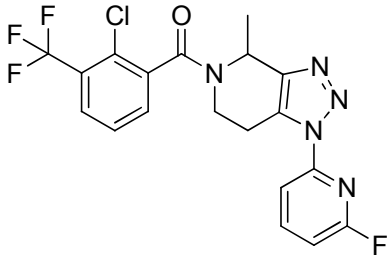
The title compound was prepared in a manner analogous to Intermediate 19 (Intermediate 17, Step 1-Intermediate 19, Step 3) substituting 6-fluoropyridin-2-amine for 2-aminopyridine in the synthesis of Intermediate 17. The product was used crude in Step 2 below.

Step 2: (2-chloro-3-(trifluoromethyl)phenyl)(1-(6-fluoropyridin-2-yl)-4-methyl-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



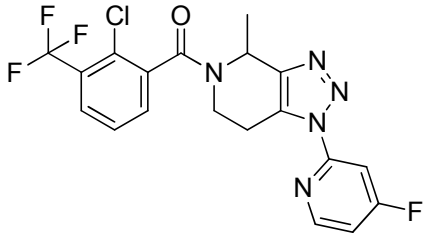
The title compound was prepared in a manner analogous to Example 72 substituting the product of Example 126, Step 5 for 1-pyrazin-2-yl-1H-[1,2,3]triazolo[4,5-c]pyridine. MS (ESI) mass calcd. $C_{19}H_{12}ClF_4N_5O$, 437.1; m/z found, 438.0 $[M+H]^+$.

Step 3: (2-chloro-3-(trifluoromethyl)phenyl)(1-(6-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example 11, Step A substituting the product of Example 137 Step 2, Step 6 for Intermediate 2. MS (ESI) mass calcd. $C_{19}H_{14}ClF_4N_5O$, 439.1; m/z found, 440.1 $[M+H]^+$.

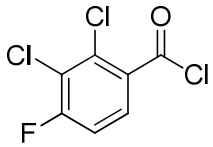
Example 138: (2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example 137 substituting 4-fluoropyridin-2-amine for 6-fluoropyridin-2-amine in Step 1. MS (ESI) mass calcd. $C_{19}H_{14}ClF_4N_5O$, 439.1; m/z found, 440.1 $[M+H]^+$.

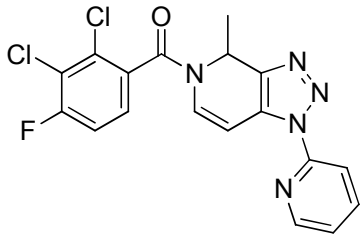
Example 139: (2,3-dichloro-4-fluorophenyl)(4-methyl-1-(pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone

Step 1: 2,3-dichloro-4-fluorobenzoyl chloride.



The title compound was prepared in a manner analogous to Intermediate 12 substituting 2,3-dichloro-4-fluorobenzoic acid for 2-chloro-3-(trifluoromethyl)benzoic acid.

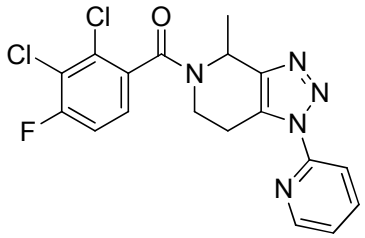
Step 2: (2,3-dichloro-4-fluorophenyl)(4-methyl-1-(pyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example 72 substituting the product of Example 139, Step 1 for 2-chloro-3-(trifluoromethyl)benzoyl chloride and Intermediate 19 for

1-pyrazin-2-yl-1H-[1,2,3]triazolo[4,5-c]pyridine. MS (ESI) mass calcd. $C_{18}H_{12}Cl_2FN_5O$, 403.0; m/z found, 403.9 $[M+H]^+$.

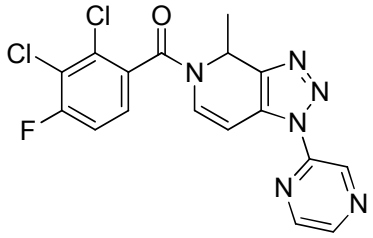
Step 3: (2,3-dichloro-4-fluorophenyl)(4-methyl-1-(pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example 11, Step A substituting the product of Example 139 Step 2, Step 6 for Intermediate 2. MS (ESI) mass calcd. $C_{18}H_{14}Cl_2FN_5O$ 405.1; m/z found, 406.0 $[M+H]^+$.

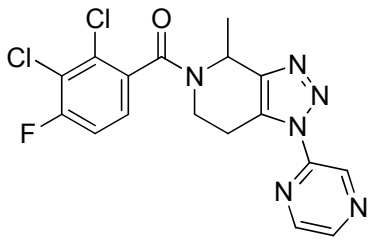
Example 140: (2,3-dichloro-4-fluorophenyl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone

Step 1: (2,3-dichloro-4-fluorophenyl)(4-methyl-1-(pyrazin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



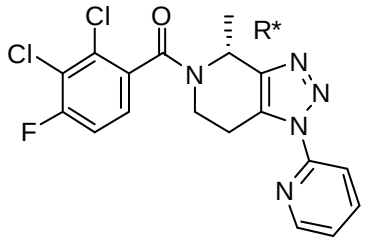
The title compound was prepared in a manner analogous to Example 72 substituting the product of Example 139, Step 1 for 2-chloro-3-(trifluoromethyl)benzoyl chloride. MS (ESI) mass calcd. $C_{17}H_{11}Cl_2FN_6O$, 404.0; m/z found, 405.0 $[M+H]^+$.

Step 2: 2,3-dichloro-4-fluorophenyl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



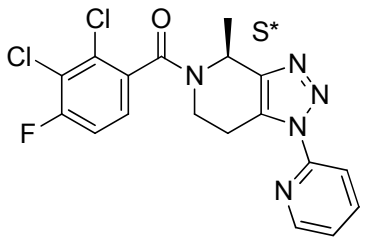
To a solution of the product of Example 140, Step 1 (350 mg, 0.864 mmol) in TFA (2 mL) was added triethylsilane (0.35 mL, 2.16 mmol). The reaction was sealed and heated at 80°C for 2 h. The reaction was diluted with CH_2Cl_2 and the organic portion washed with $NaHCO_3$. The organic portion was then dried over Na_2SO_4, concentrated and purified by chromatography on silica gel eluted with heptane/EtOAc to afford the title compound (140 mg, 40%) MS (ESI) mass calcd. $C_{17}H_{13}Cl_2FN_6O$ 406.1; m/z found, 407.0 $[M+H]^+$.

Example 141: (R*)-(2,3-Dichloro-4-fluorophenyl)(4-methyl-1-(pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 139 performed using CHIRALPAK AD-H (5µm, 250x20mm) and a mobile phase of 60% CO_2, 40% EtOH containing 0.3% $iPrNH_2$. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD-H (250x4.6mm) and a mobile phase of 60% CO_2, 40% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 3.13 min retention time). MS (ESI): mass calculated for $C_{18}H_{14}Cl_2FN_5O$, 405.1; m/z found, 405.8 $[M+H]^+$.

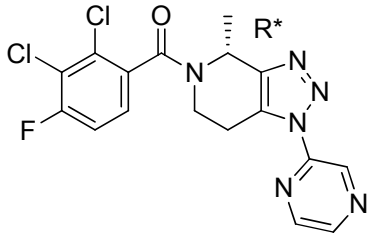
Example 142: (S*)-(2,3-Dichloro-4-fluorophenyl)(4-methyl-1-(pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 139 performed using CHIRALPAK AD-H (5µm, 250x20mm) and a mobile phase of 60% CO_2, 40% EtOH containing 0.3% $iPrNH_2$. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD-H

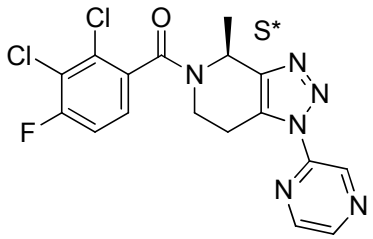
(250x4.6mm) and a mobile phase of 60% CO_2, 40% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 4.18 min retention time). MS (ESI): mass calculated for $C_{18}H_{14}Cl_2FN_5O$, 405.1; m/z found, 405.6 $[M+H]^+$.

Example 143: (R*)-(2,3-Dichloro-4-fluorophenyl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



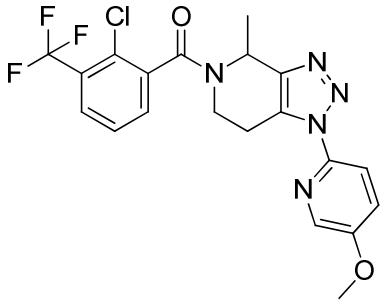
The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 140 performed using CHIRALPAK AD-H (5µm, 250x20mm) and a mobile phase of 60% CO_2, 40% EtOH containing 0.3% $iPrNH_2$. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD-H (250x4.6mm) and a mobile phase of 60% CO_2, 40% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 3.21 min retention time). MS (ESI): mass calculated for $C_{17}H_{13}Cl_2FN_6O$, 406.1; m/z found, 406.8 $[M+H]^+$.

Example 144: (S*)-(2,3-Dichloro-4-fluorophenyl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



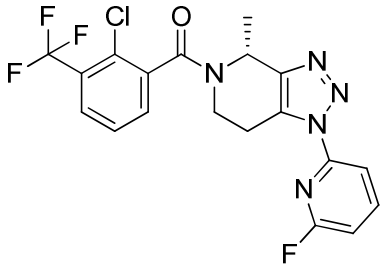
The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 140 performed using CHIRALPAK AD-H (5µm, 250x20mm) and a mobile phase of 60% CO_2, 40% EtOH containing 0.3% $iPrNH_2$. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD-H (250x4.6mm) and a mobile phase of 60% CO_2, 40% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 4.53 min retention time). MS (ESI): mass calculated for $C_{17}H_{13}Cl_2FN_6O$, 406.1; m/z found, 406.6 $[M+H]^+$.

Example 145: (2-Chloro-3-(trifluoromethyl)phenyl)(1-(5-methoxypyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



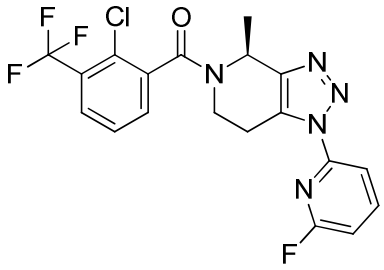
The title compound was prepared in a manner analogous to Example 140. The starting material was prepared following the route described to synthesize Intermediate 19 substituting 5-methoxy-pyridin-2-ylamine for 2-aminopyridine in Step 1, Intermediate 17. MS (ESI): mass calculated for $C_{20}H_{17}ClF_3N_5O_2$, 451.1; m/z found, 452.1 $[M+H]^+$.

Example 146: (R*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(6-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



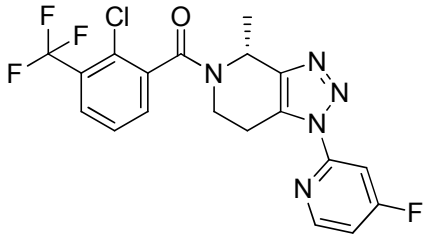
Example 137 was purified by chiral SFC on (Chiralpak AD-H 5µm 250x20mm) using a mobile phase of 80% CO_2 and 20% EtOH containing 0.3% $iPrNH_2$ to obtain the title compound as a single enantiomer of unknown configuration. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD-H (250x4.6mm) and a mobile phase of 80% CO_2, 20% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 3.42 min retention time). $[\alpha]$ = +21.2 ° (c 0.52 w/v %, DMF,). MS (ESI): mass calculated for $C_{19}H_{14}ClF_4N_5O$, 439.1; m/z found, 439.9 $[M+H]^+$.

Example 147: (S*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(6-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



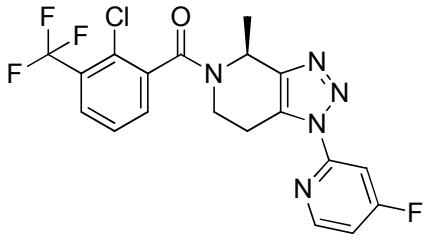
Example 137 was purified by chiral SFC on (Chiralpak AD-H 5µm 250x20mm) using a mobile phase of 80% CO_2 and 20% EtOH containing 0.3% $iPrNH_2$ to obtain the title compound as a single enantiomer of unknown configuration. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD-H (250x4.6mm) and a mobile phase of 80% CO_2, 20% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 4.06 min retention time). [α] = -22.4 (0.58 w/v%, DMF). MS (ESI): mass calculated for $C_{19}H_{14}ClF_4N_5O$, 439.1; m/z found, 439.8 $[M+H]^+$.

Example 148: (R*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



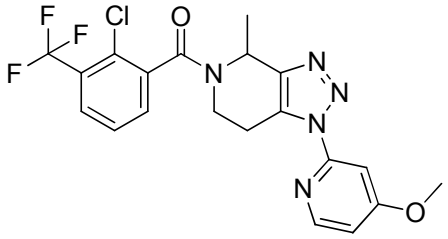
Example 138 was purified by chiral SFC on (Chiralcel OD-H 5µm 250x20mm) using a mobile phase of 80% CO_2 and 20% EtOH containing 0.3% $iPrNH_2$ to obtain the title compound as a single enantiomer of unknown configuration. The enantiomeric purity was confirmed by analytical SFC using a CHIRALCEL OD-H (250x4.6mm) and a mobile phase of 80% CO_2, 20% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 3.43 min retention time). [α] = -23.2 (0.56 w/v%, DMF). . MS (ESI): mass calculated for $C_{19}H_{14}ClF_4N_5O$, 439.1; m/z found, 439.9 $[M+H]^+$.

Example 149: (S*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



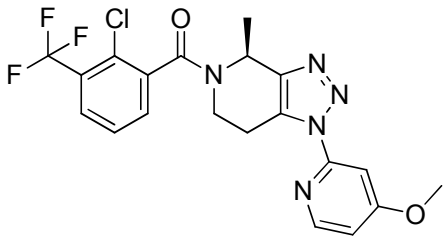
Example 138 was purified by chiral SFC on (Chiralcel OD-H 5µm 250x20mm) using a mobile phase of 80% CO_2 and 20% EtOH containing 0.3% $iPrNH_2$ to obtain the title compound as a single enantiomer of unknown configuration. The enantiomeric purity was confirmed by analytical SFC using a CHIRALCEL OD-H (250x4.6mm) and a mobile phase of 80% CO_2, 20% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 4.48 min retention time). [α] = +23.1 (0.53 w/v%, DMF). MS (ESI): mass calculated for $C_{19}H_{14}ClF_4N_5O$, 439.1; m/z found, 439.9 $[M+H]^+$.

Example 150: (2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-methoxypyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example 137 substituting 2-amino-4-methoxypyridine for 2-aminopyridine in the synthesis of Intermediate 17. MS (ESI): mass calculated for $C_{20}H_{17}ClF_3N_5O_2$, 451.1; m/z found, 452.0 $[M+H]^+$.

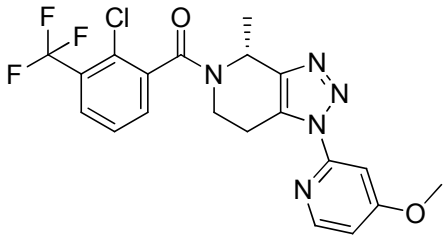
Example 151: (R*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-methoxypyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 150 performed using CHIRALCEL OD-H (5µm, 250x20mm) and a mobile phase of 85% CO_2, 15% EtOH. The enantiomeric purity was

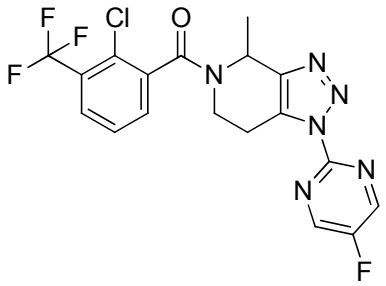
confirmed by analytical SFC using a CHIRALCEL OD-H (250x4.6mm) and a mobile phase of 80% CO_2, 20% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 4.40 min retention time). MS (ESI): mass calculated for $C_{20}H_{17}ClF_3N_5O_2$, 451.1; m/z found, 451.8 $[M+H]^+$.

Example 152: (S*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-methoxypyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 150 performed using CHIRALCEL OD-H (5µm, 250x20mm) and a mobile phase of 85% CO_2, 15% EtOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALCEL OD-H (250x4.6mm) and a mobile phase of 80% CO_2, 20% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 5.46 min retention time). $[\alpha]$ = +31.6 (0.51 w/v%, DMF). MS (ESI): mass calculated for $C_{20}H_{17}ClF_3N_5O_2$, 451.1; m/z found, 451.9 $[M+H]^+$.

Example 153: (2-Chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



Step A: 5-Fluoro-*N*-(2-methyl-3-nitropyridin-4-yl)pyrimidin-2-amine. A solution of $Pd(OAc)_2$ (0.15 g, 0.68 mmol) and BINAP (0.42 g, 0.68 mmol) were stirred in toluene (2 ml) at rt for 10 minutes. This mixture was then added to a microwave vial which contained 4-chloro-2-methyl-3-nitropyridine (3.00 g, 16.8 mmol), 2-amino-4-fluoropyrimidine (2.20

g, 18.5 mmol), and K_2CO_3 (2.6 g, 18.6 mmol) in toluene (10 ml). The reaction was irradiated in a microwave apparatus at 110 °C for 1 h. The reaction was diluted with DCM, filtered through Celite©, washed, and concentrated. Chromatography of the resulting residue (SiO_2; EtOAc:Hex) gave the desired compound (1.60 g, 38%). MS (ESI): mass calculated for $C_{10}H_8ClFN_5O_2$, 249.07; m/z found 250.0 $[M+H]^+$.

Step B: *N*-(5-Fluoropyrimidin-2-yl)-2-methylpyridine-3,4-diamine. To a solution of 5-fluoro-*N*-(2-methyl-3-nitropyridin-4-yl)pyrimidin-2-amine (4.0 g, 16.0 mmol) in degassed EtOH (100 mL) and AcOH (2mL) was added 10% Pd/C (1.70 g, 1.61 mmol) in EtOH (10 mL). The reaction was placed under a balloon of hydrogen at atmospheric pressure and let stir for 12 h. The reaction was filtered through Celite© and washed with DCM. The organic solvent was concentrated to give the title compound (3.10 g, 88%). MS (ESI): mass calculated for $C_{10}H_{10}ClFN_5$, 219.09; m/z found 220.1 $[M+H]^+$.

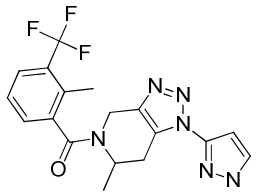
Step C: 1-(5-Fluoropyrimidin-2-yl)-4-methyl-1H-[1,2,3]triazolo[4,5-c]pyridine. A solution of *N*-(5-fluoropyrimidin-2-yl)-2-methylpyridine-3,4-diamine (0.50 g, 2.28 mmol) in THF (15 mL) and HOAc (0.14 mL, 2.51 mmol) was treated with *t*-butyl nitrite (0.45 mL, 3.42 mmol) and heated to 100 °C for 90 min. The reaction was concentrated, diluted with 1N $NaHCO_3$, and extracted with DCM (50 mL x 3). The organic layers were combined, dried (Na_2SO_4), and concentrated. Chromatography of the resulting residue (SiO_2; EtOAc:Hex) gave the title compound (0.40 g, 77%). MS (ESI): mass calcd. for $C_{10}H_7FN_6$, 230.07; m/z found, 231.1 [M+H]+.

Step D: 1-(5-Fluoropyrimidin-2-yl)-4-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo [4,5-c]pyridine. A solution of 1-(5-fluoropyrimidin-2-yl)-4-methyl-1H-imidazo[4,5-c]pyridine (0.90 g, 3.91 mmol) in AcOH (50 mL) was passed through a 10% Pt/C catalyst cartridge on an H-Cube© hydrogenation apparatus at a pressure of 60 bar, a temperature of 60 °C, and a flow rate of 1 mL/min. The reaction was concentrated, diluted with 1N NaOH, and extracted with DCM (100 mL x 3). The organic layers were combined, dried (Na_2SO_4), and concentrated. Chromatography of the resulting residue (SiO_2; MeOH (NH_3):DCM) gave the title compound (0.47 g, 51%). MS (ESI): mass calcd. for $C_{10}H_{11}FN_6$, 234.10; m/z found, 235.0 $[M+H]^+$.

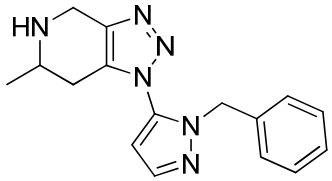
Step E: (2-Chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone. A solution of 1-(5-fluoropyrimidin-2-yl)-4-methyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine (0.30 g, 1.28 mmol), 2-chloro-3-(trifluoromethyl)benzoic acid (0.34 g, 1.54 mmol), HATU (0.38 g, 1.28 mmol), and Et_3N (0.18 mL, 1.28 mmol) in DMF (5 mL) was stirred for 30 min. The

reaction was diluted with EtOAc (30 mL) and washed with H_2O (3 x 20 mL). The organic layers were combined, dried (Na_2SO_4), and concentrated. Chromatography of the resulting residue (SiO_2; MeOH (NH_3):DCM) gave the title compound (0.51 g, 90%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.80 – 8.43 (m, 2H), 7.82 – 7.44 (m, 1H), 7.27 – 7.15 (m, 2H), 6.66 – 6.60 (m, 1H), 5.95 – 4.92 (m, 1H), 3.77 – 2.54 (m, 3H), 1.74 – 1.53 (m, 3H). MS (ESI): mass calculated for $C_{18}H_{13}ClF_4N_6O$, 440.08; m/z found, 441.0 $[M+H]^+$.

Example 154 (6-methyl-1-(1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2-methyl-3-(trifluoromethyl)phenyl)methanone

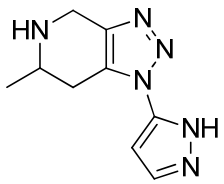


Intermediate A. 1-(1-benzyl-1H-pyrazol-5-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



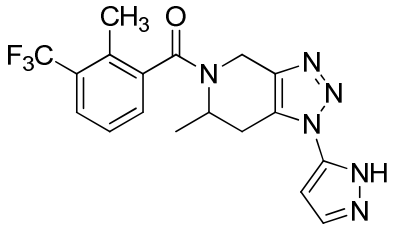
Intermediate A was prepared using the route described in Example 209 beginning from 1-benzyl-1H-pyrazol-5-amine instead of 2-aminopyrazine in step A. Subsequent steps were carried out analogous to those described in steps B-D. MS (ESI) mass calcd $C_{16}H_{18}N_6$, 294.2 m/z found, 295.2 $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.63 (d, J = 2.0 Hz, 1H), 7.25 – 7.18 (m, 3H), 7.00 – 6.94 (m, 2H), 6.37 – 6.34 (d, J = 2.0 Hz, 1H), 5.38 – 5.26 (m, 2H), 4.16 – 3.90 (m, 2H), 2.75 – 2.62 (m, 1H), 2.05 – 1.94 (m, 1H), 1.83 – 1.68 (m, 1H), 1.40 – 1.04 (m, 3H).

Intermediate B. 6-methyl-1-(1H-pyrazol-5-yl)-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine (hydrochloride salt)



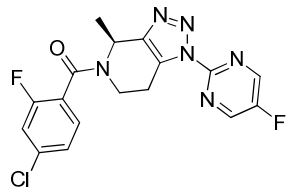
To a solution of 1-(1-benzyl-1H-pyrazol-5-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine in methanol (800 mg, 2.72 mmol) was added palladium(II)chloride (241 mg, 1.34 mmol) and 10% HCl (1 mL). The flask was evacuated and subsequently placed under an H_2 atmosphere. After stirring for 30 min at rt, additional palladium(II)chloride was added (250 mg). The reaction was stirred for 72 h, the solids were filtered away and the filtrate was concentrated *in vacuo* to give the title intermediate as a solid. MS (ESI) mass calcd $C_9H_{12}N_6$, 204.1 m/z found, 205.1 $[M+H]^+$. ^{1}H NMR (400 MHz, DMSO) δ 13.56 – 13.26 (br s, 1H), 9.98 – 9.64 (m, 1H), 8.03 – 7.98 (d, J = 2.4 Hz, 2H), 4.51 – 4.30 (m, 2H), 3.75 – 3.61 (m, 1H), 3.43 – 3.34 (m, 1H), 3.03 – 2.90 (m, 1H), 1.51 – 1.42 (d, J = 6.5 Hz, 3H).

Example 154 (6-methyl-1-(1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2-methyl-3-(trifluoromethyl)phenyl)methanone



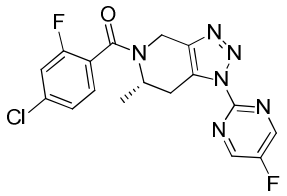
Example 154 was prepared from Intermediate B using the conditions described in Example 65. MS (ESI) mass calcd $C_{18}H_{17}F_3N_6O$, 390.1 m/z found, 391.1 $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.36 – 11.01 (s, 0.6H), 10.55 – 10.26 (s, 0.4H), 7.75 – 7.61 (m, 2H), 7.46 – 7.24 (m, 2H), 6.87 – 6.80 (m, 1H), 5.93 – 5.69 (m, 1H), 4.61 – 4.26 (m, 1.7H), 4.19 – 4.07 (m, 0.3H), 3.58 – 2.91 (m, 2H), 2.57 – 2.18 (m, 3H), 1.45 – 1.15 (m, 3H).

Example 155 (S*)-(4-chloro-2-fluorophenyl)(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



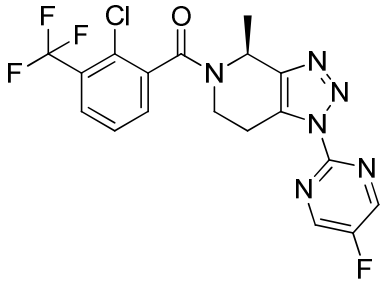
MS (ESI) mass calcd $C_{17}H_{13}ClF_2N_6O$, 390.1 m/z found, 391.1 $[M+H]^+$.

Example 156 (S)-(4-chloro-2-fluorophenyl)(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



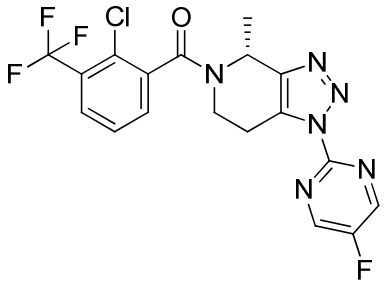
MS (ESI) mass calcd $C_{17}H_{13}ClF_2N_6O$, 390.1 m/z found, 391.1 $[M+H]^+$.

Example 157: (*S**)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



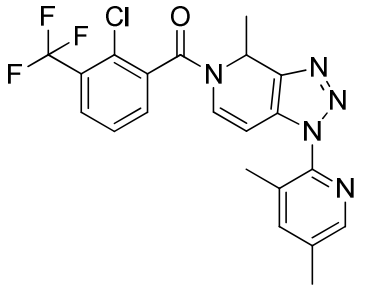
The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 153 performed using CHIRALPAK AD-H (5µm, 250x20mm) and a mobile phase of 70% CO_2, 30% EtOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) and a mobile phase of 75% CO_2, 25% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 4.07 min retention time). MS (ESI): mass calculated for $C_{18}H_{13}ClF_4N_6O$, 440.08; m/z found, 441.0 $[M+H]^+$.

Example 158: (*R*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone (Alternative syntheses of this compound are shown in Example 344.)



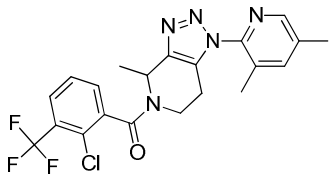
The title compound was obtained as a single enantiomer by Chiral SFC purification of Example 153 performed using CHIRALPAK AD-H (5µm, 250x20mm) and a mobile phase of 70% CO_2, 30% EtOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) and a mobile phase of 75% CO_2, 25% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 4.77 min retention time). MS (ESI): mass calculated for $C_{18}H_{13}ClF_4N_6O$, 440.08; m/z found, 441.0 $[M+H]^+$.

Intermediate C: (2-chloro-3-(trifluoromethyl)phenyl)(1-(3,5-dimethylpyridin-2-yl)-4-methyl-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone.



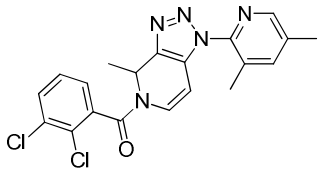
Step B: (2-chloro-3-(trifluoromethyl)phenyl)(1-(3,5-dimethylpyridin-2-yl)-4-methyl-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone. Under a nitrogen atmosphere was added 3.0 M MeMgBr in THF (0.89 mL, 2.66 mmol) to a mixture of 1-(3,5-dimethylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine (300 mg, 1.33 mmol) in THF (33 mL) at -78 °C. After 5 min, a mixture of Intermediate 12 in THF (3 mL) was slowly added dropwise to the reaction mixture. After 10 min, the reaction mixture was allowed to slowly warm to room temperature. After 1 h, the reaction mixture was quenched with saturated NH_4Cl(aq) (20 mL). Water (15 mL) was added, and the mixture was extracted using EtOAc (3 x 50 mL). The combined organics were dried over $MgSO_4$, filtered and concentrated under vacuum. The crude material was purified by chromatography on SiO_2 eluting with EtOAc/hexanes to afford the title compound. MS (ESI) mass calcd. $C_{21}H_{17}ClF_3N_5O$, 447.11; m/z found 448.10 $[M+H]^+$.

Example 159 (2-chloro-3-(trifluoromethyl)phenyl)(1-(3,5-dimethylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



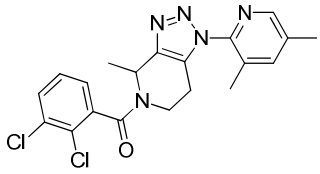
A mixture of Intermediate C and platinum(IV) oxide in THF was allowed to stir at room temperature under an hydrogen atmosphere (1 atm, balloon). After 16 hours, 60% conversion was observed and the reaction mixture was filtered through an acrodisc srynge filter. The filter was washed with DMSO. The filtrate was concentrated, dissolved in a minimum of a MeOH:DMSO (1:1) mixture and purified by chromatography on a Prep Agilent system with a XBridge C18 OBD 50x100 mm column eluting with 5 to 99% (0.05% NH_4OH in H_2O)/ACN over 17 min to afford the title compound. MS (ESI) mass calcd. $C_{21}H_{19}ClF_3N_5O$, 449.12; m/z found 450.20 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.25 – 8.06 (m, 1H), 7.75 (t, *J* = 8.5 Hz, 1H), 7.61 – 7.31 (m, 3H), 6.05 (dt, *J* = 13.4, 6.6 Hz, 0.6H), 5.06 (tt, *J* = 9.9, 5.4 Hz, 0.4H), 4.92 – 4.72 (m, 0.4H), 3.61 – 2.70 (m, 3.6H), 2.46 – 2.26 (m, 6H), 1.84 – 1.44 (m, 3H).

Intermediate D (2,3-dichlorophenyl)(1-(3,5-dimethylpyridin-2-yl)-4-methyl-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



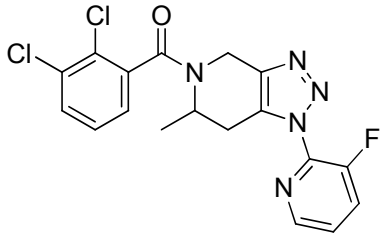
The title compound was prepared in a manner analogous to Intermediate C substituting Intermediate 14 for Intermediate 12. MS (ESI) mass calcd. $C_{20}H_{17}Cl_2N_5O$, 413.08 m/z found, 414.10 $[M+H]^+$.

Example 160 (2,3-dichlorophenyl)(1-(3,5-dimethylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



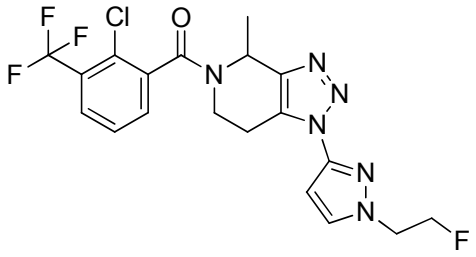
MS (ESI) mass calcd $C_{20}H_{19}Cl_2N_5O$, 415.1 m/z found, 416.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.33 - 8.08 (m, 1H), 7.71 - 7.46 (m, 2H), 7.40 - 6.98 (m, 2H), 6.22 - 5.92 (m, 0.6H), 5.13 - 5.02 (m, 0.4H), 5.00 - 4.74 (m, 0.4H), 3.69 - 2.70 (m, 3.6H), 2.51 - 2.27 (m, 6H), 1.86 - 1.43 (m, 3H).

Example 161: (2,3-Dichlorophenyl)(1-(3-fluoropyridin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



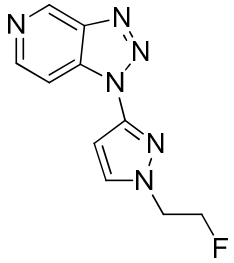
Example 161 was prepared from 6-methyl-1-(3-fluoropyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine using the conditions described in Example 63 Step 5 substituting 2,3-dichlorobenzoyl chloride for 2-chloro-3-(trifluoromethyl)benzoyl chloride . 6-Methyl-1-(3-fluoropyridin-2-yl)-4,5,6,7-tetrahydro-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine was made using the route described in Example 116 beginning from 2-amino-3-fluoropyridine instead of 2-aminopyridine in step A. Subsequent steps were carried out analogous to those described in Example 116 steps B-D. MS (ESI) mass calcd. $C_{18}H_{14}Cl_2FN_5O$, 405.06; m/z found, 406.1 $[M+H]^+$.

Example 162: (2-Chloro-3-(trifluoromethyl)phenyl)(1-(1-(2-fluoroethyl)-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



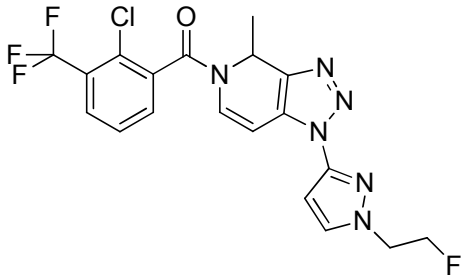
Intermediate 48

Step 1: 1-(1-(2-fluoroethyl)-1H-pyrazol-3-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine.



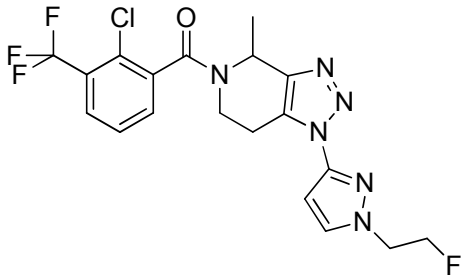
To a solution of Intermediate 48 (50 mg, 0.269 mmol) in DMF (1 mL) was added 1-bromo-2-fluoroethane (41 mg, 0.322 mmol) and Cs_2CO_3 (263 mg, 0.806 mmol). The reaction was irradiated in a microwave apparatus for 10 min at 120 °C. The resulting mixture was filtered, concentrated and purified by chromatography on silica gel eluted with 100% EtOAc to obtain the title compound (62 mg, 88%). MS (ESI) mass calcd. $C_{10}H_9FN_6$, 232.1; m/z found, 233.0 $[M+H]^+$.

Step 2: (2-chloro-3-(trifluoromethyl)phenyl)(1-(1-(2-fluoroethyl)-1H-pyrazol-3-yl)-4-methyl-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



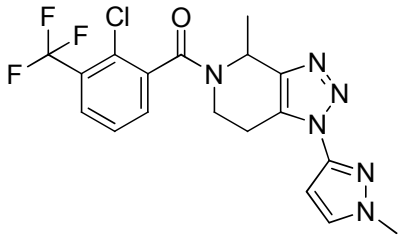
The title compound was prepared in a manner analogous to Example 72 substituting the product of Example 162, Step 1 for 1-pyrazin-2-yl-1H-[1,2,3]triazolo[4,5-c]pyridine. MS (ESI) mass calcd. $C_{19}H_{15}ClF_4N_6O$, 454.1; m/z found, 455.1 $[M+H]^+$.

Step 3: (2-chloro-3-(trifluoromethyl)phenyl)(1-(1-(2-fluoroethyl)-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



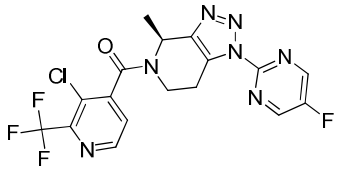
The title compound was prepared in a manner analogous to Example 73 substituting the product of Example 162 Step 2, for 5-{[2-chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrazin-2-yl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine. MS (ESI) mass calcd. $C_{19}H_{17}ClF_4N_6O$ 456.1; m/z found, 457.0 $[M+H]^+$.

Example 163: (2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(1-methyl-1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



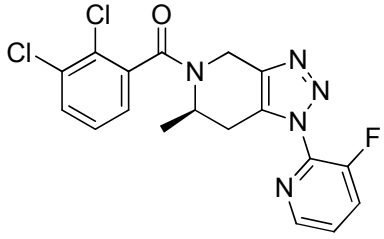
The title compound was obtained in a manner analogous to Example 162, Step 2 and 3. The starting material was obtained using the route described for Intermediate 19 substituting 1-methyl-1H-pyrazol-3-amine for 2-aminopyridine in the synthesis of Intermediate 17, Step 1. MS (ESI) mass calcd. $C_{18}H_{16}ClF_3N_6O$ 424.1; m/z found, 425.1 $[M+H]^+$.

Example 164 (S*)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



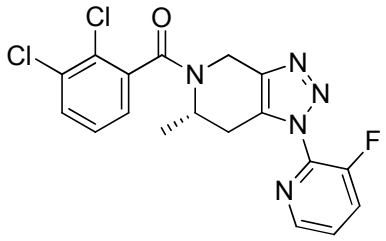
MS (ESI) mass calcd $C_{17}H_{12}ClF_4N_7O$, 441.1 m/z found, 442.1 $[M+H]^+$.

Example 165: (6R*)-5-[(2,3-Dichlorophenyl)carbonyl]-1-(3-fluoropyridin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



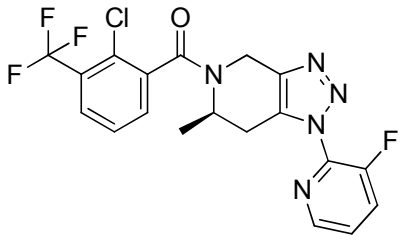
The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 161 performed using CHIRALPAK IA (5µm, 250x20mm) and a mobile phase of 65% CO_2, 35% iPrOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) and a mobile phase of 70% CO_2, 30% iPrOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 4.72 min retention time). MS (ESI) mass calcd. $C_{18}H_{14}Cl_2FN_5O$, 405.1; m/z found, 405.8 $[M+H]^+$.

Example 166: (6S*)-5-[(2,3-Dichlorophenyl)carbonyl]-1-(3-fluoropyridin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 161 performed using CHIRALPAK IA (5µm, 250x20mm) and a mobile phase of 65% CO_2, 35% iPrOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) and a mobile phase of 70% CO_2, 30% iPrOH containing 0.3% $iPrNH_2$ over 7 minutes. (98% single enantiomer, 5.55 min retention time). MS (ESI) mass calcd. $C_{18}H_{14}Cl_2FN_5O$, 405.1; m/z found, 405.8 $[M+H]^+$.

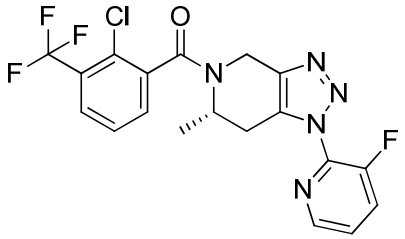
Example 167: (6R*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(3-fluoropyridin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 122 performed using CHIRALPAK IA (5µm, 250x20mm) and a mobile phase of 72% CO_2, 28% iPrOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK IA (250x4.6mm) and a mobile phase of

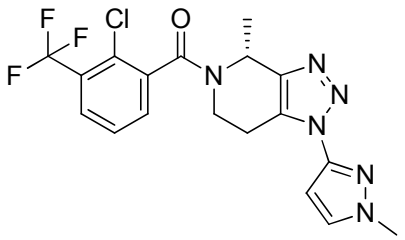
70% CO_2, 30% iPrOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 2.76 min retention time). MS (ESI) mass calcd. $C_{19}H_{14}ClF_4N_5O$, 439.1; m/z found, 439.8 $[M+H]^+$.

Example 168: (6S*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(3-fluoropyridin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



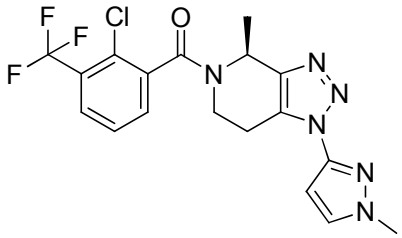
The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 122 performed using CHIRALPAK IA (5µm, 250x20mm) and a mobile phase of 72% CO_2, 28% iPrOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK IA (250x4.6mm) and a mobile phase of 70% CO_2, 30% iPrOH containing 0.3% $iPrNH_2$ over 7 minutes. (99% single enantiomer, 3.18 min retention time). MS (ESI) mass calcd. $C_{19}H_{14}ClF_4N_5O$, 439.1; m/z found, 439.8 $[M+H]^+$.

Ex**am**ple 169: (R*)-(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(1-methyl-1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



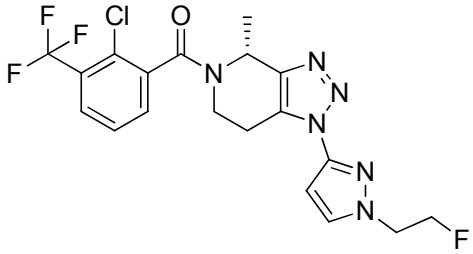
The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 163 performed using CHIRALPAK AD-H (5µm, 250x20mm) and a mobile phase of 75% CO_2, 25% EtOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) and a mobile phase of 75% CO_2, 25% iPrOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 2.80 min retention time). $[\alpha] = +13.7^o$ (0.58 w/v%, DMF). MS (ESI) mass calcd. $C_{18}H_{16}ClF_3N_6O$, 424.1; m/z found, 424.8 $[M+H]^+$.

Example 170: (S*)-(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(1-methyl-1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



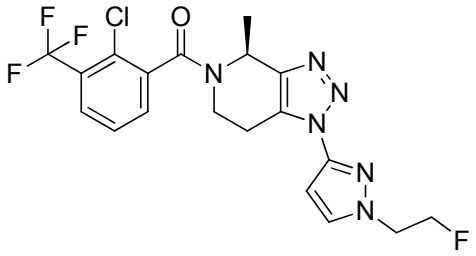
The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 163 performed using CHIRALPAK AD-H (5µm, 250x20mm) and a mobile phase of 75% CO_2, 25% EtOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) and a mobile phase of 75% CO_2, 25% iPrOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 4.02 min retention time). $[\alpha] = -14.0^o$ (0.59 w/v%, DMF). MS (ESI) mass calcd. $C_{18}H_{16}ClF_3N_6O$, 424.1; m/z found, 424.8 $[M+H]^+$.

Example 171: (R*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(1-(2-fluoroethyl)-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



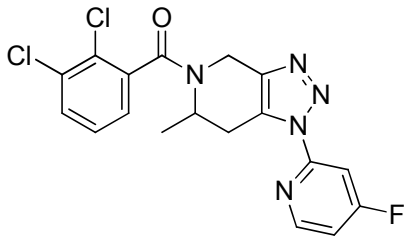
The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 162 performed using CHIRALPAK AD-H (5µm, 250x20mm) and a mobile phase of 75% CO_2, 25% EtOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) and a mobile phase of 75% CO_2, 25% iPrOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 2.64 min retention time). $[\alpha] = +11.7^o$ (0.55 w/v%, DMF). MS (ESI) mass calcd. $C_{19}H_{17}ClF_4N_6O$, 456.1; m/z found, 456.8 $[M+H]^+$.

Example 172: (S*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(1-(2-fluoroethyl)-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



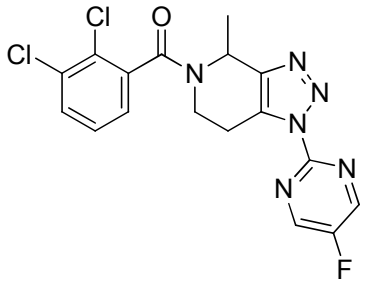
The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 162 performed using CHIRALPAK AD-H (5µm, 250x20mm) and a mobile phase of 75% CO_2, 25% EtOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) and a mobile phase of 75% CO_2, 25% iPrOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 3.72 min retention time). $[\alpha] = -12.8^o$ (0.58 w/v%, DMF). MS (ESI) mass calcd. $C_{19}H_{17}ClF_4N_6O$, 456.1; m/z found, 456.8 $[M+H]^+$.

Example 173: 5-[(2,3-Dichlorophenyl)carbonyl]-1-(4-fluoropyridin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



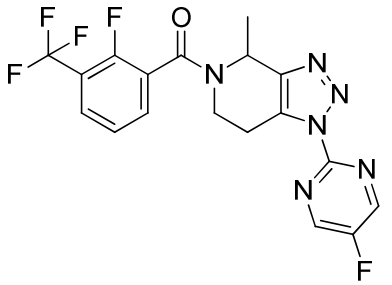
The title compound was prepared in a manner analogous to Example 116. In Intermediate 62, Step A, 4-fluoro-2-aminopyrazine was substituted for 2-aminopyridine, NaOtBu was substituted for NaH and DMSO was substituted for THF. In Intermediate 62b, Step B Pd/C in NH_3/MeOH was used in place of zinc powder in acetic acid. In Intermediate 63, Step C, isoamyl nitrite was substituted for *tert*-butyl nitrite. Step E was carried out using the conditions described for Example 63, Step 5 substituting Intermediate 14 for 2-chloro-3-(trifluoromethyl)benzoyl chloride. MS (ESI) mass calcd. $C_{18}H_{14}Cl_2FN_5O$, 405.1; m/z found, 406.0 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.52 – 8.37 (m, 1H), 7.99 – 7.89 (m, 1H), 7.57 – 7.50 (m, 1H), 7.37 – 7.04 (m, 3H), 5.88 – 5.57 (m, 1H), 4.63 – 4.06 (m, 2H), 3.60 – 3.20 (m, 2H), 1.38 – 1.17 (m, 3H).

Example 174: (2,3-Dichlorophenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



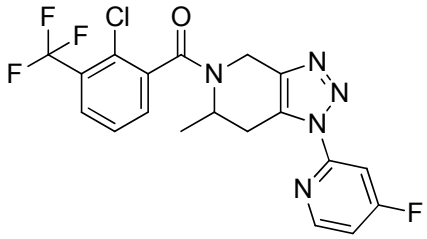
Example 174 was prepared in a manner analogous to Example 153 substituting 2,3-dichlorobenzoic acid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.81 – 8.68 (m, 1H), 8.01 (s, 1H), 7.57 – 7.50 (m, 1H), 7.38 – 7.19 (m, 2H), 6.16 – 5.91, 5.18 – 4.73 (m, 1H), 3.78 – 2.99 (m, 3H), 1.78 – 1.62 (m, 3H). $[M+H]^+$. MS (ESI): mass calculated for $C_{17}H_{13}Cl_2FN_6O$, 406.05; m/z found, 407.1

Example 175: (2-fluoro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



Example 175 was prepared in a manner analogous to Example 153 substituting 2-fluoro-3-(trifluoromethyl)benzoic acid for 2-chloro-3-(trifluoromethyl)benzoic acid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.91 – 8.61 (m, 1H), 8.02 (s, 1H), 7.88 – 7.31 (m, 2H), 6.04 (s, 1H), 5.21 – 4.85 (m, 1H), 3.82 – 3.09 (m, 3H), 1.87 – 1.47 (m, 3H). MS (ESI): mass calculated for $C_{18}H_{13}F_5N_6O$, 424.11; m/z found, 425.1 $[M+H]^+$.

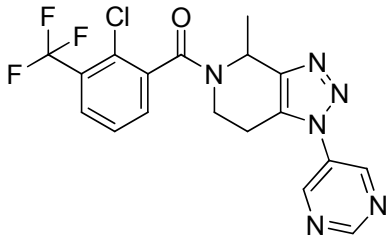
Example 176: (2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-fluoropyridin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example 173 substituting 2-chloro-3-(trifluoromethyl)benzoyl chloride for Intermediate 14. MS (ESI) mass calcd.

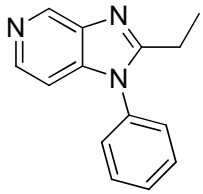
$C_{19}H_{14}ClF_4N_5O$, 439.1; m/z found, 440.0 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.53 – 8.38 (m, 1H), 8.00 – 7.89 (m, 1H), 7.82 – 7.76 (m, 1H), 7.57 – 7.40 (m, 2H), 7.14 – 7.04 (m, 1H), 5.90 – 5.59 (m, 1H), 4.68 – 4.02 (m, 2H), 3.57 – 3.19 (m, 2H), 1.41 – 1.16 (m, 3H).

Example 177: (2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrimidin-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



A solution of (2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrimidin-5-yl)-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone (237 mg, 0.56 mmol) in MeOH (12 ml) was treated with ammonium formate (147 mg, 2.3 mmol) and Pd/carbon (10 wt%, 20 mg) and the reaction was refluxed for 90 min. The reaction was filtered through celite and the filter cake washed with MeOH and concentrated to a crude solid which was re-suspended with $CHCl_3$ and filtered to remove in-organic salts then purified on 40 g SiO_2 with 0-60% EtOAc / hexanes to provide 243 mg (22%) of desired product. MS (ESI) mass calcd. $C_{18}H_{14}ClF_3N_6O$, 422.09; m/z found, 423.1 $[M+H]^+$. The enantiomers were separated by chiral SFC on (CHIRALPAK AD-H 5µm 250x20mm). Mobile phase (70% CO_2, 30% EtOH).

Intermediate 236: 2-ethyl-1-phenyl-1H-imidazo[4,5-c]pyridine



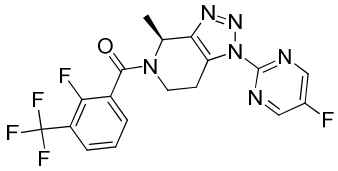
Step 1: 3-nitro-*N*-phenylpyridin-4-amine. To a mixture of 2-chloro-3-nitropyridine (15.8 g, 100 mmol) and aniline (11.1 g, 120 mmol) in dioxane (150 mL) was added was added K_2CO_3 (39 g, 120 mmol). The reaction was heated to reflux for 10h and then purified by silica gel chromatography using petroleum ether/ethyl acetate to provide the product as a yellow solid (20g, 93%).

Step 2: N^4-phenylpyridine-3,4-diamine. To a solution of 3-nitro-*N*-phenylpyridin-4-amine (20 g, 93 mmol) in MeOH (500 mL) was added 10% Pd/C. The reaction was stirred under a hydrogen atmosphere for 10h. The reaction was filtered and the filtrate was concentrated to afford the product (17.2 g, 100%).

Step 3: 2-ethyl-1-phenyl-1H-imidazo[4,5-c]pyridine. A mixture of N^4-phenylpyridine-3,4-diamine (8.0 g, 37.2 mmol), propionic acid (2.7 g, 37.2 mmol) and phosphorous oxychloride (50 mL) was stirred at reflux for 10h. The reaction was purified by silica gel chromatography using ethyl acetate to afford the product as a solid (1.6 g, 19%).

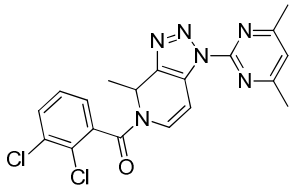
MS (ESI) mass calcd. $C_{14}H_{13}N_3$, 223.1; m/z found, 224.1 $[M+H]^+$.^{1}H NMR (400 MHz, DMSO) δ 9.12 (s, 1H), 8.38 (d, J = 5.8 Hz, 1H), 7.71-7.57 (m, 5H), 7.32 (d, J = 5.5 Hz, 1H), 2.81 (q, J = 7.5 Hz, 2H), 1.27 (t, J = 7.4 Hz, 3H).

Example 178 (S*)-(2-fluoro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



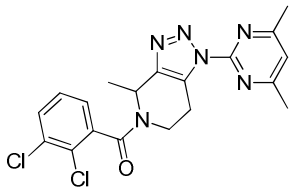
MS (ESI) mass calcd $C_{18}H_{13}F_5N_6O$, 424.1 m/z found, 425.1 $[M+H]^+$.

Intermediate E (2,3-dichlorophenyl)(1-(4,6-dimethylpyrimidin-2-yl)-4-methyl-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



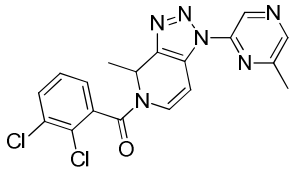
The title compound was prepared in a manner analogous to Intermediate C substituting 1-(4,6-dimethylpyrimidin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine for 1-(3,5-dimethylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine and Intermediate 14 for Intermediate 12. The reaction mixture was also cooled down to -40°C instead of -78°C. MS (ESI) mass calcd. $C_{19}H_{16}Cl_2N_6O$, 414.08 m/z found, 415.10 $[M+H]^+$.

Example 179 (2,3-dichlorophenyl)(1-(4,6-dimethylpyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



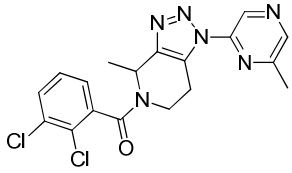
The title compound was prepared in a manner analogous to Example 159 substituting (2,3-dichlorophenyl)(1-(4,6-dimethylpyrimidin-2-yl)-4-methyl-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone for (2-chloro-3-(trifluoromethyl)phenyl)(1-(3,5-dimethylpyridin-2-yl)-4-methyl-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone. MS (ESI) mass calcd $C_{19}H_{18}Cl_2N_6O$, 416.1 m/z found, 417.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 - 7.48 (m, 1H), 7.36 - 7.18 (m, 2H), 7.14 - 6.97 (m, 1H), 6.15 - 5.95 (m, 0.5H), 5.20 - 5.06 (m, 0.5H), 5.02 - 4.72 (m, 0.5H), 3.78 - 2.92 (m, 3.5H), 2.71 - 2.48 (m, 6H), 1.81 - 1.32 (m, 3H).

Intermediate F (2,3-dichlorophenyl)(4-methyl-1-(6-methylpyrazin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



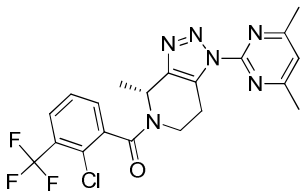
The title compound was prepared in a manner analogous to Intermediate C substituting 1-(6-methylpyrazin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine for 1-(3,5-dimethylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine and Intermediate 14 for Intermediate 12. The reaction mixture was also cooled down to -40°C instead of -78°C. MS (ESI) mass calcd. $C_{18}H_{14}Cl_2N_6O$, 400.06 m/z found, 401.10 $[M+H]^+$.

Example 180 (2,3-dichlorophenyl)(4-methyl-1-(6-methylpyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example 159 substituting (2,3-dichlorophenyl)(4-methyl-1-(6-methylpyrazin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone for (2-chloro-3-(trifluoromethyl)phenyl)(1-(3,5-dimethylpyridin-2-yl)-4-methyl-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone and EtOAc for THF. MS (ESI) mass calcd. $C_{18}H_{16}Cl_2N_6O$, 402.08 m/z found, 403.10 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 9.33 - 9.24 (m, 1H), 8.55 - 8.45 (m, 1H), 7.59 – 7.48 (d, *J* = 8.0 Hz, 1H), 7.38 – 6.98 (m, 2H), 6.13 - 5.86 (m, 0.6H), 5.17 - 5.04 (m, 0.4H), 5.03 - 4.75 (m, 0.4H), 3.73 - 2.92 (m, 3.6H), 2.69 - 2.45 (m, 3H), 1.85 - 1.40 (m, 3H). The following data was also obtained for the title compound: MS (ESI) mass calcd $C_{18}H_{16}Cl_2N_6O$, 402.1 m/z found, 403.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 9.60 - 9.11 (m, 1H), 8.88 - 8.37 (m, 1H), 7.82 - 6.86 (m, 3H), 6.34 - 5.86 (m, 0.6H), 5.39 - 5.04 (m, 0.4H), 5.03 - 4.60 (m, 0.4H), 3.92 - 2.92 (m, 3.6H), 2.78 - 2.45 (m, 3H), 1.85 - 1.40 (m, 3H).

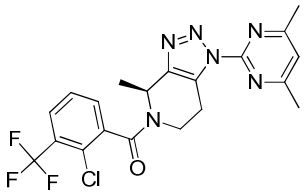
Example 181 (R*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(4,6-dimethylpyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 179 performed using a WHELK O1 (S,S) (5µm 250x21.1mm) column and a mobile phase of 50% CO_2, 50% MeOH. The enantiomeric purity was confirmed by analytical SFC using a WHELK O1 (S,S) (250x4.6mm) column and a mobile phase of 50% CO_2, 50% MeOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 3.94 min retention time). MS (ESI) mass calcd. $C_{20}H_{18}ClF_3N_6O$, 450.12 m/z found, 451.10 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 7.81 – 7.75 (m, 1H), 7.57 – 7.27 (m, 2H), 7.14 – 7.06 (m, 1H), 6.13 – 6.02 (m, 0.5H), 5.17 – 5.07 (m, 0.4H), 4.92 – 4.72 (m, 0.4H), 3.75 – 2.92 (m, 3.7H), 2.68 – 2.50 (m, 6H), 1.77 – 1.41 (m, 3H). The following data was also obtained for the title compound: MS (ESI) mass calcd $C_{20}H_{18}ClF_3N_6O$, 450.1 m/z found, 451.1 [M+H]. ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 - 7.73 (m, 1H), 7.59 - 7.25 (m, 2H), 7.17 - 7.03 (m, 1H), 6.16 - 5.98 (m, 0.6H), 5.21 - 5.05 (m,

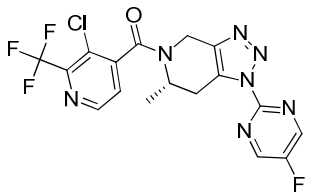
0.4H), 4.96 - 4.70 (m, 0.4H), 3.73 - 2.89 (m, 3.6H), 2.73 - 2.46 (m, 6H), 1.79 - 1.44 (m, 3H).

Example 182 (S*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(4,6-dimethylpyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



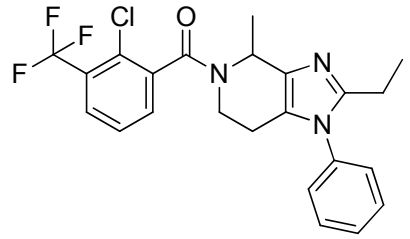
The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 179 performed using a WHELK O1 (S,S) (5µm 250x21.1mm) column and a mobile phase of 50% CO_2, 50% MeOH. The enantiomeric purity was confirmed by analytical SFC using a WHELK O1 (S,S) (250x4.6mm) column and a mobile phase of 50% CO_2, 50% MeOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 6.16 min retention time). MS (ESI) mass calcd. $C_{20}H_{18}ClF_3N_6O$, 450.12 m/z found, 451.10 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 7.81 – 7.75 (m, 1H), 7.57 – 7.27 (m, 2H), 7.14 – 7.06 (m, 1H), 6.13 – 6.02 (m, 0.5H), 5.17 – 5.07 (m, 0.4H), 4.92 – 4.72 (m, 0.4H), 3.75 – 2.92 (m, 3.7H), 2.68 – 2.50 (m, 6H), 1.77 – 1.41 (m, 3H). The following data was also obtained for the title compound: MS (ESI) mass calcd $C_{20}H_{18}ClF_3N_6O$, 450.1 m/z found, 451.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 - 7.73 (m, 1H), 7.59 - 7.25 (m, 2H), 7.17 - 7.03 (m, 1H), 6.16 - 5.98 (m, 0.6H), 5.21 - 5.05 (m, 0.4H), 4.96 - 4.70 (m, 0.4H), 3.73 - 2.89 (m, 3.6H), 2.73 - 2.46 (m, 6H), 1.79 - 1.44 (m, 3H).

Example 183 (R*)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



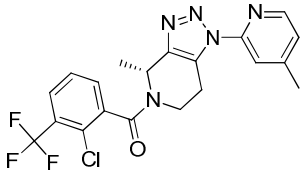
The title compound was prepared in a manner analogous to Example 220, Method II, Steps 1-2 followed by a coupling reaction analogous to that described in Example 65, replacing 3-fluoro-2-(trifluoromethyl)isonicotinic acid for 2-chloro-3-(trifluoromethyl)benzoic acid and Hunig's base for Et_3N. MS (ESI) mass calcd $C_{17}H_{12}ClF_4N_7O$, 441.1 m/z found, 442.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.81 – 8.70 (m, 2H), 8.68 – 8.58 (m, 1H), 7.70 – 7.51 (m, 1H), 5.90 – 5.70 (m, 0.5H), 5.65 – 5.55 (m, 0.5H), 4.75 – 4.48 (m, 1H), 4.43 – 4.34 (m, 0.5H), 4.19 – 4.09 (m, 0.5H), 3.78 – 3.16 (m, 2H), 1.43 – 1.23 (m, 3H).

Example 184: (2-Chloro-3-(trifluoromethyl)phenyl)(2-ethyl-4-methyl-1-phenyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example 11 substituting Intermediate 236 for Intermediate 1. 1H NMR (500 MHz, CDCl3) δ 7.77 – 7.67 (m, 1H), 7.57 – 7.35 (m, 5H), 7.27 – 7.17 (m, 2H), 5.91 – 5.71 (m, 1H), 5.32 – 5.28 (s, 1H), 5.11 – 4.78 (m, 1H), 4.74 – 4.39 (m, 1H), 3.61 – 3.27 (m, 1H), 3.27 – 3.05 (m, 1H), 2.93 – 2.04 (m, 5H), 1.30 – 1.08 (m, 3H). MS (ESI) mass calcd. $C_{23}H_{21}ClF_3N_3O$, 447.1; m/z found, 448.2 $[M+H]^+$.

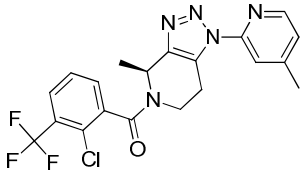
Example 185 (R*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 299 performed using a WHELK O1 (S,S) (5µm 250x21.1mm) column and a mobile phase of 50% CO_2, 50% MeOH. The enantiomeric purity was confirmed by analytical SFC using a WHELK O1 (S,S) (250x4.6mm) and a mobile phase 50% CO_2, 50% MeOH containing 0.3% $iPrNH_2$ over 7 minutes. (100%

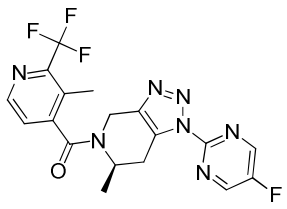
single enantiomer, 2.86 min retention time). MS (ESI) mass calcd $C_{20}H_{17}ClF_3N_5O$, 435.1 m/z found, 436.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.41 - 8.24 (m, 1H), 8.03 - 7.91 (m, 1H), 7.82 - 7.72 (m, 1H), 7.61 - 7.29 (m, 2H), 7.21 - 7.11 (m, 1H), 6.18 - 5.90 (m, 0.6H), 5.18 - 5.02 (m, 0.4H), 4.96 - 4.66 (m, 0.4H), 3.72 - 2.92 (m, 3.6H), 2.50 (s, 3H), 1.87 - 1.40 (m, 3H).

Example 186 (S*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 299 performed using a WHELK O1 (S,S) (5µm 250x21.1mm) column and a mobile phase of 50% CO_2, 50% MeOH. The enantiomeric purity was confirmed by analytical SFC using a WHELK O1 (S,S) (250x4.6mm) and a mobile phase 50% CO_2, 50% MeOH containing 0.3% $iPrNH_2$ over 7 minutes. MS (ESI) mass calcd $C_{20}H_{17}ClF_3N_5O$, 435.1 m/z found, 436.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.41 - 8.24 (m, 1H), 8.03 - 7.91 (m, 1H), 7.82 - 7.72 (m, 1H), 7.61 - 7.29 (m, 2H), 7.21 - 7.11 (m, 1H), 6.18 - 5.90 (m, 0.6H), 5.18 - 5.02 (m, 0.4H), 4.96 - 4.66 (m, 0.4H), 3.72 - 2.92 (m, 3.6H), 2.50 (s, 3H), 1.87 - 1.40 (m, 3H).

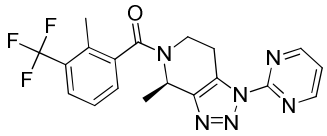
Example 187 (S*)-(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(3-methyl-2-(trifluoromethyl)pyridin-4-yl)methanone



The title compound was prepared in a manner analogous to Example 220, Method II, Steps 1-2 followed by a coupling rection analogous to that described in Example 65, replacing 3-

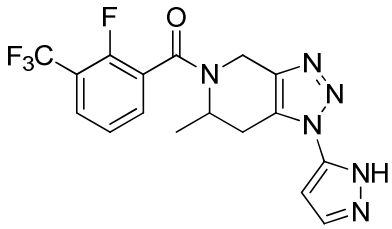
methyl-2-(trifluoromethyl)isonicotinic acid for 2-chloro-3-(trifluoromethyl)benzoic acid and Hunig's base for Et_3N. MS (ESI) mass calcd $C_{18}H_{15}F_4N_7O$, 421.1 m/z found, 422.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 – 8.71 (m, 2H), 8.68 – 8.55 (m, 1H), 7.40 – 7.19 (m, 1H), 5.91 – 5.77 (m, 0.5H), 5.71 – 5.60 (m, 0.5H), 4.52 – 4.32 (m, 1.5H), 4.11 – 3.99 (m, 0.5H), 3.54 – 3.09 (m, 2H), 2.57 – 2.20 (m, 3H), 1.40 – 1.22 (m, 3H).

Example 188 (R*)-(4-methyl-1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2-methyl-3-(trifluoromethyl)phenyl)methanone



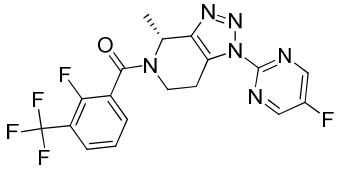
MS (ESI) mass calcd $C_{19}H_{17}F_3N_6O$, 402.1 m/z found, 403.2 $[M+H]^+$.

Example 189 (2-fluoro-3-(trifluoromethyl)phenyl)(6-methyl-1-(1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



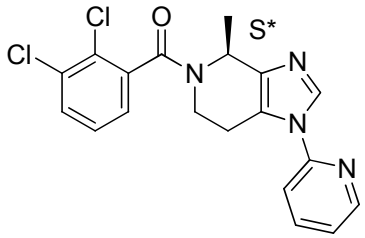
Example 189 was prepared from Intermediate B (described in Example 154) using the conditions described in Example 65.MS (ESI) mass calcd $C_{17}H_{14}F_4N_6O$, 394.1 m/z found, 395.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 10.70 – 10.39 (s, 0.6H), 10.29 – 9.98 (s, 0.4H), 7.78 – 7.31 (m, 4H), 6.90 – 6.80 (m, 1H), 5.93 – 5.58 (m, 1H), 4.73 – 4.16 (m, 2H), 3.49 – 2.96 (m, 2H), 1.44 – 1.10 (m, 3H).

Example 190 (R*)-(2-fluoro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone

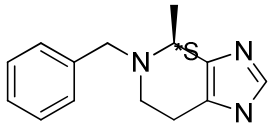


MS (ESI) mass calcd $C_{18}H_{13}F_5N_6O$, 424.1 m/z found, 425.1 $[M+H]^+$.

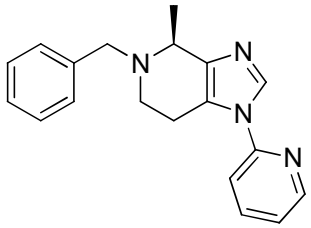
Example 191: (S*)-(2,3-Dichlorophenyl)(4-methyl-1-(pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone



Step 1: (S*)-5-benzyl-4-methyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine

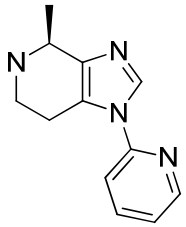


(S*)-5-benzyl-4-methyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine was obtained, absolute configuration unknown, as a single enantiomer by Chiral SFC purification of Example 11 performed using CHIRALPAK IC (5µm, 250x20mm) and a mobile phase of 70% CO_2, 30% isopropanol (0.3% NEt_3). Step 2: (S*)-5-benzyl-4-methyl-1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine



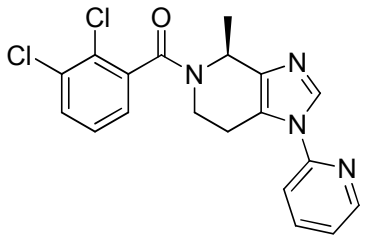
The title compound was prepared in a manner analogous to Example 24, Step B substituting the product from Example 191, Step 1 for 5-tert-butyl 4-ethyl 6,7-dihydro-1H-imidazo[4,5-c]pyridine-4,5(4H)-dicarboxylate. MS (ESI) mass calcd. $C_{19}H_2N_4$, 304.2; m/z found, 305.2 $[M+H]^+$.

Step 3: (S*)-4-methyl-1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine



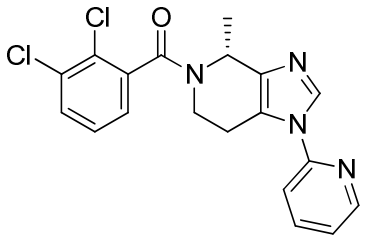
The title compound was prepared in a manner analogous to Example 153, Step D substituting the product from Example 191, Step 2 for 1-(5-fluoropyrimidin-2-yl)-4-methyl-1H-imidazo[4,5-c]pyridine, Pd/C for Pt/C and MeOH for AcOH. MS (ESI) mass calcd. $C_{12}H_{14}N_4$, 214.1; m/z found, 215.1 $[M+H]^+$.

Step 4: (S*)-(2,3-dichlorophenyl)(4-methyl-1-(pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone



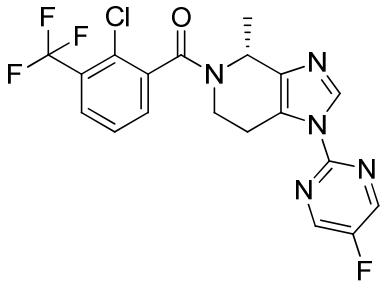
The title compound was prepared in a manner analogous to Example 1, Step C substituting the product from Example 191, Step 3 for 1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine and 2,3 dichlorobenzoic acid for 2-chloro-3-(trifluoromethyl) benzoic acid. MS (ESI) mass calcd. $C_{19}H_{16}Cl_2N_4O$, 386.1; m/z found, 387.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.62 – 8.40 (m, 1H), 8.13 – 7.96 (m, 1H), 7.96 – 7.77 (m, 1H), 7.57 – 7.42 (m, 2H), 7.41 – 7.27 (m, 2H), 5.80 (t, J = 8.0 Hz, 1H), 5.12 – 4.49 (m, 1H), 3.69 – 2.85 (m, 4H), 1.68 – 1.28 (m, 3H).

Example 192: (R*)-(2,3-Dichlorophenyl)(4-methyl-1-(pyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone



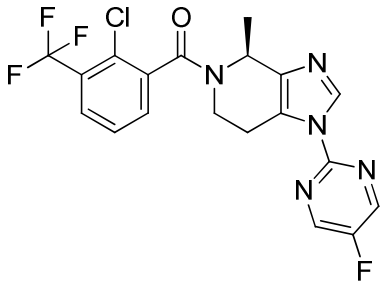
The title compound was prepared in a manner analogous to Example 191 substituting (R*)-5-benzyl-4-methyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine for (S*)-5-benzyl-4-methyl-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine in Step 1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 – 8.40 (m, 1H), 8.13 – 7.96 (m, 1H), 7.96 – 7.77 (m, 1H), 7.57 – 7.42 (m, 2H), 7.41 – 7.27 (m, 2H), 5.90 – 5.71 (t, J = 8.0 Hz, 1H), 5.12 – 4.49 (m, 1H), 3.69 – 2.85 (m, 4H), 1.68 – 1.28 (m, 3H). MS (ESI) mass calcd. $C_{19}H_{16}Cl_2N_4O$, 386.1; m/z found, 387.1 $[M+H]^+$.

Example 193: (R*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 22 performed using CHIRALCEL OD-H (5µm, 250x20mm) and a mobile phase of 72% CO_2, 28% 1:1 EtOH:iPrOH. The enantiomeric purity was confirmed by analytical SFC using Whelk-ol (S,S) (250x4.6mm) and a mobile phase of 60% CO_2, 40% MeOH over 7 minutes. (100% single enantiomer, 2.98 min retention time). MS (ESI) mass calcd. $C_{19}H_{14}ClF_4N_5O$, 439.1; m/z found, 439.8 $[M+H]^+$.

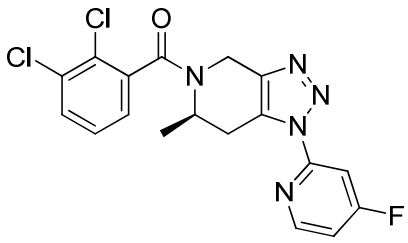
Example 194: (S*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 22 performed using CHIRALCEL OD-H (5µm, 250x20mm) and a mobile phase of 72% CO_2, 28% 1:1 EtOH:iPrOH. The enantiomeric purity was confirmed by analytical SFC using Whelk-ol (S,S) (250x4.6mm) and a mobile

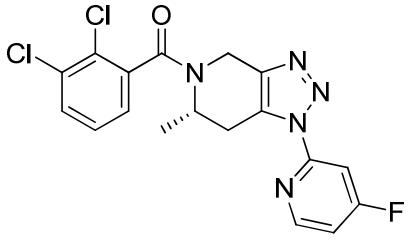
phase of 60% CO_2, 40% MeOH over 7 minutes. (100% single enantiomer, 4.03 min retention time). MS (ESI) mass calcd. $C_{19}H_{14}ClF_4N_5O$, 439.1; m/z found, 439.8 $[M+H]^+$.

Example 195: (6R*)-5-[(2,3-Dichlorophenyl)carbonyl]-1-(4-fluoropyridin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



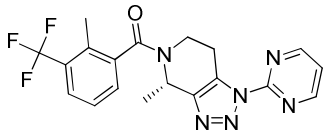
The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 173 performed using CHIRALCEL OJ-H (5µm, 250x20mm) and a mobile phase of 80% CO_2, 20% iPrOH. The enantiomeric purity was confirmed by analytical SFC using Chiralcel (250x4.6mm) and a mobile phase of 80% CO_2, 20% iPrOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 4.17 min retention time). MS (ESI) mass calcd. $C_{18}H_{14}Cl_2FN_5O$, 405.1; m/z found, 406.0 $[M+H]^+$.

Example 196: (6S*)-5-[(2,3-Dichlorophenyl)carbonyl]-1-(4-fluoropyridin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



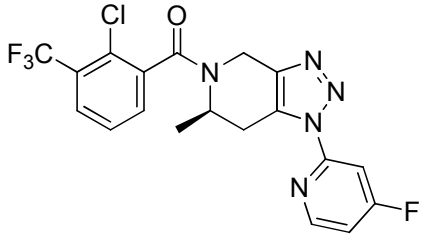
The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 173 performed using CHIRALCEL OJ-H (5µm, 250x20mm) and a mobile phase of 80% CO_2, 20% iPrOH. The enantiomeric purity was confirmed by analytical SFC using Chiralcel (250x4.6mm) and a mobile phase of 80% CO_2, 20% iPrOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 5.35 min retention time). MS (ESI) mass calcd. $C_{18}H_{14}Cl_2FN_5O$, 405.1; m/z found, 406.0 $[M+H]^+$.

Example 197 (S*)-(4-methyl-1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2-methyl-3-(trifluoromethyl)phenyl)methanone



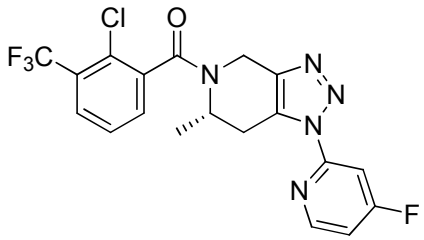
MS (ESI) mass calcd $C_{19}H_{17}F_3N_6O$, 402.1 m/z found, 403.2 $[M+H]^+$.

Example 198: (6R*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(4-fluoropyridin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 176 performed using CHIRALPAK IA (5µm, 250x20mm) and a mobile phase of 85% CO_2, 15% iPrOH. The enantiomeric purity was confirmed by analytical SFC using Chiralpak IA (250x4.6mm) and a mobile phase of 85% CO_2, 15% iPrOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 7.86 min retention time). MS (ESI) mass calcd. $C_{19}H_{14}ClF_4N_5O$, 439.1; m/z found, 440.0 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.53 – 8.38 (m, 1H), 8.00 – 7.89 (m, 1H), 7.82 – 7.76 (m, 1H), 7.57 – 7.40 (m, 2H), 7.14 – 7.04 (m, 1H), 5.90 – 5.59 (m, 1H), 4.68 – 4.02 (m, 2H), 3.57 – 3.19 (m, 2H), 1.41 – 1.16 (m, 3H).

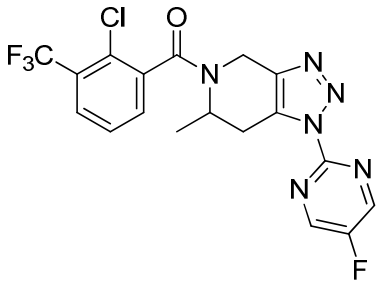
Example 199: (6S*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(4-fluoropyridin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



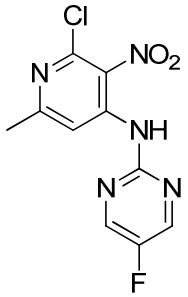
The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 176 performed using CHIRALPAK IA (5µm,

250x20mm) and a mobile phase of 85% CO_2, 15% iPrOH. The enantiomeric purity was confirmed by analytical SFC using Chiralpak IA (250x4.6mm) and a mobile phase of 85% CO_2, 15% iPrOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 8.55 min retention time). MS (ESI) mass calcd. $C_{19}H_{14}ClF_4N_5O$, 439.1; m/z found, 440.0 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.53 – 8.38 (m, 1H), 8.00 – 7.89 (m, 1H), 7.82 – 7.76 (m, 1H), 7.57 – 7.40 (m, 2H), 7.14 – 7.04 (m, 1H), 5.90 – 5.59 (m, 1H), 4.68 – 4.02 (m, 2H), 3.57 – 3.19 (m, 2H), 1.41 – 1.16 (m, 3H).

Example 200: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine

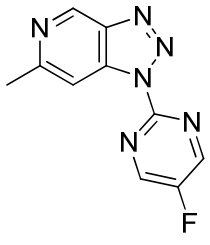


Step 1: *N*-(2-chloro-6-methyl-3-nitropyridin-4-yl)-5-fluoropyrimidin-2-amine



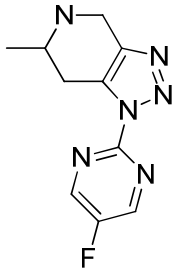
To a mixture of 5-fluoropyrimidin-2-amine (8.2 g, 72.1 mmol) and sodium hydride (5.8g, 144 mmol) in THF (100 mL) was added 2,4-dichloro-6-methyl-3-nitropyridine (15 g, 72.1 mmol). After stirring for 10 h, ethanol was added. Silica gel chromatography (5:1 Hexane:EtOAc) provided the product as a yellow solid (12.8g, 63%).

Step 2: 1-(5-Fluoropyrimidin-2-yl)-6-methyl-1H-[1,2,3]triazolo[4,5-c]pyridine



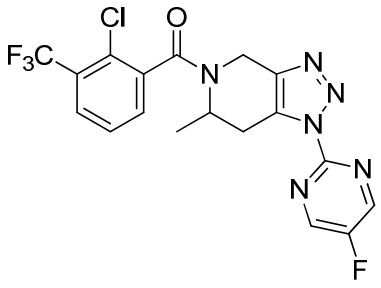
To a slurry of *N*-(2-chloro-6-methyl-3-nitropyridin-4-yl)-5-fluoropyrimidin-2-amine (13 g, 45.8 mmol) in ethanol (300 mL) was added 10% Pd/C (100 mg). The reaction was stirred for 10 h under a hydrogen atmosphere after which time the reaction was filtered and the filtrate was concentrated. The residue was diluted with ethanol (200 mL) and cooled to 0 °C. Isoamyl nitrite (4.0 g, 34.0 mmol) and HBF_4 (5.5 g, 34.0 mmol) were added and the reaction was stirred for 30 min at 0 °C followed by rt for 10h. Evaporation of the solvents followed by recrystallization afforded the product as a white solid (3.2 g, 48%). MS (ESI) mass calcd. $C_{10}H_7FN_6$, 230.07; m/z found, 231.2 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 9.44 (s, 1H), 9.17 (s, 2H), 8.14 (s, 1H), 2.70 (s, 3H).

Step 3: 1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



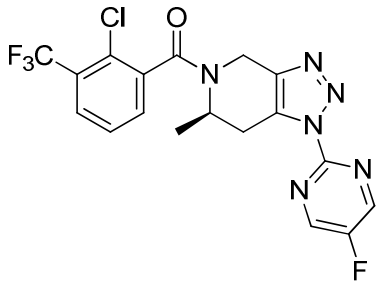
The title compound was prepared in a manner analogous to Example 50, Step A substituting the product from Example 200, Step 1 for Intermediate 2. MS (ESI) mass calcd. $C_{10}H_{11}FN_6$, 234.1; m/z found, 235.1 $[M+H]^+$.

Step 4: (-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



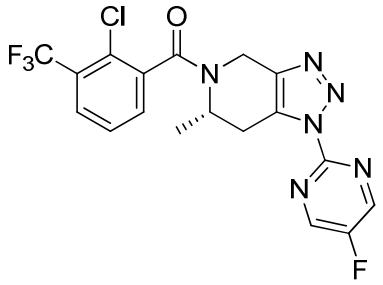
The title compound was prepared in a manner analogous to Example 63, Step 5 substituting the product from Example 200, Step 2 for 1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine, and DCM for THF. MS (ESI) mass calcd. $C_{18}H_{13}ClF_4N_6O$, 440.1; m/z found, 441.1 $[M+H]^+$.

Example 201: (6R*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



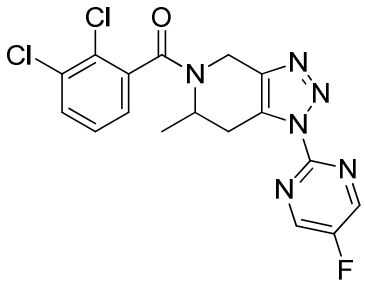
The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 200 performed using CHIRALPAK AD-H (5µm, 250x20mm) and a mobile phase of 70% CO_2, 30% 1:1 EtOH:iPrOH. The enantiomeric purity was confirmed by analytical SFC using Chiralpak AD-H (250x4.6mm) and a mobile phase of 70% CO_2, 15% iPrOH, 15% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 2.93 min retention time). MS (ESI) mass calcd. $C_{18}H_{13}ClF_4N_6O$, 440.1; m/z found, 441.0 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.80 – 8.68 (m, 2H), 7.86 – 7.73 (m, 1H), 7.61 – 7.38 (m, 2H), 5.92 – 5.60 (m, 1H), 4.69 – 4.04 (m, 2H), 3.56 – 3.06 (m, 2H), 1.43 – 1.16 (m, 3H).

Example 202: (6S*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



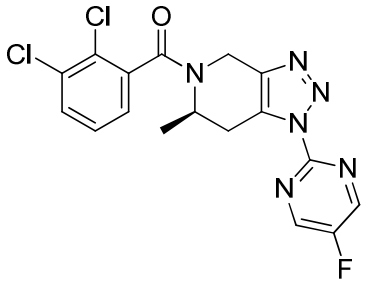
The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 200 performed using CHIRALPAK AD-H (5µm, 250x20mm) and a mobile phase of 70% CO_2, 30% 1:1 EtOH:iPrOH. The enantiomeric purity was confirmed by analytical SFC using Chiralpak AD-H (250x4.6mm) and a mobile phase of 70% CO_2, 15% iPrOH, 15% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 3.37 min retention time). MS (ESI) mass calcd. $C_{18}H_{13}ClF_4N_6O$, 440.1; m/z found, 441.0 $[M+H]^+$.

Example 203: 5-[(2,3-Dichlorophenyl)carbonyl]-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



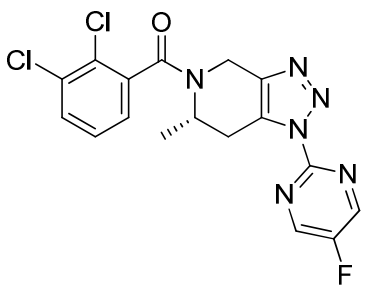
The title compound was prepared in a manner analogous to Example 200 substituting Intermediate 14 for Intermediate 12. MS (ESI) mass calcd. $C_{17}H_{13}Cl_2FN_6O$, 406.1; m/z found, 407.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.78 – 8.70 (m, 2H), 7.57 – 7.51 (m, 1H), 7.41 – 7.10 (m, 2H), 5.89 – 5.58 (m, 1H), 4.63 – 4.07 (m, 2H), 3.56 – 3.05 (m, 2H), 1.39 – 1.16 (m, 3H).

Example 204: (6R*)-5-[(2,3-Dichlorophenyl)carbonyl]-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 203 performed using CHIRALPAK AD-H (5µm, 250x20mm) and a mobile phase of 60% CO_2, 40% 1:1 MeOH:iPrOH. The enantiomeric purity was confirmed by analytical SFC using Chiralpak AD-H (250x4.6mm) and a mobile phase of 60% CO_2, 20% iPrOH, 20% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 3.49 min retention time). MS (ESI) mass calcd. $C_{17}H_{13}Cl_2FN_6O$, 406.05; m/z found, 406.9 $[M+H]^+$.

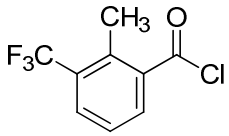
Example 205: (6S*)-5-[(2,3-Dichlorophenyl)carbonyl]-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 203 performed using CHIRALPAK AD-H (5µm, 250x20mm) and a mobile phase of 60% CO_2, 40% 1:1 MeOH:iPrOH. The enantiomeric purity was confirmed by analytical SFC using Chiralpak AD-H (250x4.6mm) and a mobile phase of 60% CO_2, 20% iPrOH, 20% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 4.04 min retention time). MS (ESI) mass calcd. $C_{17}H_{13}Cl_2FN_6O$, 406.05; m/z found, 407.0 $[M+H]^+$.

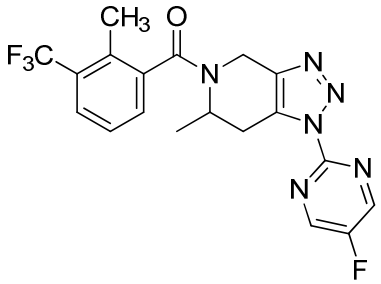
Example 206: 1-(5-Fluoropyrimidin-2-yl)-6-methyl-5-{[2-methyl-3-(trifluoromethyl)phenyl]carbonyl}-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine

Step 1: 2-methyl-3-(trifluoromethyl)benzoyl chloride



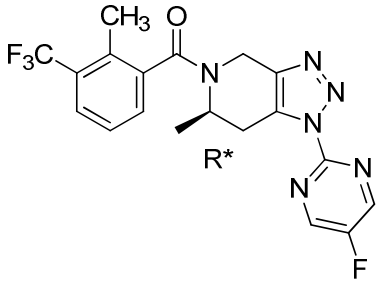
The title compound was prepared in a manner analogous to Intermediate 12 substituting 2-methyl-3-(trifluoromethyl)benzoic acid for 2-chloro-3-(trifluoromethyl)benzoic acid.

Step 2: 1-(5-Fluoropyrimidin-2-yl)-6-methyl-5-{[2-methyl-3-(trifluoromethyl)phenyl]carbonyl}-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



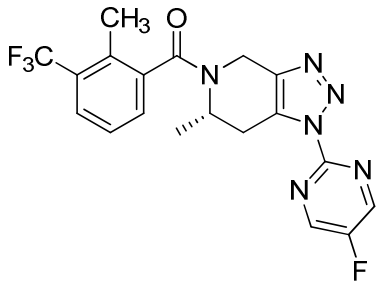
The title compound was prepared in a manner analogous to Example 200 substituting the product of Example 206, Step 1 for Intermediate 12. MS (ESI) mass calcd. $C_{19}H_{16}F_4N_6O$, 420.1; m/z found, 421.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.82 – 8.67 (m, 2H), 7.77 – 7.64 (m, 1H), 7.50 – 7.21 (m, 2H), 5.94 – 5.62 (m, 1H), 4.58 – 4.07 (m, 2H), 3.55 – 3.03 (m, 2H), 2.60 – 2.17 (m, 3H), 1.43 – 1.16 (m, 3H).

Example 207: (6R*)-1-(5-Fluoropyrimidin-2-yl)-6-methyl-5-{[2-methyl-3-(trifluoromethyl)phenyl]carbonyl}-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



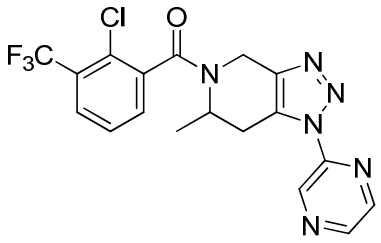
The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 206 performed using CHIRALPAK AD-H (5µm, 250x20mm) and a mobile phase of 75% CO_2, 25% EtOH . The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD-H (250x4.6mm) and a mobile phase of 75% CO_2, 25% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 2.91 min retention time). MS (ESI) mass calcd. $C_{19}H_{16}F_4N_6O$, 420.1; m/z found, 421.1 $[M+H]^+$.

Example 208: (6S*)-1-(5-Fluoropyrimidin-2-yl)-6-methyl-5-{[2-methyl-3-(trifluoromethyl)phenyl]carbonyl}-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine

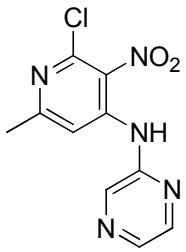


The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 206 performed using CHIRALPAK AD-H (5µm, 250x20mm) and a mobile phase of 75% CO_2, 25% EtOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD-H (250x4.6mm) and a mobile phase of 75% CO_2, 25% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 3.30 min retention time). $C_{19}H_{16}F_4N_6O$, 420.1; m/z found, 421.1 $[M+H]^+$.

Example 209: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine

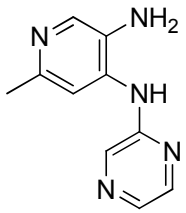


Intermediate 65: *N*-(2-Chloro-6-methyl-3-nitropyridin-4-yl)pyrazin-2-amine



Step A: *N*-(2-chloro-6-methyl-3-nitropyridin-4-yl)pyrazin-2-amine. To a solution of 2-aminopyrazine (0.900 g, 9.47 mmol) in DMSO (40 mL) was added potassium *tert*-butoxide (2.13 g, 18.9 mmol) followed by 2,4-dichloro-6-methyl-3-nitropyridine (2.00 g, 9.47 mmol). After stirring for 30 min at rt, sat. NH_4Cl solution was added. The organic layer was separated and the water layer was extracted with CH_2Cl_2 three times. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated. Chromatography on silica gel (0-70% ethyl acetate/hexanes) provided the desired product (567 mg, 23%). MS (ESI) mass calcd. $C_{10}H_8ClN_5O_2$, 265.04; m/z found, 266.0 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.69 – 8.62 (br s, 1H), 8.38 – 8.34 (m, 2H), 8.34 – 8.29 (m, 2H), 2.59 – 2.56 (m, 3H).

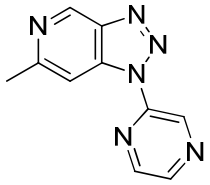
Intermediate 66: 6-Methyl-N^4-(pyrazin-2-yl)pyridine-3,4-diamine.



Step B: 6-Methyl-N^4-(pyrazin-2-yl)pyridine-3,4-diamine. A solution of *N*-(2-chloro-6-methyl-3-nitropyridin-4-yl)pryazin-2-amine (903 mg, 3.40 mmol) in 2M ammonia in methanol:THF (7:5, 120 mL) was passed through a 20% $Pd(OH)_2$ cartridge using an HCube® hydrogenation apparatus in a continuous loop overnight at 1 bar, 90 °C and 1 mL/min. The solvents were evaporated and the residue was purified by chromatography on

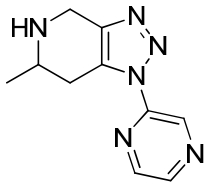
silica gel (0-10% [2M NH_3 in MeOH]/CH_2Cl_2) to provide the desired product (285 mg, 42%). MS (ESI) mass calcd. $C_{10}H_{11}N_5$, 201.10; m/z found, 202.1 $[M+H]^+$.

Intermediate 67: 6-Methyl-1-(pyrazin-2-yl)-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine.



Step C: 6-Methyl-1-(pyrazin-2-yl)-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine. To a solution of 6-methyl-N^4-(pyrazin-2-yl)pyridine-3,4-diamine (520 mg, 2.58 mmol) in THF (30 mL) was added acetic acid (0.44 mL, 7.75 mmol) and *tert*-butyl nitrite (0.51 mL, 3.88 mmol). The reaction was heated to reflux. After 30 min the reaction was cooled and filtered. The filtrate was concentrated and the residue was purified by chromatography on silica gel (0-7% [2M NH_3 in MeOH]/CH_2Cl_2) to give the desired product (127 mg, 25%). MS (ESI) mass calcd. $C_{11}H_9N_5$, 212.08; m/z found, 213.1 $[M+H]^+$.

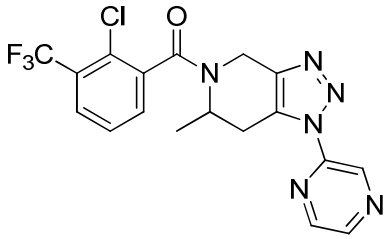
Intermediate 68: 6-Methyl-1-(pyrazin-2-yl)-4,5,6,7-tetrahydro-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine.



Step D: 6-Methyl-1-(pyrazin-2-yl)-4,5,6,7-tetrahydro-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine. To a solution of 6-methyl-1-(pyrazin-2-yl)-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine (245 mg, 1.15 mmol) in formic acid (0.70 mL, 18.5 mmol) was added dropwise triethylamine (1.28 mL, 9.24 mmol). The resulting mixture was heated to 140 ^oC for 24h. The reaction was cooled and 1M NaOH was added until the pH was 7-9. The water layer was extracted with CH_2Cl_2 three times. The organic layers were combined, dried over anhydrous $MgSO_4$, filtered and concentrated. The residue was dissolved in 3:1 isopropanol/concentrated HCl (4 mL) and stirred at 50 ^oC for 16h. The reaction was cooled and 1M NaOH was added until pH 12 was reached. The water layer was extracted with 1:4 isopropanol/CH_2Cl_2 three times. The organic layers were combined, dried over anhydrous $MgSO_4$, filtered and concentrated to a yellow solid (230 mg, 92%). MS (ESI) mass calcd. $C_{10}H_{12}N_6$, 216.11; m/z found, 217.0 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 9.51 – 9.47 (m, 1H), 8.64 – 8.60 (m, 1H), 8.49 –

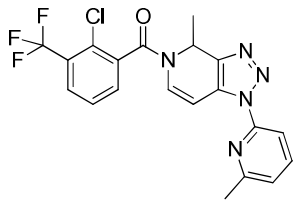
8.46 (m, 1H), 4.26 – 4.08 (m, 2H), 3.37 – 3.28 (m, 1H), 3.14 – 3.04 (m, 1H), 2.85 – 2.74 (m, 1H), 2.23 – 2.02 (br s, 1H), 1.36 (d, J = 6.3 Hz, 3H).

Example 209: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



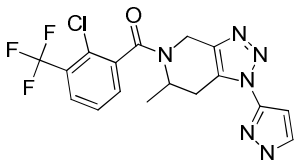
Step E: 5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine. To a solution of 6-methyl-1-(pyrizin-2-yl)-4,5,6,7-tetrahydro-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine (207 mg, 0.96 mmol) in CH_2Cl_2 (8 mL) was added triethylamine (0.40 mL, 2.88 mmol) followed by 2-chloro-3-(trifluoromethyl)-benzoic acid (279 mg, 1.15 mmol). The resulting mixture was stirred for 10 min at rt and 5% Na_2CO_3 was added. The water layer was extracted with CH_2Cl_2 three times. The organic layers were combined, dried over anhydrous $MgSO_4$, filtered and concentrated. The residue was purified by preparative basic HPLC to give the product as a white solid (200 mg, 57%). MS (ESI) mass calcd. $C_{18}H_{14}ClF_3N_6O$, 422.09; m/z found, 423.0 $[M+H]^+$.

Intermediate G: (2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-methylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone.



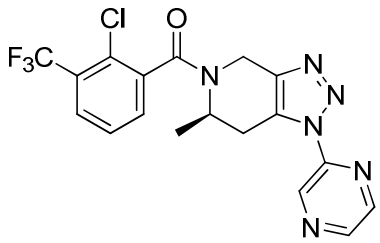
The title compound was prepared in a manner analogous to Intermediate C substituting 1-(3,5-dimethylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine for 1-(6-methylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine and cooling the reaction mixture down to -40°C instead of -78°C. MS (ESI) mass calcd. $C_{20}H_{15}F_3N_5O$, 433.09; m/z found 434.10 $[M+H]^+$.

Example 210 (2-chloro-3-(trifluoromethyl)phenyl)(6-methyl-1-(1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



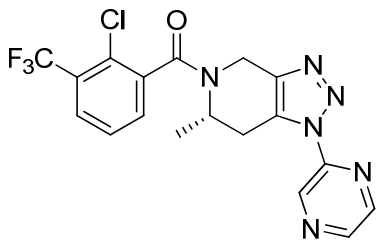
Example 210 was prepared from Intermediate B (described in Example 154) using the conditions described in Example 65. MS (ESI) mass calcd $C_{17}H_{14}ClF_3N_6O$, 410.1 m/z found, 411.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 10.99 – 10.68 (s, 0.6H), 10.39 – 10.11 (s, 0.4H), 7.83 – 7.39 (m, 4H), 6.88 – 6.80 (m, 1H), 5.94 – 5.65 (m, 1H), 4.69 – 4.30 (m, 1.7H), 4.15 – 4.03 (m, 0.3H), 3.54 – 2.94 (m, 2H), 1.44 – 1.15 (m, 3H).

Example 211: (6R*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 209 performed using CHIRALPAK IA (5µm, 250x20mm) and a mobile phase of 75% CO_2, 25% iPrOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK IA (250x4.6mm) and a mobile phase of 75% CO_2, 25% iPrOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 4.33 min retention time). MS (ESI) mass calcd. $C_{18}H_{14}ClF_3N_6O$, 422.1; m/z found, 423.1 $[M+H]^+$.

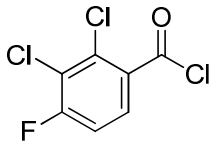
Example 212: (6S*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-1-pyrazin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 209 performed using CHIRALPAK IA (5µm, 250x20mm) and a mobile phase of 75% CO_2, 25% iPrOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK IA (250x4.6mm) and a mobile phase of 75% CO_2, 25% iPrOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 4.92 min retention time). MS (ESI) mass calcd. $C_{18}H_{14}ClF_3N_6O$, 422.1; m/z found, 423.1 $[M+H]^+$.

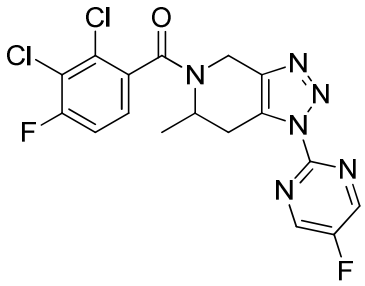
Example 213: 5-[(2,3-Dichloro-4-fluorophenyl)carbonyl]-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine

Step 1: 2,3-dichloro-4-fluorobenzoyl chloride



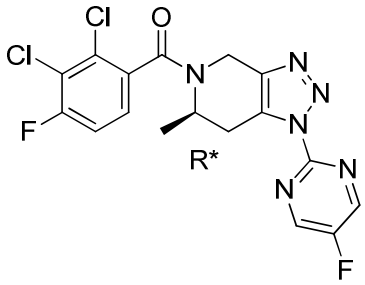
The title compound was prepared in a manner analogous to Intermediate 12 substituting 2,3-dichloro-4-fluorobenzoic acid for 2-chloro-3-(trifluoromethyl)benzoic acid.

Step 2: -[(2,3-Dichloro-4-fluorophenyl)carbonyl]-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



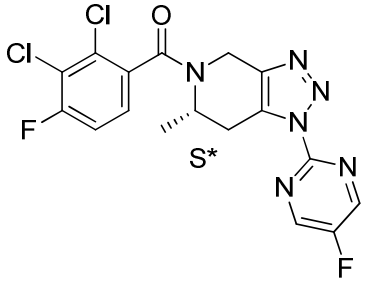
The title compound was prepared in a manner analogous to Example 200 substituting the product of Example 213, Step 1 for Intermediate 12. MS (ESI) mass calcd. $C_{17}H_{12}Cl_2F_2N_6O$, 424.0; m/z found, 424.9 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 – 8.68 (m, 2H), 7.35 – 7.10 (m, 2H), 5.91 – 5.55 (m, 1H), 4.69 – 4.05 (m, 2H), 3.58 – 3.04 (m, 2H), 1.41 – 1.14 (m, 3H).

Example 214: (6R*)-5-[(2,3-Dichloro-4-fluorophenyl)carbonyl]-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



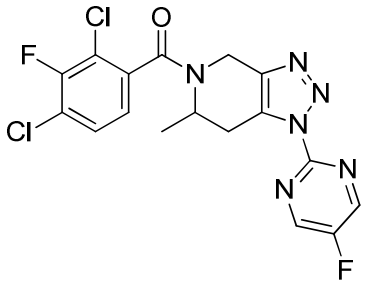
The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 213 performed using CHIRALPAK AD-H (5µm, 250x20mm) and a mobile phase of 60% CO_2, 40% MeOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) and a mobile phase of 60% CO_2, 40% MeOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 3.36 min retention time). MS (ESI) mass calcd. $C_{17}H_{12}Cl_2F_2N_6O$, 424.0; m/z found, 425.0 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.78 – 8.69 (m, 2H), 7.28 – 7.12 (m, 2H), 5.87 – 5.56 (m, 1H), 4.65 – 4.07 (m, 2H), 3.54 – 3.06 (m, 2H), 1.42 – 1.12 (m, 3H).

Example 215: (6S*)-5-[(2,3-Dichloro-4-fluorophenyl)carbonyl]-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



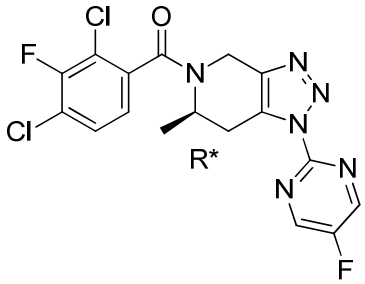
The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 213 performed using CHIRALPAK AD-H (5µm, 250x20mm) and a mobile phase of 60% CO_2, 40% MeOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) and a mobile phase of 60% CO_2, 40% MeOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 4.45 min retention time). MS (ESI) mass calcd. $C_{17}H_{12}Cl_2F_2N_6O$, 424.0; m/z found, 425.0 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.78 – 8.69 (m, 2H), 7.28 – 7.12 (m, 2H), 5.87 – 5.56 (m, 1H), 4.65 – 4.07 (m, 2H), 3.54 – 3.06 (m, 2H), 1.42 – 1.12 (m, 3H).

Example 216: 5-[(2,4-Dichloro-3-fluorophenyl)carbonyl]-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



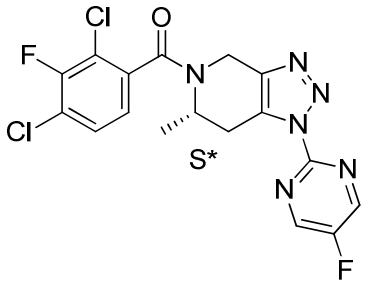
The title compound was prepared in manner analogous to Example 213 substituting 2,3-dichloro-4-fluorobenzoic acid for 2,3-dichloro-4-fluorobenzoic acid. MS (ESI) mass calcd. $C_{17}H_{12}Cl_2F_2N_6O$, 424.0; m/z found, 424.9 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.82 – 8.69 (m, 2H), 7.53 – 7.34 (m, 1H), 7.18 – 6.96 (m, 1H), 5.89 – 5.55 (m, 1H), 4.68 – 4.07 (m, 2H), 3.58 – 3.05 (m, 2H), 1.43 – 1.15 (m, 3H).

Example 217: (6R*)-5-[(2,4-Dichloro-3-fluorophenyl)carbonyl]-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



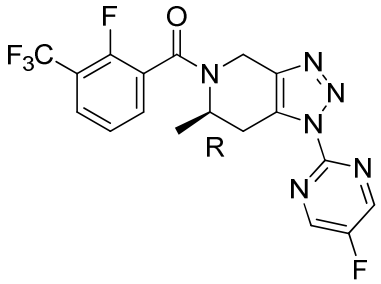
The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 216 performed using CHIRALPAK AD-H (5µm, 250x20mm) and a mobile phase of 60% CO_2, 40% MeOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) and a mobile phase of 60% CO_2, 40% MeOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 3.63 min retention time). MS (ESI) mass calcd. $C_{17}H_{12}Cl_2F_2N_6O$, 424.0; m/z found, 425.0 $[M+H]^+$.^1H NMR (500 MHz, $CDCl_3$) δ 8.79 – 8.69 (m, 2H), 7.52 – 7.33 (m, 1H), 7.17 – 6.97 (m, 1H), 5.91 – 5.56 (m, 1H), 4.68 – 4.07 (m, 2H), 3.57 – 3.05 (m, 2H), 1.42 – 1.14 (m, 3H).

Example 218: (6S*)-5-[(2,4-Dichloro-3-fluorophenyl)carbonyl]-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 216 performed using CHIRALPAK AD-H (5µm, 250x20mm) and a mobile phase of 60% CO_2, 40% MeOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) and a mobile phase of 60% CO_2, 40% MeOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 5.34 min retention time). MS (ESI) mass calcd. $C_{17}H_{12}Cl_2F_2N_6O$, 424.0; m/z found, 424.9 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.79 – 8.69 (m, 2H), 7.52 – 7.33 (m, 1H), 7.17 – 6.97 (m, 1H), 5.91 – 5.56 (m, 1H), 4.68 – 4.07 (m, 2H), 3.57 – 3.05 (m, 2H), 1.42 – 1.14 (m, 3H).

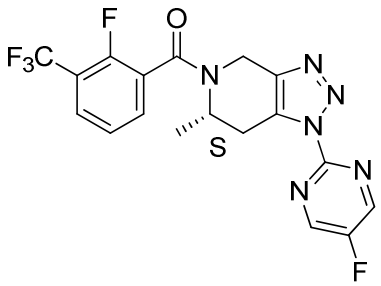
Example 219: (6R)-1-(5-Fluoropyrimidin-2-yl)-5-{[2-fluoro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



The title compound was prepared in a manner analogous to Example 213 substituting 2-fluoro-3-(trifluoromethyl)benzoic acid for 2,3-dichloro-4-fluorobenzoic acid. The racemate was purified by chiral SFC on (Chiralpak AD 5µm 250x20mm) using a mobile phase of 80% CO_2 and 20% EtOH to obtain the title compound. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) and a mobile phase of 80% CO_2, 20% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 4.49 min retention time). The absolute configuration was determined by co-injecting Example 219 with the product of Method II synthesis of Example 220 in the SFC analytical method to obtain differentiated peaks. MS (ESI) mass calcd. $C_{18}H_{13}F_5N_6O$, 424.1; m/z found, 424.8 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.79 – 8.68 (m, 2H), 7.79

– 7.54 (m, 2H), 7.46 – 7.30 (m, 1H), 5.97 – 5.55 (m, 1H), 4.77 – 4.19 (m, 2H), 3.58 – 3.11 (m, 2H), 1.43 – 1.14 (m, 3H).

Example 220: (6S)-1-(5-Fluoropyrimidin-2-yl)-5-{[2-fluoro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine

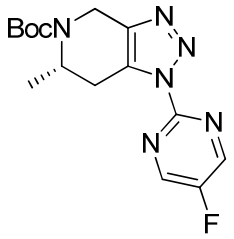


Method I:

The title compound was prepared in a manner analogous to Example 213 substituting 2-fluoro-3-(trifluoromethyl)benzoic acid for 2,3-dichloro-4-fluorobenzoic acid. The racemate was purified by chiral SFC on (Chiralpak AD 5µm 250x20mm) using a mobile phase of 80% CO_2 and 20% EtOH to obtain the title compound. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) and a mobile phase of 80% CO_2, 20% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 5.43 min retention time). The absolute configuration was determined by co-injecting the products from Method I synthesis and Method II synthesis of Example 220 in the SFC analytical method to obtain a single peak. MS (ESI) mass calcd. $C_{18}H_{13}F_5N_6O$, 424.1; m/z found, 424.8 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.79 – 8.68 (m, 2H), 7.79 – 7.54 (m, 2H), 7.46 – 7.30 (m, 1H), 5.97 – 5.55 (m, 1H), 4.77 – 4.19 (m, 2H), 3.58 – 3.11 (m, 2H), 1.43 – 1.14 (m, 3H).

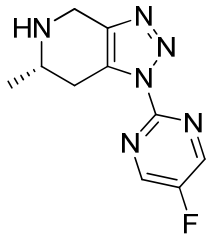
Method II:

Step 1: (S)-*tert*-butyl 1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine-5(4H)-carboxylate



(S)-*tert*-butyl 1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine-5(4H)-carboxylate . To a solution of (S)-tert-butyl 2-methyl-4-oxopiperidine-1-carboxylate (2.76 g, 12.9 mmol) in toluene (100 mL) at 100 °C was added 2-azido-5-fluoropyrimidine (2.34 g, 16.8 mmol) as a solution in toluene (15 mL) followed by pyrrolidine (1.06 mL, 12.9 mmol). After stirring for 3 h at rt, the reaction was cooled to 0 °C and CH_2Cl_2 (100 mL) was added followed by $NaHCO_3$ (2.17g, 25.9 mmol) and mCPBA (4.47g, 25.9 mmol). The reaction was allowed to warm to rt over 30 min followed by the addition of 1N NaOH (100 mL). The organic layer was separated and the water layer was extracted with CH_2Cl_2 two times. The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated. Chromatography on silica gel (0-100% ethyl acetate/hexanes) provided the desired product as a 9:1 mixture of regioisomers (9:1 = (S)-*tert*-butyl 1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine-5(4H)-carboxylate: (S)-*tert*-butyl 1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine-5(4H)-carboxylate (2.85g, 66%). The minor regioisomer was separated by SFC (Chiralpak IC 5µm 250*21mm, mobile phase 70% CO_2, 30% iPrOH) to provide the product as a white solid. MS (ESI) mass calcd. $C_{15}H_{19}FN_6O_2$, 334.16; m/z found, 335.2 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.73 (s, 2H), 5.16 (d, J = 16.1 Hz, 1H), 4.96 (br s, 1H), 4.25 (d, J = 16.4 Hz, 1H), 3.38 – 3.28 (m, 1H), 3.19 – 3.10 (m, 1H), 1.50 (s, 9H), 1.16 (d, J = 7.0 Hz, 3H).

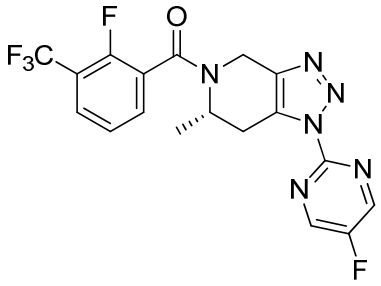
Step 2: (S)-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine- hydrochloride salt



(S)-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine- hydrochloride salt. To a solution of (S)-*tert*-butyl 1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine-5(4H)-carboxylate (0.711g, 2.13 mmol) in CH_2Cl_2 (10 mL) was added 4M HCl in dioxane (2.66 mL, 10.6 mmol). After stirring overnight at rt, the reaction was concentrated in vacuo to give the desired product as a light yellow solid (0.580 mg, 100%). MS (ESI) mass calcd. $C_{10}H_{11}FN_6$, 234.23; m/z

found, 235.1 $[M+H]^+$. ^1H NMR (400 MHz, DMSO) δ 9.97 – 9.69 (m, 1H), 9.15 (s, 2H), 4.58 – 4.35 (m, 2H), 3.80 – 3.47 (m, 2H), 3.21 – 3.03 (m, 1H), 1.46 (d, J = 6.5 Hz, 3H).

Step 3: (6S)-1-(5-Fluoropyrimidin-2-yl)-5-{[2-fluoro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



To a solution of (S)-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridinium chloride (0.575g, 2.12 mmol) in CH_2Cl_2 (10 mL) was added triethylamine (1.18 mL, 8.50 mmol) followed by 2-fluoro-3-(trifluoromethyl)benzoyl chloride (0.625 g, 2.76 mmol). After stirring for 30 min at rt, sat $NaHCO_3$ (20 mL) was added. The organic layer was separated and the water layer was extracted with CH_2Cl_2 two times. The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated. Chromatography on silica gel (0-100% ethyl acetate/hexanes) provided the desired product as a white solid (0.837 g, 93%). MS (ESI) mass calcd. $C_{18}H_{13}F_5N_6O$, 424.11; m/z found, 425.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.75 (s, 2H), 7.81 – 7.49 (m, 2H), 7.46 – 7.30 (m, 1H), 5.92 – 5.66 (m, 0.5H), 5.68 – 5.55 (m, 0.5H), 4.81 – 4.54 (m, 1H), 4.37 (d, J = 16.9 Hz, 0.5H), 4.30 – 4.18 (m, 0.5H), 3.58 – 3.40 (m, 0.8H), 3.34 – 3.12 (m, 1.2H), 1.43 – 1.12 (m, 3H).

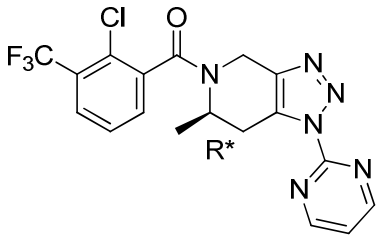
Method III:

(S)-1-(2-fluoro-3-(trifluoromethyl)benzoyl)-2-methylpiperidin-4-one: (S)-2-methylpiperidin-4-one, TFA salt (45 g, 198 mmol, 1.0 equiv.) was suspended in THF (800 mL). Et_3N (82 mL, 594 mmol, 3.0 equiv.) and 2-fluoro-3-(trifluoromethyl)benzoyl chloride (44.9 g, 198 mmol, 1.0 equiv.) were added sequentially. The reaction solution was stirred at room temperature for 1 h. The precipitated solid was filtered and washed with EtOAc. The filtrate solution was concentrated and the residue was re-dissolved in EtOAc (500 mL). The organic layer was washed with saturated $NaHCO_3$ aqueous solution, water, brine, dried over Na_2SO_4, concentrated to afford 1 (58 g, 190 mmol, 96%), which was used as it was. MS = 304.1 (positive mode).

(6S)-1-(5-Fluoropyrimidin-2-yl)-5-{[2-fluoro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine: In a 3 L, three-neck, round-bottom flask equipped with a mechanic stirring, Dean-Stark trap, reflux condenser, and an internal thermometer, to the solution of (S)-1-(2-fluoro-3-(trifluoromethyl)benzoyl)-2-methylpiperidin-4-one (53 g, 174 mmol, 1.0 equiv.) in toluene (800 mL), piperidine (20.7 mL, 210 mmol, 1.2 equiv.) and 2-azido-5-fluoropyrimidine (29.2 g, 210 mmol, 1.2 equiv.) were added sequentially. The reaction mixture was heated at reflux temperature for 4 hours and then cooled to room temperature. $NaHCO_3$ (29.4 g, 350 mmol, 2.0 equiv.) and mCPBA (86 g, 349 mmol, 2.0 equiv.) solution in EtOAC (~250 mL) were added sequentially. After stirring at room temperature for 1 hour, water and EtOAc were added. The organic layer was washed with 1M Na_2SO_3, saturated $NaHCO_3$ aqueous solution, and brine, dried over Na_2SO_4, and concentrated to afford a mixture of (S)-(2-fluoro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone and 2 in 10:1 ratio.

The crude mixture was recrystallized from hot EtOAc (~150 mL) to provide (6S)-1-(5-Fluoropyrimidin-2-yl)-5-{[2-fluoro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine (38.5 g). The mother liquor was concentrated and the recystallization process was repeated to afford another crop of pure (6S)-1-(5-Fluoropyrimidin-2-yl)-5-{[2-fluoro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine(6.0 g).

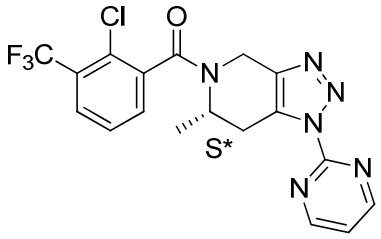
Example 221: (6R*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-1-pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



The title compound was prepared using the conditions described in Example 209 Steps A-E beginning from 2-aminopyrimidine instead of 2-aminopyrazine in step A Intermediate 65. Chiral separation of the product of Step E by SFC (CHIRALPAK AD-H 5µm 250x20mm, mobile phase 80% CO_2/20% EtOH) provided the title compound. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) and a mobile phase of 80% CO_2, 20% EtOH containing 0.3% $iPrNH_2$ over 7

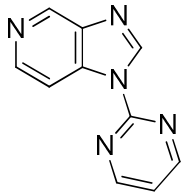
minutes. (100% single enantiomer, 5.98 min retention time). MS (ESI) mass calcd. $C_{18}H_{14}ClF_3N_6O$, 422.09; m/z found, 422.9 $[M+H]^+$.

Example 222: (6S*)-5-{[2-Chloro-3-(trifluoromethyl)phenyl]carbonyl}-6-methyl-1-pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



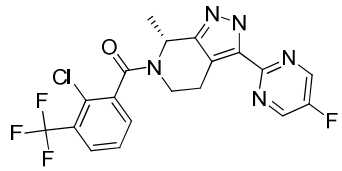
The title compound was prepared using the conditions described in Example 209 Steps A-E beginning from 2-aminopyrimidine instead of 2-aminopyrazine in step A Intermediate 65. Chiral separation of the product of Step E by SFC (CHIRALPAK AD-H 5µm 250x20mm, mobile phase 80% CO_2/20% EtOH) provided the title compound. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) and a mobile phase of 80% CO_2, 20% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 6.74 min retention time). MS (ESI) mass calcd. $C_{18}H_{14}ClF_3N_6O$, 422.09; m/z found, 422.9 $[M+H]^+$.

Intermediate 69: 3-(Pyridin-2-yl)-3H-imidazo[4,5-c]pyridine.

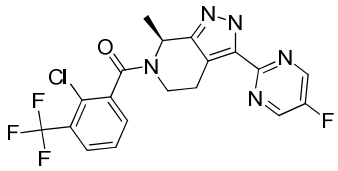


Intermediate 69 was prepared in a manner analogous to Intermediate 1, substituting 2-bromopyrimidine for 2-bromo-fluoropyridine. MS (ESI): mass calculated for $C_{11}H_8N_4$, 196.07; m/z found 197.1 $[M+H]^+$.

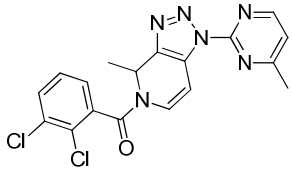
Example 223 (R*)-(2-chloro-3-(trifluoromethyl)phenyl)(3-(5-fluoropyrimidin-2-yl)-7-methyl-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone



Example 224 (S*)-(2-chloro-3-(trifluoromethyl)phenyl)(3-(5-fluoropyrimidin-2-yl)-7-methyl-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone

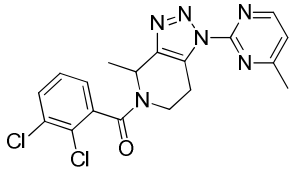


Intermediate H (2,3-dichlorophenyl)(4-methyl-1-(4-methylpyrimidin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Intermediate C substituting 1-(3,5-dimethylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine for 1-(4-methylpyrimidin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine and Intermediate 12 for Intermediate 14. The reaction mixture was also cooled down to -40°C instead of -78°C. MS (ESI) mass calcd. $C_{18}H_{14}Cl_2N_6O$, 400.06 m/z found, 401.10 $[M+H]^+$.

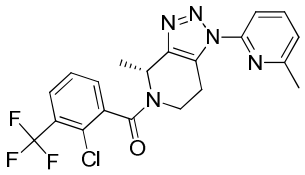
Example 225 (2,3-dichlorophenyl)(4-methyl-1-(4-methylpyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example 159 substituting (2,3-dichlorophenyl)(4-methyl-1-(4-methylpyrimidin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone for (2-chloro-3-(trifluoromethyl)phenyl)(1-(3,5-dimethylpyridin-2-yl)-4-methyl-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone.. MS (ESI) mass calcd. $C_{18}H_{16}Cl_2N_6O$, 402.08 m/z found, 403.10 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.74 - 8.63 (m, 1H), 7.58 - 7.48 (m, 1H), 7.39 - 6.97 (m, 3H), 6.16 - 5.98 (m, 0.6H), 5.20 - 5.05 (m, 0.4H), 5.02 - 4.74 (m, 0.4H), 3.79 - 2.93 (m, 3.6H), 2.75 - 2.57 (m, 3H), 1.77 - 1.44 (m,

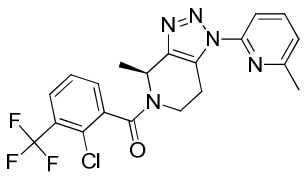
3H). The following data was also obtained for the title compound: MS (ESI) mass calcd $C_{18}H_{16}Cl_2N_6O$, 402.1 m/z found, 403.1 [M+H. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 - 8.57 (m, 1H), 7.58 - 7.48 (m, 1H), 7.39 - 6.97 (m, 3H), 6.16 - 5.98 (m, 0.6H), 5.20 - 5.05 (m, 0.4H), 5.02 - 4.74 (m, 0.4H), 3.79 - 2.93 (m, 3.6H), 2.75 - 2.57 (m, 3H), 1.77 - 1.44 (m, 3H).

Example 226 (R*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 302 performed using a CHIRALPAK AD-H (5µm 250x20mm) column and a mobile phase of 75% CO_2, 25% MeOH/iPrOH 50/50 v/v containing 0.3% $iPrNH_2$. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) and a mobile phase of 75% CO_2, 25% MeOH/iPrOH 50/50 v/v containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 2.73 min retention time). MS (ESI) mass calcd. $C_{20}H_{17}ClF_3N_5O$, 435.11 m/z found, 436.10 $[M+H]^+$. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 – 7.88 (m, 1H), 7.82 – 7.74 (m, 2H), 7.58 – 7.29 (m, 2H), 7.23 – 7.14 (m, 1H), 6.12 – 5.99 (m, 0.6H), 5.17 – 5.07 (m, 0.4H), 4.90 – 4.72 (m, 0.4H), 3.68 – 2.95 (m, 3.6H), 2.63 – 2.46 (m, 3H), 1.77 – 1.44 (m, 3H).

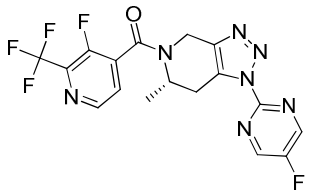
Example 227 (S*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 302 performed using a CHIRALPAK AD-H (5µm 250x20mm) column and a mobile phase of 75% CO_2, 25% MeOH/iPrOH 50/50 v/v

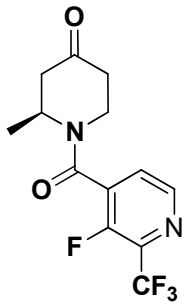
containing 0.3% $iPrNH_2$. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) and a mobile phase of 75% CO_2, 25% MeOH/iPrOH 50/50 v/v containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 3.36 min retention time). MS (ESI) mass calcd. $C_{20}H_{17}ClF_3N_5O$, 435.11 m/z found, 436.10 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 7.97 – 7.88 (m, 1H), 7.82 – 7.74 (m, 2H), 7.58 – 7.29 (m, 2H), 7.23 – 7.14 (m, 1H), 6.12 – 5.99 (m, 0.6H), 5.17 – 5.07 (m, 0.4H), 4.90 – 4.72 (m, 0.4H), 3.68 – 2.95 (m, 3.6H), 2.63 – 2.46 (m, 3H), 1.77 – 1.44 (m, 3H).

Example 228 (S)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared as described in Example 65, substituting (S)-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine-hydrochloride salt (prepared as Step 2 intermediate of method II synthesis) in Example 220 for 1-pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine, 3-fluoro-2-(trifluoromethyl)isonicotinic acid for 2-chloro-3-(trifluoromethyl)benzoic acid and Hunig's base (3.0 equiv) for Et_3N. The powder x-ray diffraction pattern for this compound is shown in Figure 2. Alternatively, the title compound was synthesized using the following procedure:

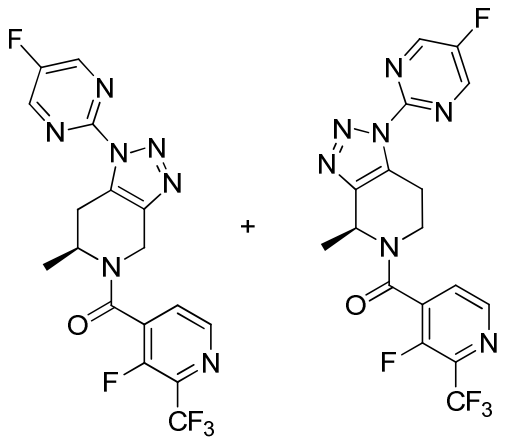
Step 1: (S)-1-(3-fluoro-2-(trifluoromethyl)isonicotinoyl)-2-methylpiperidin-4-one



(S)-1-(3-fluoro-2-(trifluoromethyl)isonicotinoyl)-2-methylpiperidin-4-one.: (S)-2-methylpiperidin-4-one, TFA salt (108 g, 478 mmol, 1.0 equiv.) was suspended in DCM (1.4 L). Et_3N (265 mL, 1.9 mol, 4.0 equiv.) and 3-fluoro-2-(trifluoromethyl)isonicotinoyl

chloride (119 g, 526 mmol, 1.1 equiv.) were added sequentially. The reaction solution was stirred at room temperature for 1 h. The precipitated solid was filtered and washed with EtOAc. The filtrate solution was concentrated and the residue was re-dissolved in EtOAc (500 mL). The organic layer was washed with saturated $NaHCO_3$ aqueous solution, water and brine, dried over Na_2SO_4, and concentrated. The crude product was triturated from EtOAc/hexanes to afford (S)-1-(3-fluoro-2-(trifluoromethyl)isonicotinoyl)-2-methylpiperidin-4-one (103 g, 368 mmol, 77%), which was used without further purification. MS = 305.1 (positive mode)

Step 2: (S)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone and (S)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



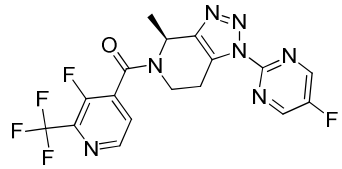
In a 5 L, three-neck, round-bottom flask equipped with a mechanic stirring, Dean-Stark trap, reflux condenser and an internal thermometer, to the solution of (S)-1-(3-fluoro-2-(trifluoromethyl)isonicotinoyl)-2-methylpiperidin-4-one, prepared in Step 1 above (100 g, 328 mmol, 1.0 equiv.) in toluene (1.5 L), *p*-toluenesulphonic acid (0.62 g, 3.29 mmol, 0.01 equiv.), pyrrolidine (33 mL, 394 mmol, 1.2 equiv.) and 2-azido-5-fluoropyrimidine (59.4 g, 427 mmol, 1.3 equiv.) were added sequentially. The reaction mixture was heated to reflux temperature for 4 hours and then cooled to room temperature. $NaHCO_3$ (55.2 g, 657 mmol, 2.0 equiv.) and mCPBA (162 g, 657 mmol, 2.0 equiv.) solution in EtOAC (~250 mL) were added sequentially. After stirring at room temperature for 2 hours, water and EtOAc were added. The organic layer was washed sequentially with 1M Na_2SO_3, saturated $NaHCO_3$ aqueous solution, and brine, dried over Na_2SO_4, and concentrated. The crude product was purified via column chromatography to afford a mixture of (S)-(3-fluoro-2-

(trifluoromethyl)pyridin-4-yl)(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone and (S)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone in a 10:1 ratio (97 grams).

Step 3: (S)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone

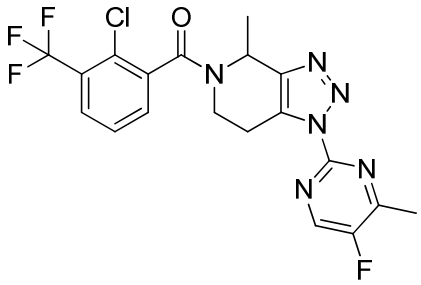
HPLC purification of the mixture from Step 2 was performed via achiral SFC (Stationary phase: Chiralcel OD-H 5µm 250x30mm), (Mobile phase: 75% CO_2, 25% MeOH) to afford pure (S)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone (73 gram, 172 mmol, 52%). MS (ESI) mass calcd $C_{17}H_{12}F_5N_7O$, 425.1 m/z found, 426.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.84 – 8.69 (m, 2H), 8.68 – 8.57 (m, 1H), 7.71 – 7.49 (m, 1H), 5.90 – 5.68 (d, J = 16.4 Hz, 0.5H), 5.66 – 5.54 (m, 0.5H), 4.76 – 4.58 (d, J = 15.8 Hz, 0.5H), 4.58 – 4.48 (m, 0.5H), 4.45 – 4.33 (m, 0.5H), 4.20 – 4.09 (m, 0.5H), 3.56 – 3.12 (m, 2H), 1.48 – 1.18 (m, 3H).

Example 229 (S*)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



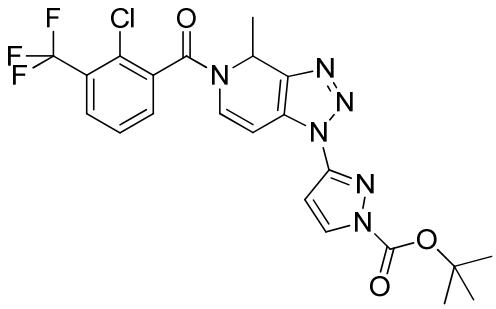
The title compound was prepared as described in Example 65, substituting (S)-1-(5-fluoropyrimidin-2-yl)-4-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine-hydrochloride salt (prepared from the minor isomer obtained in Step 1 of Method II Example 220 synthesis using conditions described in Step 2, Method II in Example 220) for 1-pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine, 3-fluoro-2-(trifluoromethyl)isonicotinic acid for 2-chloro-3-(trifluoromethyl)benzoic acid and Hunig's base (3.0 equiv) for Et_3N. MS (ESI) mass calcd $C_{17}H_{12}F_5N_7O$, 425.1 m/z found, 426.1 $[M+H]^+$.

Example 230: (2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone.



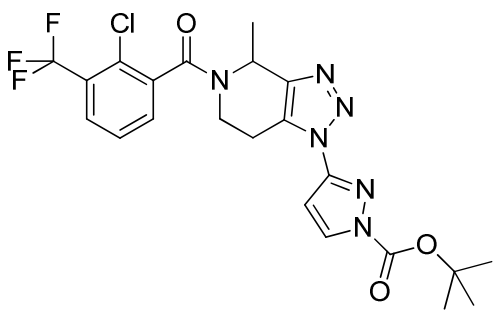
Example 230 was prepared in a manner analogous to Example 11 substituting Intermediate 51 and excess MeMgBr in Step A. MS (ESI): mass calculated for $C_{19}H_{15}ClF_4N_6O$, 454.09; m/z found, 455.1 $[M+H]^+$.

Intermediate 231: tert-butyl 3-(5-(2-chloro-3-(trifluoromethyl)benzoyl)-4-methyl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-1-yl)-1H-pyrazole-1-carboxylate



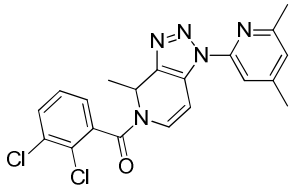
Was made in a fashion analogous to compound Example 11, Step A substituting Intermediate 49 for Intermediate 1. MS (ESI) mass calcd. $C_{22}H_{20}ClF_3N_6O_3$, 508.88; m/z found, 509.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$); 8.14 (t, J = 2.6 Hz, 1H), 7.89 - 7.77 (m, 1H), 7.68 - 7.40 (m, 2H), 7.01 - 6.92 (m, 1H), 6.59 - 6.47 (m, 1H), 6.39 - 6.23 (m, 1H), 4.12 (q, J = 7.1 Hz, 1H), 1.73 - 1.55 (m, 12H).

Intermediate 232: tert-Butyl 3-(5-(2-chloro-3-(trifluoromethyl)benzoyl)-4-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridin-1-yl)-1H-pyrazole-1-carboxylate



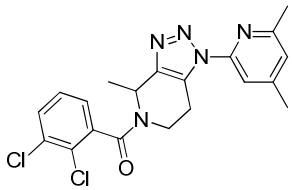
A solution of *tert*-butyl 3-(5-(2-chloro-3-(trifluoromethyl)benzoyl)-4-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridin-1-yl)-1H-pyrazole-1-carboxylate (34 mg, 0.07 mmol) in MeOH 92.5 ml) was treated with Pd/carbon (5 wt%, 14 mg) and put under 1 atmosphere of H_2 and reaction stirred for 16 h. Reaction filtered, and concentrated and the crude product was purified on 16 g SiO_2 with 0–40 % EtOAc/ hexanes. MS (ESI) mass calcd. $C_{22}H_{22}ClF_3N_6O_3$, 510.90; m/z found, 511.2 $[M+H]^+$.

Intermediate I (2,3-dichlorophenyl)(1-(4,6-dimethylpyridin-2-yl)-4-methyl-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Intermediate C substituting 1-(3,5-dimethylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine for 1-(4,6-dimethylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine and Intermediate 12 for Intermediate 14. The reaction mixture was also cooled down to -40°C instead of -78°C. MS (ESI) mass calcd $C_{20}H_{17}Cl_2N_5O$, 413.08 m/z found, 414.10 $[M+H]^+$.

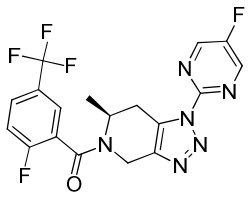
Example 231 (2,3-dichlorophenyl)(1-(4,6-dimethylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example C substituting (2,3-dichlorophenyl)(1-(4,6-dimethylpyridin-2-yl)-4-methyl-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone for (2-chloro-3-(trifluoromethyl)phenyl)(1-(3,5-dimethylpyridin-2-yl)-4-methyl-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone. MS (ESI) mass calcd $C_{20}H_{19}Cl_2N_5O$, 415.1 m/z found, 416.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 7.81 - 7.67 (m, 1H), 7.60 - 7.47 (m, 1H), 7.38 - 7.19 (m, 2H), 7.06 - 6.96 (m, 1H), 6.11 - 5.96 (m,

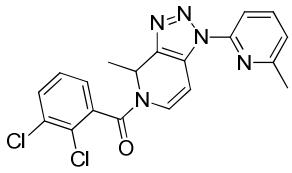
0.6H), 5.21 - 5.04 (m, 0.4H), 4.98 - 4.70 (m, 0.4H), 3.69 - 2.94 (m, 3.6H), 2.59 - 2.39 (m, 6H), 1.77 - 1.40 (m, 3H).

Example 232 (S*)-(2-fluoro-5-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



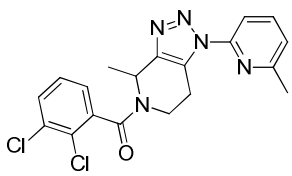
MS (ESI) mass calcd $C_{18}H_{13}F_5N_6O$, 424.1 m/z found, 425.1 $[M+H]^+$.

Intermediate J (2,3-dichlorophenyl)(4-methyl-1-(6-methylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Intermediate C substituting 1-(6-methylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine for 1-(3,5-dimethylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine and Intermediate 14 for Intermediate 12. The reaction mixture was also cooled down to -40°C instead of -78°C. MS (ESI) mass calcd. $C_{19}H_{15}Cl_2N_5O$, 399.07 m/z found, 400.10 $[M+H]^+$.

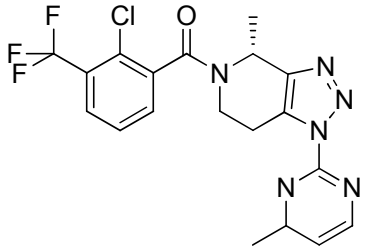
Example 233 (2,3-dichlorophenyl)(4-methyl-1-(6-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example C substituting (2,3-dichlorophenyl)(4-methyl-1-(6-methylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-

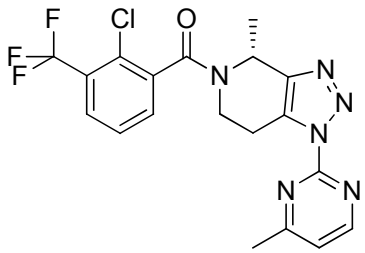
yl)methanone for (2-chloro-3-(trifluoromethyl)phenyl)(1-(3,5-dimethylpyridin-2-yl)-4-methyl-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone. MS (ESI) mass calcd $C_{19}H_{17}Cl_2N_5O$, 401.1 m/z found, 402.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 7.99 – 7.87 (m, 1H), 7.85 – 7.71 (m, 1H), 7.62 – 7.49 (m, 1H), 7.39 – 6.99 (m, 3H), 6.17 – 5.95 (m, 0.6H), 5.17 – 5.04 (m, 0.4H), 5.00 – 4.67 (m, 0.4H), 3.79 – 2.94 (m, 3.6H), 2.70 – 2.42 (m, 3H), 1.83 – 1.41 (m, 3H).

Example 234: (4*R**)-(2-Chloro-3-(trifluoromethyl)phenyl)((4R)-4-methyl-1-(6-methyl-1,6-dihydropyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



A solution of (4R*)-5-{[2-2hloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrimidin-2-yl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine (45 mg, 0.11 mmol) in THF was cooled to -30 °C and treated with 2.0 MeMgBr in THF (0.04 ml, 0.12 ml) and the reaction was warmed to 0 °C and diluted with EtOAc and washed with water. The EtOAc solution was dried and concentrated and purified on 4 g SiO_2 with 0-40% EtOAc/DCM. MS (ESI) mass calcd. $C_{19}H_{18}ClF_3N_6O$, 438.12; m/z found, 439.2 $[M+H]^+$.

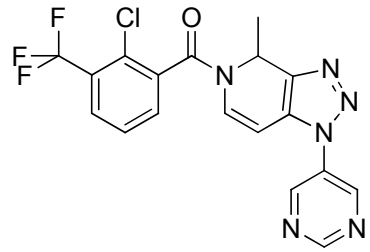
Example 235: (4*R**)-(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(4-methylpyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



A solution of (4*R**)-(2-chloro-3-(trifluoromethyl)phenyl)((4R)-4-methyl-1-(6-methyl-1,6-dihydropyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone (41 mg, 0.9 mmol) in DCM was treated with DDQ (50 mg, 0.21 mmol). After 2 min, the reaction was complete and the crude reaction was applied directly to a 12 g SiO2 column and eluted with 0-4% NH_3 MeOH / DCM to provide desired product (24 mg, 59%) MS (ESI) mass calcd. $C_{19}H_{16}ClF_3N_6O$, 436.10; m/z found, 437.2 $[M+H]^+$. ^1H NMR (400 MHz,

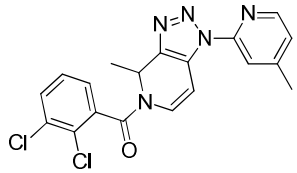
$CDCl_3$) δ 8.71 (dd, *J* = 5.0, 2.5 Hz, 0.5H), 8.69 - 8.64 (m, 0.5H), 7.81 - 7.73 (m, 1H), 7.58 - 7.36 (m, 2H), 7.31 - 7.27 (m, 0.3H), 7.25 - 7.20 (m, 0.7H), 6.13 - 6.02 (m, 0.5H), 5.16 - 5.10 (m, 0.4H), 4.92 - 4.85 (m, 0.1H), 4.80 - 4.75 (m, 0.3H), 3.67 - 3.11 (m, 3.3H), 3.07 - 2.95 (m, 0.4H), 2.68 – 2.67 (m, 1.3H), 2.65 (s, 0.6H), 2.63 (s, 1H), 1.72 (d, *J* = 6.9 Hz, 0.9H), 1.70 (d, *J* = 7.0 Hz, 0.6H), 1.58 (d, *J* = 7.1 Hz, 0.5H), 1.50 (d, *J* = 6.7 Hz, 0.9H).

Example 236: (2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrimidin-5-yl)-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



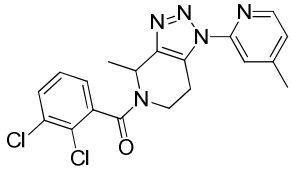
The title compound was prepared in a manner analogous to Example 72 substituting 5-aminopyrimidine for 2-aminopyrazine in the synthesis of 1-pyrazin-2-yl-1H-[1,2,3]triazolo[4,5-c]pyridine. MS (ESI) mass calcd. $C_{18}H_{12}ClF_3N_6O$, 420.07; m/z found, 421.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 9.34 (s, 1H), 9.16 - 9.02 (m, 2H), 7.85 (ddd, J = 7.7, 3.5, 1.6 Hz, 1H), 7.70 - 7.44 (m, 2H), 6.43 - 6.30 (m, 2H), 5.85 - 5.74 (m, 1H), 1.66 (d, J = 1.8 Hz, 3H).

Intermediate K: (2,3-dichlorophenyl)(4-methyl-1-(4-methylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Intermediate C substituting 1-(4-methylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine for 1-(3,5-dimethylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine and Intermediate 14 for Intermediate 12. The reaction mixture was also cooled down to -40°C instead of -78°C. MS (ESI) mass calcd. $C_{19}H_{15}Cl_2N_5O$, 399.07; m/z found 400.10 $[M+H]^+$.

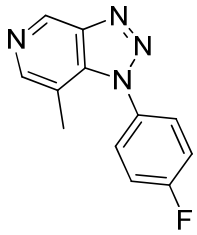
Example 237 (2,3-dichlorophenyl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example 159 substituting (2,3-dichlorophenyl)(4-methyl-1-(4-methylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone for (2-chloro-3-(trifluoromethyl)phenyl)(1-(3,5-dimethylpyridin-2-yl)-4-methyl-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone for. MS (ESI) mass calcd $C_{19}H_{17}Cl_2N_5O$, 401.08 m/z found, 402.10 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.40 - 8.24 (m, 1H), 8.01 - 7.93 (m, 1H), 7.62 - 7.47 (m, 1H), 7.40 - 6.98 (m, 3H), 6.17 - 5.92 (m, 0.6H), 5.15 - 5.04 (m, 0.4H), 5.00 - 4.74 (m, 0.4H), 3.68 - 2.95 (m, 3.6H), 2.52 - 2.38 (m, 3H), 1.75 - 1.41 (m, 3H). The following data was also obtained for the title compound: MS (ESI) mass calcd $C_{19}H_{17}Cl_2N_5O$, 401.1 m/z found, 402.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.47 - 8.19 (m, 1H), 8.05 - 7.88 (m, 1H), 7.62 - 7.47 (m, 1H), 7.40 - 6.98 (m, 3H), 6.17 - 5.92 (m, 0.6H), 5.15 - 5.04 (m, 0.4H), 5.00 - 4.74 (m, 0.4H), 3.75 - 2.92 (m, 3.6H), 2.58 - 2.37 (m, 3H), 1.82 - 1.39 (m, 3H).

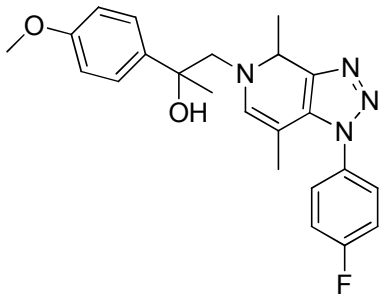
Example 238: (2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-fluorophenyl)-4,7-dimethyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone

Step 1: 1-(4-fluorophenyl)-7-methyl-1H-[1,2,3]triazolo[4,5-c]pyridine.



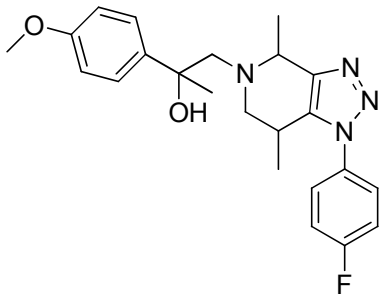
The title compound was prepared in a manner analogous to Intermediate 17, Step 1 through Intermediate 19, Step 3 substituting 4-chloro-3-methyl-5-nitro-pyridine for 4-chloro-3-nitropyridine and 4-fluoroaniline for 2-aminopyridine in the synthesis of Intermediate 17, Step 1. MS (ESI) mass calcd. $C_{12}H_9FN_4$, 228.1; m/z found, 229.1 $[M+H]^+$.

Step 2: 1-(1-(4-fluorophenyl)-4,7-dimethyl-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)-2-(4-methoxyphenyl)propan-2-ol.



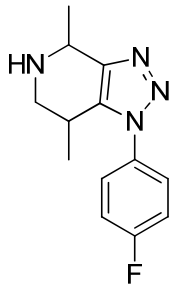
The title compound was prepared in a manner analogous to Example 72 substituting 2-bromo-4'-methoxyacetophenone for 2-chloro-3-(trifluoromethyl)benzoyl chloride. MS (ESI) mass calcd. $C_{23}H_{25}FN_4O_2$, 408.2; m/z found 409.18 $[M+H]^+$.

Step 3: 1-(1-(4-fluorophenyl)-4,7-dimethyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)-2-(4-methoxyphenyl)propan-2-ol.



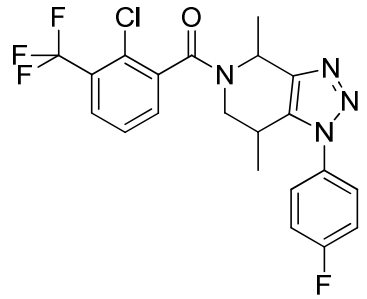
To a solution of the product of Example 238, Step 2 (200 mg, 0.49 mmol) in MeOH (2 mL) was added Pd/C (52 mg, 0.049 mmol) and ammonium formate (93 mg, 1.45 mmol). The reaction vessel was sealed and heated 80°C for 16 h. The reaction mixture was then filtered through Celite, concentrated and purified on silica gel with 0-2% NH_3 MeOH / CH_2Cl_2 to afford the title compound (93 mg, 46%). MS (ESI) mass calcd. $C_{23}H_{27}FN_4O_2$, 410.2; m/z found, 411.20 $[M+H]^+$.

Step 4: 1-(4-fluorophenyl)-4,7-dimethyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



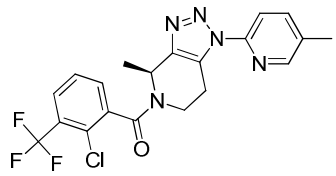
The product of Example 238, Step 3 (90 mg, 0.22 mmol) was dissolved in a solution of HCl in dioxane (4M, 2 mL). The reaction was heated at 90 °C for 16 h. The solvent was removed *in vacuo* to afford the title compound (50 mg, 92%). MS (ESI) mass calcd. $C_{13}H_{15}FN_4$, 246.10; m/z found, 247.16 $[M+H]^+$.

Step 5: (2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-fluorophenyl)-4,7-dimethyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example 63, Step 5 substituting the product of Example 238, Step 4 for 1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine and DIPEA for TEA. MS (ESI) mass calcd. $C_{21}H_{17}ClF_4N_4O$, 452.1; m/z found, 453.1 $[M+H]^+$.

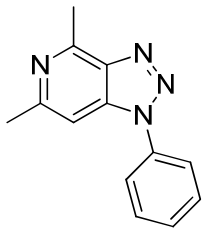
Example 239 (S*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(5-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 301 performed using a WHELK O1 (S,S) (5µm 250x21.1mm) column and a mobile phase of 60% CO_2, 40% MeOH. The enantiomeric purity was confirmed by analytical SFC using a WHELK O1 (S,S) (250x4.6mm) and a mobile phase 60% CO_2, 40% MeOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 5.70 min retention time). After the Chiral SFC purification, purification by chromatography on SiO_2 eluting with EtOAc/hexanes was done. MS (ESI) mass calcd. MS (ESI) mass calcd $C_{20}H_{17}ClF_3N_5O$, 435.1 m/z found, 435.7 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.41 - 8.16 (m, 1H), 8.12 - 7.94 (m, 1H), 7.85 - 7.64 (m, 2H), 7.63 - 7.28 (m, 2H), 6.16 - 5.96 (m, 0.6H), 5.20 - 5.05 (m, 0.4H), 4.93 - 4.68 (m, 0.4H), 3.66 - 2.96 (m, 3.6H), 2.59 - 2.28 (m, 3H), 1.82 - 1.44 (m, 3H).

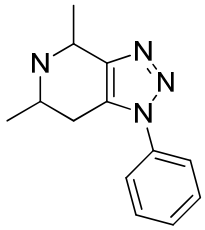
Example 240: (2-Chloro-3-(trifluoromethyl)phenyl)(4,6-dimethyl-1-phenyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone

Step 1: 4,6-dimethyl-1-phenyl-1H-[1,2,3]triazolo[4,5-c]pyridine.



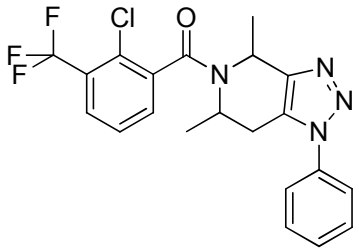
The title compound was prepared in a manner analogous to Intermediate 17, Step 1 through Intermediate 19, Step 3. In the synthesis of Intermediate 17, Step 1 $Pd(OAc)_2$ and BINAP were eliminated and these substitutions were made: 4-chloro-2,6-dimethyl-3-nitropyridine for 4-chloro-3-nitropyridine, aniline for 2-aminopyridine, NaH for K_2CO_3, and THF for toluene, and the reaction was carried out for 24 h at room temperature. MS (ESI) mass calcd. $C_{13}H_{12}N_4$, 224.1; m/z found, 225.1 $[M+H]^+$.

Step 2: 4,6-dimethyl-1-phenyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine



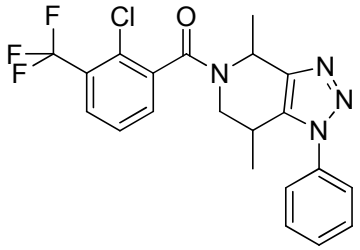
The title compound was prepared in a manner analogous to Intermediate 68, Step D Substituting the product of Example 240, Step 1 for 6-methyl-1-(pyrazin-2-yl)-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine. MS (ESI) mass calcd. $C_{13}H_{16}N_4$, 228.1; m/z found, 229.1 $[M+H]^+$.

Step 3: 2-Chloro-3-(trifluoromethyl)phenyl)(4,6-dimethyl-1-phenyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



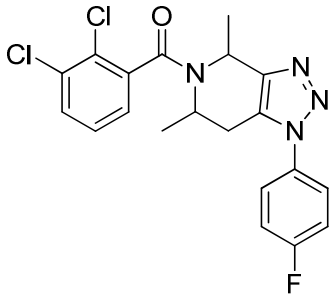
The title compound was prepared in a manner analogous to Example 63, Step 5 substituting the product of Example 238, Step 4 for 1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine. MS (ESI) mass calcd. $C_{21}H_{18}ClF_3N_4O$, 434.1; m/z found, 435.1 $[M+H]^+$.

Example 241: (2-Chloro-3-(trifluoromethyl)phenyl)(4,7-dimethyl-1-phenyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



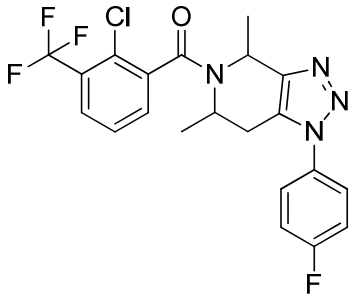
The title compound was prepared in a manner analogous to Example 238 substituting aniline for 4-fluoroaniline in Step 1, acetyl chloride for 2-bromo-4'-methoxyacetophenone in Step 2 and HCl (12N) in MeOH/H_2O (3:1) for HCl (4N in dioxane) in MeOH in Step 4. MS (ESI) mass calcd. $C_{21}H_{18}ClF_3N_4O$, 434.1; m/z found, 435.1 $[M+H]^+$.

Example 242: (2,3-Dichlorophenyl)(1-(4-fluorophenyl)-4,6-dimethyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example 240 substituting 4-fluoroaniline for aniline in the synthesis of example 240, step 1 and substituting 2,3-dichlorobenzoyl chloride for 2-chloro-3-(trifluoromethyl)benzoyl chloride in the synthesis of Example 240, Step 3. MS (ESI) mass calcd. $C_{20}H_{17}Cl_2FN_4O$, 418.1; m/z found, 419.0 $[M+H]^+$.

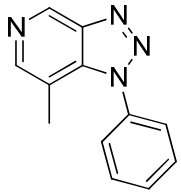
Example 243: (2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-fluorophenyl)-4,6-dimethyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example 240 substituting 4-fluoroaniline for aniline in the synthesis of example 240, step 1. MS (ESI) mass calcd. $C_{21}H_{17}ClF_4N_4O$, 452.1; m/z found, 453.2 $[M+H]^+$.

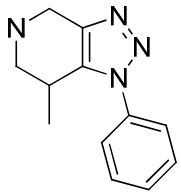
Example 244: (2,3-Dichlorophenyl)(7-methyl-1-phenyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone

Step 1: 7-methyl-1-phenyl-1H-[1,2,3]triazolo[4,5-c]pyridine.



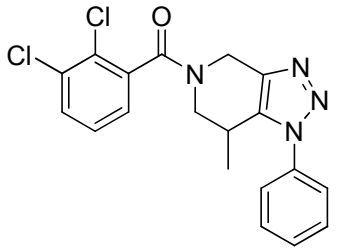
The title compound was prepared in a manner analogous to Intermediate 17, Step 1 through Intermediate 19, Step 3 substituting 4-chloro-3-methyl-5-nitro-pyridine for 4-chloro-3-nitropyridine, and aniline for 2-aminopyridine. MS (ESI) mass calcd. $C_{12}H_{10}N_4$, 210.1; m/z found, 225.1 $[M+H]^+$.

Step 2: 7-methyl-1-phenyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



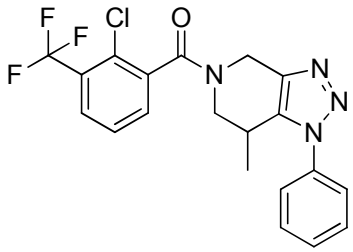
The title compound was prepared in a manner analogous to Intermediate 68, Step D Substituting the product of Example 244, Step 1 for 6-methyl-1-(pyrazin-2-yl)-1*H*-[1,2,3]triazolo[4,5-*c*]pyridine. MS (ESI) mass calcd. $C_{12}H1_4N$, 214.1; m/z found, 215.1 $[M+H]^+$.

Step 3: (2,3-Dichlorophenyl)(7-methyl-1-phenyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



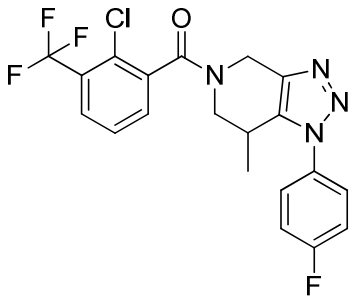
The title compound was prepared in a manner analogous to Example 63, Step 5 substituting the product of Example 244, Step 2 for 1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine, 2,3-dichlorobenzoyl chloride for 2-chloro-3-(trifluoromethyl)benzoyl chloride and DIPEA for TEA. MS (ESI) mass calcd. $C_{19}H_{16}Cl_2N_4O$, 386.1; m/z found, 387.1 $[M+H]^+$.

Example 245: (2-Chloro-3-(trifluoromethyl)phenyl)(7-methyl-1-phenyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



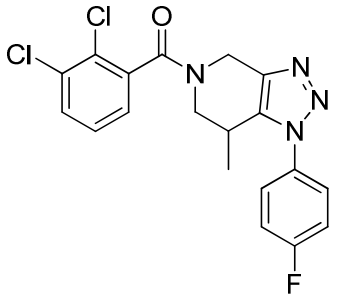
The title compound was prepared in a manner analogous to Example 244 substituting 2-chloro-3-(trifluoromethyl)benzoyl chloride for 2,3-dichlorobenzoyl chloride in the final step. MS (ESI) mass calcd. $C_{20}H_{16}ClF_3N_4O$, 420.1; m/z found, 421.2 $[M+H]^+$.

Example 246: (2-Chloro-3-(trifluoromethyl)phenyl)(1-(4-fluorophenyl)-7-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



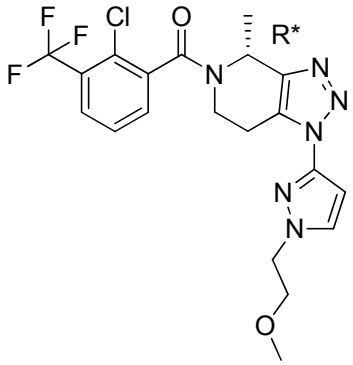
The title compound was prepared in a manner analogous to Example 244 substituting 4-fluoroaniline for aniline in Example 244, Step 1 and 2-chloro-3-(trifluoromethyl)benzoyl chloride for 2, 3-dichlorobenzoyl chloride in Step 3. MS (ESI) mass calcd. $C_{20}H_{15}ClF_4N_4O$, 438.1; m/z found, 439.1 $[M+H]^+$.

Example 247: (2,3-Dichlorophenyl)(1-(4-fluorophenyl)-7-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



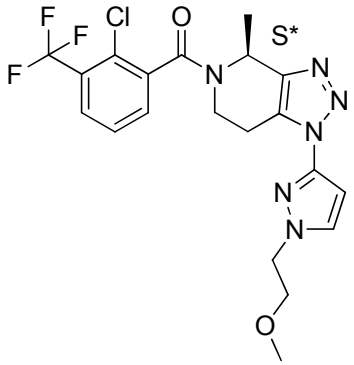
The title compound was prepared in a manner analogous to Example 244 substituting 4-fluoroaniline for aniline in Example 244, Step 1. MS (ESI) mass calcd. $C_{19}H_{15}Cl_2FN_4O$, 404.1; m/z found, 405.2 $[M+H]^+$.

Example 248: (R*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(1-(2-methoxyethyl)-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The racemic mixture of the title compound was prepared in a manner analogous to Example 162 substituting 2-bromoethyl methyl ether for 1-bromo-2-fluoroethane in Example 162, Step 2. The title compound was obtain by chiral SFC purification of the racemic mixture (Chiralpak AD-H 5µm 250x20mm) using a mobile phase of 80% CO_2 and 20% EtOH to obtain the title compound. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) and a mobile phase of 80% CO_2, 20% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 4.66 min retention time). MS (ESI) mass calcd. $C_{20}H_{20}ClF_3N_6O_2$, 468.1; m/z found, 469.1 $[M+H]^+$.

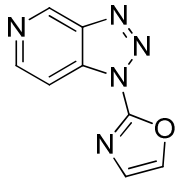
Example 249: (S*)-(2-Chloro-3-(trifluoromethyl)phenyl)(1-(1-(2-methoxyethyl)-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The racemic mixture of the title compound was prepared in a manner analogous to Example 162 substituting 2-bromoethyl methyl ether for 1-bromo-2-fluoroethane in Example 162, Step 2. The title compound was obtain by chiral SFC purification of the racemic mixture (Chirapak AD-H 5µm 250x20mm) using a mobile phase of 80% CO_2 and 20% EtOH to obtain the title compound. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) and a mobile phase of 80% CO_2, 20% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 6.61 min retention time). MS (ESI) mass calcd. $C_{20}H_{20}ClF_3N_6O_2$, 468.1; m/z found, 469.1 $[M+H]^+$.

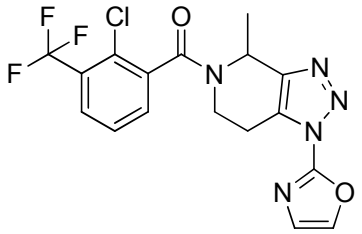
Example 250: (2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(oxazol-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone

Step 1: 2-(1H-[1,2,3]triazolo[4,5-c]pyridin-1-yl)oxazole.



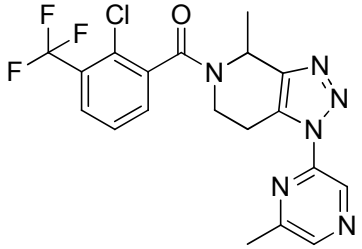
The title compound was prepared in a manner analogous to Intermediate 17, Step 1 through Intermediate 19, Step 3. In the synthesis of Intermediate 17, Step 1 $Pd(OAc)_2$ and BINAP were eliminated and these substitutions were made: 2-aminooxazole for 2-aminopyridine, NaOtBu for K_2CO_3, and *tert*-amyl alcohol for toluene, reaction carried out for 0.5 h at room temperature. MS (ESI) mass calcd. $C_8H_5N_5O$, 187.0; m/z found, 188.1 $[M+H]^+$.

Step 2: (2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(oxazol-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared following the route to prepare Example 73 using the product of Example 250, Step 1 as starting material. MS (ESI) mass calcd $C_{17}H_{13}ClF_3N_5O_2$, 411.1; m/z found, 412.1 $[M+H]^+$.

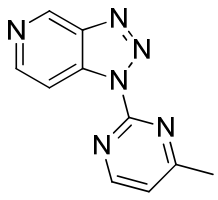
Example 251: (2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-methylpyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was obtained using the route described to synthesize Example 73. The starting material was obtained in a manner analogous to Intermediate 20, Step 4 substituting 2-amino-6-methylpyraizine for 2-aminopyridine, Xantphos for BINAP, Cs_2CO_3 for K_2CO_3 and dioxane for toluene in the synthesis of Intermediate 17, Step 1. MS (ESI) mass calcd $C_{19}H_{16}ClF_3N_6O$, 436.1; m/z found, 437.1 $[M+H]^+$.

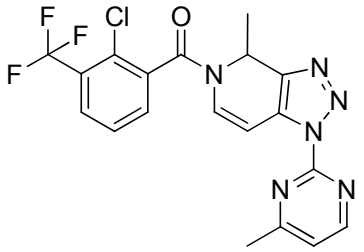
Example 252: (2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(4-methylpyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone

Step 1: 1-(4-methylpyrimidin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine.



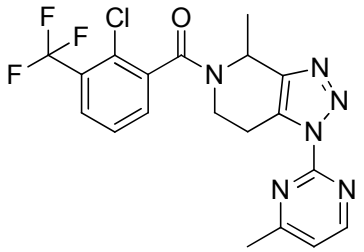
The title compound was prepared in a manner analogous to Intermediate 17, Step 1 through Intermediate 19, Step 3. In the synthesis of Intermediate 17, Step 1 these substitutions were made: 4-methylpyrimidin-2-amine for 2-aminopyridine, Cs_2CO_3 for K_2CO_3, and dioxane for toluene, reaction carried out for 0.5 h at room temperature. MS (ESI) mass calcd. $C_{10}H_8N_6$, 212.1; m/z found, 213.1 $[M+H]^+$.

Step 2: (2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(4-methylpyrimidin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



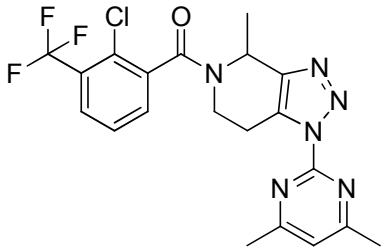
To a suspension of the product of Example 252, Step 1 (200 mg, 0.94 mmol) in THF (30 mL) cooled to -78°C was added Intermediate 12 (251 mg, 1.04 mmol). Trimethylsilyl trifluoromethanesulfonate (0.188 mL, 1.04 mmol) was then added and the reaction was stirred at -78°C for 30 min. The resulting mixture was treated with MeMgBr (3.0 M solution in Et_2O, 0.94 mL, 2.83 mmol) and stirred for 1 h. The reaction was quenched with NH_4Cl and extracted with EtOAc, dried over $MgSO_4$ and concentrated. The residue was purified by chromatography on silica gel (0-5% MeOH/DCM) to provide the desired product (66 mg, 16%). MS (ESI) mass calcd. $C_{19}H_{14}ClF_3N_6O$, 434.1; m/z found, 435.1 $[M+H]^+$.

Step 3: (2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(4-methylpyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



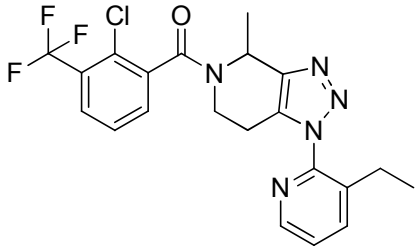
The title compound was prepared in a manner analogous to Example 73 substituting the product of Example 252, Step 2 for the 5-{[2-chloro-3-(trifluoromethyl)phenyl]carbonyl}-4-methyl-1-pyrazin-2-yl-4,5-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridine. MS (ESI) mass calcd. $C_{19}H_{16}ClF_3N_6O$, 436.1; m/z found, 437.1 $[M+H]^+$.

Example 253: (2-Chloro-3-(trifluoromethyl)phenyl)(1-(4,6-dimethylpyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



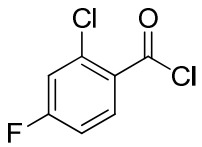
The title compound was prepared in a manner analogous to Example 252 substituting 4,6-dimethylpyrimidin-2-amine for 4-methylpyrimidin-2-amine in Step 1. MS (ESI) mass calcd. $C_{20}H_{18}ClF_3N_6O$, 450.1; m/z found, 451.2 $[M+H]^+$.

Example 254: (2-Chloro-3-(trifluoromethyl)phenyl)(1-(3-ethylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



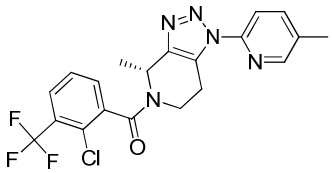
The title compound was prepared in a manner analogous to Example 252 substituting 3-ethylpyridin-2-amine for 4-methylpyrimidin-2-amine in Step 1 and triisopropylsilyl trifluoromethanesulfonate for trimethylsilyl trifluoromethanesulfonate in Step 2. MS (ESI) mass calcd. $C_{21}H_{19}ClF_3N_5O$, 449.1; m/z found, 450.0 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.50 - 8.34 (m, 1H), 7.89 - 7.68 (m, 2H), 7.63 - 7.34 (m, 3H), 6.18 - 6.04 (m, 0.5H), 5.18 - 5.04 (m, 0.4H), 5.00 - 4.71 (m, 0.4H), 3.64 – 2.65 (m, 4.7H), 1.76-1.68 (m, 2H), 1.51 (d, J = 6.8 Hz, 1H), 1.25 - 1.11 (m, 4H).

Intermediate 234: 2-chloro-4-fluorobenzoyl chloride



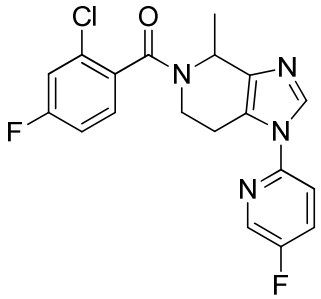
The title compound was prepared in a manner analogous to Intermediate 12 substituting 2-chloro-4-fluorobenzoic acid for 2-chloro-3-(trifluoromethyl)benzoic acid.

Example 255 (R*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(5-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



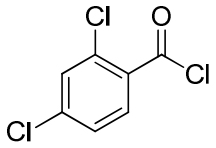
The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 301 performed using a WHELK O1 (S,S) (5µm 250x21.1mm) column and a mobile phase of 60% CO_2, 40% MeOH. The enantiomeric purity was confirmed by analytical SFC using a WHELK O1 (S,S) (250x4.6mm) and a mobile phase 60% CO_2, 40% MeOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 3.80 min retention time). After the Chiral SFC purification, purification by chromatography on SiO_2 eluting with EtOAc/hexanes was done. MS (ESI) mass calcd. MS (ESI) mass calcd $C_{20}H_{17}ClF_3N_5O$, 435.1 m/z found, 435.7 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.41 – 8.16 (m, 1H), 8.12 – 7.94 (m, 1H), 7.85 – 7.64 (m, 2H), 7.63 – 7.28 (m, 2H), 6.16 – 5.96 (m, 0.6H), 5.20 – 5.05 (m, 0.4H), 4.93 – 4.68 (m, 0.4H), 3.66 – 2.96 (m, 3.6H), 2.59 – 2.28 (m, 3H), 1.82 – 1.44 (m, 3H).

Example 256: (2-chloro-4-fluorophenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone



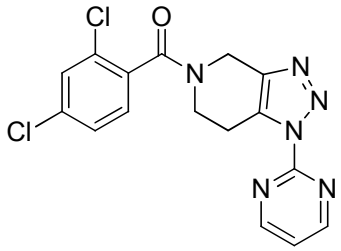
The title compound was prepared in a manner analogous to Example 11 substituting Intermediate 234 for Intermediate 12 in Step A as well as the addition of triisopropylsilyl trifluoromethanesulfonate (1 eq) to Step A. ^1H NMR (500 MHz, $CDCl_3$) δ 8.46 – 8.30 (m, 1H), 8.13 – 7.87 (m, 1H), 7.66 – 7.41 (m, 1H), 7.40 – 7.00 (m, 4H), 5.83 – 5.73 (q, J = 6.7 Hz, 1H), 5.14 – 4.46 (m, 1H), 3.66 – 3.24 (m, 1H), 3.24 – 2.64 (m, 3H), 1.72 – 1.51 (m, 3H). MS (ESI) mass calcd. $C_{19}H_{15}ClF_2N_4O$, 388.1; m/z found, 389.1 $[M+H]^+$.

Intermediate 235: 2,4-dichlorobenzoyl chloride



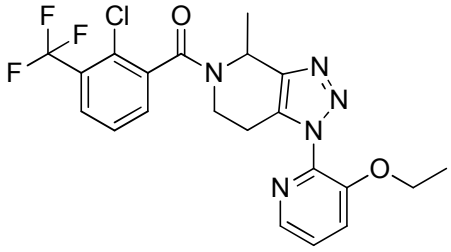
The title compound was prepared in a manner analogous to Intermediate 12 substituting 2,4-dichlorobenzoic acid for 2-chloro-3-(trifluoromethyl)benzoic acid.

Example 257: (2,4-dichlorophenyl)(1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example 63, Step 5 substituting Intermediate 50 for 1-(pyridin-2-yl)-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine and Intermediate 235 for 2-chloro-3-(trifluoromethyl)benzoyl chloride. MS (ESI) mass calcd. $C_{16}H_{12}Cl_2N_6O$, 374.0; m/z found, 375.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.97 - 8.77 (dd, J = 13.6, 4.8 Hz, 2H), 7.63 - 7.10 (m, 6H), 5.43 - 5.24 (s, 0.5H), 5.24 - 4.90 (m, 1H), 4.71 - 4.29 (m, 1H), 4.33 - 3.94 (m, 1H), 3.68 - 3.40 (m, 2H), 3.39 - 3.12 (m, 1H).

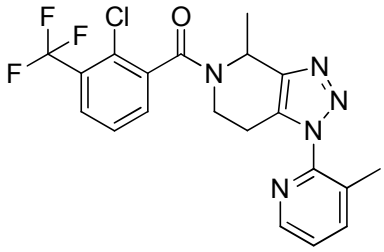
Example 258: (2-Chloro-3-(trifluoromethyl)phenyl)(1-(3-ethoxypyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example 252 substituting 3-ethoxypyridin-2-amine for 4-methylpyrimidin-2-amine in Step 1 and triisopropylsilyl trifluoromethanesulfonate for trimethylsilyl trifluoromethanesulfonate in Step 2. MS (ESI) mass calcd. $C_{21}H_{19}ClF_3N_5O_2$, 465.1; m/z found, 466.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.27 - 8.13 (m, 1H), 7.82 - 7.68 (m, 1H), 7.64 - 7.39 (m, 4H), 6.24 - 6.01 (m, 0.5H), 5.16 - 4.98 (m, 0.5H), 4.96 - 4.71 (m, 0.5H), 4.22 - 4.00 (m, 2H), 3.64 - 3.45 (m,

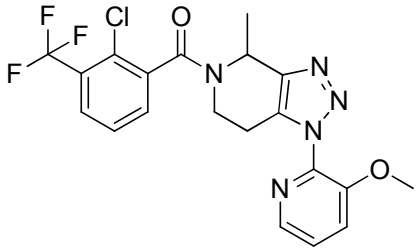
0.7H), 3.40 - 2.96 (m, 1.5H), 2.82 - 2.59 (m, 1.3H), 1.75-1.66 (m, 1.5H), 1.59-1.47 (m, 1.5H), 1.44 - 1.29 (m, 3H).

Example 259: (2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(3-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



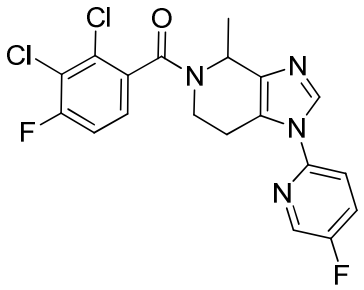
The title compound was prepared in a manner analogous to Example 252 substituting 3-methylpyridin-2-amine for 4-methylpyrimidin-2-amine in Step 1 and triisopropylsilyl trifluoromethanesulfonate for trimethylsilyl trifluoromethanesulfonate in Step 2. MS (ESI) mass calcd. $C_{20}H_{17}ClF_3N_5O$, 435.1; m/z found, 436.0 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.49 - 8.28 (m, 1H), 7.84 - 7.70 (m, 2H), 7.59 - 7.40 (m, 2H), 7.41 - 7.29 (m, 1H), 6.16 - 6.01 (m, 0.6H), 5.15 - 5.04 (m, 0.4H), 4.95 - 4.72 (m, 0.4H), 3.64 - 3.33 (m, 1.2H), 3.29 - 2.81 (m, 2.4H), 2.54 - 2.39 (m, 3H), 1.78-1.67 (m, 2H), 1.62-1.43 (m, 1H).

Example 260: (2-Chloro-3-(trifluoromethyl)phenyl)(1-(3-methoxypyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



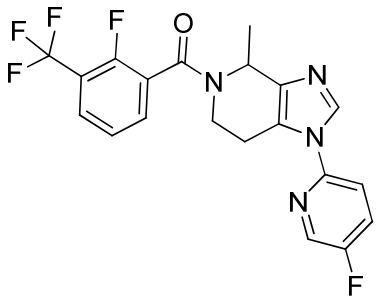
The title compound was prepared in a manner analogous to Example 252 substituting 3-methoxypyridin-2-amine for 4-methylpyrimidin-2-amine in Step 1 and triisopropylsilyl trifluoromethanesulfonate for trimethylsilyl trifluoromethanesulfonate in Step 2. MS (ESI) mass calcd. $C_{20}H_{17}ClF_3N_5O_2$, 451.1; m/z found, 436.0 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.28 - 8.12 (m, 1H), 7.83 - 7.73 (m, 1H), 7.59 - 7.33 (m, 4H), 6.22 - 5.99 (m, 0.5H), 5.14 - 5.01 (m, 0.4H), 4.96-4.74 (m, 0.4H), 3.99 - 3.81 (m, 3H), 3.61 - 3.31 (m, 1.1H), 3.29 - 2.97 (m, 1.1H), 2.84 - 2.59 (m, 1.5H), 1.76-1.66 (m, 1.5H), 1.60-1.44 (m, 1.5H).

Example 261: (2,3-dichloro-4-fluorophenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone



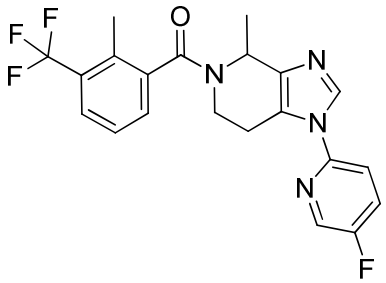
The title compound was prepared in a manner analogous to Example 252 substituting Intermediate 1 for the product of Example 252, Step 1, 2,3-dichloro-4-fluorobenzoyl chloride for Intermediate 12 and excluding trimethylsilyl trifluoromethanesulfonate in Step 2. MS (ESI) mass calcd. $C_{19}H_{14}Cl_2F_2N_4O$, 422.1; m/z found, 423.1 $[M+H]^+$. ^1H NMR (600 MHz, CDCl3) δ 8.42 – 8.29 (m, 1H), 8.00 – 7.89 (m, 1H), 7.67 – 7.55 (m, 1H), 7.37 – 7.30 (m, 1H), 7.25 – 7.05 (m, 2H), 5.87 – 5.40 (m, 1H), 5.08 – 3.80 (m, 2H), 3.71 – 2.69 (m, 3H), 1.83 – 1.29 (m, 3H)

Example 262: (2-fluoro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example 252 substituting Intermediate 1 for the product of Example 252, Step 1, 2-fluoro-3-(trifluoromethyl)benzoyl chloride for Intermediate 12 and excluding trimethylsilyl trifluoromethanesulfonate in Step 2. MS (ESI) mass calcd. $C_{20}H_{15}F_5N_4O$, 422.1; m/z found, 423.2 $[M+H]^+$. ^1H NMR (600 MHz, $CDCl_3$) δ 8.43 – 8.32 (m, 1H), 7.98 – 7.83 (m, 1H), 7.74 – 7.54 (m, 3H), 7.40 – 7.30 (m, 2H), 5.87 – 5.48 (m, 1H), 5.09 – 4.55 (m, 1H), 4.41 – 3.57 (m, 1H), 3.29 – 2.69 (m, 2H), 2.16 – 1.35 (m, 3H).

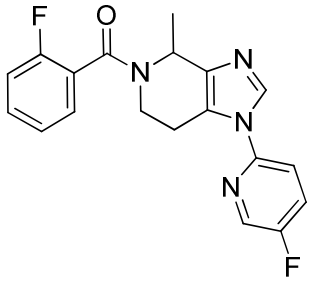
Example 263: (1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-methyl-3-(trifluoromethyl)phenyl)methanone



The title compound was prepared in a manner analogous to Example 252 substituting Intermediate 1 for the product of Example 252, Step 1, 2-methyl-3-(trifluoromethyl)benzoyl chloride for Intermediate 12 and excluding trimethylsilyl trifluoromethanesulfonate in Step 2. MS (ESI) mass calcd. $C_{21}H_{18}F_4N_4O$, 418.1; m/z found, 419.2 $[M+H]^+$. ^1H NMR (600 MHz, $CDCl_3$) δ 8.48 – 8.26 (m, 1H), 8.07 – 7.77 (m, 1H), 7.77 – 7.50 (m, 2H), 7.50 – 7.32 (m, 3H), 5.17 – 4.03 (s, 1H), 3.74 – 2.66 (m, 3H), 2.33 – 1.89 (m, 2H), 1.63 – 1.09 (m, 5H).

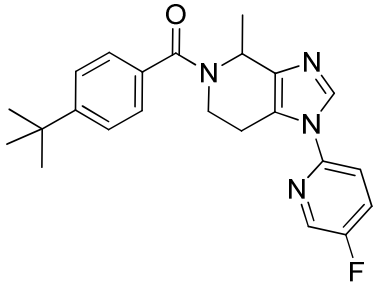
Example 264: (2-fluorophenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone

Step 1:



MS (ESI) mass calcd. $C_{19}H_{16}F_2N_4O$, 354.1; m/z found, 355.2 $[M+H]^+$.

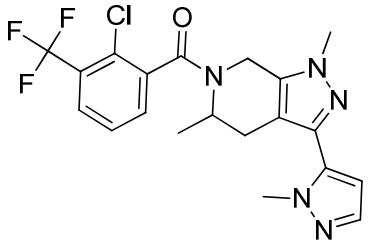
Example 265: (4-(tert-butyl)phenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example 252 substituting Intermediate 1 for the product of Example 252, Step 1, 4-(tert-butyl)benzoyl chloride for

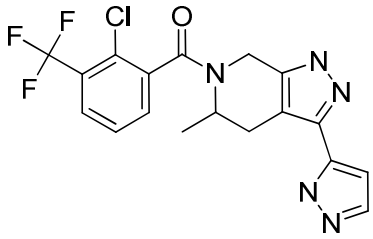
Intermediate 12 and excluding trimethylsilyl trifluoromethanesulfonate in Step 2. MS (ESI) mass calcd. $C_{23}H_{25}FN_4O$, 392.2; m/z found,393.3 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.53 – 8.17 (s, 1H), 8.07 – 7.78 (s, 1H), 7.70 – 7.27 (m, 6H), 5.05 – 4.58 (s, 1H), 3.43 – 2.73 (m, 3H), 1.67 – 1.46 (s, 4H), 1.43 – 1.17 (m, 9H).

Example 266: (2-chloro-3-(trifluoromethyl)phenyl)(1,5-dimethyl-3-(1-methyl-1H-pyrazol-5-yl)-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone



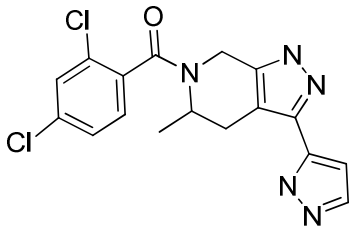
^1H NMR (400 MHz, $CDCl_3$) δ 7.81 - 7.73 (m, 1H), 7.54 - 7.39 (m, 1H), 7.35 (d, J = 2.3 Hz, 1H), 6.53 (dd, J = 2.3, 1.7 Hz, 1H), 5.61 (ddd, J = 21.5, 16.8, 1.2 Hz, 1H), 4.21 - 4.10 (m, 1H), 3.97 - 3.85 (m, 5H), 3.73 (s, 6H), 2.89 - 2.71 (m, 1H), 1.29 (d, J = 6.8 Hz, 2H), 1.15 (d, J = 6.8 Hz, 1H). MS (ESI) mass calcd. $C_{20}H_{19}ClF_3N_5O$, 437.1; m/z found, 438.4 $[M+H]^+$.

Example 267: (2-chloro-3-(trifluoromethyl)phenyl)(5-methyl-3-(1H-pyrazol-5-yl)-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone



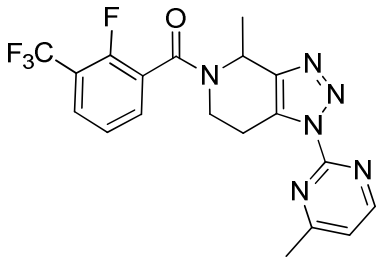
^1H NMR (400 MHz, $CDCl_3$) δ 7.85 - 7.72 (m, 1H), 7.71 - 7.62 (m, 1H), 7.55 - 7.42 (m, 3H), 6.58 - 6.34 (m, 1H), 6.09 - 5.83 (m, 1H), 5.59 (d, J = 6.6 Hz, 1H), 4.30 (d, J = 8.9 Hz, 0.29H), 4.04 (s, 2H), 3.21 (s, 2H), 2.89 (s, 0.36H), 2.82 - 2.55 (m, 3H), 1.35 (dd, J = 6.8, 4.8 Hz, 3H). MS (ESI) mass calcd. $C_{18}H_{15}ClF_3N_5O$, 409.1; m/z found, 410.3 $[M+H]^+$.

Example 268: (2,4-dichlorophenyl)(5-methyl-3-(1H-pyrazol-5-yl)-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone



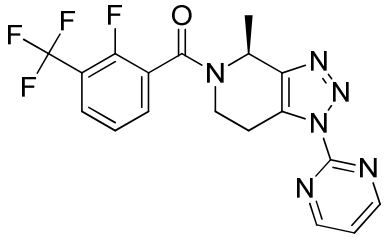
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (dd, J = 7.8, 2.4 Hz, 1H), 7.50 (dd, J = 9.5, 2.0 Hz, 1H), 7.46 - 7.38 (m, 1.6H), 7.38 - 7.28 (m, 1H), 7.23 (d, J = 8.2 Hz, 1H), 6.51 (d, J = 2.5 Hz, 0.5H), 6.44 (dd, J = 8.9, 2.4 Hz, 0.82H), 6.05 (dd, J = 39.7, 17.0 Hz, 1H), 5.56 (s, 0.5H), 4.41 - 4.21 (m, 1.5H), 4.13 - 3.99 (m, 1H), 3.22 (dd, J = 15.1, 5.7 Hz, 1H), 2.79 - 2.45 (m, 0.5H), 1.38 - 1.25 (m, 3H). MS (ESI) mass calcd. $C_{17}H_{15}Cl_2N_5O$, 375.1; m/z found, 376.3 $[M+H]^+$.

Example 269: (2-fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(4-methylpyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



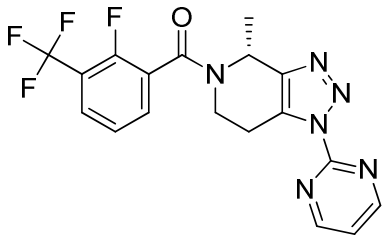
MS (ESI) mass calcd. $C_{19}H_{16}F_4N_6O$, 420.1; m/z found, 421.1 $[M+H]^+$.

Example 270: (S*)-(2-fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



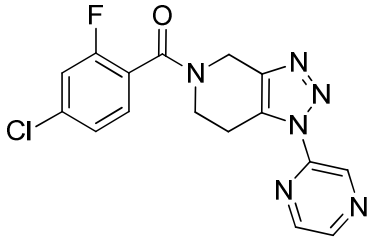
MS (ESI) mass calcd. $C_{18}H_{14}F_4N_6O$, 406.1; m/z found, 407.1 $[M+H]^+$.

Example 271: (R*)-(2-fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



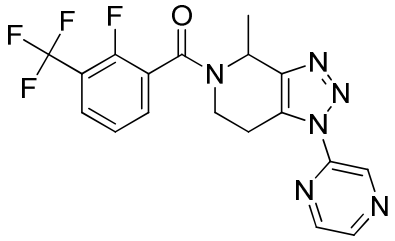
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (dd, *J* = 11.2, 4.8 Hz, 2H), 7.82 – 7.46 (m, 2H), 7.47 – 7.29 (m, 2H), 5.09 (dd, *J* = 13.0, 5.2 Hz, 0.59H), 4.92 (d, *J* = 6.7 Hz, 0.60H), 3.73 (t, *J* = 7.4 Hz, 0.73H), 3.60 – 3.04 (m, 3.46H), 1.70 (d, *J* = 6.7 Hz, 1.82H), 1.26 (s, 1.55H).
MS (ESI) mass calcd. $C_{18}H_{14}F_4N_6O$, 406.1; m/z found, 407.1 $[M+H]^+$.

Example 272: (4-chloro-2-fluorophenyl)(1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



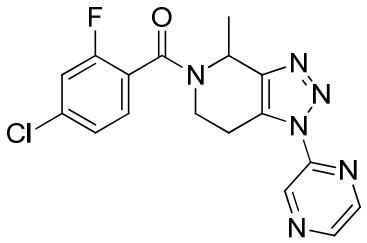
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.52 (d, J = 16.3 Hz, 1H), 8.65 (dd, J = 6.0, 2.5 Hz, 1H), 8.56 - 8.37 (m, 1H), 7.39 (dt, J = 15.8, 7.6 Hz, 1H), 7.20 (dd, J = 9.3, 1.9 Hz, 2H), 5.06 (s, 1H), 4.66 (s, 1H), 3.66 (s, 1H), 3.48 - 3.13 (m, 3H). MS (ESI) mass calcd. $C_{16}H_{12}ClFN_6O$, 358.1; m/z found, 359.1$[M+H]^+$.

Example 273: (2-fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



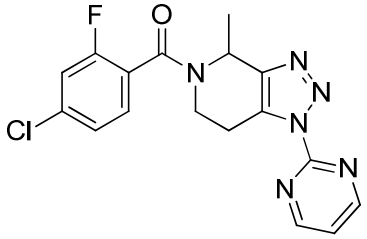
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.63 - 9.39 (m, 1H), 8.73 - 8.60 (m, 1H), 8.55 - 8.39 (m, 1H), 7.81 - 7.31 (m, 3H), 6.05 (s, 1H), 5.17 - 4.84 (m, 1H), 3.74 (d, J = 11.4 Hz, 1H), 3.60 - 3.03 (m, 3H), 1.70 (d, J = 6.7 Hz, 2H). MS (ESI) mass calcd. $C_{18}H_{14}F_4N_6O$, 406.1; m/z found, 407.1 $[M+H]^+$.

Example 274: (4-chloro-2-fluorophenyl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



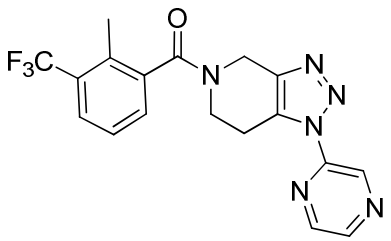
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.59 - 9.45 (m, 1H), 8.73 - 8.57 (m, 1H), 8.53 - 8.39 (m, 1H), 7.19 (dd, J = 9.2, 1.9 Hz, 1H), 6.02 (d, J = 7.1 Hz, 1H), 4.95 (d, J = 7.0 Hz, 1H), 3.78 (d, J = 11.4 Hz, 1H), 3.54 - 3.28 (m, 2H), 3.23 (q, J = 7.3 Hz, 2H), 1.68 (d, J = 6.7 Hz, 3H). MS (ESI) mass calcd. $C_{17}H_{14}ClFN_6O$, 372.1; m/z found, 373.1$[M+H]^+$.

Example 275: (4-chloro-2-fluorophenyl)(4-methyl-1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (dd, J = 11.3, 4.8 Hz, 2H), 7.39 (q, J = 4.7 Hz, 1.66H), 7.25-7.10(m, 1.6H), 6.02 (d, J = 7.5 Hz, 1H), 5.15 - 4.90 (m, 1H), 3.78 (d, J = 12.6 Hz, 1H), 3.58 - 3.05 (m, 3H), 1.68 (d, J = 6.8 Hz, 1.6H). MS (ESI) mass calcd. $C_{17}H_{14}ClFN_6O$, 372.1; m/z found, 373.1 $[M+H]^+$.

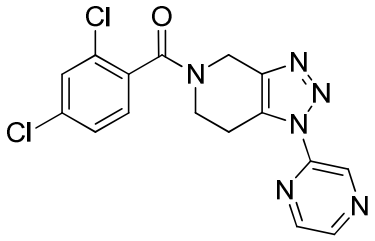
Example 276: (2-methyl-3-(trifluoromethyl)phenyl)(1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



^{1}H NMR (400 MHz, $CDCl_3$) δ 9.64 - 9.44 (m, 1H), 8.66 (ddd, J = 11.5, 2.5, 0.5 Hz, 1H), 8.46 (ddd, J = 33.8, 2.5, 1.4 Hz, 1H), 7.79 - 7.62 (m, 1H), 7.45 - 7.31 (m, 2H), 5.41 - 5.18 (m, 0.70H), 5.05 - 4.87 (m, 0.63H), 4.50 (d, J = 1.4 Hz, 1.2H), 4.38 - 3.96 (m, 1H), 3.71 -

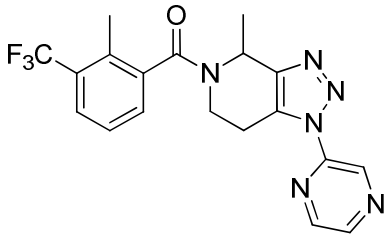
3.09 (m, 3H), 2.41 (dd, J = 39.2, 1.7 Hz, 3H). MS (ESI) mass calcd. $C_{18}H_{15}F_3N_6O$, 388.1; m/z found, 389.2 $[M+H]^+$.

Example 277: (2,4-dichlorophenyl)(1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



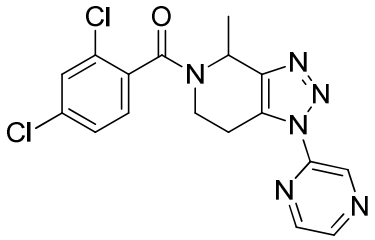
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.69 - 9.38 (m, 1H), 8.65 (dd, J = 9.1, 2.5 Hz, 1H), 8.46 (ddd, J = 29.7, 2.6, 1.5 Hz, 1H), 7.57 - 7.43 (m, 1H), 7.34 (dd, J = 8.4, 1.9 Hz, 2H), 5.24 - 4.91 (m, 1H), 4.71 - 4.39 (m, 1H), 4.37 - 3.96 (m, 1.3H), 3.59 (q, J = 6.1 Hz, 1H), 3.51 - 3.08 (m, 1.86H). MS (ESI) mass calcd. $C_{16}H_{12}Cl_2N_6O$, 374.1; m/z found, 375.1 $[M+H]^+$.

Example 278: (4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2-methyl-3-(trifluoromethyl)phenyl)methanone



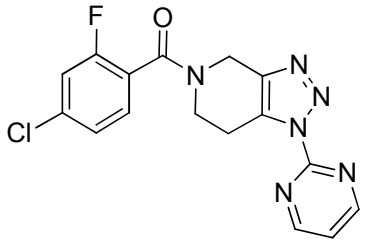
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.58 - 9.46 (m, 1H), 8.74 - 8.58 (m, 1H), 8.54 - 8.36 (m, 1H), 7.77 - 7.65 (m, 1H), 7.51 - 7.32 (m, 2H), 6.19 - 6.03 (m, 0.71H), 5.23 - 4.71 (m, 1.49H), 3.75 - 2.94 (m, 3H), 2.58 - 2.38 (m, 2H), 2.21 (d, J = 1.8 Hz, 1H), 1.79 - 1.63 (m, 1.66H), 1.53 - 1.43 (m, 1.32H). MS (ESI) mass calcd. $C_{19}H_{17}F_3N_6O$, 402.1; m/z found, 403.2 $[M+H]^+$.

Example 279: (2,4-dichlorophenyl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



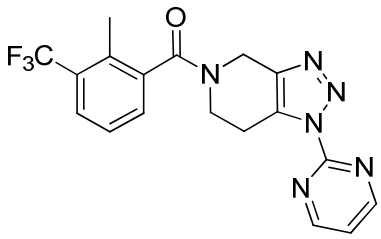
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.60 - 9.45 (m, 1H), 8.72 - 8.59 (m, 0.81H), 8.50 (s, 0.39H), 8.41 (dd, J = 2.5, 1.5 Hz, 0.44H), 7.60 - 7.28 (m, 3H), 6.06 (d, J = 6.8 Hz, 0.56H), 5.14-4.80 (m, 1.23H), 3.74 - 2.83 (m, 3.62H), 1.77 - 1.64 (m, 1.36H). MS (ESI) mass calcd. $C_{17}H_{14}Cl_2N_6O$, 388.1; m/z found, 389.1 $[M+H]^+$.

Example 280: (4-chloro-2-fluorophenyl)(1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



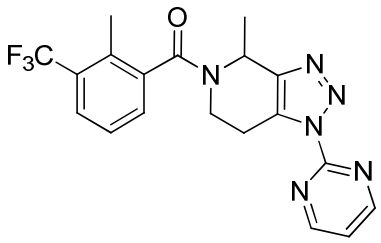
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.06 - 8.74 (m, 2H), 7.57 - 7.30 (m, 2H), 7.25 - 7.11 (m, 2.5H), 5.47 - 4.95 (m, .088H), 4.66 (s, 1.31H), 3.66 (s, 1H), 3.51 - 3.19 (m, 2H). MS (ESI) mass calcd. $C_{16}H_{12}ClFN_6O$, 358.1; m/z found, 359.1 $[M+H]^+$.

Example 281: (2-methyl-3-(trifluoromethyl)phenyl)(1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone Duncan fix



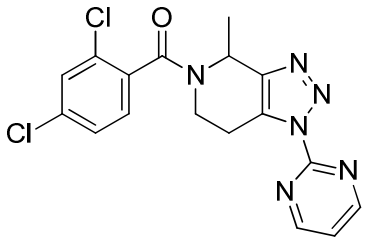
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 – 8.78 (m, 2H), 7.71 (td, *J* = 6.4, 2.6 Hz, 1H), 7.48 – 7.32 (m, 3H), 5.29 (d, *J* = 16.6 Hz, 0.57H), 4.97 (d, *J* = 16.4 Hz, 0.58H), 4.50 (d, *J* = 1.1 Hz, 1H), 4.37 – 4.21 (m, 0.48H), 4.09 (d, *J* = 6.5 Hz, 0.63H), 3.71 – 3.48 (m, 1H), 3.45 (d, *J* = 5.1 Hz, 1H), 3.22 (s, 0.88H), 2.41 (dd, *J* = 41.9, 1.7 Hz, 3H).
MS (ESI) mass calcd. $C_{18}H_{15}F_3N_6O$, 388.1; m/z found, 389.1 $[M+H]^+$.

Example 282: (4-methyl-1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2-methyl-3-(trifluoromethyl)phenyl)methanone



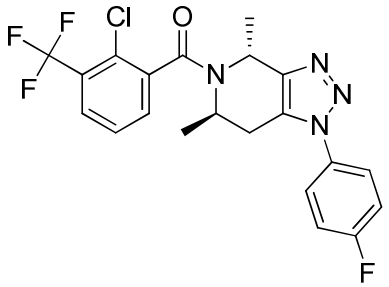
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (d, J = 4.8 Hz, 1H), 8.85 (d, J = 4.8 Hz, 1H), 7.70 (d, J = 6.6 Hz, 1H), 7.50 - 7.33 (m, 3H), 6.19 - 6.04 (m, 0.5H), 5.24 - 4.65 (m, 1.5H), 3.77 - 2.96 (m, 2H), 2.57 - 2.36 (m, 3H), 2.20 (d, J = 1.8 Hz, 1H), 1.77 - 1.65 (m 1H), 1.53 - 1.43 (m, 2H). MS (ESI) mass calcd. $C_{19}H_{17}F_3N_6O$, 402.1; m/z found, 403.2$[M+H]^+$.

Example 283: (2,4-dichlorophenyl)(4-methyl-1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



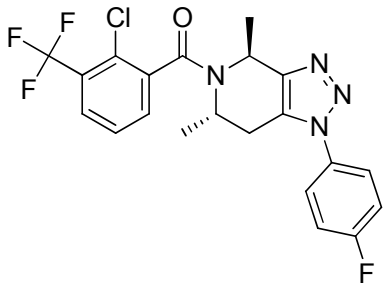
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 - 8.79 (m, 2H), 7.48 (d, J = 2.0 Hz, 1H), 7.45 - 7.29 (m, 1H), 6.06 (q, J = 6.8 Hz, 0.5H), 5.11 (dd, J = 13.2, 5.4 Hz, 0.5H), 4.81 (d, J = 6.9 Hz, 0.5H), 3.75 - 2.87 (m, 4H), 1.77 - 1.64 (m, 1.5H), 1.49 (d, J = 6.8 Hz, 0.5H). MS (ESI) mass calcd. $C_{17}H_{14}Cl_2N_6O$, 388.1; m/z found, 389.1 $[M+H]^+$.

Example 284: (2-chloro-3-(trifluoromethyl)phenyl)((4R,6R)-1-(4-fluorophenyl)-4,6-dimethyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



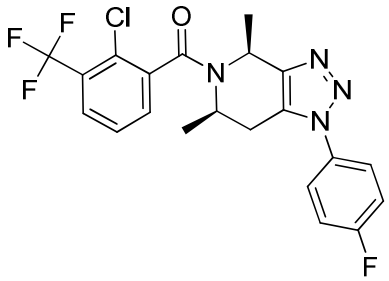
MS (ESI) mass calcd. $C_{21}H_{17}ClF_4N_4O$, 452.1; m/z found, 452.8 $[M+H]^+$.

Example 285: (2-chloro-3-(trifluoromethyl)phenyl)((4S,6S)-1-(4-fluorophenyl)-4,6-dimethyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



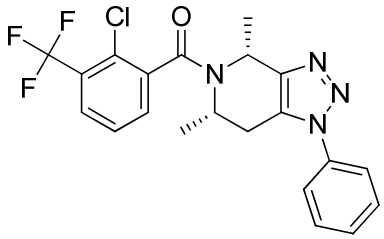
MS (ESI) mass calcd. $C_{21}H_{17}ClF_4N_4O$, 452.1; m/z found, 452.8 $[M+H]^+$.

Example 286: (2-chloro-3-(trifluoromethyl)phenyl)((4S,6R)-1-(4-fluorophenyl)-4,6-dimethyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



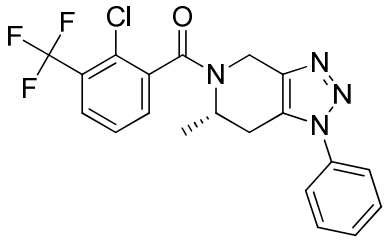
MS (ESI) mass calcd. $C_{21}H_{17}ClF_4N_4O$, 452.1; m/z found, 452.8 $[M+H]^+$.

Example 287: (2-chloro-3-(trifluoromethyl)phenyl)((4R,6S)-1-(4-fluorophenyl)-4,6-dimethyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



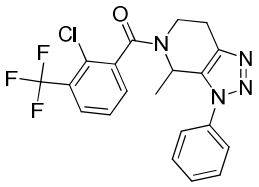
MS (ESI) mass calcd. $C_{21}H_{17}ClF_4N_4O$, 452.1; m/z found, 452.8 $[M+H]^+$.

Example 288: (S)-(2-chloro-3-(trifluoromethyl)phenyl)(6-methyl-1-phenyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



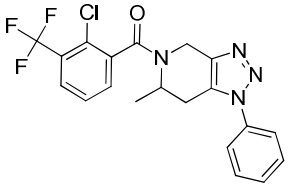
MS (ESI) mass calcd. $C_{20}H_{16}ClF_3N_4O$, 420.1; m/z found, 421.0 $[M+H]^+$.

Example 289: (2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-3-phenyl-6,7-dihydro-3H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



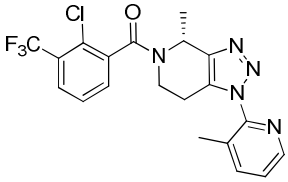
MS (ESI) mass calcd. $C_{20}H_{16}ClF_3N_4O$, 420.1; m/z found, 421.0 $[M+H]^+$.

Example 290: (2-chloro-3-(trifluoromethyl)phenyl)(6-methyl-1-phenyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



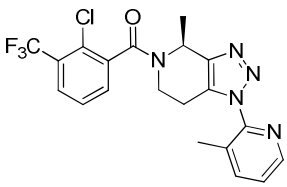
MS (ESI) mass calcd. $C_{20}H_{16}ClF_3N_4O$, 420.1; m/z found, 421.0 $[M+H]^+$.

Example 291: (R*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(3-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



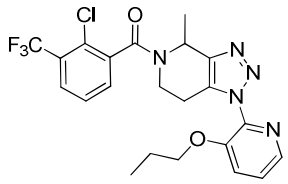
MS (ESI) mass calcd. $C_{20}H_{17}ClF_3N_5O$, 435.1; m/z found, 436.0 $[M+H]^+$.

Example 292: (S*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(3-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



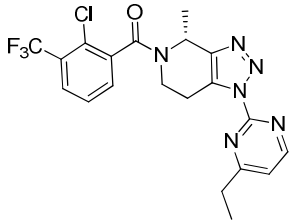
MS (ESI) mass calcd. $C_{20}H_{17}ClF_3N_5O$, 435.1; m/z found, 436.0 $[M+H]^+$.

Example 293: (2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(3-propoxypyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



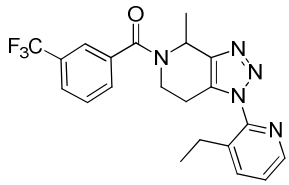
MS (ESI) mass calcd. $C_{22}H_{21}ClF_3N_5O_2$, 479.1; m/z found, 480.0 $[M+H]^+$.

Example 294: (R*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(4-ethylpyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



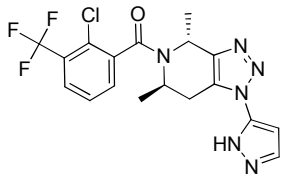
MS (ESI) mass calcd. $C_{20}H_{18}ClF_3N_6O$, 450.1; m/z found, 451.0 $[M+H]^+$.

Example 295: (1-(3-ethylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(3-(trifluoromethyl)phenyl)methanone



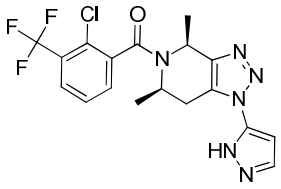
MS (ESI) mass calcd. $C_{21}H_{20}F_3N_5O$, 415.1; m/z found, 416.1 $[M+H]^+$.

Example 296: (2-chloro-3-(trifluoromethyl)phenyl)((4R,6R)-4,6-dimethyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



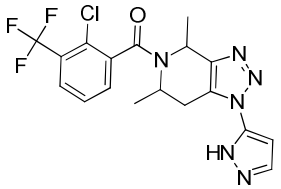
MS (ESI) mass calcd. $C_{18}H_{16}ClF_3N_6O$, 424.1; m/z found, $[M+H]^+$.

Example 297: (2-chloro-3-(trifluoromethyl)phenyl)((4S,6R)-4,6-dimethyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



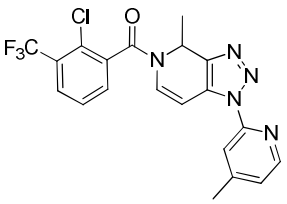
MS (ESI) mass calcd. $C_{18}H_{16}ClF_3N_6O$, 424.1; m/z found, 425.1 $[M+H]^+$.

Example 298: (2-chloro-3-(trifluoromethyl)phenyl)(4,6-dimethyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



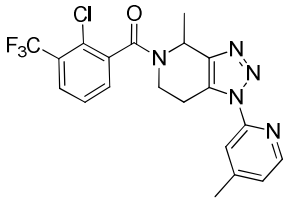
MS (ESI) mass calcd. $C_{18}H_{16}ClF_3N_6O$, 424.1; m/z found, 425.2 $[M+H]^+$.

Intermediate L: (2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(4-methylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



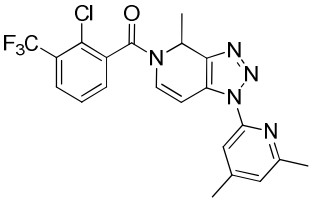
The title compound was prepared in a manner analogous to Intermediate C substituting 1-(4-methylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine for 1-(3,5-dimethylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine and cooling the reaction mixture down to -40°C instead of -78°C. MS (ESI) mass calcd. $C_{20}H_{15}ClF_3N_5O$, 433.09; m/z found 434.10 $[M+H]^+$.

Example 299: (2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



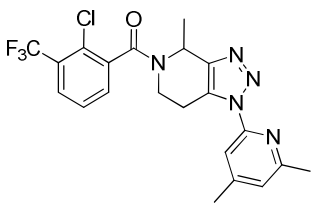
The title compound was prepared in a manner analogous to Example 159 substituting (2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(4-methylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone for (2-chloro-3-(trifluoromethyl)phenyl)(1-(3,5-dimethylpyridin-2-yl)-4-methyl-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone and THF for EtOAc. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 - 8.24 (m, 1H), 8.03 - 7.91 (m, 1H), 7.82 - 7.72 (m, 1H), 7.61 - 7.29 (m, 2H), 7.21 - 7.11 (m, 1H), 6.18 - 5.90 (m, 0.6H), 5.18 - 5.02 (m, 0.4H), 4.96 - 4.66 (m, 0.4H), 3.72 - 2.92 (m, 3.6H), 2.63 - 2.37 (s, 3H), 1.87 - 1.40 (m, 3H).MS (ESI) mass calcd $C_{20}H_{17}ClF_3N_5O$, 435.1; m/z found, 436.1 $[M+H]^+$.

Intermediate M: (2-chloro-3-(trifluoromethyl)phenyl)(1-(4,6-dimethylpyridin-2-yl)-4-methyl-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Intermediate C substituting 1-(4,6-dimethylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine for 1-(3,5-dimethylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine for and cooling the reaction mixture down to -40°C instead of -78°C. MS (ESI) mass calcd. $C_{21}H_{17}ClF_3N_5O$, 447.11; m/z found 448.10 $[M+H]^+$.

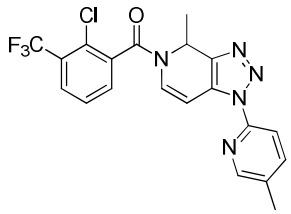
Example 300: (2-chloro-3-(trifluoromethyl)phenyl)(1-(4,6-dimethylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example 159 substituting (2-

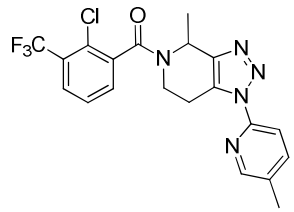
chloro-3-(trifluoromethyl)phenyl)(1-(4,6-dimethylpyridin-2-yl)-4-methyl-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone for (2-chloro-3-(trifluoromethyl)phenyl)(1-(3,5-dimethylpyridin-2-yl)-4-methyl-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone and THF was replaced by EtOAc. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 - 7.69 (m, 2H), 7.60 - 7.29 (m, 2H), 7.09 - 6.93 (m, 1H), 6.19 - 5.92 (m, 0.6H), 5.25 - 5.01 (m, 0.4H), 4.94 - 4.66 (m, 0.4H), 3.68 - 2.93 (m, 3.6H), 2.62 - 2.33 (m, 6H), 1.81 - 1.42 (m, 3H). MS (ESI) mass calcd $C_{21}H_{19}ClF_3N_5O$, 449.1; m/z found, 450.1 $[M+H]^+$.

Intermediate N: (2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(5-methylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Intermediate C substituting 1-(5-methylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine for 1-(3,5-dimethylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine and cooling the reaction mixture down to -40°C instead of -78°C. MS (ESI) mass calcd. $C_{20}H_{15}ClF_3N_5O$, 433.09; m/z found 434.10 $[M+H]^+$.

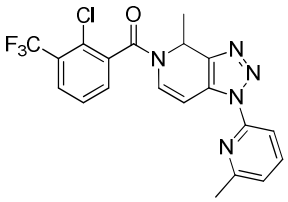
Example 301: (2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(5-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example 159 substituting (2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(5-methylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone for (2-chloro-3-(trifluoromethyl)phenyl)(1-(3,5-dimethylpyridin-2-yl)-4-methyl-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone and THF was replaced by EtOAc. Platinum(IV) oxide was added in two loads of 0.2 eq. in 16 hour intervals. The title compound was purified by chromatography on SiO_2 eluting with EtOAc/hexanes followed by chromatography on a

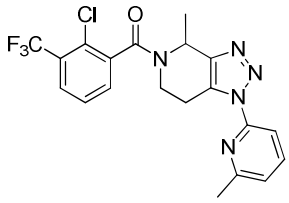
Prep Agilent system with a XBridge C18 OBD 50x100 mm column eluting with 5 to 99% (0.05% NH_4OH in H_2O)/ACN over 17 min to afford the title compound. ^1H NMR (400 MHz, $CDCl_3$) δ 8.36 - 8.19 (m, 1H), 8.10 - 7.95 (m, 1H), 7.85 - 7.66 (m, 2H), 7.61 - 7.29 (m, 2H), 6.14 - 5.95 (m, 0.6H), 5.19 - 5.05 (m, 0.4H), 4.93 - 4.69 (m, 0.4H), 3.67 - 2.89 (m, 3.6H), 2.54 - 2.26 (d, J = 10.0 Hz, 3H), 1.82 - 1.41 (m, 3H). MS (ESI) mass calcd $C_{20}H_{17}ClF_3N_5O$, 435.1; m/z found, 436.1 $[M+H]^+$.

Intermediate O: (2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-methylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone.



The title compound was prepared in a manner analogous to Intermediate C substituting 1-(6-methylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine for 1-(3,5-dimethylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine and cooling the reaction mixture down to -40°C instead of -78°C. MS (ESI) mass calcd. $C_{20}H_{15}ClF_3N_5O$, 433.09; m/z found 434.10 $[M+H]^+$.

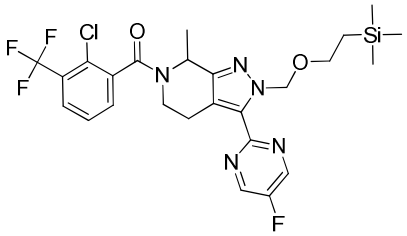
Example 302: (2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example 159 substituting (2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-methylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone for (2-chloro-3-(trifluoromethyl)phenyl)(1-(3,5-dimethylpyridin-2-yl)-4-methyl-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone and THF was replaced by EtOAc. The title compound was purified by chromatography on SiO_2 eluting with EtOAc/hexanes. ^1H NMR (400 MHz, $CDCl_3$) δ 8.00 - 7.88 (m, 1H), 7.85 - 7.73 (m, 2H), 7.61 - 7.29 (m, 2H), 7.24 - 7.12 (m, 1H), 6.16 - 5.95 (m, 0.6H), 5.21 - 5.03 (m, 0.4H), 4.95 - 4.67 (m, 0.4H), 3.71 - 2.94 (m, 3.6H),

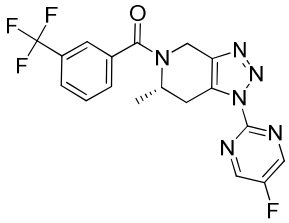
2.70 - 2.39 (m, 3H), 1.84 - 1.41 (m, 3H). MS (ESI) mass calcd $C_{20}H_{17}ClF_3N_5O$, 435.1; m/z found, 436.1 $[M+H]^+$.

Example 303: (2-chloro-3-(trifluoromethyl)phenyl)(3-(5-fluoropyrimidin-2-yl)-7-methyl-2-((2-(trimethylsilyl)ethoxy)methyl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone



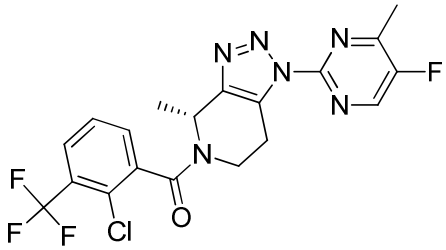
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 - 8.60 (m, 2H), 7.75 (td, J = 7.2, 6.8, 1.7 Hz, 1H), 7.60 - 7.28 (m, 2H), 6.23 - 5.86 (m, 2H), 5.08 - 4.56 (m, 1H), 3.67 - 3.26 (m, 3H), 3.26 - 2.61 (m, 2H), 1.70 - 1.41 (m, 4H), 0.91 - 0.73 (m, 2H), -0.04 - -0.19 (m, 9H). MS (ESI) mass calcd $C_{24}H_{32}FN_5OSi$, 569.2; m/z found, 570.1 $[M+H]^+$.

Example 304: (S)-(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(3-(trifluoromethyl)phenyl)methanone



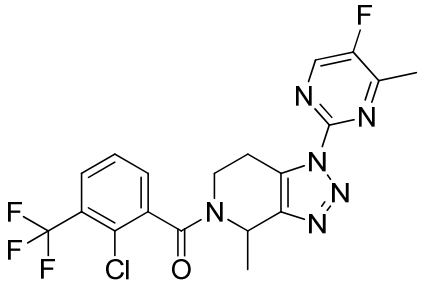
MS (ESI) mass calcd $C_{18}H_{14}F_4N_6O$, 406.1; m/z found, 407.2 $[M+H]^+$.

Example 305: (R*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



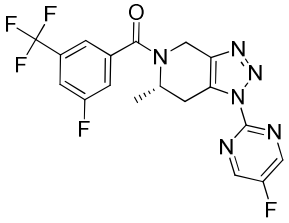
MS (ESI) mass calcd $C_{19}H_{15}ClF_4N_6O$, 454.1; m/z found, 454.8 $[M+H]^+$.

Example 306: (S*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



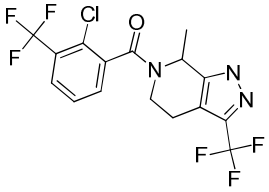
MS (ESI) mass calcd $C_{19}H_{15}ClF_4N_6O$, 454.1; m/z found, 454.8 $[M+H]^+$.

Example 307: (S)-(3-fluoro-5-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



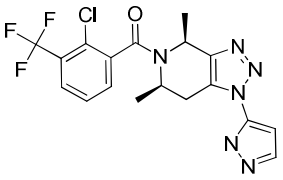
MS (ESI) mass calcd $C_{18}H_{13}F_5N_6O$, 424.1; m/z found, 425.1 $[M+H]^+$.

Example 308: (2-chloro-3-(trifluoromethyl)phenyl)(7-methyl-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone



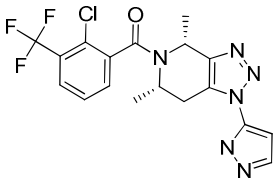
MS (ESI) mass calcd $C_{16}H_{12}ClF_6N_3O$, 411.1; m/z found, 412.0 $[M+H]^+$.

Example 309: (2-chloro-3-(trifluoromethyl)phenyl)((4S,6R)-4,6-dimethyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



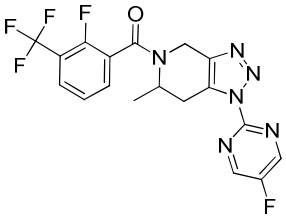
MS (ESI) mass calcd $C_{18}H_{16}ClF_3N_6O$, 424.1; m/z found, 424.7 $[M+H]^+$.

Example 310: (2-chloro-3-(trifluoromethyl)phenyl)((4R,6S)-4,6-dimethyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



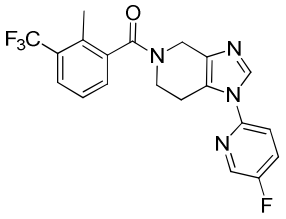
MS (ESI) mass calcd $C_{18}H_{16}ClF_3N_6O$, 424.1; m/z found, 424.7 $[M+H]^+$.

Example 311: (2-fluoro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



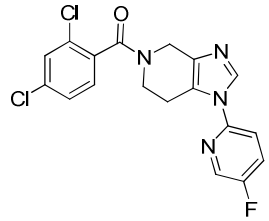
MS (ESI) mass calcd $C_{18}H_{13}F_5N_6O$, 424.1; m/z found, 425.1 $[M+H]^+$.

Example 312: (1-(5-fluoropyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)(2-methyl-3-(trifluoromethyl)phenyl)methanone



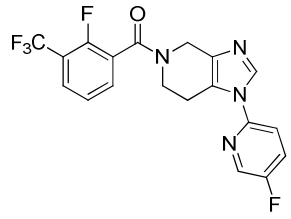
^{1}H NMR (400 MHz, DMSO- d_6) δ 8.57 (d, J = 3.0 Hz, 0.35H), 8.53 (d, J = 3.0 Hz, 0.65H), 8.26 (s, 0.65H), 8.19 (s, 0.35H), 8.00 (tdd, J = 8.7, 6.4, 3.1 Hz, 1H), 7.82 - 7.73 (m, 2H), 7.60 (d, J = 7.5 Hz, 0.65H), 7.51 (p, J = 4.5 Hz, 1.35H), 4.88 (d, J = 15.9 Hz, 0.65H), 4.56 (d, J = 16.0 Hz, 0.65H), 4.25 - 4.06 (m, 1H), 3.89 (dd, J = 12.7, 6.3 Hz, 0.3H), 3.47 - 3.39 (m, 1.4H), 3.03 (t, J = 5.8 Hz, 0.7H), 2.88 (d, J = 6.9 Hz, 0.65H), 2.79 (d, J = 16.1 Hz, 0.65H), 2.35 (d, J = 1.9 Hz, 2H), 2.27 (q, J = 1.7 Hz, 1H). MS (ESI) mass calcd $C_{20}H_{16}F_4N_4O$, 404.1; m/z found, 405.1 $[M+H]^+$.

Example 313: (2,4-dichlorophenyl)(1-(5-fluoropyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone



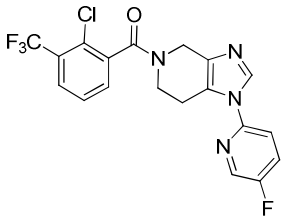
^{1}H NMR (400 MHz, DMSO- d_6) δ 8.57 (d, J = 2.9 Hz, 0.35H), 8.53 (d, J = 3.1 Hz, 0.65H), 8.26 (d, J = 4.9 Hz, 0.65H), 8.19 (d, J = 3.0 Hz, 0.35H), 8.04 - 7.96 (m, 1H), 7.82 - 7.73 (m, 2H), 7.58 - 7.42 (m, 2H), 4.78 (d, J = 16.0 Hz, 0.5H), 4.58 (d, J = 16.0 Hz, 0.5H), 4.30 (s, 0.2H), 4.18 (d, J = 1.9 Hz, 0.5H), 4.07 - 3.87 (m, 0.6H), 3.59 - 3.40 (m, 1.4H), 3.01 (s, 0.8H), 2.88 (t, J = 5.8 Hz, 1.5H). MS (ESI) mass calcd $C_{18}H_{13}Cl_2FN_4O$, 390.1; m/z found, 391.0 $[M+H]^+$.

Example 314: (2-fluoro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone



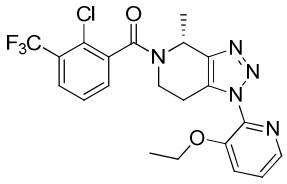
^{1}H NMR (400 MHz, DMSO- d_6) δ 8.57 (d, J = 3.0 Hz, 0.35H), 8.54 (d, J = 3.1 Hz, 0.65H), 8.27 (s, 0.65H), 8.20 (s, 0.35H), 8.00 (tt, J = 8.3, 3.1 Hz, 1H), 7.95 - 7.89 (m, 1.3H), 7.86 (t, J = 7.0 Hz, 0.7H), 7.80 (d, J = 4.0 Hz, 0.65H), 7.77 (d, J = 3.7 Hz, 0.35H), 7.54 (td, J = 7.8, 4.7 Hz, 1H), 4.70 (s, 1H), 4.30 (s, 0.65H), 4.00 (t, J = 5.8 Hz, 0.65H), 3.54 (t, J = 5.7 Hz, 1.3H), 3.02 (s, 0.90H), 2.91 (s, 1.10H). MS (ESI) mass calcd $C_{19}H_{13}F_5N_4O$, 408.1; m/z found, 409.1 $[M+H]^+$.

Example 315: (2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone



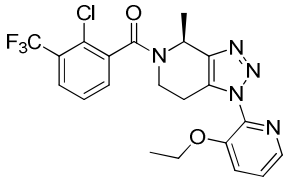
^{1}H NMR (400 MHz, DMSO- d_6) δ 8.57 (d, J = 3.1 Hz, 0.35H), 8.53 (d, J = 3.0 Hz,0.652H), 8.27 (s, 0.65H), 8.19 (s, 0.35H), 8.05 - 7.93 (m, 2H), 7.84 - 7.72 (m, 2H), 7.67 (td, J = 7.7, 3.8 Hz, 1H), 4.83 (d, J = 16.0 Hz, 0.65H), 4.60 (d, J = 16.1 Hz, 0.35H), 4.18 (d, J = 3.0 Hz, 0.7H), 4.08 - 3.91 (m, 0.8H), 3.45 (q, J = 5.9 Hz, 1.4H), 3.04 (d, J = 6.2 Hz, 0.6H), 2.94 - 2.82 (m, 1.2H). MS (ESI) mass calcd $C_{19}H_{13}ClF_4N_4O$, 424.1; m/z found, 425.1 $[M+H]^+$.

Example 316: (R*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(3-ethoxypyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



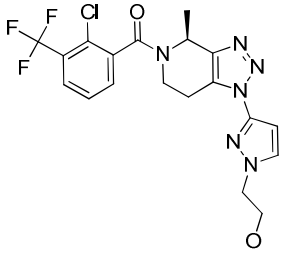
MS (ESI) mass calcd $C_{21}H_{19}ClF_3N_5O_2$, 465.1; m/z found, 465.8 $[M+H]^+$.

Example 317: (S*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(3-ethoxypyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



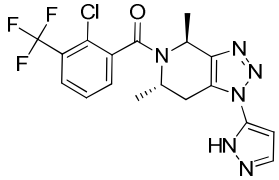
MS (ESI) mass calcd $C_{21}H_{19}ClF_3N_5O_2$, 465.1; m/z found, 465.8 $[M+H]^+$.

Example 318: (S*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(1-(2-hydroxyethyl)-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



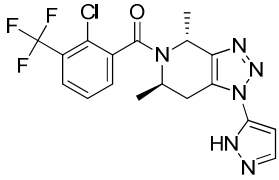
MS (ESI) mass calcd $C_{19}H_{18}ClF_3N_6O_2$, 454.1; m/z found, 455.1 $[M+H]^+$.

Example 319: (2-chloro-3-(trifluoromethyl)phenyl)((4S,6S)-4,6-dimethyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



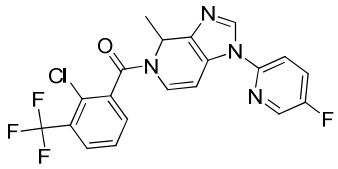
MS (ESI) mass calcd $C_{18}H_{16}ClF_3N_6O$, 424.1; m/z found, 425.1 $[M+H]^+$.

Example 320: (2-chloro-3-(trifluoromethyl)phenyl)((4R,6R)-4,6-dimethyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



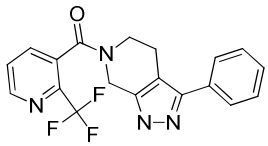
MS (ESI) mass calcd $C_{18}H_{16}ClF_3N_6O$, 424.1; m/z found, 425.1 $[M+H]^+$.

Example 321: (2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone



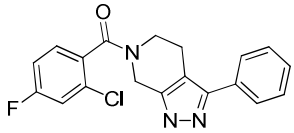
MS (ESI) mass calcd $C_{20}H_{13}ClF_4N_4O$, 436.1; m/z found, 437.1 $[M+H]^+$.

Example 322: (3-phenyl-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)(2-(trifluoromethyl)pyridin-3-yl)methanone



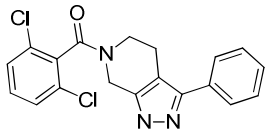
MS (ESI) mass calcd $C_{19}H_{15}F_3N_4O$, 372.1; m/z found, 373.1 $[M+H]^+$.

Example 323: (2-chloro-4-fluorophenyl)(3-phenyl-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone



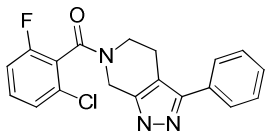
MS (ESI) mass calcd $C_{19}H_{15}ClFN_3O$, 355.1; m/z found, 356.1 $[M+H]^+$.

Example 324: (2,6-dichlorophenyl)(3-phenyl-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone



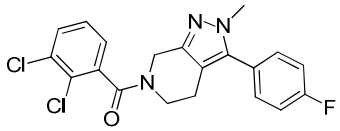
MS (ESI) mass calcd $C_{19}H_{15}Cl_2N_3O$, 371.1; m/z found, 372.1 $[M+H]^+$.

Example 325: (2-chloro-6-fluorophenyl)(3-phenyl-4,5-dihydro-1H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone



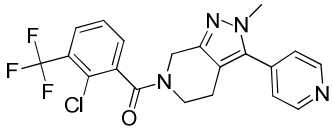
MS (ESI) mass calcd $C_{19}H_{15}ClFN_3O$, 355.1; m/z found, 356.1 $[M+H]^+$.

Example 326: (2,3-dichlorophenyl)(3-(4-fluorophenyl)-2-methyl-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone



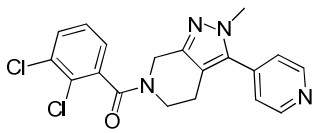
MS (ESI) mass calcd $C_{20}H_{16}Cl_2FN_3O$, 403.1; m/z found, 404.1 $[M+H]^+$.

Example 327: (2-chloro-3-(trifluoromethyl)phenyl)(2-methyl-3-(pyridin-4-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone



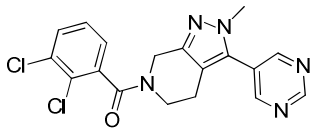
MS (ESI) mass calcd $C_{20}H_{16}ClF_3N_4O$, 420.1; m/z found, 421.1 $[M+H]^+$.

Example 328: (2,3-dichlorophenyl)(2-methyl-3-(pyridin-4-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone



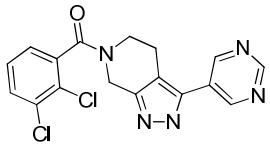
MS (ESI) mass calcd $C_{19}H_{16}Cl_2N_4O$, 386.1; m/z found, 387.1 $[M+H]^+$.

Example 329: (2,3-dichlorophenyl)(2-methyl-3-(pyrimidin-5-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone



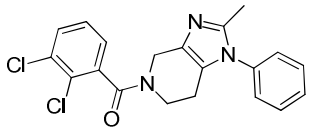
MS (ESI) mass calcd $C_{18}H_{15}Cl_2N_5O$, 387.1; m/z found, $[M+H]^+$.

Example 330: (2,3-dichlorophenyl)(3-(pyrimidin-5-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone



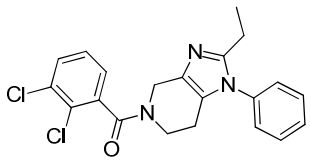
MS (ESI) mass calcd $C_{17}H_{13}Cl_2N_5O$, 373.0; m/z found, 374.1 $[M+H]^+$.

Example 331: (2,3-dichlorophenyl)(2-methyl-1-phenyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone



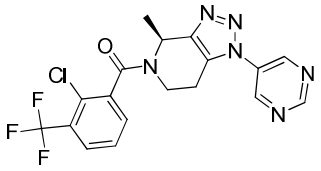
MS (ESI) mass calcd $C_{20}H_{17}Cl_2NO$, 385.1; m/z found, 385.9 m/z $[M+H]^+$.

Example 332 (2,3-dichlorophenyl)(2-ethyl-1-phenyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone



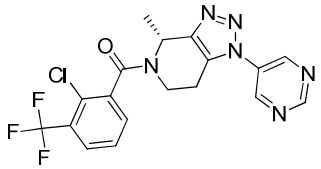
MS (ESI) mass calcd $C_{21}H_{19}Cl_2N_3O$, 399.1; m/z found, 400.0 $[M+H]^+$.

Example 333 (S)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrimidin-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



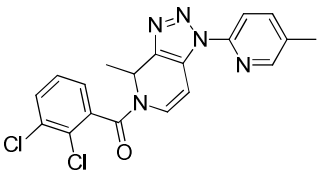
MS (ESI) mass calcd $C_{18}H_{14}ClF_3N_6O$, 422.1; m/z found, 423.1 $[M+H]^+$.

Example 334 (R*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrimidin-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



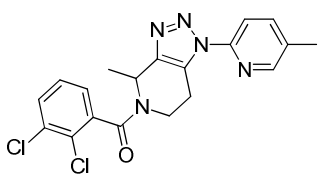
MS (ESI) mass calcd $C_{18}H_{14}ClF_3N_6O$, 422.1 m/z found, 423.1 $[M+H]^+$.

Intermediate P: (2,3-dichlorophenyl)(4-methyl-1-(5-methylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Intermediate C substituting 1-(5-methylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine for 1-(3,5-dimethylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridineand Intermediate 14 for 12. The reaction mixture was also cooled down to -40°C instead of -78°C. MS (ESI) mass calcd. $C_{19}H_{15}Cl_2N_5O$, 399.07; m/z found 400.10 $[M+H]^+$.

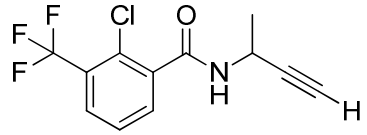
Example 336 (2,3-dichlorophenyl)(4-methyl-1-(5-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example 159 substituting (2,3-dichlorophenyl)(4-methyl-1-(5-methylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone for (2-chloro-3-(trifluoromethyl)phenyl)(1-(3,5-dimethylpyridin-2-yl)-4-methyl-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone and THF was replaced by EtOAc. MS (ESI) mass calcd $C_{19}H_{17}Cl_2N_5O$, 401.1 m/z found, 402.1 $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 - 8.19 (m, 1H), 8.09 - 7.94 (m, 1H), 7.79 - 7.64 (m, 1H), 7.59 - 7.46 (m, 1H), 7.42 - 6.98 (m, 2H), 6.20 - 5.92 (m, 0.6H), 5.17 - 5.04 (m, 0.4H), 4.99 - 4.69 (m, 0.4H), 3.82 - 2.90 (m, 3.6H), 2.57 - 2.24 (m, 3H), 2.12 - 1.25 (m, 3H).

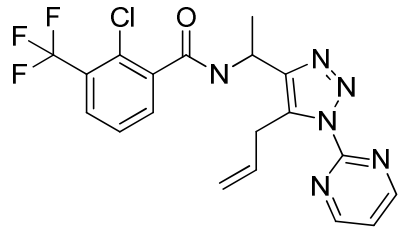
Example 337 Alternative synthesis of Example 88: (2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone

Intermediate 501: N-(but-3-yn-2-yl)-2-chloro-3-(trifluoromethyl)benzamide



To the suspension of but-3-yn-2-amine·HCl salt (10 g, 94.7 mmol, 1.0 equiv.) in THF (150 mL), Et_3N (27.5 mL, 199 mmol, 2.1 equiv.) and (2-chloro-3-(trifluoromethyl)benzoyl chloride (23.1 g, 94.7 mmol, 1.0 equiv.) were added sequentially at 0 ^{o}C. The reaction mixture was then stirred at room temperature for 16 hours. The precipitate was filtered off and washed with THF. The filtrate solution was concentrated and re-dissolved in EtOAc. The EtOAc solution was washed with saturated $NaHCO_3$ and brine, dried over Na_2SO_4, concentrated. Trituration of the crude product from EtOAc/hexanes afforded Intermediate 501: (23 g, 83.8 mmol, 88%) as a white solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.82 – 7.75 (dd, J = 7.9, 1.6 Hz, 1H), 7.73 – 7.66 (dd, J = 7.7, 1.6 Hz, 1H), 7.48 – 7.41 (dd, J = 8.2, 7.3 Hz, 1H), 6.35 – 6.02 (d, J = 7.9 Hz, 1H), 5.09 – 4.90 (dqd, J = 8.1, 6.9, 2.3 Hz, 1H), 2.47 – 2.20 (m, 1H), 1.58 – 1.54 (d, J = 6.9 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.7, 137.9, 132.5, 129.4 (q, J_{C-F} = 31.5 Hz), 129.1, 129.0 (q, J_{C-F} = 5.2 Hz), 127.1, 122.5 (q, J_{C-F} = 273.4 Hz), 83.2, 71.2, 37.8, 22.1. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{12}H_{10}ClF_3NO$, 276.0398; found, 276.0390.

Intermediate 502: N-(1-(5-allyl-1-(pyrimidin-2-yl)-1H-1,2,3-triazol-4-yl)ethyl)-2-chloro-3-(trifluoromethyl)benzamide

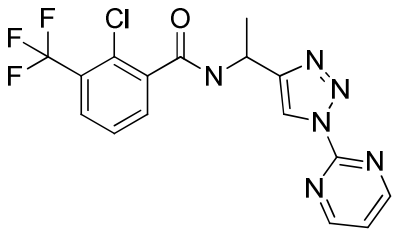


Method 1: To the suspension of Intermediate 501 (138 mg, 0.5 mmol, 1.0 equiv), tetrazolo[1,5-a]pyrimidine (67 mg, 0.55 mmol, 1.1 equiv.), allyl bromide (73 mg, 0.6 mmol, 1.2 equiv.) and Cs_2CO_3(0.49 g, 1.5 mmol, 3.0 equiv.) in THF (2 mL), CuI (48 mg, 0.25 mmol, 0.5 equiv.) was added at room temperature in one portion under N_2. The reaction mixture was then stirred at room temperature under N_2 for 16 hours. Celite and EtOAc (5 mL) were added and the suspension was stirred for 20 minutes. The insoluble solid was filtered off and washed with EtOAc. The filtrate solution was washed with brine, dried over Na_2SO_4 and concentrated. The crude product was purified by column chromatography with EtOAc/hexanes as eluents to afford compound Intermediate 502 (146 mg, 0.34 mmol, 67% yield) as a white solid. As byproducts Intermediate 503 (30 mg, 0.075 mmol, 15% yield) and Intermediate 237 (2% yield) were also isolated.

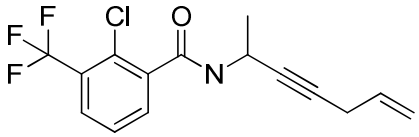
Method 2: To the suspension of compound Intermediate 501 (138 mg, 0.5 mmol, 1.0 equiv), tetrazolo[1,5-a]pyrimidine (67 mg, 0.55 mmol, 1.1 equiv.) and Hunig's base (0.3 mL, 1.75 mmol, 3.5 equiv.), $(CuOTf)_2 \cdot$Benzene (150 mg, 0.6 mmol, 1.2 equiv.) was added at room temperature in one portion under N_2. After 6 hours at room temperature, HPLC analysis indicated the complete consumption of Intermediate 501. Allyl bromide (242 mg, 2.0 mmol, 4.0 euqiv.) was added and the reaction solution was stirred for another 2 hours. The same workup/purification procedure were followed to afford Intermediate 502 (113 mg, 0.26 mml, 52% yield) along with Intermediate 503 (49 mg, 0.12 mmol, 25% yield).

Intermediate 502: N-(1-(5-allyl-1-(pyrimidin-2-yl)-1H-1,2,3-triazol-4-yl)ethyl)-2-chloro-3-(trifluoromethyl)benzamide: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.95 – 8.85 (d, J = 4.8 Hz, 2H), 7.78 – 7.72 (dd, J = 7.8, 1.6 Hz, 1H), 7.67 – 7.61 (dd, J = 7.7, 1.6 Hz, 1H), 7.46 – 7.43 (s, 1H), 7.43 – 7.38 (td, J = 7.8, 0.9 Hz, 1H), 6.93 – 6.79 (d, J = 8.3 Hz, 1H), 5.96 – 5.85 (dddd, J = 16.7, 10.1, 6.4, 5.5 Hz, 1H), 5.57 – 5.47 (dq, J = 8.3, 6.8 Hz, 1H), 5.08 – 4.92 (m, 2H), 4.15 – 4.05 (m, 1H), 4.04 – 3.95 (m, 1H), 1.76 – 1.71 (d, J = 6.9 Hz, 3H). ^{13}C

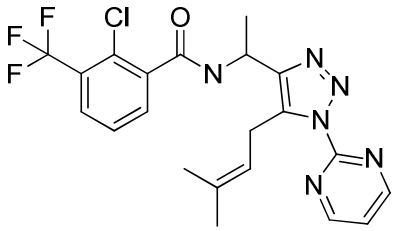
NMR (151 MHz, $CDCl_3$) δ 165.1, 159.1, 155.7, 146.8, 138.3, 133.2, 132.6, 132.2, 129.3 (q, J_{C-F} = 31.5 Hz), 129.3, 128.7 (q, J_{C-F} = 5.2 Hz), 126.9, 122.5 (q, J_{C-F} = 273.4 Hz), 120.8, 117.2, 41.3, 27.9, 21.5. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{19}H_{17}ClF_3N_6O$, 437.1099; found, 437.1088.



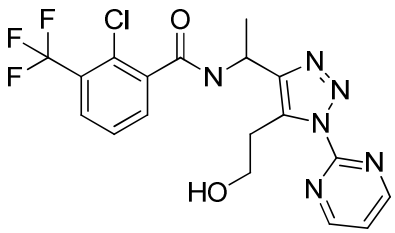
Intermediate 503: 2-chloro-N-(1-(1-(pyrimidin-2-yl)-1H-1,2,3-triazol-4-yl)ethyl)-3-(trifluoromethyl)benzamide: ^1H NMR (600 MHz, $CDCl_3$) δ 8.91 – 8.84 (d, J = 4.8 Hz, 2H), 8.65 – 8.57 (s, 1H), 7.81 – 7.74 (dd, J = 7.8, 1.6 Hz, 1H), 7.72 – 7.64 (dd, J = 7.7, 1.6 Hz, 1H), 7.51 – 7.38 (m, 2H), 6.80 – 6.64 (d, J = 8.1 Hz, 1H), 5.71 – 5.49 (p, J = 7.1 Hz, 1H), 1.87 – 1.69 (d, J = 7.0 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.3, 159.3, 154.4, 149.0, 138.2, 132.4, 129.3 (q, J_{C-F} = 31.5 Hz), 129.2, 128.7 (q, J_{C-F} = 5.2 Hz), 127.0, 122.5 (q, J_{C-F} = 273.4 Hz), 120.8, 120.1, 42.5, 21.1. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{16}H_{13}ClF_3N_6O$, 397.0786; found, 397.0780.



Intermediate 237: 2-chloro-N-(hept-6-en-3-yn-2-yl)-3-(trifluoromethyl)benzamide: ^1H NMR (600 MHz, $CDCl_3$) δ 7.81 – 7.72 (dd, J = 7.7, 1.7 Hz, 1H), 7.70 – 7.60 (dd, J = 7.6, 1.7 Hz, 1H), 7.52 – 7.37 (t, J = 7.8 Hz, 1H), 6.37 – 6.21 (d, J = 8.2 Hz, 1H), 5.86 – 5.72 (ddt, J = 17.1, 10.2, 5.2 Hz, 1H), 5.37 – 5.27 (m, 1H), 5.18 – 5.07 (dq, J = 10.8, 1.9 Hz, 1H), 5.06 – 4.92 (ddt, J = 8.4, 4.5, 2.3 Hz, 1H), 3.13 – 2.76 (dq, J = 5.1, 2.0 Hz, 2H), 1.61 – 1.32 (d, J = 6.8 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.6, 138.2, 132.4, 132.1, 129.3 (q, J_{C-F} = 31.5 Hz), 129.1, 128.8 (q, J_{C-F} = 5.2 Hz), 127.0, 122.5 (q, J_{C-F} = 273.4 Hz), 116.2, 81.9, 80.0, 38.3, 22.9, 22.5. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{15}H_{14}ClF_3NO$, 316.0711; found, 316.0726.

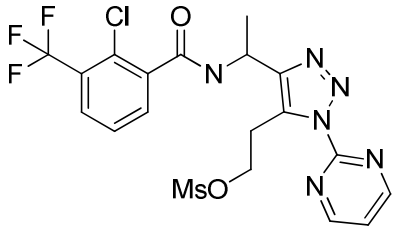


Intermediate 238: 2-chloro-N-(1-(5-(3-methylbut-2-en-1-yl)-1-(pyrimidin-2-yl)-1H-1,2,3-triazol-4-yl)ethyl)-3-(trifluoromethyl)benzamide: Following Method l described above for Intermediate 502 substituting dimethylallyl bromide for allyl bromide, the title compound was isolated in 77% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.94 – 8.87 (d, *J* = 4.8 Hz, 2H), 7.77 – 7.70 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.67 – 7.61 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.47 – 7.43 (t, *J* = 4.8 Hz, 1H), 7.43 – 7.36 (t, *J* = 7.7 Hz, 1H), 7.04 – 6.91 (d, *J* = 8.3 Hz, 1H), 5.58 – 5.48 (m, 1H), 5.10 – 5.02 (m, 1H), 3.98 – 3.90 (d, *J* = 6.8 Hz, 2H), 1.76 – 1.72 (s, 3H), 1.72 – 1.68 (d, *J* = 6.8 Hz, 3H), 1.65 – 1.60 (d, *J* = 1.5 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.0, 159.0, 155.8, 146.1, 138.4, 134.7, 134.3, 132.2, 129.3 (q, J_{C-F} = 31.5 Hz), 129.3, 128.7 (q, J_{C-F} = 5.2 Hz), 126.9, 122.5 (q, J_{C-F} = 273.4 Hz), 120.7, 118.8, 41.4, 25.5, 23.1, 21.6, 18.1. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{21}H_{21}ClF_3N_6O$, 465.1412; found, 465.1393.

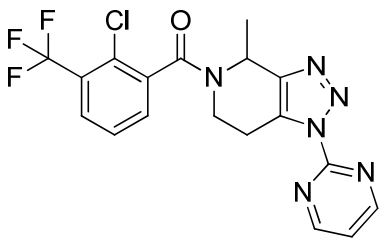


Intermediate 239: 2-chloro-N-(1-(5-(2-hydroxyethyl)-1-(pyrimidin-2-yl)-1H-1,2,3-triazol-4-yl)ethyl)-3-(trifluoromethyl)benzamide: A stream of O_3 generated from an ozonator was passed though the solution of Intermediate 238 (200 mg, 0.43 mmol, 1.0 equiv.) in MeOH (30 mL) at -78 ^{o}C until the color of the reaction solution became blue (~10 min). $NaBH_4$ (49 mg, 1.3 mmol, 3.0 equiv.) was added at -78 ^{o}C. The reaction solution was warmed to room temperature and partitioned between EtOAc and brine. The organic layer was separated, dried over Na_2SO_4 and concentrated. The crude product was purified by column chromatography with EtOAc/hexanes as eluents to afford the title compound (140 mg, 0.30 mmol, 70% yield) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.95 – 8.88 (d, *J* = 4.9 Hz, 2H), 7.81 – 7.73 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.67 – 7.58 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.50 –

7.44 (t, *J* = 4.9 Hz, 1H), 7.43 – 7.36 (t, *J* = 7.8 Hz, 1H), 6.95 – 6.83 (d, *J* = 8.1 Hz, 1H), 5.62 – 5.44 (m, 1H), 4.06 – 3.89 (m, 2H), 3.66 – 3.56 (ddd, *J* = 14.7, 6.1, 4.6 Hz, 1H), 3.44 – 3.34 (ddd, *J* = 14.7, 7.7, 4.9 Hz, 1H), 3.20 – 3.14 (t, *J* = 5.9 Hz, 1H), 1.88 – 1.71 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.5, 159.0, 155.5, 147.4, 138.3, 133.1, 132.2, 129.2, 129.1 (q, J_{C-F} = 31.5 Hz), 128.5 (q, J_{C-F} = 5.2 Hz), 126.8, 122.5 (q, J_{C-F} = 273.4 Hz), 120.7, 61.1, 41.4, 27.3, 20.7. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{18}H_{17}ClF_3N_6O_2$, 441.1048; found, 441.1038.



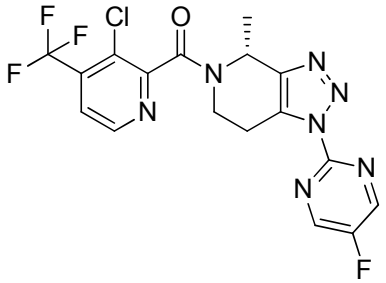
Intermediate 240: To the solution of Intermediate 239 (100 mg, 0.22 mmol, 1.0 equiv.) in THF (10 mL), Et_3N (37 uL, 0.27 mmol, 1.2 equiv.) and MsCl (29 mg, 0.24 mmol, 1.1 equiv.) was added sequentially. The reaction solution was stirred at room temperature for 16 hours. EtOAc and water were added. The organic layer was separated, dried over Na_2SO_4 and concentrated. The crude product (112 mg, 0.21 mmol, 95% yield) was used directly in the next reaction without further purification. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.97 – 8.88 (d, *J* = 4.8 Hz, 2H), 7.80 – 7.72 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.66 – 7.59 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.50 – 7.45 (t, *J* = 4.8 Hz, 1H), 7.44 – 7.36 (t, *J* = 7.8 Hz, 1H), 6.86 – 6.77 (d, *J* = 8.3 Hz, 1H), 5.60 – 5.47 (dd, *J* = 8.3, 7.0 Hz, 1H), 4.66 – 4.57 (ddd, *J* = 7.5, 6.0, 3.9 Hz, 2H), 3.92 – 3.79 (m, 1H), 3.73 – 3.59 (d, *J* = 14.6 Hz, 1H), 3.04 – 2.95 (s, 3H), 1.83 – 1.72 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.3, 159.3, 155.5, 148.2, 138.1, 132.2, 129.8, 129.4 (q, J_{C-F} = 31.5 Hz), 129.2, 128.9 (q, J_{C-F} = 5.2 Hz), 127.0, 122.5 (q, J_{C-F} = 273.4 Hz), 120.9, 67.6, 41.1, 37.3, 24.4, 21.0. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{19}H_{19}ClF_3N_6O_4S$, 519.0824; found, 519.0805.



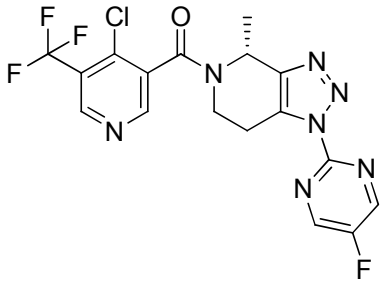
(2-Chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone: To the solution of Intermediate 240 (112 mg, 0.21 mmol, 1.0 equiv.) in THF (20 mL), NaH (60 wt% in mineral oil, 30 mg, 0.74 mmol, 3.5 equiv.) was added in one portion. The reaction solution was heated to reflux temperature for 3 hours and then cooled to room temperature. The reaction solution was partitioned between EtOAc and brine. The organic layer was separated, dried over Na_2SO_4 and concentrated. The crude product was purified by column chromatography to afford (2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(pyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone (68 mg, 0.16 mmol, 75% yield) as a white solid. ^{1}H NMR (600 MHz, MeOD) δ 8.97 – 8.86 (m, 2H), 7.98 – 7.88 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.83 – 7.52 (m, 3H), [6.05 – 5.78 (m), 4.87 – 4.82 (m), 4.72 – 4.66 (m), 1H] [5.04 – 4.98 (m), 3.94 – 2.86 (m), 4H], [1.72 – 1.66 (m), 1.59 – 1.48 (m), 3 H]. ^{13}C NMR (151 MHz, MeOD) δ 168.36, 168.27, 168.25, 160.68, 160.64, 160.63, 156.44, 156.42, 156.40, 146.71, 146.59, 146.46, 139.78, 139.59, 139.56, 139.37, 134.20, 133.93, 133.22, 132.96, 132.90, 132.61, 132.47, 130.47, 130.37, 130.27, 130.16, 130.06, 129.85, 129.82, 129.78, 129.76, 129.72, 129.69, 129.65, 129.59, 129.57, 129.48, 129.46, 129.33, 129.30, 129.13, 129.04, 126.83, 125.03, 124.91, 123.22, 123.10, 122.50, 122.47, 122.41, 121.41, 51.90, 51.40, 46.88, 46.66, 41.78, 41.01, 36.04, 35.83, 26.17, 25.75, 25.21, 25.17, 20.28, 20.13, 18.84, 18.51. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{18}H_{15}ClF_3N_6O$, 423.0942; found, 423.0937.

Examples 338 to 343 are made in accordance with the synthetic schemes, and in light of the specific examples, provided above.

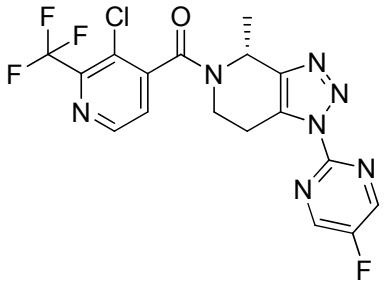
Example 338: (R*)-(3-chloro-4-(trifluoromethyl)pyridin-2-yl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



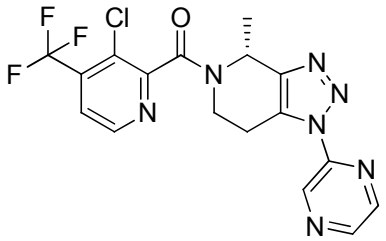
Example 339: (R*)-(4-chloro-5-(trifluoromethyl)pyridin-3-yl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



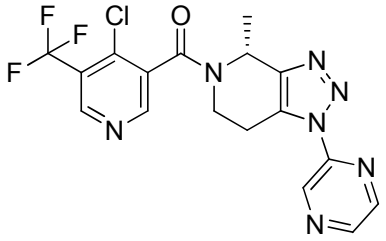
Example 340: (R*)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



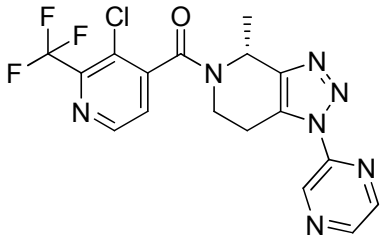
Example 341: (R*)-(3-chloro-4-(trifluoromethyl)pyridin-2-yl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



Example 342: (R*)-(4-chloro-5-(trifluoromethyl)pyridin-3-yl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone

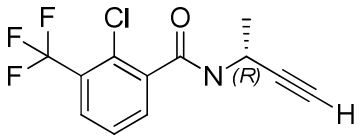


Example 343: (R*)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(pyrazin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



Example 344: (R)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone (An alternative synthesis of this compound is shown in Example 158.)

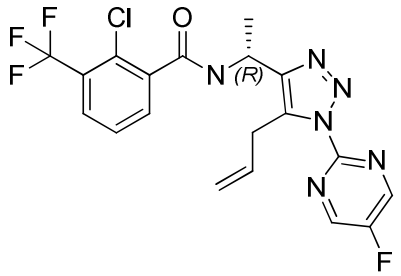
Intermediate 241: (R)-*N*-(but-3-yn-2-yl)-2-chloro-5-fluoro-3-(trifluoromethyl)benzamide



Intermediate 241: (R)-*N*-(but-3-yn-2-yl)-2-chloro-5-fluoro-3-(trifluoromethyl)benzamide: To the suspension of (R) but-3-yn-2-amine·HCl salt (10 g, 94.7 mmol, 1.0 equiv.) in THF (150 mL), Et_3N (27.5 mL, 199 mmol, 2.1 equiv.) and (2-chloro-3-(trifluoromethyl)benzoyl chloride (23.1 g, 94.7 mmol, 1.0 equiv.) were added sequentially at 0 ^oC. The reaction mixture was then stirred at room temperature for 16 hours. The precipitate was filtered off and washed with THF. The filtrate solution was concentrated and re-dissolved in EtOAc. The EtOAc solution was washed with saturated $NaHCO_3$ and brine, dried over Na_2SO_4, concentrated. Trituration of the crude product from EtOAc/hexanes afforded the title compound (23 g, 83.8 mmol, 88%) as a white solid. An alternative synthesis method for Intermediate 241: (*R*)-But-3-yn-2-amine HCl (1.0 eq., 40.2 g, 380.8 mmol) was suspended in THF (350 mL) followed by dropwise addition of Et_3N (2.1 eq., 110.85 mL, 799.7 mmol) at 0 °C. 2-Chloro-3-(trifluoromethyl)benzoyl chloride (1.0 eq., 92.54 g, 380.8 mmol) in THF (350 mL) was then added at 0 °C for over 30 minutes and the reaction mixture was stirred at room temperature overnight. Insoluble solids in the reaction mixture were filtered off and washed with EtOAc. The solvent was evaporated and the residue was partitioned between EtOAc and $NaHCO_3$ aqueous solution. The EtOAc layer was washed with brine, dried with Na_2SO_4 and then concentrated. The crude product was triturated from hot EtOAc/hexanes to afford 91.5 grams of the title comound in 87% yield as white solid. ^1H NMR (600 MHz, $CDCl_3$) δ 7.82 – 7.75 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.73 – 7.66 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.48 – 7.41 (dd, *J* = 8.2, 7.3 Hz, 1H), 6.35 – 6.02 (d, *J* = 7.9 Hz, 1H), 5.09

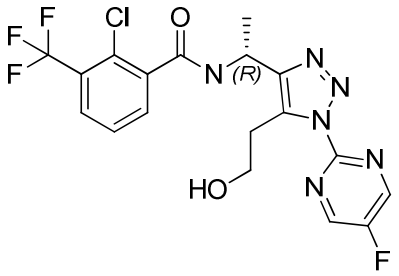
– 4.90 (dqd, J = 8.1, 6.9, 2.3 Hz, 1H), 2.47 – 2.20 (m, 1H), 1.58 – 1.54 (d, J = 6.9 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.7, 137.9, 132.5, 129.4 (q, J_{C-F} = 31.5 Hz), 129.1, 129.0 (q, J_{C-F} = 5.2 Hz), 127.1, 122.5 (q, J_{C-F} = 273.4 Hz), 83.2, 71.2, 37.8, 22.1. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{12}H_{10}ClF_3NO$, 276.0398; found, 276.0390.

Intermediate 242: (R)-*N*-(1-(5-allyl-1-(5-fluoropyrimidin-2-yl)-1H-1,2,3-triazol-4-yl)ethyl)-2-chloro-3-(trifluoromethyl)benzamide



To the suspension of Intermediate 241 (41.93 g, 152.11 mmol, 1.0 equiv), 2-azido-5-fluoropyrimidine (25.43 g, 182.85 mmol, 1.2 equiv.), allyl bromide (16.73 mL, 197.74 mmol, 1.3 equiv.) and Cs_2CO_3(148.68 g, 456.33 mmol, 3.0 equiv.) in 2-methyl-tetrahydrofuran (1000 mL) was added CuI (28.97 g, 152.11 mmol, 1.0 equiv.) at room temperature in one portion under N_2. The reaction mixture was vigorously stirred at room temperature under N_2(g) for 16 hours. Celite was added to the reaction mixture and the insoluble solid was filtered off. The solids were re-suspended in EtOAc (500 mL) and the solids were filtered off again. This filtrate was combined with the prior filtrate and they were concentrated to ½ their volume under reduced pressure. This filtrate was then washed with 1N KOH (700 mL) and EtOAc (300 mL) was added. The organic layer was separated, dried over Na_2SO_4 and concentrated. The crude product was slurried in 4/1 EtOAc/TMBE 400 mL/100 mL for 48 hours then filtered to recover Intermediate 242: (R)-*N*-(1-(5-allyl-1-(5-fluoropyrimidin-2-yl)-1H-1,2,3-triazol-4-yl)ethyl)-2-chloro-3-(trifluoromethyl)benzamide as a light yellow solid. Subsequent trituration and then chromatography of the crude reaction mixture provided the title compound**.** (56.5 g, 124.27 mmol, 82%). MS-ESI (m/z): $[M+H]^+$ calcd for $C_{19}H_{15}ClF_4N_6O$, 454.81; found, 455.10.

Intermediate 243: (R)-2-chloro-N-(1-(1-(5-fluoropyrimidin-2-yl)-5-(2-hydroxyethyl)-1H-1,2,3-triazol-4-yl)ethyl)-3-(trifluoromethyl)benzamide:

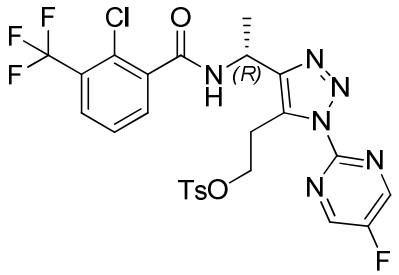


Intermediate 243: (R)-2-chloro-N-(1-(1-(5-fluoropyrimidin-2-yl)-5-(2-hydroxyethyl)-1H-1,2,3-triazol-4-yl)ethyl)-3-(trifluoromethyl)benzamide: A stream of ozone (O_3) generated from an ozonator was passed though the solution of Intermediate 242 (8 g, 17.59 mmol, 1.0 equiv.) in MeOH (350 mL) and CH_2Cl_2 at -78 ^oC until the color of the reaction solution became blue (~45 min). Removed O_3(g) and bubbled in N_2(g) for 15 minutes. Slowly, $NaBH_4$ (2 g, 52.77 mmol, 3.0 equiv.) was added at -78 ^oC and stirred for 30 minutes. The reaction solution was warmed above 0 ^oC by quenching with ice and CH_2Cl_2. The organic layer was separated, dried over Na_2SO_4 and concentrated. The crude product was purified by column chromatography with 9/1 EtOAc/hexanes as eluents to afford the title compound (Intermediate 243: (R)-2-chloro-N-(1-(1-(5-fluoropyrimidin-2-yl)-5-(2-hydroxyethyl)-1H-1,2,3-triazol-4-yl)ethyl)-3-(trifluoromethyl)benzamide) (5.7 g, 12.42 mmol, 71% yield) as a foam oil. MS-ESI (m/z): $[M+H]^+$ calcd for $C_{18}H_{15}ClF_4N_6O_2$, 458.80; found, 459.10.

Intermediate 243: Alternative procedure: (*R*)-2-chloro-N-(1-(1-(5-fluoropyrimidin-2-yl)-5-(2-hydroxyethyl)-1H-1,2,3-triazol-4-yl)ethyl)-3-(trifluoromethyl)benzamide: A stream of O_3 generated from an ozonator was passed though the solution of Intermediate 242 (69.32 g, 152.41 mmol, 1.0 equiv.) in MeOH (500 mL) and THF (750 mL) at -65 ^oC until the color of the reaction solution became light yellow (~50 min). Removed O_3(g) and bubbled in N_2(g) for 15 minutes. Slowly, $NaBH_4$ (4.16 g, 109.94 mmol, 0.72 equiv.) was added in three portions at -60 ^oC and stirred for 30 minutes. The reaction was slowly quenched with 0.5 M sodium phosphate buffer pH 7.5 (200 mL) and allowed to warm up to room temperature for 60 minutes. Inorganic solids in the mixture were filtered off and washed with CH_2Cl_2 (250 mL). The filtrate was concentrated to 1/2 volume at room temperature then washed with CH_2Cl_2 (3 x 250 ml) and extracted. The combined organic layers were dried with Na_2SO_4, filtered and concentrated to recover 80 grams of crude oil. The material was purified via plugged silica gel (330 g) with 3/2 EtOAc/hexane then increasing the eluent to 9/1 EtOAc/hexane. The product was isolated and dried under high vacuum overnight to afford the title compound Intermediate 243: (R)-2-chloro-N-(1-(1-(5-

fluoropyrimidin-2-yl)-5-(2-hydroxyethyl)-1H-1,2,3-triazol-4-yl)ethyl-3-(trifluoromethyl)benzamide (58.53 g, 127.57 mmol, 83.7% yield) as a foam oil. MS-ESI (m/z): $[M+H]^+$ calcd for $C_{18}H_{15}ClF_4N_6O_2$, 458.80; found, 459.10.

Intermediate 244: (R)-2-(4-(1-(2-chloro-3-(trifluoromethyl)benzamido)ethyl)-1-(5-fluoropyrimidin-2-yl)-1H-1,2,3-triazol-5-yl)ethyl 4-methylbenzenesulfonate:

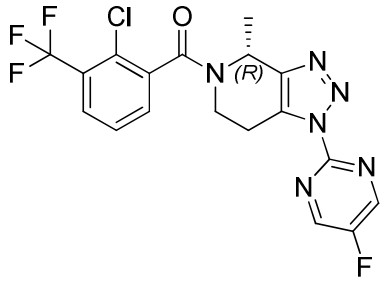


Intermediate 244**:** To the solution of Intermediate 243 (10 g, 21.80 mmol, 1.0 equiv.) in CH_2Cl_2 (80 mL) was added TsCl (5.0 g, 26.16 mmol, 1.2 equiv.), DMAP (0.27 g, 2.18 mmol, 0.1 equiv.) and trimethyl amine HCl (0.42 g, 4.36 mmol, 0.2 eqiv.). Slowly, Et_3N (3.9 mL, 28.33 mmol, 1.3 equiv.) was added drop wise. The reaction solution was stirred at room temperature for 16 hours then quenched with H_2O. The organic layer was separated, dried over Na_2SO_4 and concentrated.

The crude product was purified by column chromatography using 3/2 EtOAc/hexane to recover Intermediate 244 (12.90 g, 21.04 mmol, 96% yield).

An alternative synthesis of the title compound: In a 1 liter round bottom flask with a magnetic stir bar, Intermediate 243 (1 eq., 51.95 g, 113.23 mmol) was combined with DMAP (0.1 eq., 1.38 g, 11.32 mmol), trimethyl amine HCl (0.2 eq., 2.16 g, 22.65 mmol) and tosyl Cl (1.3 eq., 28.10 g, 147.39 mmol) in CH_2Cl_2 (360 mL) at room temperature. Slowly, TEA (1.4 eq, 22.40 mL, 161.15 mmol) was added dropwise over a period of 12 minutes to the reaction mixture. Mild exotherm occurred during the addition of TEA. After stirring for 2 hours, another 0.1 equivalents of tosyl Cl (2.16 g, 11.32 mmol) and TEA (1.58 mL, 11.32 mmol) was added then the reaction was stirred overnight. The mixture was quenched with H_2O (275 mL) and the organic phase extracted. The aqueous layer was washed with CH_2Cl_2 (2 x 75 ml CH_2Cl_2) and extracted. The combined organic layers were dried with Na_2SO_4, filtered and concentrated to recover 70 grams of Intermediate 244 as a dark oil in quantitative yield. The material was used in the next step without further purification. MS-ESI (m/z): $[M+H]^+$ calcd for $C_{25}H_{21}ClF_4N_6O_4S$, 612.99; found, 613.4.

Example 344: (R)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone:

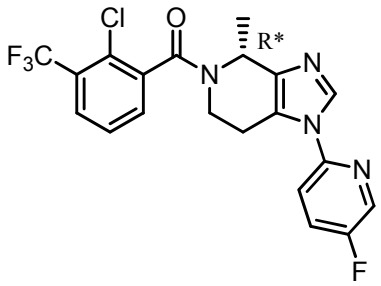


To the solution of Intermediate 244 (12.9 g, 21.04 mmol, 1.0 equiv.) in THF (150 mL) was added NaH (60 wt% in mineral oil, 4.5 g, 112.38 mmol, 5.3 equiv.). The reaction solution was heated to 60 ^{o}C for 3 hours and then cooled to room temperature. The reaction was quenched with cold H_2O and EtOAc. The organic layer was separated, dried over Na_2SO_4 and concentrated. The crude product was purified by column chromatography to afford Example 344: (R)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone (6.70 g, 15.20 mmol, 72% yield) as a white solid. MS-ESI (m/z): $[M+H]^+$ calcd for $C_{18}H_{13}ClF_4N_6O$, 440.79; found, 440.90. CHN analysis calcd for $C_{18}H_{13}ClF_4N_6O$: 49.04% C, 2.98% H, 19.05 N; found, 48.93% C, 3.25% H, 19.02 N. Chiral HPLC analysis: Chiral Pak AD-H column, 0.4 mL/min, 80% EtOH / 20% hexane, major isomer 12.56 min, minor isomer 11.28 min.

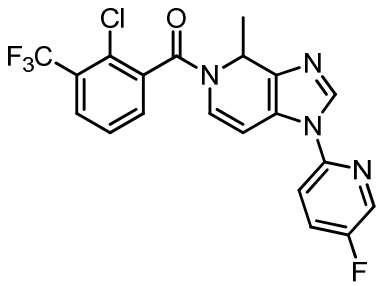
An alternative synthesis of Example 344: In a 1-neck, 1 liter round bottom flask with a magnetic stir bar, 60% NaH (3.0 eq., 14.0 g. 350.03 mol) was slurried in THF (350 mL) and heated to 60 °C. Intermediate 244, (1 eq., 69.41 g, 113.23 mmol) was also diluted in THF (125 mL) then slowly added into the NaH mixture over 15 minutes. Mild gas evolution occurred during the addition. After the reaction was completed in 2 - 3 hours, the mixture was cooled to room temperature then slowly poured into a cold ice/water mixture (400 mL) with vigorous stirring. The mixture was then treated with EtOAc (300 mL) and the organic layer was extracted. The aqueous phase was washed with EtOAc (3 x 100 mL) and also extracted. The combined organic layers were dried with Na_2SO_4, filtered and concentrated to a dark foamy solid. The crude product was diluted and stirred in EtOH/TBME (150 mL/ 50 mL) overnight to form precipitated solids. The solids were filtered and washed with 9/1 TBME/EtOH to recover 21.51 grams of tan product. The product was refluxed in EtOH (350 mL) until dissolved then hot H_2O (175 mL) was added.

The solids slowly precipitated after stirring overnight. The solids were filtered and dried under high vacuum at 90 °C overnight to recover 18.2 grams of product. The filtrate was recrystallized again to recover another 1.9 grams of product. All the remaining filtrates were combined and purified via ISCO column using silica gel with 1/1 EtOAc/hexane then increasing the eluent to 4/1 EtOAc/hexane to recover 7.3 grams of 78% pure product. The material was slurried in TBME (50 mL) for 2 hours then filtered to recover 5.1 grams of pure product. The solids were refluxed in EtOH (80 mL) until dissolved then hot water (50 mL) was added. The precipitated mixture was allowed to stir overnight then filtered and washed with water to recover 4.9 grams of solvent-free enantiomeric pure product. A combined total of 25 grams of (R)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyrimidin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone was isolated in 50% yield. Chiral Pak AD-H column (250 x 4.6 mm), 0.4 mL/min, 80% hexane/20% EtOH. Elution of the *R* enantiomer is at 15.46 minutes. (For reference the *S* enantiomer elutes at 12.60 minutes.) MS 441.0 (M^+H).

Example 345: (R*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone



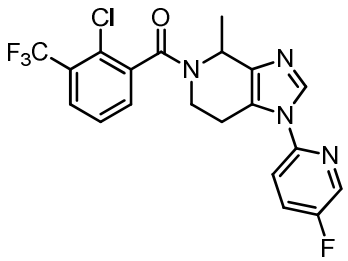
Intermediate 245: (2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone



In a three-neck round-bottom flask equipped with a mechanic stirring, an internal thermal couple and an addition funnel, 1-(5-fluoropyridin-2-yl)-1H-imidazo[4,5-c]pyridine (70 g,

326 mmol) was suspended in THF (1.7 L) and then warmed to 50 ^{o}C to form a clear solution. The clear solution was cooled to -78 ^{o}C and a lot of solid precipitated out. Under N_2, MeMgBr (3.0 mol/L in THF, 109 mL, 326 mmol) was added over 30 min while the internal temperature was maintained at <-70 ^{o}C. After 20 min, the solution of Intermediate 12 (87 g, 359 mmol) in THF (100 mL) was added over 30 min with the internal temperature maintained at <-70 ^{o}C. The rest of MeMgBr (3.0 mol/L in THF, 130 mL, 390 mmol) was then added over 30 min. The reaction was stirred at -78 ^{o}C for 1 hour. The cold bath was removed and the reaction solution was warmed to 0 ^{o}C. With an ice/water bath, 2 mol/L HCl aqueous solution was slowly added to quench the reaction while the internal temperature was maintained at <5 ^{o}C. Concentrated NH_4Cl aqueous solution was then added until clear phase separation was obtained. The aqueous layer was extracted with EtOAc twice (300 mL). The organic layers were combined, dried over Na_2SO_4, and concentrated. The crude product was recrystallized from hot EtOAc(250 mL)/MTBE (500 mL). The precipitated solid was collected by filtration, washed with cold MTBE (500 mL) to afford Intermediate 245 as a white solid (117 g, 82%). MS-EI (m/z): $[M+H]^+$ observed: 437.0.

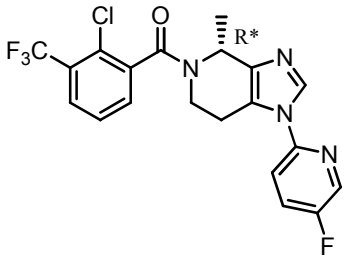
Alternative Synthesis of Example 11. (2-Chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone.



Intermediate 245 (80 g, 183 mmol) was dissolved in the mixed solvent of THF (450 mL), EtOH (600 mL), AcOH (80 mL) at 50 ^{o}C. The solution was poured into Pd/C (23 g, 10 wt% dry base, 1:1 with water). The hydrogenation was performed on a Parr shaker at 55 ^{o}C, 30 PSI overnight. After the reaction was complete, Pd/C was filtered off under N_2 and washed with EtOH. The filtrate solution was concentrated and repartitioned between EtOAc/saturated aqueous $NaHCO_3$ solution. The EtOAc layer was washed with brine, dried on Na_2SO_4 and concentrated. The residue was recrystallized from hot EtOAc(200 mL)/TBME (400 mL) to afford a white, free-flowing solid. Recrystallization from hot

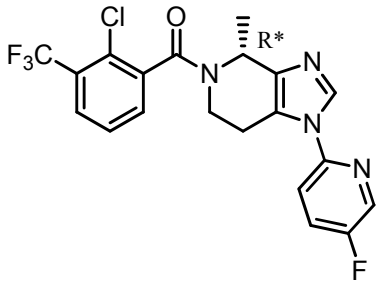
EtOAc (700 mL) afforded pure Example 11 as a white solid (54.3 g, 124 mmol, 67%). MS-EI (m/z): $[M+H]^+$ observed: 439.0.

Alternative Chiral Separation of Example 11: (R*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone



Chiral separation of Example 11 (54.3 g) was performed on chiral SFC (Stationary phase: CHIRALCEL OD-H 5µm 250x20mm), Mobile phase: 85% CO_2, 15% EtOH). 26.7 grams of enantiopure compound was obtained. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.45 – 8.29 (m, H), 7.99 – 7.86 (m, H), 7.81 – 7.70 (m, 1H), 7.64 – 7.29 (m, 4H), 5.87 – 5.75 (m, 0.7H), 5.15 – 5.01 (m, 0.6H), 4.71 – 4.58 (m, 0.3H), 4.57 – 4.46 (m, 0.4H), 3.61 – 3.46 (m, 1H), 3.44 – 3.33 (m, 0.3H), 3.27 – 3.09 (m, 1.2H), 3.00 – 2.72 (m, 1.5H), 1.67 – 1.59 (m, 1.7H), 1.51 – 1.46 (d, *J* = 6.8 Hz, 0.8H), 1.44 – 1.39 (d, *J* = 6.9 Hz, 0.5H).

Alternative Synthesis of Example 345: (R*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone



(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone: In a three-neck round-bottom flask equipped with a mechanic stirring, an internal thermal couple and an addition funnel, 1-(5-fluoropyridin-2-yl)-1H-imidazo[4,5-c]pyridine (70 g, 326 mmol) was suspended in THF (1.7 L) and then warmed to 50 ^{o}C to form a clear solution. The clear solution was cooled to -78 ^{o}C and a lot

of solid precipitated out. Under N_2, MeMgBr (3.0 mol/L in THF, 109 mL, 326 mmol) was added over 30 min while the internal temperature was maintained at <-70 ^oC. After 20 min, the solution of 2-chloro-3-(trifluoromethyl)benzoyl chloride (87 g, 359 mmol) in THF (100 mL) was added over 30 min with the internal temperature maintained at <-70 ^oC. The rest of MeMgBr (3.0 mol/L in THF, 130 mL, 390 mmol) was then added over 30 min. The reaction was stirred at -78 ^oC for 1 hour. The cold bath was removed and the reaction solution was warmed to 0 ^oC. With an ice/water bath, 2 mol/L HCl aqueous solution was slowly added to quench the reaction while the internal temperature was maintained at <5 ^oC. Concentrated NH4Cl aqueous solution was then added until clear phase separation was obtained. The aqueous layer was extracted with EtOAc twice (300 mL). The organic layers were combined, dried over Na2SO4, and concentrated. The crude product was recrystallized from hot EtOAc(250 mL)/MTBE (500 mL). The precipitated solid was collected by filtration, washed with cold MTBE (500 mL) to afford a white solid (117 g, 82%). MS-EI (m/z): [M+H]+ observed: 437.0.

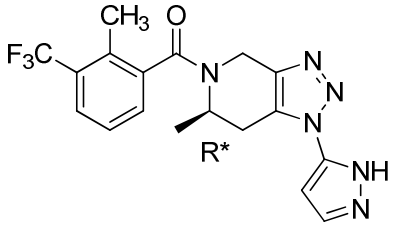
(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone: (2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone (80 g, 183 mmol) was dissolved in the mixed solvent of THF (450 mL), EtOH (600 mL), AcOH (80 mL) at 50 ^oC. The solution was poured into Pd/C (23 g, 10 wt% dry base, 1:1 with water). The hydrogenation was performed on a Parr shaker at 55 ^oC, 30 PSI overnight. After the reaction was complete, Pd/C was filtered off under N2 and washed with EtOH. The filtrate solution was concentrated and repartitioned between EtOAc/saturated aqueous NaHCO3 solution. The EtOAc layer was washed with brine, dried on Na2SO4 and concentrated. The residue was recrystallized from hot EtOAc(200 mL)/TBME (400 mL) to afford a white, free-flowing solid. Recrystallization from hot EtOAc (700 mL) afforded pure (2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-6,7-dihydro-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone as a white solid (54.3 g, 124 mmol, 67%). MS-EI (m/z): [M+H]+ observed: 439.0.

<u>(R*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone:</u>

Chiral separation of (2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone (54.3 g) was performed on chiral SFC (Stationary phase: CHIRALCEL OD-H 5µm 250x20mm), Mobile phase: 85% CO2, 15% EtOH). 26.7 grams of (R*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoropyridin-2-yl)-4-methyl-1H-imidazo[4,5-c]pyridin-5(4H)-yl)methanone was obtained.
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.45 – 8.29 (m, H), 7.99 – 7.86 (m, H), 7.81 – 7.70 (m, 1H), 7.64 – 7.29 (m, 4H), 5.87 – 5.75 (m, 0.7H), 5.15 – 5.01 (m, 0.6H), 4.71 – 4.58 (m, 0.3H), 4.57 – 4.46 (m, 0.4H), 3.61 – 3.46 (m, 1H), 3.44 – 3.33 (m, 0.3H), 3.27 – 3.09 (m, 1.2H), 3.00 – 2.72 (m, 1.5H), 1.67 – 1.59 (m, 1.7H), 1.51 – 1.46 (d, J = 6.8 Hz, 0.8H), 1.44 – 1.39 (d, J = 6.9 Hz, 0.5H). Elemental analysis: Theory: C, 54.74, H, 3.45, N, 12.77; observed: C, 54.58, H, 3.58, N, 12.70.

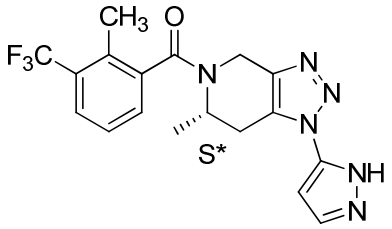
Examples 346 and 347 were prepared by separation of the enantiomers of Example 154 using SFC (Chiralcel OD-H 5µm 250*20mm, mobile phase 80% CO_2, 20% mixture of EtOH/iPrOH 50/50 v/v(+0.3% $iPrNH_2$)).

Example 346 (*R**)-(6-methyl-1-(1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2-methyl-3-(trifluoromethyl)phenyl)methanone



MS (ESI) mass calcd $C_{18}H_{17}F_3N_6O$, 390.1 m/z found; 391.1 $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.36 – 11.01 (s, 0.6H), 10.55 – 10.26 (s, 0.4H), 7.75 – 7.61 (m, 2H), 7.46 – 7.24 (m, 2H), 6.87 – 6.80 (m, 1H), 5.93 – 5.69 (m, 1H), 4.61 – 4.26 (m, 1.7H), 4.19 – 4.07 (m, 0.3H), 3.58 – 2.91 (m, 2H), 2.57 – 2.18 (m, 3H), 1.45 – 1.15 (m, 3H).

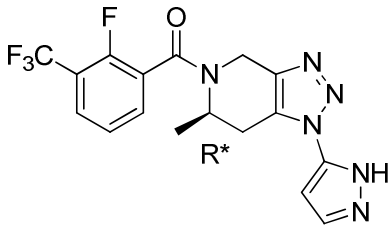
Example 347 (*S**)-(6-methyl-1-(1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2-methyl-3-(trifluoromethyl)phenyl)methanone



MS (ESI) mass calcd $C_{18}H_{17}F_3N_6O$, 390.1 m/z found; 391.1 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 11.36 – 11.01 (s, 0.6H), 10.55 – 10.26 (s, 0.4H), 7.75 – 7.61 (m, 2H), 7.46 – 7.24 (m, 2H), 6.87 – 6.80 (m, 1H), 5.93 – 5.69 (m, 1H), 4.61 – 4.26 (m, 1.7H), 4.19 – 4.07 (m, 0.3H), 3.58 – 2.91 (m, 2H), 2.57 – 2.18 (m, 3H), 1.45 – 1.15 (m, 3H).

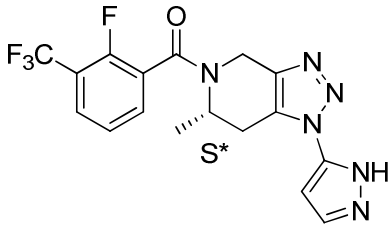
Examples 348 and 349 were prepared by separation of the enantiomers of Example 189 using SFC (Chiralpak AD-H 5µm 250*20mm, mobile phase 80% CO_2, 20% mixture of EtOH/iPrOH 50/50 v/v(+0.3% $iPrNH_2$)).

Example 348 (*R**)-(2-fluoro-3-(trifluoromethyl)phenyl)(6-methyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



MS (ESI) mass calcd $C_{17}H_{14}F_4N_6O$, 394.1 m/z found; 395.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 10.70 – 10.39 (s, 0.6H), 10.29 – 9.98 (s, 0.4H), 7.78 – 7.31 (m, 4H), 6.90 – 6.80 (m, 1H), 5.93 – 5.58 (m, 1H), 4.73 – 4.16 (m, 2H), 3.49 – 2.96 (m, 2H), 1.44 – 1.10 (m, 3H).

Example 349 (*S**)-(2-fluoro-3-(trifluoromethyl)phenyl)(6-methyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone

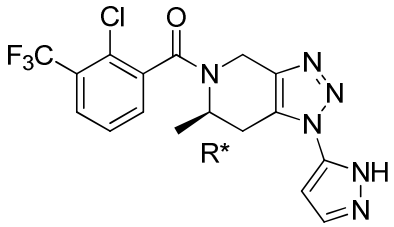


MS (ESI) mass calcd $C_{17}H_{14}F_4N_6O$, 394.1 m/z found; 395.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 10.70 – 10.39 (s, 0.6H), 10.29 – 9.98 (s, 0.4H), 7.78 – 7.31 (m, 4H), 6.90 – 6.80

(m, 1H), 5.93 – 5.58 (m, 1H), 4.73 – 4.16 (m, 2H), 3.49 – 2.96 (m, 2H), 1.44 – 1.10 (m, 3H).

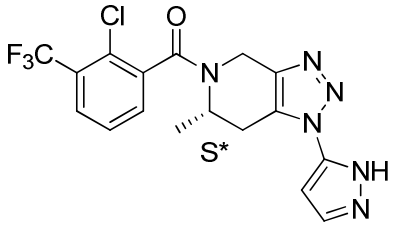
Examples 350 and 351 were prepared by separation of the enantiomers of Example 210 using SFC (Chiralpak AD-H 5µm 250*20mm, mobile phase 80% CO_2, 20% mixture of EtOH/iPrOH 50/50 v/v(+0.3% $iPrNH_2$)).

Example 350 (*R**)-(2-chloro-3-(trifluoromethyl)phenyl)(6-methyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



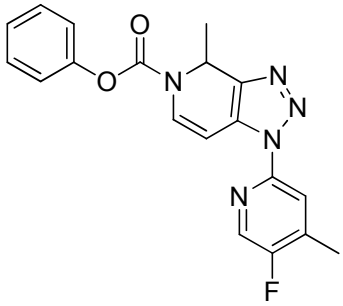
MS (ESI) mass calcd $C_{17}H_{14}ClF_3N_6O$, 410.1 m/z found; 411.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 10.99 – 10.68 (s, 0.6H), 10.39 – 10.11 (s, 0.4H), 7.83 – 7.39 (m, 4H), 6.88 – 6.80 (m, 1H), 5.94 – 5.65 (m, 1H), 4.69 – 4.30 (m, 1.7H), 4.15 – 4.03 (m, 0.3H), 3.54 – 2.94 (m, 2H), 1.44 – 1.15 (m, 3H).

Example 351 (*S**)-(2-chloro-3-(trifluoromethyl)phenyl)(6-methyl-1-(1H-pyrazol-5-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



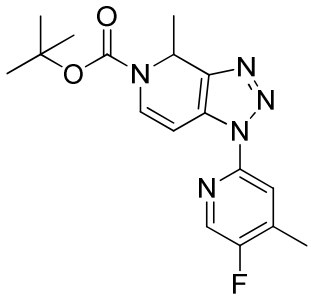
MS (ESI) mass calcd $C_{17}H_{14}ClF_3N_6O$, 410.1 m/z found, 411.1 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 10.99 – 10.68 (s, 0.6H), 10.39 – 10.11 (s, 0.4H), 7.83 – 7.39 (m, 4H), 6.88 – 6.80 (m, 1H), 5.94 – 5.65 (m, 1H), 4.69 – 4.30 (m, 1.7H), 4.15 – 4.03 (m, 0.3H), 3.54 – 2.94 (m, 2H), 1.44 – 1.15 (m, 3H).

Intermediate Q: phenyl 1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-1H-[1,2,3]triazolo[4,5-c]pyridine-5(4H)-carboxylate.



Step A: phenyl 1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-1H-[1,2,3]triazolo[4,5-c]pyridine-5(4H)-carboxylate. Under a nitrogen atmosphere was added 3.0 M MeMgBr in Et_2O (2.04 mL, 6.11 mmol) to a mixture of 1-(5-fluoro-4-methylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine (700 mg, 3.05 mmol) in THF at -78C. After 5 minutes, phenyl chloroformate (0.58 mL, 4.58 mmol) was slowly added to the reaction mixture at -78C. The reaction mixture was allowed to sitr at -78C for another 10 min and was then allowed to slowly warm to r.t. After 1 h, the reaction mixture was quenched with saturated NH_4Cl(aq) (30 mL). Water (15 mL) was added, and the mixture was extracted using EtOAc (3 x 50 mL). The combined organics were dried over MgSO4, filtered and concentrated under vacuum. The crude material was purified by chromatography on SiO_2 eluting with EtOAc/hexanes to afford the title compound. MS (ESI) mass calcd. $C_{19}H_{16}FN_5O_2$, 365.13; m/z found 366.10 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.26 (s, 1H), 8.04 (d, *J* = 5.4 Hz, 1H), 7.51 – 7.37 (m, 2H), 7.31 – 7.25 (m, 1H), 7.23 – 7.15 (m, 3H), 6.75 – 6.61 (m, 1H), 6.08 – 5.87 (m, 1H), 2.48 – 2.41 (m, 3H), 1.68 – 1.37 (m, 3H).

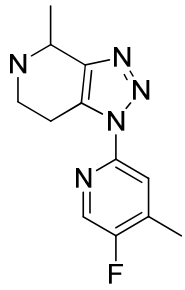
Intermediate R: tert-butyl 1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-1H-[1,2,3]triazolo[4,5-c]pyridine-5(4H)-carboxylate.



Step B: tert-butyl 1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-1H-[1,2,3]triazolo[4,5-c]pyridine-5(4H)-carboxylate. Under a nitrogen atmosphere was added a suspension of KOtBu (332 mg, 2.96 mmol) in THF (3 mL) to a mixture of phenyl 1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-1H-[1,2,3]triazolo[4,5-c]pyridine-5(4H)-carboxylate (900 mg, 2.46 mmol) in THF at room temperature. After 1h, water (30 mL) was added to the

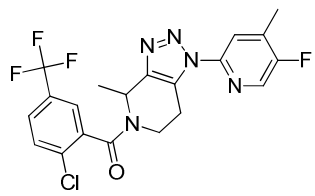
reaction mixture. The mixture was extracted using EtOAc (3 x 45 mL). The combined organics layers were washed with NaOH 0.5N (1 x 150 mL), dried over $MgSO_4$, filtered and concentrated under vacuum to afford the title product. MS (ESI) mass calcd. $C_{17}H_{20}FN_5O_2$, 345.16; m/z found 346.00 $[M+H]^+$.

Intermediate S: 1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine.



Step C: 1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine. A mixture of 1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine (250 mg, 0.72 mmol) and Platinum oxide(IV) (65.7 mg, 0.29 mmol) in MeOH (9 mL) was allowed to stir at room temperature under a hydrogen atmosphere (1 atm, balloon). After 16 hours, complete conversion was observed and the reaction mixture was filtered through an acrodisc serynge filter. The crude material was then dissolved in DCM (20 mL). The reaction mixture was purged with nitrogen and TFA (2.31 mL, 30.2 mmol) was added to the reaction mixture at room temperature. After completion, the reaction mixture was quenched with saturated $NaHCO_3$(aq) (40 mL). The mixture was extracted using DCM (3 x 50 mL). The combined organics were combined, dried over MgSO4, filtered and concentrated under vacuum to afford the title product. MS (ESI) mass calcd. $C_{12}H_{14}FN_5$, 247.12; m/z found 248.00 $[M+H]^+$.

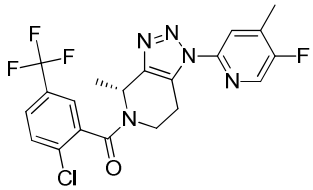
Example 352: (2-chloro-5-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



HATU (126.9 mg, 0.33 mmol) was added to a mixture of Intermediate S (75 mg, 0.30 mmol), 2-chloro-5-(trifluoromethyl)benzoic acid (68.1 mg, 0.30) and Hunig's base (0.11 mL, 0.61 mmol) in DMF (5 mL) at room temperature. After completion, saturated

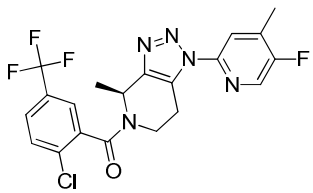
NaHCO3(aq) (15 mL) and DCM (15 mL) were added. The mixture was extracted with DCM (3 x 25 mL). The combined organics were dried over $MgSO_4$, filtered and concentrated under vacuum. The title product was purified by chromatography on a Prep Agilent system with a XBridge C18 OBD 50x100 mm column eluting with 5 to 99% (0.05% NH_4OH in H_2O)/ACN over 17 min. MS (ESI) mass calcd. $C_{20}H_{16}ClF_4N_5O$, 453.10; m/z found 453.90 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.28 – 8.14 (m, 1H), 8.07 – 7.99 (m, 1H), 7.69 – 7.37 (m, 3H), 6.10 – 6.00 (m, 0.6H), 5.16 – 5.04 (m, 0.4H), 4.93 – 4.70 (m, 0.4H), 3.65 – 2.95 (m, 3.6H), 2.43 (s, 3H), 1.77 – 1.43 (m, 3H).

Example 353 (R*)-(2-chloro-5-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 352 performed using a CHIRALPAK AD-H (5µm, 250x20mm) column and a mobile phase of 80% CO_2, 20% MeOH/iPrOH 50/50 v/v. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) and a mobile phase of 80% CO_2, 20% MeOH/iPrOH 50/50 v/v containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 3.59 min retention time). MS (ESI) mass calcd. $C_{20}H_{16}ClF_4N_5O$, 453.10; m/z found 453.90 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.28 – 8.14 (m, 1H), 8.07 – 7.99 (m, 1H), 7.69 – 7.37 (m, 3H), 6.10 – 6.00 (m, 0.6H), 5.16 – 5.04 (m, 0.4H), 4.93 – 4.70 (m, 0.4H), 3.65 – 2.95 (m, 3.6H), 2.43 (s, 3H), 1.77 – 1.43 (m, 3H).

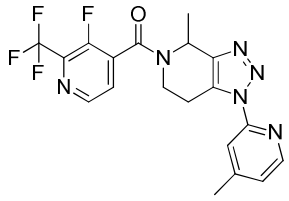
Example 354 (S*)-(2-chloro-5-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 352 performed using a CHIRALPAK AD-H (5µm, 250x20mm) column and a mobile phase of 80% CO_2, 20% MeOH/iPrOH 50/50 v/v. The

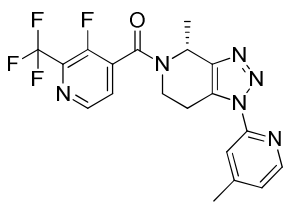
enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) and a mobile phase of 80% CO_2, 20% MeOH/iPrOH 50/50 v/v containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 4.35 min retention time). MS (ESI) mass calcd. $C_{20}H_{16}ClF_4N_5O$, 453.10; m/z found 453.90 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.28 – 8.14 (m, 1H), 8.07 – 7.99 (m, 1H), 7.69 – 7.37 (m, 3H), 6.10 – 6.00 (m, 0.6H), 5.16 – 5.04 (m, 0.4H), 4.93 – 4.70 (m, 0.4H), 3.65 – 2.95 (m, 3.6H), 2.43 (s, 3H), 1.77 – 1.43 (m, 3H).

Example 355 (3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example 352 substituting 3-fluoro-2-(trifluoromethyl)isonicotinic acid for 2-chloro-5-(trifluoromethyl)benzoic acid and 1-(4-methylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine for 1-(5-fluoro-4-methylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine in Step A, and substituting platinum oxide(IV) with Pd/C 10% (0.05 eq.) in Step C. MS (ESI) mass calcd. $C_{19}H_{16}F_4N_6O$, 420.13; m/z found 420.90 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.66 – 8.56 (m, 1H), 8.38 – 8.26 (m, 1H), 8.03 – 7.91 (m, 1H), 7.64 – 7.45 (m, 1H), 7.21 – 7.11 (m, 1H), 6.01 (q, *J* = 6.7 Hz, 0.6H), 5.09 – 5.00 (m, 0.4H), 4.80 (q, *J* = 6.7 Hz, 0.4H), 3.66 – 3.08 (m, 3.6H), 2.48 (s, 3H), 1.73 – 1.54 (m, 3H).

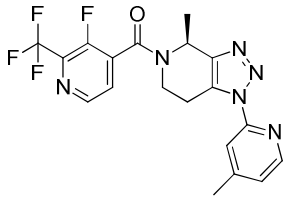
Example 356 (R*)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 355 performed using a CHIRALCEL OD-H (5µm,

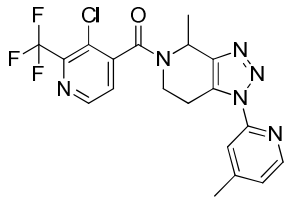
250x20mm) column and a mobile phase of 70% CO_2, 30% iPrOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALCEL OD-H (250x4.6mm) and a mobile phase of 70% CO_2, 30% iPrOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 2.87 min retention time). MS (ESI) mass calcd. $C_{19}H_{16}F_4N_6O$, 420.13; m/z found 420.90 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.66 – 8.56 (m, 1H), 8.38 – 8.26 (m, 1H), 8.03 – 7.91 (m, 1H), 7.64 – 7.45 (m, 1H), 7.21 – 7.11 (m, 1H), 6.01 (q, *J* = 6.7 Hz, 0.6H), 5.09 – 5.00 (m, 0.4H), 4.80 (q, *J* = 6.7 Hz, 0.4H), 3.66 – 3.08 (m, 3.6H), 2.48 (s, 3H), 1.73 – 1.54 (m, 3H).

Example 357 (S*)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



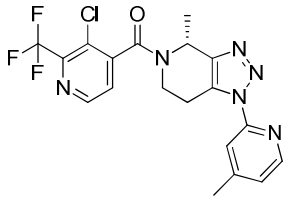
The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 355 performed using a CHIRALCEL OD-H (5µm, 250x20mm) column and a mobile phase of 70% CO_2, 30% iPrOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALCEL OD-H (250x4.6mm) and a mobile phase of 70% CO_2, 30% iPrOH containing 0.3% $iPrNH_2$ over 7 minutes. (99.53% single enantiomer, 3.97 min retention time). MS (ESI) mass calcd. $C_{19}H_{16}F_4N_6O$, 420.13; m/z found 420.90 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.66 – 8.56 (m, 1H), 8.38 – 8.26 (m, 1H), 8.03 – 7.91 (m, 1H), 7.64 – 7.45 (m, 1H), 7.21 – 7.11 (m, 1H), 6.01 (q, *J* = 6.7 Hz, 0.6H), 5.09 – 5.00 (m, 0.4H), 4.80 (q, *J* = 6.7 Hz, 0.4H), 3.66 – 3.08 (m, 3.6H), 2.48 (s, 3H), 1.73 – 1.54 (m, 3H).

Example 358 (3-chloro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



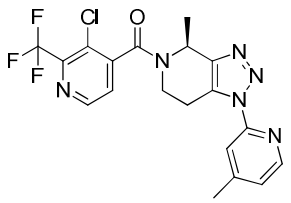
The title compound was prepared in a manner analogous to Example 355 substituting 3-chloro-2-(trifluoromethyl)isonicotinic acid for 3-fluoro-2-(trifluoromethyl)isonicotinic acid. MS (ESI) mass calcd. $C_{19}H_{16}ClF_3N_6O$, 436.10; m/z found 436.90 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.79 – 8.58 (m, 1H), 8.40 – 8.24 (m, 1H), 8.04 – 7.92 (m, 1H), 7.55 – 7.12 (m, 2H), 6.10 – 5.99 (m, 0.6H), 5.14 – 5.04 (m, 0.4H), 4.85 – 4.63 (m, 0.4H), 3.62 – 2.99 (m, 3.6H), 2.55 – 2.45 (s, 3H), 1.77 – 1.48 (m, 3H).

Example 359 (R*)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 358 performed using a CHIRALCEL OD-H (5µm, 250x20mm) column and a mobile phase of 70% CO_2, 30% iPrOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALCEL OD-H (250x4.6mm) and a mobile phase of 70% CO_2, 30% iPrOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 3.60 min retention time). MS (ESI) mass calcd. $C_{19}H_{16}ClF_3N_6O$, 436.10; m/z found 436.90 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.75 – 8.59 (m, 1H), 8.39 – 8.26 (m, 1H), 8.02 – 7.94 (m, 1H), 7.54 – 7.12 (m, 2H), 6.09 – 5.99 (m, 0.6H), 5.14 – 5.04 (m, 0.4H), 4.84 – 4.64 (m, 0.4H), 3.62 – 3.00 (m, 3.6H), 2.49 (s, 3H), 1.79 – 1.48 (m, 3H).

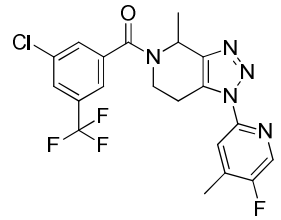
Example 360 (S*)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 358 performed using a CHIRALCEL OD-H (5µm, 250x20mm) column and a mobile phase of 70% CO_2, 30% iPrOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALCEL OD-H (250x4.6mm) and a mobile

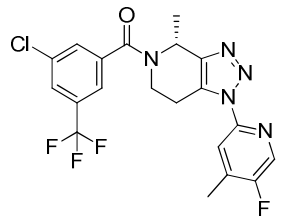
phase of 70% CO_2, 30% iPrOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 4.57 min retention time). MS (ESI) mass calcd. $C_{19}H_{16}ClF_3N_6O$, 436.10; m/z found 436.90 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.75 – 8.59 (m, 1H), 8.39 – 8.26 (m, 1H), 8.02 – 7.94 (m, 1H), 7.54 – 7.12 (m, 2H), 6.09 – 5.99 (m, 0.6H), 5.14 – 5.04 (m, 0.4H), 4.84 – 4.64 (m, 0.4H), 3.62 – 3.00 (m, 3.6H), 2.49 (s, 3H), 1.79 – 1.48 (m, 3H).

Example 361 (3-chloro-5-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example 352 substituting 3-chloro-5-(trifluoromethyl)benzoic acid for 2-chloro-5-(trifluoromethyl)benzoic acid . MS (ESI) mass calcd. $C_{20}H_{16}ClF_4N_5O$, 453.10; m/z found 453.90 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.27 – 8.18 (m, 1H), 8.09 – 7.97 (m, 1H), 7.73 – 7.70 (m, 1H), 7.64 – 7.56 (m, 2H), 6.06 – 5.82 (m, 0.5H), 5.19 – 4.76 (m, 0.8H), 3.98 – 3.68 (m, 0.5H), 3.62 – 3.02 (m, 3.2H), 2.44 (s, 3H), 1.79 – 1.48 (m, 3H).

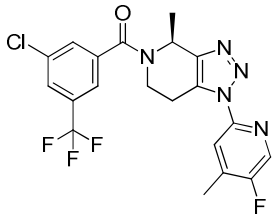
Example 362 (R*)-(3-chloro-5-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 361 performed using a CHIRALPAK AD-H (5µm, 250x20mm) column and a mobile phase of 80% CO_2, 20% MeOH/iPrOH 50/50 v/v. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) and a mobile phase of 80% CO_2, 20% MeOH/iPrOH 50/50 v/v containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 3.13 min retention time). MS (ESI) mass calcd. $C_{20}H_{16}ClF_4N_5O$, 453.10; m/z found 453.90 $[M+H]^+$. ^1H NMR (400 MHz,

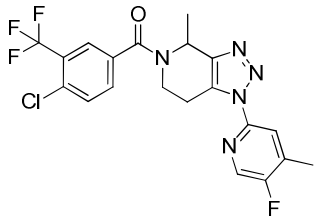
$CDCl_3$) δ 8.27 – 8.18 (m, 1H), 8.09 – 7.97 (m, 1H), 7.73 – 7.70 (m, 1H), 7.64 – 7.56 (m, 2H), 6.06 – 5.82 (m, 0.5H), 5.19 – 4.76 (m, 0.8H), 3.98 – 3.68 (m, 0.5H), 3.62 – 3.02 (m, 3.2H), 2.44 (s, 3H), 1.79 – 1.48 (m, 3H).

Example 363 (S*)-(3-chloro-5-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 361 performed using a CHIRALPAK AD-H (5µm, 250x20mm) column and a mobile phase of 80% CO_2, 20% MeOH/iPrOH 50/50 v/v. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) and a mobile phase of 80% CO_2, 20% MeOH/iPrOH 50/50 v/v containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 4.05 min retention time). MS (ESI) mass calcd. $C_{20}H_{16}ClF_4N_5O$, 453.10; m/z found 453.90 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.27 – 8.18 (m, 1H), 8.09 – 7.97 (m, 1H), 7.73 – 7.70 (m, 1H), 7.64 – 7.56 (m, 2H), 6.06 – 5.82 (m, 0.5H), 5.19 – 4.76 (m, 0.8H), 3.98 – 3.68 (m, 0.5H), 3.62 – 3.02 (m, 3.2H), 2.44 (s, 3H), 1.79 – 1.48 (m, 3H).

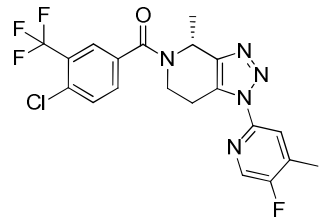
Example 364 (4-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example 352 substituting 4-chloro-3-(trifluoromethyl)benzoic acid for 2-chloro-5-(trifluoromethyl)benzoic acid . MS (ESI) mass calcd. $C_{20}H_{16}ClF_4N_5O$, 453.10; m/z found 453.90 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.22 (s, 1H), 8.11 – 7.96 (m, 1H), 7.79 (d, J = 2.0 Hz, 1H), 7.62 – 7.53 (m, 2H),

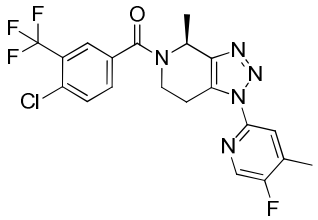
6.07 – 5.80 (m, 0.4H), 5.21 – 4.73 (s, 0.8H), 4.07 – 3.66 (m, 0.4H), 3.59 – 2.96 (m, 3.4H), 2.49 – 2.35 (m, 3H), 1.69 – 1.61 (m, 3H).

Example 365 (R*)-(4-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 364 performed using a CHIRALPAK AD-H (5µm, 250x20mm) column and a mobile phase of 80% CO_2, 20% MeOH/iPrOH 50/50 v/v. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) and a mobile phase of 75% CO_2, 25% MeOH/iPrOH 50/50 v/v containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 3.85 min retention time). MS (ESI) mass calcd. $C_{20}H_{16}ClF_4N_5O$, 453.10; m/z found 453.90 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 8.11 – 7.96 (m, 1H), 7.79 (d, *J* = 2.0 Hz, 1H), 7.62 – 7.53 (m, 2H), 6.07 – 5.80 (m, 0.4H), 5.21 – 4.73 (s, 0.8H), 4.07 – 3.66 (m, 0.4H), 3.59 – 2.96 (m, 3.4H), 2.49 – 2.35 (m, 3H), 1.69 – 1.61 (m, 3H).

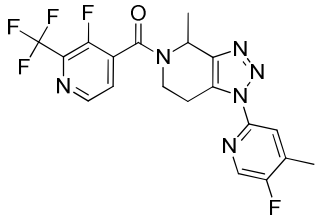
Example 366 (S*)-(4-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 364 performed using a CHIRALPAK AD-H (5µm, 250x20mm) column and a mobile phase of 80% CO_2, 20% MeOH/iPrOH 50/50 v/v. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) and a mobile phase of 75% CO_2, 25% MeOH/iPrOH 50/50 v/v containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 4.63 min retention time). MS

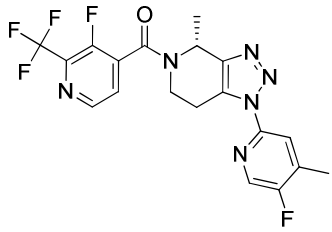
(ESI) mass calcd. $C_{20}H_{16}ClF_4N_5O$, 453.10; m/z found 453.90 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 8.11 – 7.96 (m, 1H), 7.79 (d, *J* = 2.0 Hz, 1H), 7.62 – 7.53 (m, 2H), 6.07 – 5.80 (m, 0.4H), 5.21 – 4.73 (s, 0.8H), 4.07 – 3.66 (m, 0.4H), 3.59 – 2.96 (m, 3.4H), 2.49 – 2.35 (m, 3H), 1.69 – 1.61 (m, 3H).

Example 367 (3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example 352 substituting 3-fluoro-2-(trifluoromethyl)isonicotinic acid for 2-chloro-5-(trifluoromethyl)benzoic acid. MS (ESI) mass calcd. $C_{19}H_{15}F_5N_6O$, 438.12; m/z found 438.90 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.66 – 8.56 (m, 1H), 8.28 – 8.15 (m, 1H), 8.08 – 7.97 (m, 1H), 7.66 – 7.46 (m, 1H), 6.01 (q, *J* = 6.6 Hz, 0.6H), 5.08 – 5.00 (m, 0.4H), 4.80 (q, *J* = 6.6 Hz, 0.4H), 3.71 – 3.03 (m, 3.6H), 2.52 – 2.38 (m, 3H), 1.78 – 1.56 (m, 3H).

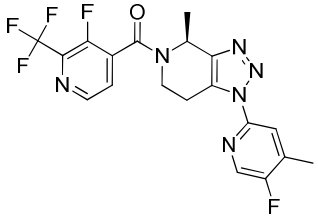
Example 368 (R*)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 367 performed using a CHIRALCEL OD-H (5µm, 250x20mm) column and a mobile phase of 70% CO_2, 30% iPrOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALCEL OD-H (250x4.6mm) column and a mobile phase of 70% CO_2, 30% iPrOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 2.78 min retention time). MS (ESI) mass calcd. $C_{19}H_{15}F_5N_6O$, 438.12; m/z found 439.3 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.66 – 8.56 (m, 1H), 8.28 – 8.15

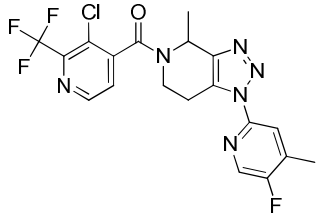
(m, 1H), 8.08 – 7.97 (m, 1H), 7.66 – 7.46 (m, 1H), 6.01 (q, *J* = 6.6 Hz, 0.6H), 5.08 – 5.00 (m, 0.4H), 4.80 (q, *J* = 6.6 Hz, 0.4H), 3.71 – 3.03 (m, 3.6H), 2.52 – 2.38 (m, 3H), 1.78 – 1.56 (m, 3H).

Example 369 (S*)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 367 performed using a CHIRALCEL OD-H (5µm, 250x20mm) column and a mobile phase of 70% CO_2, 30% iPrOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALCEL OD-H (250x4.6mm) column and a mobile phase of 70% CO_2, 30% iPrOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 5.52 min retention time). MS (ESI) mass calcd. $C_{19}H_{15}F_5N_6O$, 438.12; m/z found 439.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.66 – 8.56 (m, 1H), 8.28 – 8.15 (m, 1H), 8.08 – 7.97 (m, 1H), 7.66 – 7.46 (m, 1H), 6.01 (q, *J* = 6.6 Hz, 0.6H), 5.08 – 5.00 (m, 0.4H), 4.80 (q, *J* = 6.6 Hz, 0.4H), 3.71 – 3.03 (m, 3.6H), 2.52 – 2.38 (m, 3H), 1.78 – 1.56 (m, 3H).

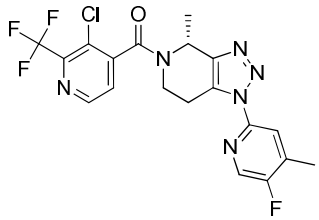
Example 370 (3-chloro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example 352 substituting 3-chloro-2-(trifluoromethyl)isonicotinic acid for 2-chloro-5-(trifluoromethyl)benzoic acid. MS (ESI) mass calcd. $C_{19}H_{15}ClF_4N_6O$, 454.09; m/z found 454.90 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.73 – 8.59 (m, 1H), 8.26 – 8.15 (m, 1H), 8.07 – 7.99 (m, 1H), 7.52 – 7.26

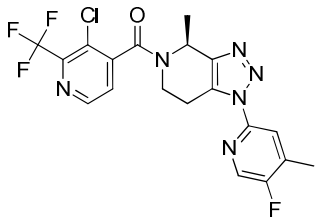
(m, 1H), 6.08 – 5.98 (m, 0.6H), 5.12 – 5.04 (m, 0.4H), 4.83 – 4.63 (m, 0.4H), 3.60 – 2.97 (m, 3.6H), 2.49 – 2.40 (m, 3H), 1.76 – 1.48 (m, 3H).

Example 371 (R*)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 370 performed using a CHIRALCEL OD-H (5µm, 250x20mm) column and a mobile phase of 70% CO_2, 30% iPrOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALCEL OD-H (250x4.6mm) column and a mobile phase of 70% CO_2, 30% iPrOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 3.38 min retention time). MS (ESI) mass calcd. $C_{19}H_{15}ClF_4N_6O$, 454.09; m/z found 454.90 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.73 – 8.59 (m, 1H), 8.26 – 8.15 (m, 1H), 8.07 – 7.99 (m, 1H), 7.52 – 7.26 (m, 1H), 6.08 – 5.98 (m, 0.6H), 5.12 – 5.04 (m, 0.4H), 4.83 – 4.63 (m, 0.4H), 3.60 – 2.97 (m, 3.6H), 2.49 – 2.40 (m, 3H), 1.76 – 1.48 (m, 3H).

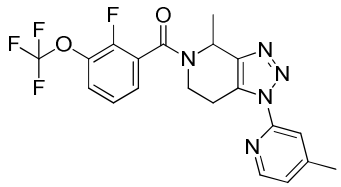
Example 372 (S*)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 370 performed using a CHIRALCEL OD-H (5µm, 250x20mm) column and a mobile phase of 70% CO_2, 30% iPrOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALCEL OD-H (250x4.6mm) column and a mobile phase of 70% CO_2, 30% iPrOH containing 0.3% $iPrNH_2$ over 7 minutes. (99.1% single enantiomer, 5.24 min retention time). MS (ESI) mass calcd. $C_{19}H_{15}ClF_4N_6O$,

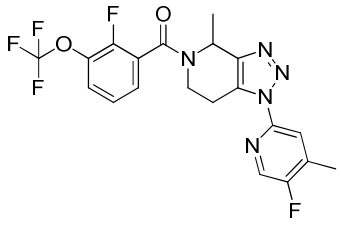
454.09; m/z found 454.90 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.73 – 8.59 (m, 1H), 8.26 – 8.15 (m, 1H), 8.07 – 7.99 (m, 1H), 7.52 – 7.26 (m, 1H), 6.08 – 5.98 (m, 0.6H), 5.12 – 5.04 (m, 0.4H), 4.83 – 4.63 (m, 0.4H), 3.60 – 2.97 (m, 3.6H), 2.49 – 2.40 (m, 3H), 1.76 – 1.48 (m, 3H).

Example 373 (2-fluoro-3-(trifluoromethoxy)phenyl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



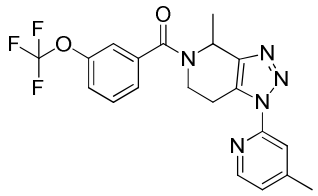
The title compound was prepared in a manner analogous to Example 355 substituting 2-fluoro-3-(trifluoromethoxy)benzoic acid for 3-fluoro-2-(trifluoromethyl)isonicotinic acid. MS (ESI) mass calcd. $C_{20}H_{17}F_4N_5O_2$, 435.13; m/z found 435.90 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.41 – 8.20 (m, 1H), 8.05 – 7.89 (m, 1H), 7.49 – 7.05 (m, 4H), 6.10 – 5.94 (m, 0.6H), 5.10 – 5.01 (m, 0.4H), 4.95 – 4.86 (m, 0.4H), 3.79 – 2.94 (m, 3.6H), 2.48 (s, 3H), 1.77 – 1.44 (m, 3H).

Example 374 (2-fluoro-3-(trifluoromethoxy)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



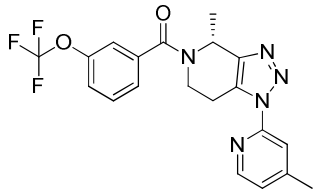
The title compound was prepared in a manner analogous to Example 352 substituting 2-fluoro-3-(trifluoromethoxy)benzoic acid for 2-chloro-5-(trifluoromethyl)benzoic acid. MS (ESI) mass calcd. $C_{20}H_{16}F_5N_5O_2$, 453.12; m/z found 453.90 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.29 – 8.14 (m, 1H), 8.09 – 7.97 (m, 1H), 7.47 – 7.20 (m, 3H), 6.09 – 5.95 (m, 0.6H), 5.08 – 5.01 (m, 0.4H), 4.93 – 4.86 (m, 0.4H), 3.76 – 3.67 (m, 0.6H), 3.54 – 2.99 (m, 3H), 2.48 – 2.40 (m, 3H), 1.72 – 1.50 (m, 3H).

Example 375 (4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(3-(trifluoromethoxy)phenyl)methanone



The title compound was prepared in a manner analogous to Example 159 substituting 1-(4-methylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine for 1-(3,5-dimethylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine and 3-(trifluoromethoxy)benzoic acid in step A for Intermediate 12. Title compound was purified by chromatography on SiO_2 eluting with EtOAc/hexanes to afford the title compound MS (ESI) mass calcd. $C_{20}H_{18}F_3N_5O_2$, 417.14; m/z found 417.95 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.41 – 8.22 (m, 1H), 8.06 – 7.87 (m, 1H), 7.55 – 7.07 (m, 5H), 6.08 – 5.81 (m, 0.5H), 5.19 – 4.74 (m, 0.8H), 4.04 – 3.71 (m, 0.4H), 3.57 – 2.97 (m, 3.3H), 2.59 – 2.26 (s, 3H), 1.82 – 1.40 (s, 3H).

Example 376 (R*)-(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(3-(trifluoromethoxy)phenyl)methanone

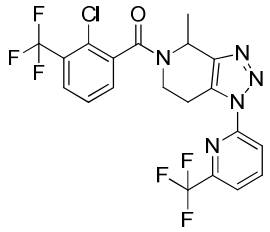


The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 375 performed using a CHIRALPAK AD-H (5µm, 250x20mm) column and a mobile phase of 80% CO_2, 20% MeOH/iPrOH 50/50 v/v. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (5µm, 250x4.6mm) column and a mobile phase of 80% CO_2, 20% MeOH/iPrOH 50/50 v/v containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 3.48 min retention time). MS (ESI) mass calcd. $C_{20}H_{18}F_3N_5O_2$, 417.14; m/z found 417.90 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.41 – 8.22 (m, 1H), 8.06 – 7.87 (m, 1H), 7.55 – 7.07 (m, 5H), 6.08 – 5.81 (m, 0.5H), 5.19 – 4.74 (m, 0.8H), 4.04 – 3.71 (m, 0.4H), 3.57 – 2.97 (m, 3.3H), 2.59 – 2.26 (s, 3H), 1.82 – 1.40 (s, 3H).

Example 377 (S*)-(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(3-(trifluoromethoxy)phenyl)methanone

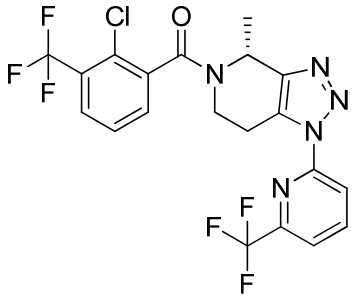
The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 375 performed using a CHIRALPAK AD-H (5µm, 250x20mm) column and a mobile phase of 80% CO_2, 20% MeOH/iPrOH 50/50 v/v. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) column and a mobile phase of 80% CO_2, 20% MeOH/iPrOH 50/50 v/v over 7 minutes. (100% single enantiomer, 4.08 min retention time). MS (ESI) mass calcd. $C_{20}H_{18}F_3N_5O_2$, 417.14; m/z found 417.90 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.41 – 8.22 (m, 1H), 8.06 – 7.87 (m, 1H), 7.55 – 7.07 (m, 5H), 6.08 – 5.81 (m, 0.5H), 5.19 – 4.74 (m, 0.8H), 4.04 – 3.71 (m, 0.4H), 3.57 – 2.97 (m, 3.3H), 2.59 – 2.26 (s, 3H), 1.82 – 1.40 (s, 3H).

Example 378 (2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-(trifluoromethyl)pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



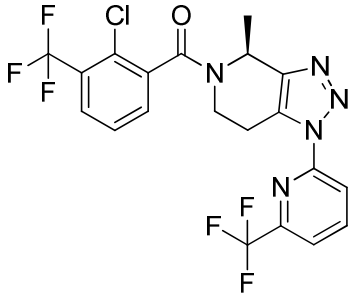
The title compound was prepared in a manner analogous to Example 159 substituting 1-(3,5-dimethylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine for 1-(6-(trifluoromethyl)pyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine in step A. Title compound was purified by chromatography on SiO_2 eluting with EtOAc/hexanes followed by chromatography on a Prep Agilent system with a XBridge C18 OBD 50x100 mm column eluting with 5 to 99% (0.05% NH_4OH in H_2O)/ACN over 17 min to afford the title compound. MS (ESI) mass calcd. $C_{20}H_{14}ClF_6N_5O$, 489.08; m/z found 489.80 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.46 – 8.37 (m, 1H), 8.17 – 8.09 (m, 1H), 7.83 – 7.68 (m, 2H), 7.59 – 7.28 (m, 2H), 6.14 – 6.01 (m, 0.6H), 5.19 – 5.10 (m, 0.3H), 4.91 – 4.72 (m, 0.4H), 3.71 – 2.98 (m, 3.7H), 1.74 – 1.47 (m, 3H).

Example 379 (R*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-(trifluoromethyl)pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 378 performed using a WHELK O1 (S,S) (5µm, 250x21.1mm) column and a mobile phase of 60% CO_2, 40% EtOH. The enantiomeric purity was confirmed by analytical SFC using a WHELK O1 (S,S) (250x4.6mm) and a mobile phase of 60% CO_2, 40% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 3.39 min retention time). MS (ESI) mass calcd. $C_{20}H_{14}ClF_6N_5O$, 489.08; m/z found 489.80 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.46 – 8.37 (m, 1H), 8.17 – 8.09 (m, 1H), 7.83 – 7.68 (m, 2H), 7.59 – 7.28 (m, 2H), 6.14 – 6.01 (m, 0.6H), 5.19 – 5.10 (m, 0.3H), 4.91 – 4.72 (m, 0.4H), 3.71 – 2.98 (m, 3.7H), 1.74 – 1.47 (m, 3H).

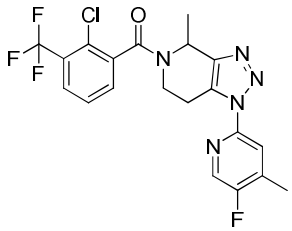
Example 380 (S*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-(trifluoromethyl)pyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 378 performed using a WHELK O1 (S,S) (5µm, 250x21.1mm) column and a mobile phase of 60% CO_2, 40% EtOH. The enantiomeric purity was confirmed by analytical SFC using a WHELK O1 (S,S) (250x4.6mm) and a mobile phase of 60% CO_2, 40% EtOH containing 0.3% $iPrNH_2$ over 7 minutes.. (100% single enantiomer, 5.51 min retention time). MS (ESI) mass calcd. $C_{20}H_{14}ClF_6N_5O$, 489.08; m/z found 489.80 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.46 – 8.37 (m, 1H),

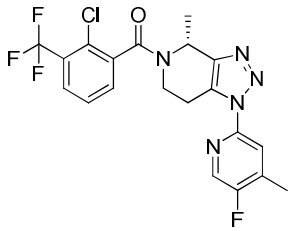
8.17 – 8.09 (m, 1H), 7.83 – 7.68 (m, 2H), 7.59 – 7.28 (m, 2H), 6.14 – 6.01 (m, 0.6H), 5.19 – 5.10 (m, 0.3H), 4.91 – 4.72 (m, 0.4H), 3.71 – 2.98 (m, 3.7H), 1.74 – 1.47 (m, 3H).

Example 381 (2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example 159 substituting for 1-(5-fluoro-4-methylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine in step A for 1-(3,5-dimethylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine. Title compound was purified by chromatography on SiO_2 eluting with EtOAc/hexanes. MS (ESI) mass calcd. $C_{20}H_{16}ClF_4N_5O$, 453.10; m/z found 454.10 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 8.27 – 8.13 (m, 1H), 8.07 – 7.98 (m, 1H), 7.81 – 7.75 (m, 1H), 7.58 – 7.28 (m, 2H), 6.10 – 6.01 (m, 0.6H), 5.15 – 5.07 (m, 0.4H), 4.89 – 4.70 (m, 0.4H), 3.64 – 2.94 (m, 3.6H), 2.47 – 2.37 (m, 3H), 1.72 – 1.42 (m, 3H).

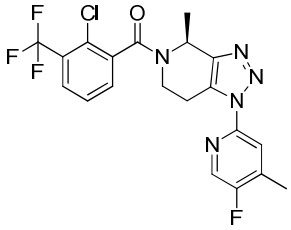
Example 382 (R*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 381 performed using a WHELK O1 (S,S) (5µm, 250x21.1mm) column and a mobile phase of 65% CO_2, 35% MeOH. The enantiomeric purity was confirmed by analytical SFC using a WHELK O1 (S,S) (250x4.6mm) and a mobile phase of 50% CO_2, 50% MeOH over 7 minutes. (100% single enantiomer, 2.84 min retention time). MS (ESI) mass calcd. $C_{20}H_{16}ClF_4N_5O$, 453.10; m/z found 453.90 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.27 – 8.13 (m, 1H), 8.07 – 7.98 (m, 1H), 7.81 – 7.75 (m,

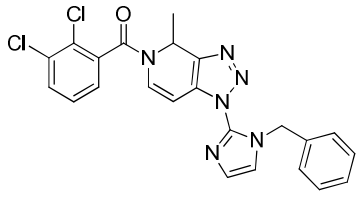
1H), 7.58 – 7.28 (m, 2H), 6.10 – 6.01 (m, 0.6H), 5.15 – 5.07 (m, 0.4H), 4.89 – 4.70 (m, 0.4H), 3.64 – 2.94 (m, 3.6H), 2.47 – 2.37 (m, 3H), 1.72 – 1.42 (m, 3H).

Example 383 (S*)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(5-fluoro-4-methylpyridin-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



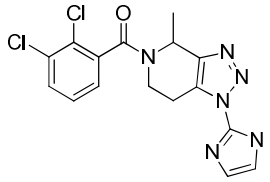
The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 381 performed using a WHELK O1 (S,S) (5µm, 250x21.1mm) column and a mobile phase of 65% CO_2, 35% MeOH. The enantiomeric purity was confirmed by analytical SFC using a WHELK O1 (S,S) (250x4.6mm) and a mobile phase of 50% CO_2, 50% MeOH over 7 minutes. (100% single enantiomer, 3.85 min retention time). MS (ESI) mass calcd. $C_{20}H_{16}ClF_4N_5O$, 453.10; m/z found 453.90 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.27 – 8.13 (m, 1H), 8.07 – 7.98 (m, 1H), 7.81 – 7.75 (m, 1H), 7.58 – 7.28 (m, 2H), 6.10 – 6.01 (m, 0.6H), 5.15 – 5.07 (m, 0.4H), 4.89 – 4.70 (m, 0.4H), 3.64 – 2.94 (m, 3.6H), 2.47 – 2.37 (m, 3H), 1.72 – 1.42 (m, 3H).

Intermediate T: (1-(1-benzyl-1H-imidazol-2-yl)-4-methyl-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2,3-dichlorophenyl)methanone



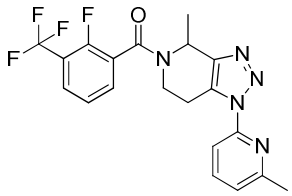
The title compound was prepared in a manner analogous to Intermediate 159 substituting 1-(1-benzyl-1H-imidazol-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine for 1-(3,5-dimethylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine and Intermediate 14 for Intermediate 12 in Step A. Title compound was not purified furthermore after the extraction. MS (ESI) mass calcd. $C_{23}H_{18}Cl_2N_6O$, 464.09; m/z found 465.10 $[M+H]^+$.

Example 384 (1-(1H-imidazol-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2,3-dichlorophenyl)methanone



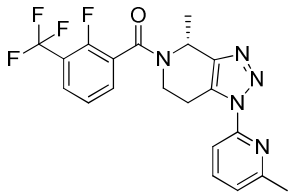
A mixture of Intermediate T (80 mg, 0.17 mmol) and of $Pd(OH)_2/C$ 20% (18.0 mg, 0.03 mmol) in MeOH was allowed to stir at room temperature under hydrogen (balloon, 1 atm) After completion, the reaction mixture was filtered through an acrodisc serynge filter. The filtrate was concentrated under vacuum and title compound was purified by chromatography on SiO_2 eluting with EtOAc/hexanes followed by chromatography on a Prep Agilent system with a XBridge C18 OBD 50x100 mm column eluting with 5 to 99% (0.05% NH_4OH in H_2O)/ACN over 17 min to afford the title compound. MS (ESI) mass calcd. $C_{16}H_{14}Cl_2N_6O$, 376.06; m/z found 377.10 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 10.15 – 9.91 (m, 1H), 7.57 – 7.49 (m, 1H), 7.38 – 6.98 (m, 4H), 6.10 – 5.98 (m, 0.6H), 5.18 – 5.11 (m, 0.4H), 4.95 – 4.72 (m, 0.4H), 3.71 – 2.91 (m, 3.6H), 1.70 – 1.43 (m, 3H).

Example 385 (2-fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



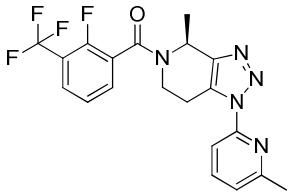
The title compound was prepared in a manner analogous to Example 159 substituting 1-(6-methylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine for 1-(3,5-dimethylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine and Intermediate 13 by Intermediate 12 in step A. Title compound was purified by chromatography on SiO_2 eluting with EtOAc/hexanes. MS (ESI) mass calcd. $C_{20}H_{17}F_4N_5O$, 419.14; m/z found 420.10 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 7.97 – 7.88 (m, 1H), 7.83 – 7.76 (m, 1H), 7.75 – 7.68 (m, 1H), 7.68 – 7.48 (m, 1H), 7.41 – 7.29 (m, 1H), 7.22 – 7.12 (m, 1H), 6.10 – 5.97 (m, 0.6H), 5.11 – 5.01 (m, *J* = 13.2, 5.3 Hz, 0.4H), 4.95 – 4.85 (m, 0.4H), 3.77 – 3.68 (m, 0.6H), 3.61 – 2.95 (m, 3H), 2.63 – 2.49 (m, 3H), 1.76 – 1.48 (m, 3H).

Example 386 (R*)-(2-fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 385 performed using a CHIRALAK AD-H (5µm, 250x20mm) column and a mobile phase of 75% CO_2, 25% EtOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALAK AD-H (250x4.6mm) column and a mobile phase of 80% CO_2, 20% EtOH over 7 minutes. (100% single enantiomer, 2.74 min retention time). MS (ESI) mass calcd. $C_{20}H_{17}F_4N_5O$, 419.14; m/z found 420.10 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 – 7.88 (m, 1H), 7.83 – 7.76 (m, 1H), 7.75 – 7.68 (m, 1H), 7.68 – 7.48 (m, 1H), 7.41 – 7.29 (m, 1H), 7.22 – 7.12 (m, 1H), 6.10 – 5.97 (m, 0.6H), 5.11 – 5.01 (m, *J* = 13.2, 5.3 Hz, 0.4H), 4.95 – 4.85 (m, 0.4H), 3.77 – 3.68 (m, 0.6H), 3.61 – 2.95 (m, 3H), 2.63 – 2.49 (m, 3H), 1.76 – 1.48 (m, 3H).

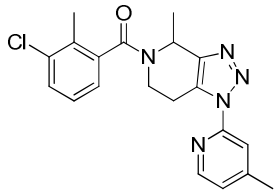
Example 387 (S*)-(2-fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 385 performed using a CHIRALAK AD-H (5µm, 250x20mm) column and a mobile phase of 75% CO_2, 25% EtOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALAK AD-H (250x4.6mm) column and a mobile phase of 80% CO_2, 20% EtOH over 7 minutes. (100% single enantiomer, 3.63 min retention time). MS (ESI) mass calcd. $C_{20}H_{17}F_4N_5O$, 419.14; m/z found 420.10 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 – 7.88 (m, 1H), 7.83 – 7.76 (m, 1H), 7.75 – 7.68 (m, 1H), 7.68 – 7.48 (m, 1H), 7.41 – 7.29 (m, 1H), 7.22 – 7.12 (m, 1H), 6.10 – 5.97 (m, 0.6H),

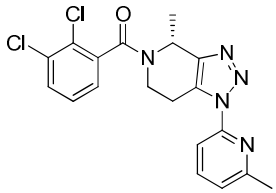
5.11 – 5.01 (m, *J* = 13.2, 5.3 Hz, 0.4H), 4.95 – 4.85 (m, 0.4H), 3.77 – 3.68 (m, 0.6H), 3.61 – 2.95 (m, 3H), 2.63 – 2.49 (m, 3H), 1.76 – 1.48 (m, 3H).

Example 388 (3-chloro-2-methylphenyl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was prepared in a manner analogous to Example 159 substituting 1-(4-methylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine for 1-(3,5-dimethylpyridin-2-yl)-1H-[1,2,3]triazolo[4,5-c]pyridine and 3-chloro-2-methylbenzoyl chloride for Intermediate 12 in step A. Title compound was purified by chromatography on SiO_2 eluting with EtOAc/hexanes. MS (ESI) mass calcd. $C_{20}H_{20}ClN_5O$, 381.14; m/z found 382.20 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.40 – 8.20 (m, 1H), 8.01 – 7.87 (m, 1H), 7.48 – 7.33 (m, 1H), 7.30 – 6.85 (m, 3H), 6.14 – 5.99 (m, 0.5H), 5.17 – 4.96 (m, 0.5H), 4.77 (q, *J* = 6.7 Hz, 0.3H), 3.74 – 2.94 (m, 3.7H), 2.55 – 2.06 (m, 6H), 1.77 – 1.56 (m, 3H).

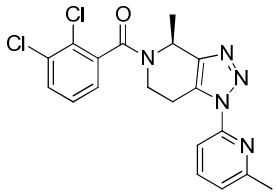
Example 389 (R*)-(2,3-dichlorophenyl)(4-methyl-1-(6-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 233 performed using a CHIRALAK AD (5µm, 250x30mm) column and a mobile phase of 50% CO_2, 50% MeOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALAK AD (250x4.6mm) column and a mobile phase of 60% CO_2, 40% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 2.50 min retention time). MS (ESI) mass calcd. $C_{19}H_{17}Cl_2N_5O$, 401.08 m/z found, 402.10 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 – 7.87 (m, 1H), 7.82 –

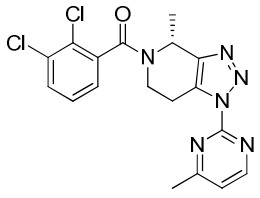
7.73 (m, 1H), 7.56 – 7.49 (m, 1H), 7.35 – 6.99 (m, 3H), 6.10 – 5.98 (m, 0.6H), 5.14 – 5.03 (m, 0.4H), 4.98 – 4.73 (m, 0.4H), 3.70 – 2.95 (m, 3.6H), 2.62 – 2.46 (m, 3H), 1.74 – 1.43 (m, 3H).

Example 390 (S*)-(2,3-dichlorophenyl)(4-methyl-1-(6-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 233 performed using a CHIRALAK AD (5µm, 250x30mm) column and a mobile phase of 50% CO_2, 50% MeOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALAK AD (250x4.6mm) column and a mobile phase of 60% CO_2, 40% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 3.59 min retention time). MS (ESI) mass calcd. $C_{19}H_{17}Cl_2N_5O$, 401.08 m/z found, 402.10 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 – 7.87 (m, 1H), 7.82 – 7.73 (m, 1H), 7.56 – 7.49 (m, 1H), 7.35 – 6.99 (m, 3H), 6.10 – 5.98 (m, 0.6H), 5.14 – 5.03 (m, 0.4H), 4.98 – 4.73 (m, 0.4H), 3.70 – 2.95 (m, 3.6H), 2.62 – 2.46 (m, 3H), 1.74 – 1.43 (m, 3H).

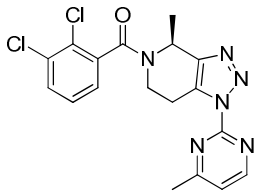
Example 391 (R*)-(2,3-dichlorophenyl)(4-methyl-1-(4-methylpyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 225 performed using a CHIRALAK AD-H (5µm, 250x20mm) column and a mobile phase of 60% CO_2, 40% EtOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALAK AD (250x4.6mm) column and a

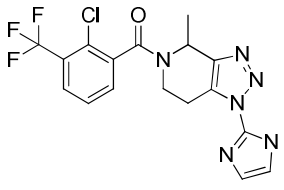
mobile phase of 60% CO_2, 40% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 2.83 min retention time). MS (ESI) mass calcd. $C_{18}H_{16}Cl_2N_6O$, 402.08 m/z found, 403.10 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.73 – 8.63 (m, 1H), 7.56 – 7.49 (m, 1H), 7.37 – 6.96 (m, 3H), 6.14 – 5.99 (m, 0.5H), 5.16 – 5.06 (m, 0.5H), 5.00 – 4.74 (m, 0.5H), 3.70 – 2.95 (m, 3.5H), 2.70 – 2.59 (m, 3H), 1.75 – 1.45 (m, 3H).

Example 392 (S*)-(2,3-dichlorophenyl)(4-methyl-1-(4-methylpyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 225 performed using a CHIRALAK AD-H (5µm, 250x20mm) column and a mobile phase of 60% CO_2, 40% EtOH. The enantiomeric purity was confirmed by analytical SFC using a CHIRALAK AD (250x4.6mm) column and a mobile phase of 60% CO_2, 40% EtOH containing 0.3% $iPrNH_2$ over 7 minutes. (100% single enantiomer, 3.79 min retention time). MS (ESI) mass calcd. $C_{18}H_{16}Cl_2N_6O$, 402.08 m/z found, 403.10 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.73 – 8.63 (m, 1H), 7.56 – 7.49 (m, 1H), 7.37 – 6.96 (m, 3H), 6.14 – 5.99 (m, 0.5H), 5.16 – 5.06 (m, 0.5H), 5.00 – 4.74 (m, 0.5H), 3.70 – 2.95 (m, 3.5H), 2.70 – 2.59 (m, 3H), 1.75 – 1.45 (m, 3H).

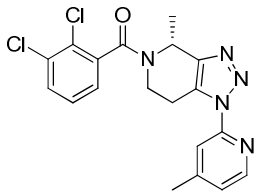
Example 393 (1-(1H-imidazol-2-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2-chloro-3-(trifluoromethyl)phenyl)methanone



The title compound was prepared in a manner analogous to Example 384 substituting Intermediate 12 by Intermediate 14 in Step A, and $Pd(OH)_2$/C 20% by Pd/C 10% (0.3 eq.). The hydrogenation occurred in a Parr shaker at room temperature under hydrogen (30 PSI).

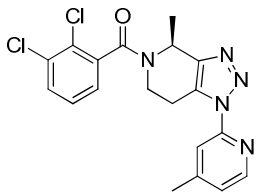
Title compound was purified by chromatography on a Prep Agilent system with a XBridge C18 OBD 50x100 mm column eluting with 5 to 99% (0.05% NH_4OH in H_2O)/ACN over 17 min followed by chromatography on SiO_2 eluting with EtOAc/hexanes. MS (ESI) mass calcd. $C_{17}H_{14}ClF_3N_6O$, 410.09; m/z found 411.10 $[M+H]^+$. ^1H NMR (500 MHz, $CDCl_3$) δ 10.16 – 9.88 (m, 1H), 7.82 – 7.75 (m, 1H), 7.59 – 7.28 (m, 2H), 7.13 – 7.02 (m, 2H), 6.11 – 5.99 (m, 0.7H), 5.19 – 5.12 (m, 0.3H), 4.89 – 4.70 (m, 0.3H), 3.68 – 3.11 (m, 3.3H), 3.02 – 2.89 (m, 0.4H), 1.73 – 1.45 (m, 3H).

Example 394 (R*)-(2,3-dichlorophenyl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



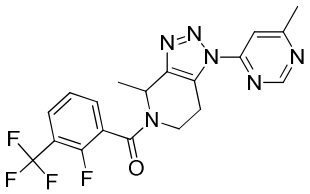
The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 237 performed using a CHIRALCEL OD-H (5µm, 250x20mm) column and a mobile phase of 70% CO_2, 30% EtOH/iPrOH 50/50 v/v containing 0.3% $iPrNH_2$. The enantiomeric purity was confirmed by analytical SFC using a CHIRALCEL OD (250x4.6mm) column and a mobile phase of 70% CO_2, 30% EtOH/iPrOH 50/50 v/v containing 0.3% $iPrNH_2$. (100% single enantiomer, 5.16 min retention time). MS (ESI) mass calcd. $C_{19}H_{17}Cl_2N_5O$, 401.08 m/z found, 402.10 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.42 – 8.21 (m, 1H), 8.01 – 7.93 (m, 1H), 7.56 – 7.49 (m, 1H), 7.37 – 7.00 (m, 3H), 6.13 – 5.99 (m, 0.6H), 5.15 – 5.04 (m, 0.4H), 4.98 – 4.73 (m, 0.4H), 3.67 – 2.96 (m, 3.6H), 2.52 – 2.40 (m, 3H), 1.80 – 1.42 (m, 3H).

Example 395 (S*)-(2,3-dichlorophenyl)(4-methyl-1-(4-methylpyridin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



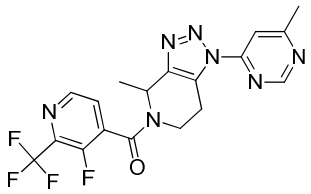
The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 237 performed using a CHIRALCEL OD-H (5µm, 250x20mm) column and a mobile phase of 70% CO_2, 30% EtOH/iPrOH 50/50 v/v containing 0.3% $iPrNH_2$. The enantiomeric purity was confirmed by analytical SFC using a CHIRALCEL OD (250x4.6mm) column and a mobile phase of 70% CO_2, 30% EtOH/iPrOH 50/50 v/v containing 0.3% $iPrNH_2$. (100% single enantiomer, 6.41 min retention time). MS (ESI) mass calcd. $C_{19}H_{17}Cl_2N_5O$, 401.08 m/z found, 402.10 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 8.42 – 8.21 (m, 1H), 8.01 – 7.93 (m, 1H), 7.56 – 7.49 (m, 1H), 7.37 – 7.00 (m, 3H), 6.13 – 5.99 (m, 0.6H), 5.15 – 5.04 (m, 0.4H), 4.98 – 4.73 (m, 0.4H), 3.67 – 2.96 (m, 3.6H), 2.52 – 2.40 (m, 3H), 1.80 – 1.42 (m, 3H).

Example 396 (2-fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-methylpyrimidin-4-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



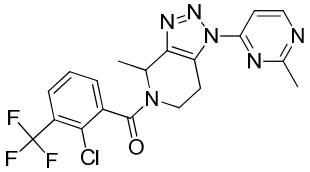
MS (ESI) mass calcd. $C_{19}H_{16}F_4N_6O$, 420.1; m/z found 421.0 $[M+H]^+$. ^1H NMR (DMSO) δ 9.06 (s, 1H), 8.11 (s, 1H), 7.93 (t, J = 7.5 Hz, 1H), 7.88 (t, J = 7.0 Hz, 1H), 7.55 (t, J = 7.6 Hz, 1H), 5.77 (q, J = 6.7 Hz, 1H), 3.69-3.58 (m, 1H), 3.55-3.44 (m, 1H), 3.30-3.23 (m, 1H), 3.20-2.98 (m, 1H), 2.62 (s, 3H), 1.57 (d, J = 6.7 Hz, 3H).

Example 397 (3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(6-methylpyrimidin-4-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



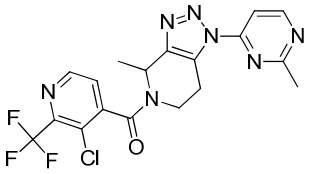
MS (ESI) mass calcd. $C_{18}H_{15}F_4N_7O$, 421.1; m/z found 422.0 $[M+H]^+$. ^1H NMR (DMSO) δ 9.07 (s, 1H), 8.72 (d, J = 4.6 Hz, 1H), 8.12 (s, 1H), 8.02 (t, J = 4.6 Hz, 1H), 5.76 (q, J = 6.7 Hz, 1H), 3.73 (d, J = 14.2 Hz, 1H), 3.54-3.45 (m, 1H), 3.31-3.24 (m, 1H), 3.22-3.08 (m, 1H), 2.62 (s, 3H), 1.58 (d, J = 6.8 Hz, 3H).

Example 398 (2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(2-methylpyrimidin-4-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



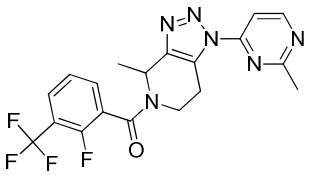
MS (ESI) mass calcd. $C_{19}H_{16}ClF_3N_6O$, 436.1; m/z found 436.9 $[M+H]^+$. ^1H NMR (DMSO) δ 8.92 (d, J = 5.2 Hz, 1H), 8.11-7.93 (m, 2H), 7.93-7.75 (m, 1H), 7.75-7.52 (m, 1H), 5.89-5.70 (m, 1H), 3.64-3.42 (m, 2H), 3.24-2.96 (m, 1H), 2.64 (s, 3H), 1.71-1.50 (m, 3H).

Example 399 (3-chloro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(2-methylpyrimidin-4-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



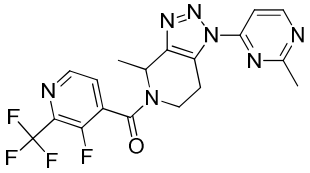
MS (ESI) mass calcd. $C_{18}H_{15}ClF_3N_7O$, 437.1; m/z found 438.0 $[M+H]^+$. ^1H NMR (XXX MHz, DMSO) δ 8.92 (d, J = 5.2 Hz, 1H), 8.81 (d, J = 4.5 Hz, 1H), 7.99-7.91 (m, 2H), 5.88-5.78 (m, 1H), 3.65-3.41 (m, 2H), 3.33-3.26 (m, 1H), 3.24-3.03 (m, 1H), 2.65 (s, 3H), 1.62-1.56 (m, 3H).

Example 400 (2-fluoro-3-(trifluoromethyl)phenyl)(4-methyl-1-(2-methylpyrimidin-4-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



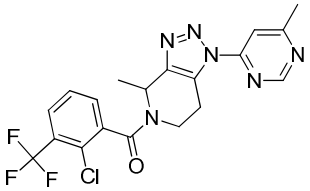
MS (ESI) mass calcd. $C_{19}H_{16}F_4N_6O$, 420.1; m/z found 421.0 $[M+H]^+$. ^1H NMR (DMSO) δ 8.97-8.88 (m, 1H), 7.98 (d, J = 5.5 Hz, 1H), 7.96-7.91 (m, 1H), 7.91-7.80 (m, 1H), 7.55 (t, J = 7.9 Hz, 1H), 5.81-5.74 (m, 1H), 3.72-3.60 (m, 1H), 3.56-3.45 (m, 1H), 3.42-3.31 (m, 1H), 3.24-2.95 (m, 2H), 2.65 (s, 3H), 1.56 (d, J = 6.6 Hz, 2H).

Example 401 (3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(2-methylpyrimidin-4-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



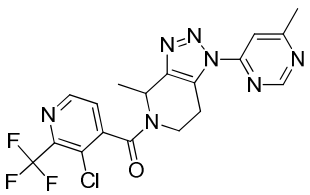
MS (ESI) mass calcd. $C_{18}H_{15}F_4N_7O$, 421.1; m/z found 422.1 $[M+H]^+$. ^1H NMR (DMSO) δ 8.93 (d, J = 5.3 Hz, 1H), 8.72 (d, J = 4.5 Hz, 1H), 8.02 (t, J = 4.5 Hz, 1H), 7.97 (d, J = 5.5 Hz, 1H), 5.76 (q, J = 6.7 Hz, 1H), 3.84-3.67 (m, 1H), 3.58-3.47 (m, 1H), 3.25-3.03 (m, 2H), 2.66 (s, 3H), 1.56 (d, J = 6.5 Hz, 3H).

Example 402 (2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(6-methylpyrimidin-4-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



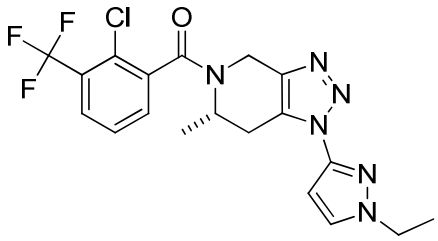
MS (ESI) mass calcd. $C_{19}H_{16}ClF_3N_6O$, 436.1; m/z found 437.0 $[M+H]^+$. ^1H NMR (DMSO) δ 9.04 (s, 1H), 8.10 (s, 1H), 7.97 (d, J = 7.7 Hz, 1H), 7.94-7.58 (m, 2H), 5.87-5.84 (m, 1H), 3.61-3.41 (m, 2H), 3.28-2.99 (m, 2H), 2.61 (s, 3H), 1.57 (d, J = 6.7 Hz, 3H).

Example 403 (3-chloro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(6-methylpyrimidin-4-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



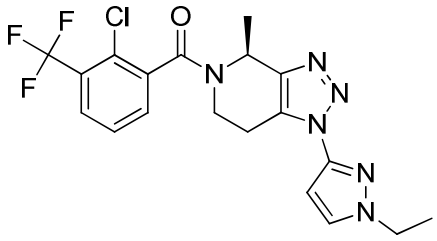
MS (ESI) mass calcd. $C_{18}H_{15}ClF_3N_7O$, 437.1; m/z found 438.0 $[M+H]^+$. ^1H NMR (DMSO) δ 9.06 (s, 1H), 8.81 (d, J = 5.0 Hz, 1H), 8.12 (s, 1H), 7.90 (d, J = 4.5 Hz, 1H), 5.78 (q, J = 6.7 Hz, 1H), 3.58-3.41 (m, 2H), 3.27-3.20 (m, 1H), 3.20-3.04 (m, 1H), 2.61 (s, 3H), 1.59 (d, J = 6.5 Hz, 3H).

Example 404: (S)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(1-ethyl-1H-pyrazol-3-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



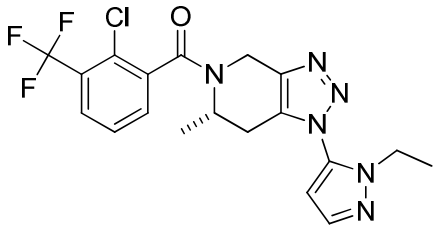
The title compound was prepared using the conditions described in Example 220, Method II, using 3-azido-1-ethyl-1H-pyrazole instead of 2-azido-5-fluoropyrimidine in Step 1 and 2-chloro-3-(trifluoromethyl)benzoyl chloride instead of 2-fluoro-3-(trifluoromethyl)benzoyl chloride in Step 3. The compound was purified by achiral SFC (Stationary phase: CHIRALCEL OJ-H 5µm 250x20mm), Mobile phase: 85% CO_2, 15% iPrOH). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 – 7.72 (m, 1H), 7.57 – 7.38 (m, 3H), 6.72 – 6.63 (m, 1H), 5.86 – 5.61 (m, 1H), 4.62 – 4.03 (m, 4H), 3.42 – 2.91 (m, 2H), 1.58 – 1.47 (m, 3H), 1.37 – 1.16 (m, 3H). MS (ESI) mass calcd. $C_{19}H_{18}ClF_3N_6O$, 438.8; m/z found, 439.3 $[M+H]^+$.

Example 405: (S)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(1-ethyl-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



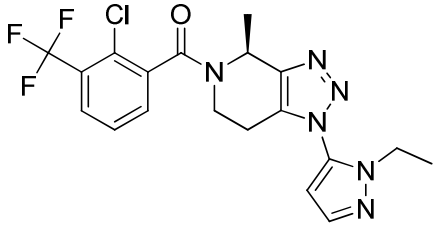
The title compound was prepared using the conditions described in Example 404 using the minor regio-isomer instead of the major regio-isomer in Step 1. The compound was purified by achiral SFC (Stationary phase: CHIRALCEL OJ-H 5µm 250x20mm), Mobile phase: 85% CO_2, 15% iPrOH). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 – 7.74 (m, 1H), 7.56 – 7.28 (m, 3H), 6.70 – 6.63 (m, 1H), 6.11 – 5.06 (m, 1H), 4.89 – 2.79 (m, 6H), 1.75 – 1.44 (m, 6H). MS (ESI) mass calcd. $C_{19}H_{18}ClF_3N_6O$, 438.8; m/z found, 439.3 $[M+H]^+$.

Example 406: (S)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(1-ethyl-1H-pyrazol-5-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



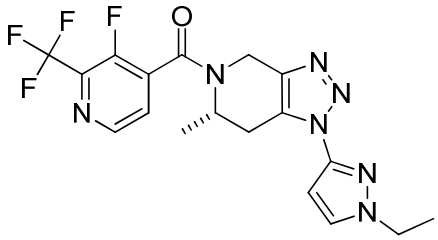
The title compound was prepared using the conditions described in Example 220, Method II, using 5-azido-1-ethyl-1H-pyrazole instead of 2-azido-5-fluoropyrimidine in Step 1 and 2-chloro-3-(trifluoromethyl)benzoyl chloride instead of 2-fluoro-3-(trifluoromethyl)benzoyl chloride in Step 3. The compound was purified by achiral SFC (Stationary phase: CHIRALCEL OJ-H 5µm 250x20mm), Mobile phase: 88% CO_2, 12% iPrOH). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 – 7.76 (m, 1H), 7.67 – 7.60 (m, 1H), 7.56 – 7.38 (m, 2H), 6.38 – 6.27 (m, 1H), 5.89 – 5.61 (m, 1H), 4.63 – 4.05 (m, 4H), 3.17 – 2.35 (m, 2H), 1.44 – 1.36 (m, 3H), 1.34 – 1.15 (m, 3H).MS (ESI) mass calcd. $C_{19}H_{18}ClF_3N_6O$, 438.8; m/z found, 439.3 $[M+H]^+$.

Example 407: (S)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(1-ethyl-1H-pyrazol-5-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



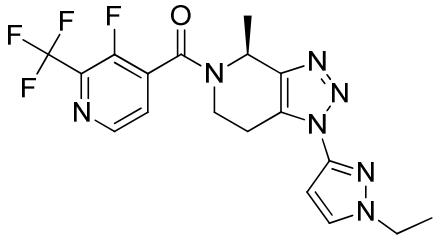
The title compound was prepared using the conditions described in Example 406 using the minor regio-isomer instead of the major regio-isomer in Step 1. The compound was purified by achiral SFC (Stationary phase: CHIRALCEL OJ-H 5µm 250x20mm), Mobile phase: 88% CO_2, 12% iPrOH). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 – 7.75 (m, 1H), 7.68 – 7.59 (m, 1H), 7.58 – 7.31 (m, 2H), 6.39 – 6.27 (m, 1H), 6.13 – 5.09 (m, 1H), 4.93 – 3.08 (m, 4H), 2.99 – 2.44 (m, 2H), 1.77 – 1.34 (m, 6H). MS (ESI) mass calcd. $C_{19}H_{18}ClF_3N_6O$, 438.8; m/z found, 439.3 $[M+H]^+$.

Example 408: (S)-(1-(1-ethyl-1H-pyrazol-3-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)methanone



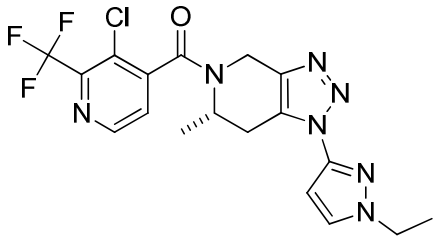
The title compound was prepared using the conditions described in Example 220, Method II, using 3-azido-1-ethyl-1H-pyrazole instead of 2-azido-5-fluoropyrimidine in Step 1 and 3-fluoro-2-(trifluoromethyl)isonicotinic acid instead of 2-fluoro-3-(trifluoromethyl)benzoyl chloride in Step 3. The compound was purified by achiral SFC (Stationary phase: CHIRALPAK IC 5µm 250x20mm), Mobile phase: 60% CO_2, 40% iPOH(0.3% iPrNH2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.68 – 8.53 (m, 1H), 7.65 – 7.41 (m, 2H), 6.73 – 6.60 (m, 1H), 6.07 – 5.00 (m, 1H), 4.82 – 2.89 (m, 6H), 1.71 – 1.48 (m, 6H). MS (ESI) mass calcd. $C_{18}H_{17}F_4N_7O$, 423.8; m/z found, 424.1 $[M+H]^+$.

Example 409: (S)-(1-(1-ethyl-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)methanone



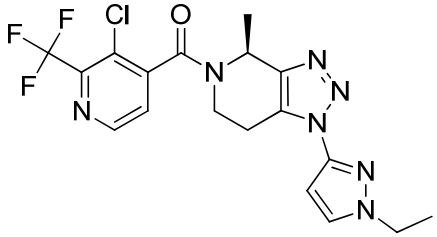
The title compound was prepared using the conditions described in Example 408 using the minor regio-isomer instead of the major regio-isomer in Step 1. The compound was purified by achiral SFC (Stationary phase: CHIRALPAK IC 5µm 250x20mm), Mobile phase: 60% CO_2, 40% iPOH(0.3% iPrNH2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.65 – 8.57 (m, 1H), 7.69 – 7.43 (m, 2H), 6.73 – 6.65 (m, 1H), 5.88 – 5.50 (m, 1H), 4.73 – 4.05 (m, 4H), 3.40 – 3.03 (m, 2H), 1.57 – 1.24 (m, 6H). MS (ESI) mass calcd. $C_{18}H_{17}F_4N_7O$, 423.8; m/z found, 424.1 $[M+H]^+$.

Example 410: (S)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(1-(1-ethyl-1H-pyrazol-3-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



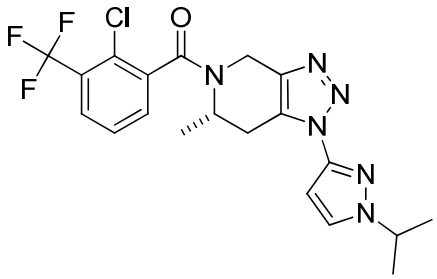
The title compound was prepared using the conditions described in Example 220, Method II, using 3-azido-1-ethyl-1H-pyrazole instead of 2-azido-5-fluoropyrimidine in Step 1 and 3-chloro-2-(trifluoromethyl)isonicotinic acid instead of 2-fluoro-3-(trifluoromethyl)benzoyl chloride in Step 3. The compound was purified by achiral SFC (Stationary phase: CHIRALPAK AD-H 5µm 250x20mm), Mobile phase: 85% CO_2, 15% MeOH). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.72 – 8.61 (m, 1H), 7.51 – 7.35 (m, 2H), 6.73 – 6.65 (m, 1H), 5.85 – 5.57 (m, 1H), 4.65 – 3.95 (m, 4H), 3.43 – 2.97 (m, 2H), 1.57 – 1.20 (m, 6H). MS (ESI) mass calcd. $C_{18}H_{17}ClF_3N_7O$, 439.8; m/z found, 440.1 $[M+H]^+$.

Example 411: (S)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(1-(1-ethyl-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



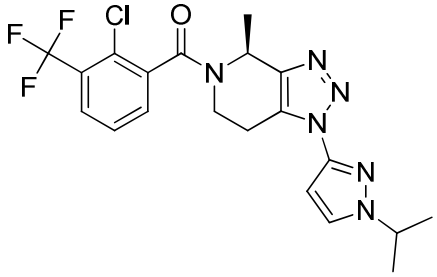
The title compound was prepared using the conditions described in Example 410 using the minor regio-isomer instead of the major regio-isomer in Step 1. The compound was purified by achiral SFC (Stationary phase: CHIRALPAK AD-H 5µm 250x20mm), Mobile phase: 85% CO_2, 15% MeOH). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.74 – 8.59 (m, 1H), 7.52 – 7.41 (m, 2H), 6.72 – 6.64 (m, 1H), 6.08 – 5.04 (m, 1H), 4.83 – 2.84 (m, 6H), 1.72 – 1.46 (m, 6H). MS (ESI) mass calcd. $C_{18}H_{17}ClF_3N_7O$, 439.8; m/z found, 440.1 $[M+H]^+$.

Example 412: (S)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(1-isopropyl-1H-pyrazol-3-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



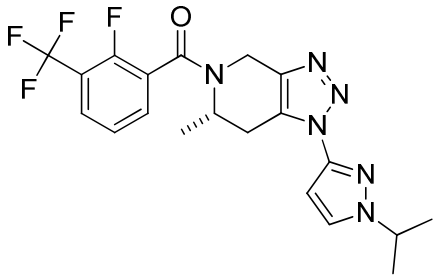
The title compound was prepared using the conditions described in Example 220, Method II, using 3-azido-1-isopropyl-1H-pyrazole instead of 2-azido-5-fluoropyrimidine in Step 1 and 2-chloro-3-(trifluoromethyl)benzoyl chloride instead of 2-fluoro-3-(trifluoromethyl)benzoyl chloride in Step 3. The compound was purified by achiral SFC (Stationary phase: CHIRALCEL OJ-H 5µm 250x20mm), Mobile phase: 92% CO_2, 8% iPrOH). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 – 7.74 (m, 1H), 7.56 – 7.39 (m, 3H), 6.72 – 6.63 (m, 1H), 5.86 – 5.60 (m, 1H), 4.63 – 4.03 (m, 3H), 3.44 – 2.94 (m, 2H), 1.59 – 1.17 (m, 9H). MS (ESI) mass calcd. $C_{20}H_{20}ClF_3N_6O$, 452.8; m/z found, 453.1 $[M+H]^+$.

Example 413: (S)-(2-chloro-3-(trifluoromethyl)phenyl)(1-(1-isopropyl-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



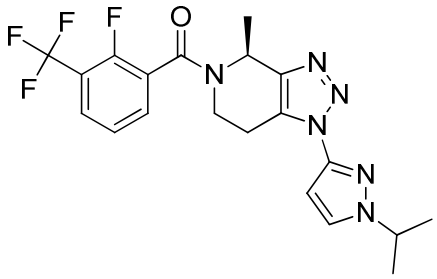
The title compound was prepared using the conditions described in Example 412 using the minor regio-isomer instead of the major regio-isomer in Step 1. The compound was purified by achiral SFC (Stationary phase: CHIRALCEL OJ-H 5µm 250x20mm), Mobile phase: 92% CO_2, 8% iPrOH). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 – 7.74 (m, 1H), 7.57 – 7.28 (m, 3H), 6.69 – 6.62 (m, 1H), 6.12 – 5.08 (m, 1H), 4.89 – 2.80 (m, 5H), 1.74 – 1.44 (m, 9H). MS (ESI) mass calcd. $C_{20}H_{20}ClF_3N_6O$, 452.8; m/z found, 453.1 $[M+H]^+$.

Example 414: (S)-(2-fluoro-3-(trifluoromethyl)phenyl)(1-(1-isopropyl-1H-pyrazol-3-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



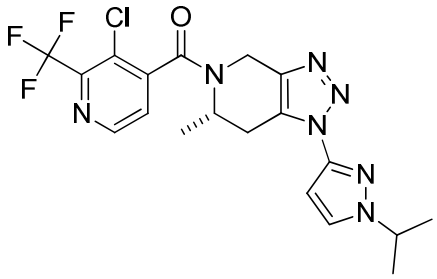
The title compound was prepared using the conditions described in Example 220, Method II, using 3-azido-1-isopropyl-1H-pyrazole instead of 2-azido-5-fluoropyrimidine in Step 1. The compound was purified by achiral SFC (Stationary phase: CHIRALPAK IC 5µm 250x20mm), Mobile phase: 60% CO_2, 40% iPOH(0.3% iPrNH2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 – 7.29 (m, 4H), 6.71 – 6.57 (m, 1H), 6.08 – 5.00 (m, 1H), 4.93 – 3.68 (m, 2H), 3.64 – 2.78 (m, 3H), 1.71 – 1.61 (m, 3H), 1.59 – 1.46 (m, 6H). MS (ESI) mass calcd. $C_{20}H_{20}F_4N_6O$, 436.4; m/z found, 437.1 $[M+H]^+$.

Example 415: (S)-(2-fluoro-3-(trifluoromethyl)phenyl)(1-(1-isopropyl-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



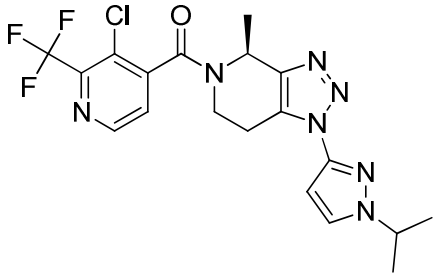
The title compound was prepared using the conditions described in Example 414 using the minor regio-isomer instead of the major regio-isomer in Step 1. The compound was purified by achiral SFC (Stationary phase: CHIRALPAK IC 5µm 250x20mm), Mobile phase: 60% CO_2, 40% iPOH(0.3% iPrNH2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 – 7.30 (m, 4H), 6.75 – 6.62 (m, 1H), 5.90 – 5.53 (m, 1H), 4.73 – 4.18 (m, 3H), 3.43 – 2.98 (m, 2H), 1.57 – 1.47 (m, 6H), 1.38 – 1.16 (m, 3H). MS (ESI) mass calcd. $C_{20}H_{20}F_4N_6O$, 436.4; m/z found, 437.1 $[M+H]^+$.

Example 416: (S)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(1-(1-isopropyl-1H-pyrazol-3-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



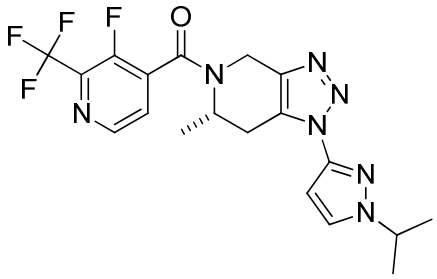
The title compound was prepared using the conditions described in Example 220, Method II, using 3-azido-1-isopropyl-1H-pyrazole instead of 2-azido-5-fluoropyrimidine in Step 1 and 3-chloro-2-(trifluoromethyl)isonicotinic acid instead of 2-fluoro-3-(trifluoromethyl)benzoyl chloride in Step 3. The compound was purified by achiral SFC (Stationary phase: CHIRALCEL OJ-H 5µm 250x20mm), Mobile phase: 92% CO_2, 8% iPrOH). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.74 – 8.58 (m, 1H), 7.53 – 7.35 (m, 2H), 6.73 – 6.61 (m, 1H), 5.84 – 5.54 (m, 1H), 4.67 – 3.94 (m, 3H), 3.46 – 2.98 (m, 2H), 1.58 – 1.48 (m, 6H), 1.39 – 1.22 (m, 3H). MS (ESI) mass calcd. $C_{19}H_{19}ClF_3N_7O$, 453.8; m/z found, 454.1 $[M+H]^+$.

Example 417: (S)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(1-(1-isopropyl-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



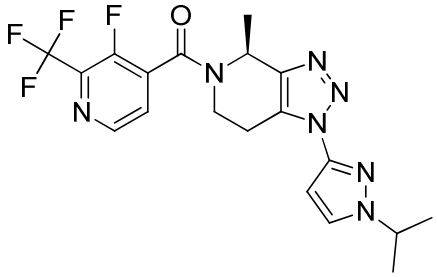
The title compound was prepared using the conditions described in Example 416 using the minor regio-isomer instead of the major regio-isomer in Step 1. The compound was purified by achiral SFC (Stationary phase: CHIRALCEL OJ-H 5µm 250x20mm), Mobile phase: 92% CO_2, 8% iPrOH). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.76 – 8.55 (m, 1H), 7.54 – 7.39 (m, 2H), 6.71 – 6.62 (m, 1H), 6.06 – 5.06 (m, 1H), 4.84 – 2.84 (m, 5H), 1.72 – 1.67 (m, 2H), 1.60 – 1.48 (m, 7H). MS (ESI) mass calcd. $C_{19}H_{19}ClF_3N_7O$, 453.8; m/z found, 454.1 $[M+H]^+$.

Example 418: (S)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(1-(1-isopropyl-1H-pyrazol-3-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



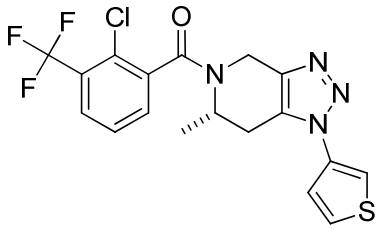
The title compound was prepared using the conditions described in Example 220, Method II, using 3-azido-1-isopropyl-1H-pyrazole instead of 2-azido-5-fluoropyrimidine in Step 1 and 3-fluoro-2-(trifluoromethyl)isonicotinic acid instead of 2-fluoro-3-(trifluoromethyl)benzoyl chloride in Step 3. The compound was purified by achiral SFC (Stationary phase: CHIRALPAK IC 5µm 250x20mm), Mobile phase: 60% CO_2, 40% iPOH(0.3% iPrNH2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.67 – 8.54 (m, 1H), 7.67 – 7.44 (m, 2H), 6.72 – 6.61 (m, 1H), 6.07 – 5.01 (m, 1H), 4.85 – 3.61 (m, 2H), 3.60 – 2.93 (m, 3H), 1.71 – 1.66 (m, 2H), 1.59 – 1.50 (m, 7H). MS (ESI) mass calcd. $C_{19}H_{19}F_4N_7O$, 437.4; m/z found, 438.1 $[M+H]^+$.

Example 419: (S)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(1-(1-isopropyl-1H-pyrazol-3-yl)-4-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



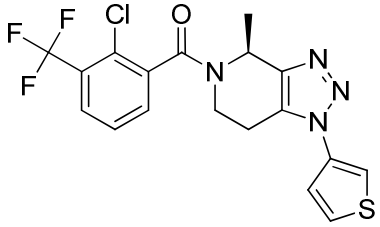
The title compound was prepared using the conditions described in Example 418 using the minor regio-isomer instead of the major regio-isomer in Step 1. The compound was purified by achiral SFC (Stationary phase: CHIRALPAK IC 5µm 250x20mm), Mobile phase: 60% CO_2, 40% iPOH(0.3% iPrNH2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.71 – 8.51 (m, 1H), 7.67 – 7.43 (m, 2H), 6.73 – 6.63 (m, 1H), 5.86 – 5.50 (m, 1H), 4.70 – 4.06 (m, 3H), 3.44 – 3.02 (m, 2H), 1.58 – 1.48 (m, 6H), 1.39 – 1.23 (m, 3H). MS (ESI) mass calcd. $C_{19}H_{19}F_4N_7O$, 437.4; m/z found, 438.1 $[M+H]^+$.

Example 420: (S)-(2-chloro-3-(trifluoromethyl)phenyl)(6-methyl-1-(thiophen-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



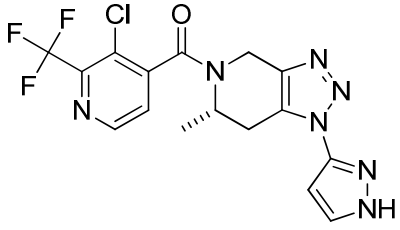
The title compound was prepared using the conditions described in Example 220, Method II, using 3-azidothiophene instead of 2-azido-5-fluoropyrimidine in Step 1 and 2-chloro-3-(trifluoromethyl)benzoyl chloride instead of 2-fluoro-3-(trifluoromethyl)benzoyl chloride in Step 3. The compound was purified by achiral SFC (Stationary phase: CHIRALCEL OJ-H 5µm 250x20mm), Mobile phase: 80% CO_2, 20% iPrOH). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 – 7.75 (m, 1H), 7.56 – 7.37 (m, 5H), 5.87 – 5.63 (m, 1H), 4.64 – 4.04 (m, 2H), 3.38 – 2.58 (m, 2H), 1.38 – 1.14 (m, 3H). MS (ESI) mass calcd. $C_{18}H_{14}ClF_3N_4OS$, 426.8; m/z found, 427.1 $[M+H]^+$.

Example 421: (S)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(thiophen-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



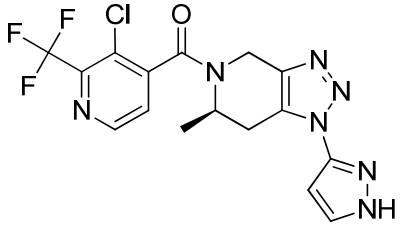
The title compound was prepared using the conditions described in Example 420 using the minor regio-isomer instead of the major regio-isomer in Step 1. The compound was purified by achiral SFC (Stationary phase: CHIRALCEL OJ-H 5µm 250x20mm), Mobile phase: 80% CO_2, 20% iPrOH). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 – 7.76 (m, 1H), 7.58 – 7.31 (m, 5H), 6.12 – 5.10 (m, 1H), 4.91 – 2.70 (m, 4H), 1.73 – 1.47 (m, 3H). MS (ESI) mass calcd. $C_{18}H_{14}ClF_3N_4OS$, 426.8; m/z found, 427.1 $[M+H]^+$.

Example 422: (S*)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(6-methyl-1-(1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



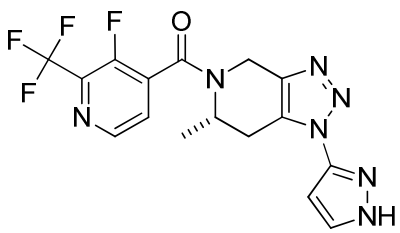
To a solution of 6-methyl-1-(1H-pyrazol-5-yl)-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine (prepared in an analogus manner to Example 220, Method II) (0.125g, 0.519 mmol) in CH_2Cl_2 (5 mL) was added Hunig's base (0.181 mL, 1.039 mmol) followed by 3-chloro-2-(trifluoromethyl)isonicotinic acid (0.175 g, 0.779 mmol) and HATU (0.236g, 0.623 mmol). After stirring for 30 min at rt, sat $NaHCO_3$ (20 mL) was added. The organic layer was separated and the water layer was extracted with CH_2Cl_2 two times. The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated. Chromatography on silica gel (0-100% ethyl acetate/hexanes) provided the racemic product as a white solid (0.07 g, 33%). Enantiomers were separated by chiral SFC (Stationary phase: CHIRALPAK AD-H 5µm 250x20mm, Mobile phase: 80% CO_2, 20% EtOH(0.3% iPrNH2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.80 – 10.03 (s, 1H), 8.73 – 8.62 (m, 1H), 7.72 – 7.62 (m, 1H), 7.52 – 7.36 (m, 1H), 6.89 – 6.79 (m, 1H), 5.87 – 5.61 (m, 1H), 4.67 – 3.95 (m, 2H), 3.47 – 2.99 (m, 2H), 1.33 – 1.19 (m, 3H). MS (ESI) mass calcd. $C_{16}H_{13}ClF_3N_7O$, 411.7; m/z found, 411.9 $[M+H]^+$.

Example 423: (S*)-(3-chloro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



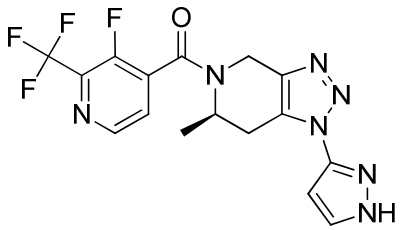
The title compound was obtained via separation of the racemic mixture described in Example 422. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.38 – 10.02 (s, 1H), 8.74 – 8.61 (m, 1H), 7.72 – 7.63 (m, 1H), 7.54 – 7.36 (m, 1H), 6.88 – 6.80 (m, 1H), 5.88 – 5.58 (m, 1H), 4.68 – 3.95 (m, 2H), 3.76 – 2.99 (m, 2H), 1.33 – 1.20 (m, 3H). MS (ESI) mass calcd. $C_{16}H_{13}ClF_3N_7O$, 411.7; m/z found, 411.9 $[M+H]^+$.

Example 424: (S*)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(6-methyl-1-(1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



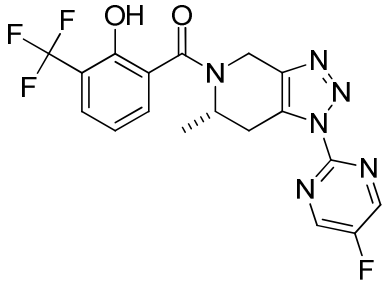
The title compound was prepared using the conditions described in Example 422, using 3-fluoro-2-(trifluoromethyl)isonicotinic acid instead of 3-chloro-2-(trifluoromethyl)isonicotinic acid. The resulting racemic mixture was separated by chiral SFC (Stationary phase: CHIRALPAK AD-H 5µm 250x20mm, Mobile phase: 80% CO_2, 20% EtOH(0.3% iPrNH2)). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.66 – 8.56 (m, 2H), 7.71 – 7.51 (m, 3H), 6.88 – 6.81 (m, 2H), 5.86 – 5.53 (m, 2H), 4.72 – 4.07 (m, 4H), 3.44 – 2.99 (m, 3H), 1.34 – 1.17 (m, 6H), 10.61 – 9.82 (m, 1H). MS (ESI) mass calcd. $C_{16}H_{13}F_4N_7O$, 395.3; m/z found, 396.1 $[M+H]^+$.

Example 425: (S*)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(4-methyl-1-(1H-pyrazol-3-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound was obtained via separation of the racemic mixture described in Example 424. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.49 – 10.07 (s, 1H), 8.67 – 8.56 (m, 1H), 7.71 – 7.48 (m, 2H), 6.89 – 6.79 (m, 1H), 5.86 – 5.56 (m, 1H), 4.70 – 4.08 (m, 2H), 3.43 – 3.04 (m, 2H), 1.34 – 1.20 (m, 3H). MS (ESI) mass calcd. $C_{16}H_{13}F_4N_7O$, 395.3; m/z found, 396.1 $[M+H]^+$.

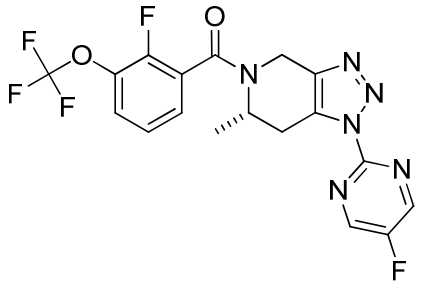
Example 426: (S)-(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2-hydroxy-3-(trifluoromethyl)phenyl)methanone



To a solution of (S)-1-(5-fluoropyrimidin-2-yl)-6-methyl-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo[4,5-c]pyridine (prepared in an analogus manner to Example 220, Method II) (0.2g, 0.845 mmol) in CH_2Cl_2 (5 mL) was added Hunig's base (0.294 mL, 1.708 mmol) followed by 2-hydroxy-3-(trifluoromethyl)benzoic acid (0.194 g, 0.939 mmol) and HATU (0.39g, 1.025 mmol). After stirring for 30 min at rt, sat $NaHCO_3$ (20 mL) was added. The

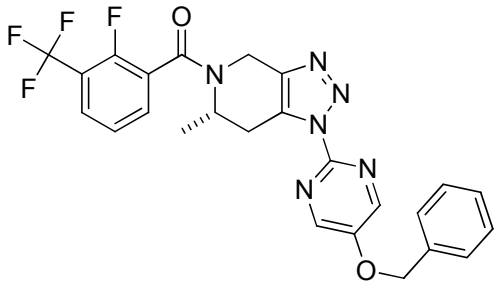
organic layer was separated and the water layer was extracted with CH_2Cl_2 two times. The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated. Chromatography on silica gel (0-100% ethyl acetate/hexanes) provided the desired product as a white solid (0.04 g, 13%).^{1}H NMR (500 MHz, $CDCl_3$) δ 8.75 – 8.74 (s, 2H), 7.70 – 7.66 (m, 1H), 7.53 – 7.50 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.03 – 6.98 (m, 1H), 5.31 – 5.15 (m, 2H), 4.72 – 4.60 (d, *J* = 15.7 Hz, 1H), 3.57 – 3.50 (m, 1H), 3.29 – 3.23 (m, 1H), 1.38 – 1.33 (d, *J* = 7.0 Hz, 3H). MS (ESI) mass calcd. $C_{18}H_{14}F_4N_6O_2$, 422.3; m/z found, 423.1 $[M+H]^+$.

Example 427: (S)-(2-fluoro-3-(trifluoromethoxy)phenyl)(1-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



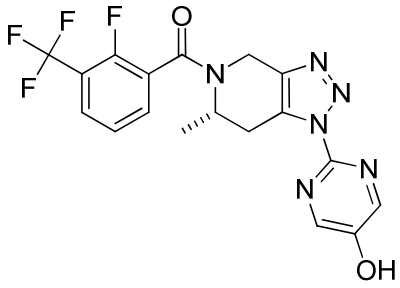
The title compound was prepared using the conditions described in Example 426, using 2-fluoro-3-(trifluoromethoxy)benzoic acid instead of 2-hydroxy-3-(trifluoromethyl)benzoic acid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.79 – 8.68 (m, 2H), 7.47 – 7.22 (m, 3H), 5.94 – 5.54 (m, 1H), 4.73 – 4.16 (m, 2H), 3.57 – 3.09 (m, 2H), 1.41 – 1.12 (m, 3H).MS (ESI) mass calcd. $C_{18}H_{13}F_5N_6O_2$, 440.3; m/z found, 441.2 $[M+H]^+$.

Intermediate U: (S)-(1-(5-(benzyloxy)pyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)(2-fluoro-3-(trifluoromethyl)phenyl)methanone



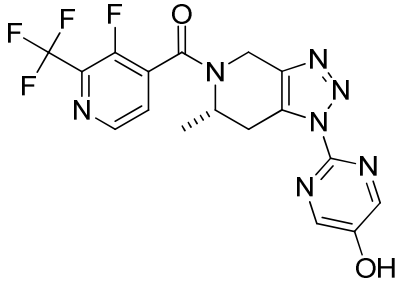
The title compound was prepared using the conditions described in Example 220, Method II, using 2-azido-5-(benzyloxy)pyrimidine instead of 2-azido-5-fluoropyrimidine in Step 1.

Example 428: (S)-(2-fluoro-3-(trifluoromethyl)phenyl)(1-(5-hydroxypyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



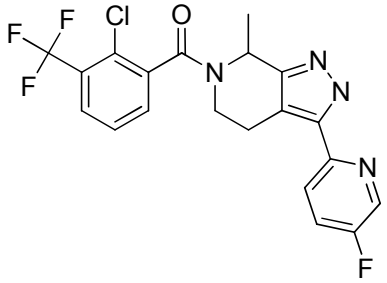
To a solution of Intermediate U (0.120g, 0.237 mmol) in ethanol (5 mL) was added ammonium formate (0.07g, 1.183 mmol) followed by 10% Palladium on carbon (0.251 g, 0.237 mmol. After stirring at reflux for 2 hours, the reaction mixture was cooled to rt. and filtered through a celite pad. The organic layer was concentrated and purified via chromatography on silica gel (0-100% ethyl acetate/hexanes) providing the desired product as a white solid (0.04 g, 13%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.64 – 7.30 (m, 5H), 5.90 – 5.52 (m, 1H), 4.75 – 4.12 (m, 2H), 3.55 – 2.71 (m, 2H), 1.44 – 1.09 (m, 3H). MS (ESI) mass calcd. $C_{18}H_{14}F_4N_6O_2$, 422.3; m/z found, 423.1 $[M+H]^+$.

Example 429: (S)-(3-fluoro-2-(trifluoromethyl)pyridin-4-yl)(1-(5-hydroxypyrimidin-2-yl)-6-methyl-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone

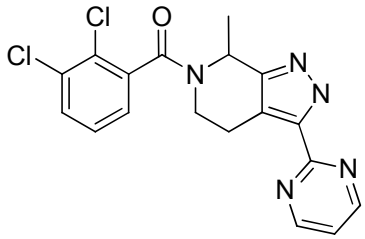


The title compound was prepared using the conditions described in Example 428, using 3-fluoro-2-(trifluoromethyl)isonicotinic acid instead of 2-fluoro-3-(trifluoromethyl)benzoic acid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.66 – 8.54 (m, 1H), 8.46 – 8.32 (d, J = 32.9 Hz, 2H), 7.65 – 7.54 (m, 1H), 5.75 – 5.49 (m, 1H), 4.70 – 4.04 (m, 2H), 3.44 – 3.09 (m, 2H), 1.39 – 1.14 (m, 3H), 6.78 – 5.95 (m, 1H). MS (ESI) mass calcd. $C_{17}H_{13}F_4N_7O_2$, 423.3; m/z found, 424.1 $[M+H]^+$.

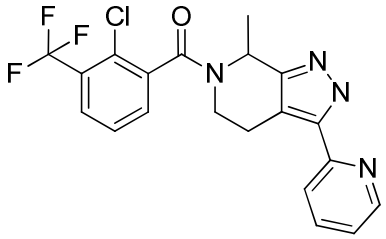
Example 430: (2-chloro-3-(trifluoromethyl)phenyl)(3-(5-fluoropyridin-2-yl)-7-methyl-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone.



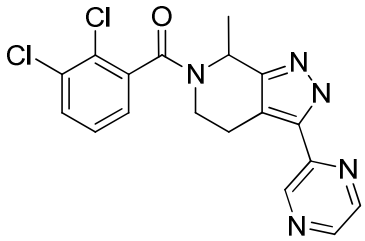
Example 431: (2,3-dichlorophenyl)(7-methyl-3-(pyrimidin-2-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone.



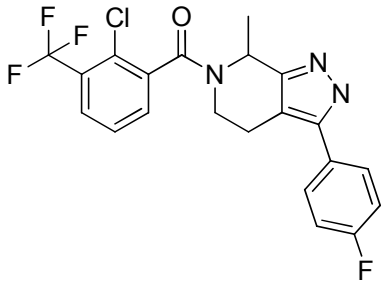
Example 432: (2-chloro-3-(trifluoromethyl)phenyl)(7-methyl-3-(pyridin-2-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone.



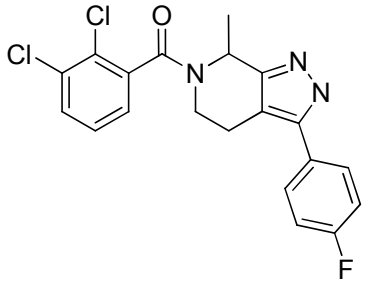
Example 433: (2,3-dichlorophenyl)(7-methyl-3-(pyrazin-2-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone.



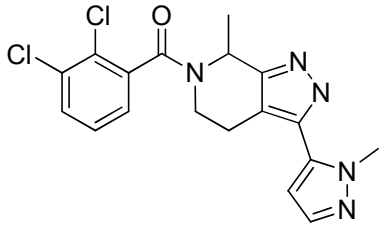
Example 434: (2-chloro-3-(trifluoromethyl)phenyl)(3-(4-fluorophenyl)-7-methyl-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone.



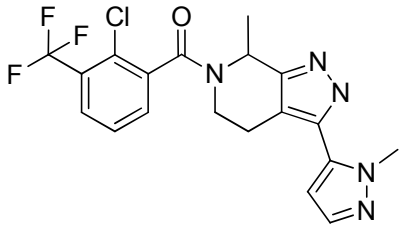
Example 435: (2,3-dichlorophenyl)(3-(4-fluorophenyl)-7-methyl-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone.



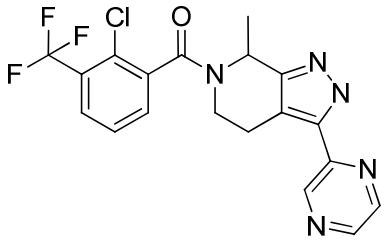
Example 436: (2,3-dichlorophenyl)(7-methyl-3-(1-methyl-1H-pyrazol-5-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone.



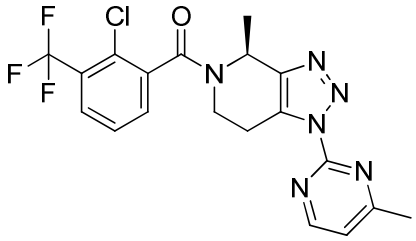
Example 437: (2-chloro-3-(trifluoromethyl)phenyl)(7-methyl-3-(1-methyl-1H-pyrazol-5-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone.



Example 438: (2-chloro-3-(trifluoromethyl)phenyl)(7-methyl-3-(pyrazin-2-yl)-4,5-dihydro-2H-pyrazolo[3,4-c]pyridin-6(7H)-yl)methanone.



Example 439: (S*)-(2-chloro-3-(trifluoromethyl)phenyl)(4-methyl-1-(4-methylpyrimidin-2-yl)-6,7-dihydro-1H-[1,2,3]triazolo[4,5-c]pyridin-5(4H)-yl)methanone



The title compound, absolute configuration unknown, was obtained as a single enantiomer by Chiral SFC purification of Example 252 performed using a CHIRALPAK AD-H (5µm, 250x20mm) column and a mobile phase of 75% CO_2, 25% EtOH/iPrOH 50/50 v/v containing 0.3% $iPrNH_2$. The enantiomeric purity was confirmed by analytical SFC using a CHIRALPAK AD (250x4.6mm) column and a mobile phase of 75% CO_2, 25% EtOH/iPrOH 50/50 v/v containing 0.3% $iPrNH_2$. (100% single enantiomer, 4.30 min retention time). MS (ESI) mass calcd. $C_{19}H_{16}ClF_3N_6O$, 436.10 m/z found, 437.20 $[M+H]^+$. ^1H NMR (400 MHz, CDCl3) δ 8.73 – 8.62 (m, 1H), 7.82 – 7.73 (m, 1H), 7.59 – 7.19 (m, 3H), 6.13 – 6.01 (m, 0.6H), 5.17 – 5.07 (m, 0.4H), 4.92 – 4.73 (m, 0.4H), 3.69 – 2.94 (m, 3.6H), 2.75 – 2.55 (m, 3H), 1.77 – 1.46 (m, 3H).

Pharmacological examples

The in vitro affinity of the compounds of the invention for the rat and human P2X7 receptor was determined using a human peripheral blood mononuclear cells (PBMCs), ahuman whole blood assay, a Ca^{2+} flux and radioligand binding assay in recombinant human P2X7 cells and recombinant rat P2X7 cells.In Tables 2 and 3, when the data cell has been left blank, it is intended to mean that the compound was not tested in that assay. The data represented in Tables 2 and 3 may represent a value from a single determination or when the experiment was run more than once, the data represent averages from between 2-12 runs.

P2X7 antagonism in human peripheral blood mononuclear cells (PBMCs) and Human Whole Blood.

Human blood was collected using a blood donor program. PBMCs were isolated from blood using a Ficoll density gradient technique. Briefly, blood was laid on Ficoll solution and centrifuged at RT for 20 minutes at 2000 rpm. The buffy layer (between red blood cells and plasma) was carefully collected by aspiration, washed with PBS and centrifuged again at 1500 rpm for 15 minutes. The resulting cell pellet was washed and plated on 96 well-plates for experiments. For the Human Whole Blood experiments, 150 μl of human blood was platted on 96 well-plates. Lipopolysaccharide (LPS) (30 ng/ml) was added to each well and incubated for 1 hour. Test compounds were then added and incubated for 30 minutes. The P2X7 agonist, 2'(3')-O-(4-benzoylbenzoyl) adenosine 5' –triphosphate (Bz-ATP) was then added at a final concentration of 0.5 mM (PBMC) or 1 mM (blood). Cells were incubated for an additional 1.5 hours. At that point, supernatant was collected and stored for IL-1β assay using manufacturer's protocol for enzyme-linked immunosorbent assay (ELISA). Data was expressed as percent control, where control is defined as the difference in IL-1β release in LPS+Bz-ATP samples and LPS only samples. Data was plotted as response (% control) versus concentration to generate IC_{50} values. In Tables 2 and 3, this data is represented by PBMC 1 μM (% control) and PBMC 10 μM (%control) and human whole blood IC_{50} (μM). Data are analyzed and graphed on Graphpad Prism 5. For analysis, each concentration

point is averaged from triplicate values and the averaged values are plotted on Graphpad Prism. The IC_{50} for each compound is then uploaded into 3DX.

P2X7 antagonism in recombinant human P2X7 cells or recombinant rat P2X7 cells: (a) Ca^{2+} flux and (b) radioligand binding

(a) Ca^{2+} flux: 1321N1 cells expressing the recombinant human or rat P2X7 channel was cultured in HyQ DME/(HyClone/Dulbecco's Modified Eagle Medium) high glucose supplemented with 10% Fetal Bovine Serum **(**FBS) and appropriate selection marker. Cells were seeded at a density of 25000 cells/well (96-well clear bottom black walled plates) in 100 µl volume/well. On the day of the experiment, cell plates were washed with assay buffer, containing (in mM): 130 NaCl, 2 KCl, 1 $CaCl_2$, 1 $MgCl_2$, 10 HEPES, 5 glucose; pH 7.40 and 300 mOs. After the wash, cells were loaded with the Calcium-4 dye (Molecular Device) and incubated in the dark for 60 minutes. Test compounds were prepared at 250X the test concentration in neat DMSO. Intermediate 96-well compound plates were prepared by transferring 1.2 µL of the compound into 300 µL of assay buffer. A further 3X dilution occurred when transferring 50 µL/well of the compound plate to 100 µL/well in the cell plate. Cells were incubated with test compounds and dye for 30 minutes. Calcium dye fluorescence was monitored in FLIPR as the cells were challenged by adding 50 µL/well of BzATP (final concentration is 250 µM BzATP (human and rat)). The fluorescence change was measured 180 seconds after adding the agonist. Peak fluorescence was plotted as a function of BzATP concentration using Origin 7 software and the resultant IC_{50} is shown in Tables 2 and 3 under the column headings FLIPR (human) IC_{50} (µM) and FLIPR (rat) IC_{50} (µM).

(b) Radioligand binding: human or rat P2X7-1321N1 cells were collected and frozen @ -80 °C. On the day of the experiment, cell membrane preparations were made according to standard published methods. The total assay volume was 100 µl:10 µl compound (10x) + (b) 40 µl tracer (2.5x) + 50 µl membrane (2x). The tracer used for the assay was tritiated A-804598. The compound can be prepared as described in the literature. (Donnelly-Roberts, D. *Neuropharmacology* 2008, *56* (1), 223-229.) Compounds, tracer and membranes were incubated for 1 hour @ 4 °C. The assay was terminated by filtration (GF/B filters pre-soaked with 0.3% PEI)

and washed with washing buffer (Tris-HCl 50 mM). The IC_{50} generated in the binding assay was corrected for tracer concentration and affinity of the tracer to derive at the affinity (K_i) of the test compounds. The data are presented in Tables 2 and 3 under the headings: P2X7 human K_i (μM) and P2X7 rat K_i (μM). Data are analyzed and graphed on Graphpad Prism 5. For analysis, each concentration point is averaged from triplicate values and the averaged values are plotted on Graphpad Prism.

Table 2: P2X7 activity of the compounds of Formula (I, Ia, IIa or IIb) in a panel of in-vitro assays

Example	PBMC 1 µM (% control)	PBMC 10 µM (% control)	P2X7 human K_i (µM)	P2X7 rat K_i (µM)	FLIPR (human) IC_{50} (µM)	FLIPR (rat) IC_{50} (µM)	Human whole blood IC_{50} (µM)
1	11.5		0.0759		0.0061	1.2078	
2	7.9		0.0871		0.0184	1.9409	
3	23.0		0.0603		0.0811	4.4771	
4		-3.7	0.0251		0.0465	2.5704	
5		11.6	0.0316		0.0124	0.3236	
6	14.3		0.0427		0.0094	1.7824	
7	98.7						
8	83.1						
9	83.7						
10	76.5						
11		25.2	0.1259		0.0223	0.6714	1.585
12	11.2		0.0851	0.1349	0.0061	1.3213	0.631
13	27.9		0.0794		0.0126	0.1259	
14	12.8		0.0794		0.0830	0.1409	
15	9.1		0.1585		0.0875	0.1791	
16	8.5		0.2512		0.1038	0.4560	
17	6.5		0.0501		0.0259	0.1560	
18	5.3		0.1000		0.0773	0.9162	
19		11.6	0.1000		0.0352	0.4539	
20		8.6	0.5012		0.9311	2.3714	
21		1.6	0.1259		0.0785	1.6069	
22		-15.9	0.1259		0.0131	1.6256	
23		6.4	0.0398		0.0344	0.0906	
24	2.9		0.0912		0.0350	0.0342	
25	9.7		0.0741		0.1114	3.2659	
26	14.0		0.0851		0.0098	0.0710	
27	39.2		1.3804		0.1799	1.8923	
28	4.8		0.0794		0.0138	0.0165	
29	34.7		0.0380		0.0798	2.0701	
30	87.0		0.3981		1.3677	6.1376	
31	50.8		0.3162		0.1563	0.1074	
32		1.9	0.0372		0.0105	0.0655	0.251
33	100.7						
34	29.8		0.6310		0.1585	0.1585	
35	31.6		0.3162		0.3162	0.3162	
36	16.6				3.0832	10.0693	
37		-9.1	0.0794		0.0993	1.5311	
38		-0.3	0.2512		0.0143	0.1265	
39		112.0					
40		36.5	0.0071	0.0078	0.0040	0.1152	0.092

41		40.5			1.6118	10.0000	
42		5.8	0.0398	0.0141	0.0557	0.0883	2.512
43		77.8		1.9953	5.2360	>10	
44		44.7	0.0316		0.0150	0.1164	
45		29.4			1.6106	14.9969	
46		2.1	0.0398		0.0603	0.4721	3.981
47		-1.1	0.3162		0.1486	2.0417	
48	90.1						
49	93.5						
50	96.0						
51	97.6						
52	98.9						
53	99.0		0.7413		0.9750	4.9545	
54	8.6		0.0437		0.1984	4.1115	
55	11.3		0.1259		0.0167	0.2594	
56	10.1		0.0794		0.0251	0.3981	
57		46.7	0.7943		0.7178	0.2198	
58		-2.0	0.1259		0.0107	0.7656	
59		10.2	0.5012		0.3784	0.5272	
60		8.4	0.1000		0.0557	1.6482	
61	-0.1		0.0389		0.0047	1.3996	
62	5.2		0.0437		0.0762	4.2756	
63	12.6		0.0117		0.0033	1.0864	
64		-9.2	0.0316	0.0263	0.0143	2.4434	0.251
65		5.8	0.0158		0.0063	0.0087	0.079
66		2.7	0.0158		0.0174	0.2065	0.363
67		6.5	0.0079		0.0030	0.0789	0.158
68		12.9	0.0182		0.0169	0.1845	
69		6.8	0.0141		0.1058	1.4571	
70		10.6	0.0126		0.0075	1.3274	0.501
71		11.1	0.2512		0.0490	0.3972	
72	-5.7		0.0295		0.0042	0.1687	0.126
73	4.3		0.2512	0.0191	0.0145	0.0408	0.016
74	102.6		13.1826	2.2387	13.3660	19.2309	5.012
75	5.2	-0.3	0.0447	0.0062	0.0034	0.0091	0.013
76	1.6		0.3631		0.0244	0.0324	
77	31.7		0.3981		0.1259	0.0063	
78	57.7		0.1000		0.0631	0.5012	
79	23.2		0.0316		0.0062	0.0865	
80		4.6	0.0398		0.0207	0.0187	0.016
81		5.9	0.0631		0.0735	0.1076	
82		7.9	0.0575		0.0173	0.1545	
83		4.5	0.1585		0.0169	0.3972	
84		8.5	0.0398		0.0177	0.1871	0.200
85		24.7	0.0398		0.0141	0.0146	
86		13.0	0.0398		0.0129	0.1361	
87		21.7	1.2589	0.7943	2.5050	5.2180	3.311
88		13.3	0.0126	0.0022	0.0022	0.0020	0.002

89	-1.5		0.0158		0.0055	0.9078	
90	13.3		0.0295		0.0103	0.9727	
91	6.1		0.0234	0.0162	0.0029	1.4928	0.316
92	2.8		0.0263		0.0054	0.4395	
93	9.0		0.0398		0.0079	0.2512	
94		10.8	0.0316		0.0124	0.1230	
95		14.4	0.3162		0.2042	>10	
96		3.6	0.0148		0.0025	0.1786	
97		12.7	0.0200		0.0045	2.2909	
98		32.5	0.0141		0.0066	0.5483	
99	7.0		0.0813	0.7413	0.0115	0.1948	
100	9.2		0.0759		0.0062	1.6387	
101	7.6		0.0851		0.1285	3.4594	
102	18.0		0.1096		0.2299	5.9361	
103	56.0		0.2754		0.3917	8.3560	
104	8.9		0.0501		0.2046	1.6088	
105	51.0		0.1995		0.0794	1.2589	
106	64.4		0.2512		0.1585	1.5849	
107	24.7		0.0794		0.0158	0.7943	
108	1.1		0.1000		0.0126	0.7943	
109	94.1				0.2512	3.1623	
110	-15.1		0.1820		0.0100	1.2589	
111	15.7		0.0794		0.1585	1.5849	
112	51.9		0.2512		0.1259	3.9811	
113		42.6	0.3981		0.8551	>10	
114	20.4		0.2512		0.0631	1.2589	
115		-3.3			1.0691	>10	
116		45.3	0.0063		0.0088	0.0041	
117		4.3			2.2182	>10	
118		12.6	0.7943		1.1858	1.7378	
119		20.0	0.0063	0.0025	0.0013	0.0015	0.013
120		-3.8	0.0063		0.0059	0.0556	
121		-0.2	0.0112		0.0032	0.0065	
122		0.2	0.0200		0.0048	0.0120	
123	22.0		0.0631		0.0501	1.0000	
124	94.7						
125	83.4		0.2512		0.1585	1.2589	
126	71.7		0.0933		0.0855	1.4109	
127		9.2	0.0398		0.0221	0.0891	
128		23.1			2.1086	>10	
129		8.4			0.3664	3.3497	
130		3.7	0.0501		0.0036	0.1545	0.501
131		8.3	0.0501		0.0029	0.0515	0.316
132		3.8	0.0501		0.0783	4.4259	
133		-0.2	0.0100	0.0016	0.0022	0.0093	
134		12.3	3.9811		6.6989	10.8643	
135		1.7	0.1000		0.0482	1.3804	
136		5.3	0.0158		0.0093	0.1327	0.063

137							
138							
139							
140							
141		40.5			9.5940	>10	
142		33.8	0.0100		0.0020	0.1432	
143		58.0			>10	>10	
144		19.6	0.0032		0.0097	0.0552	
145		15.2			2.3068	13.7721	
146		30.9			2.7040	>10	
147		-8.9	0.0398		0.0113	0.5070	
148		-9.6	0.0316		0.0085	0.0118	
149		3.5			2.4917	17.2783	
150							
151		19.5	0.0501		0.0057	0.0216	
152		15.4			0.9795	1.9770	
153		28.9	0.0631		0.0051	0.0303	
154		-0.6			0.0165	0.0102	
155		111.6					
156		1.8			0.0144	0.6039	
157		-1.4	3.1623		1.5346	3.2961	
158		1.1	0.0094	0.0055	0.0030	0.0188	0.008
159		54.1			>10	>10	
160		101.5			>10	>10	
161		-0.9	0.0158		0.0181	0.1791	
162							
163							
164		98.1					
165		60.7			9.7949	>10	
166		0.6	0.0025		0.0024	0.0185	
167		4.2			10.4713	>10	
168		-4.2	0.0032		0.0036	0.0049	
169		95.0					
170		-5.7	0.0200	0.0032	0.0089	0.0102	
171		28.7			2.0277	>10	
172		-6.0	0.0316	0.0050	0.0117	0.0054	
173		8.8	0.0158		0.0089	0.0102	
174		4.2	0.0501		0.0033	1.6827	
175		4.5	0.0398		0.0181	2.8774	
176		7.3	0.0316		0.0080	0.0072	
177		8.6	0.0794		0.2270	>10	
178		-4.7			0.0051	0.1180	
179		-4.3			1.0568	>10	
180		-3.7			0.5916	>10	
181		-0.1			0.0944	>10	
182		62.5					
183		-1.2			0.0204	0.0083	
184		-0.7	0.3715		0.1059	1.6406	

185		-3.7			0.0052	0.0195	
186		-0.5			9.0365	11.6950	
187		-0.6			0.0446	6.4714	
188		-0.7	0.0079		0.0027	0.0085	
189		0.5	0.0135		0.0039	0.0063	
190		7.1			1.5560	1.2912	
191		5.2	0.0251		0.0122	1.3002	
192		-6.3			2.5119	10.0000	
193		1.4	0.0224		0.0532	0.2382	
194		-12.8	1.3804		3.9811	>10	
195		14.4	0.0100		0.0034	0.0108	
196		-3.1	0.5012		0.3908	2.6182	
197		2.1			0.6622	0.6714	
198		1.3	0.6310		0.1803	4.9774	
199		0.0	0.0398		0.0086	0.0025	
200		3.2	0.0251		0.0370	0.0173	
201		20.4			1.2503	7.6208	
202		24.1	0.0100	0.0025	0.0017	0.0037	
203		0.6	0.0079		0.0105	0.1132	
204		180.6					
205		17.1	0.0040		0.0010	0.1084	
206		-1.0	0.0282		0.0159	0.0800	
207		45.0			8.5507	>10	
208		20.9	0.0100	0.0020	0.0126	0.0200	0.015
209		-1.0	0.0158		0.0142	0.0021	
210		0.8	0.0050		0.0102	0.0077	
211		28.5			6.3096	5.0119	
212		17.4	0.0050		0.0050	0.0016	
213		0.3	0.0251		0.0133	0.0106	
214		8.2			8.4918	46.2381	
215		2.7	0.0100		0.0020	0.0019	
216		0.6	0.0126		0.0126	0.0834	
217		60.8					
218		6.1	0.0025		0.0124	0.0180	
219		76.5			7.4131	>10	
220		15.1	0.0056	0.0012	0.0048	0.0059	0.063
221		17.8			0.5058	6.6834	
222		11.8	0.0251		0.0011	0.0010	
223		1.8	0.0447		0.0250	0.5636	
224		103.3					
225		-1.0	0.0091		0.0062	0.0423	
226		58.0					
227		-0.4	0.0200		0.0072	0.0102	
228		0.1	0.0048		0.0051	0.0082	
229		116.4					
230		2.9	0.0589		0.0139	0.0895	
231		-4.8			0.4989	38.1944	
232		7.5			5.5976	>10	

233		-0.1	0.1000		0.0060	0.1324	
234		-40.9	0.0794		0.1995	1.9953	
235		-3.7	0.0141	0.0031	0.0054	0.0066	0.017
236		9.3			1.1858	>10	
237		-5.1	0.0363		0.0032	0.1276	
238		-4.1	0.0794		0.0271	0.7244	
239		86.9					
240		-8.9	2.5119		0.1002	0.0226	
241		6.5	1.9953		2.5823	>10	
242		-3.4	0.0251		0.0815	0.0604	
243		1.0	0.0631		0.0160	0.0150	
244		-2.3			1.1429	13.5207	
245		-7.3	0.1000		0.1607	2.0701	
246		-3.1	0.1738		0.2296	6.5313	
247		-0.8			2.3281	8.2035	
248		74.3					
249		5.1	0.0200	0.0022	0.0127	0.0038	
250		-1.3	0.0398		0.0086	0.6699	
251		11.6	0.1445		0.1237	9.1096	
252		-0.8	0.0282		0.0188	0.0223	
253		-2.6	0.1950		0.1849	12.6911	
254		0.9	0.0447		0.0223	4.2560	
255		-5.5	0.0724		0.0160	0.2113	
256		7.1			2.3878	>10	
257		7.1	0.0158		0.6516	6.1660	
258		-3.2	0.0631		0.0855	4.8417	
259		-3.5	0.0575		0.0406	10.0925	
260		1.4	0.0355		0.0270	6.9343	
261		-3.1	0.0363		0.0194	1.2331	
262		-3.6	0.0398		0.1276	1.5453	
263		-1.6	0.0550		0.0161	1.2531	
264		89.5			>10	>10	
265		76.5					
266		5.8	0.0200		0.0127	0.0126	
267		-50.8	0.0100		0.0081	0.0095	
268		-59.9			0.5998	1.2190	
269		16.3	0.0200		0.0131	0.0206	
270		98.5					
271		-3.7	0.0059		0.0033	0.0111	
272		-7.6	0.1000		0.6223	3.0200	
273		-2.1	0.0182		0.0076	0.0832	
274		-4.8	0.0417		0.0745	1.8793	
275		-8.3	0.0245		0.0469	0.6730	
276		-0.9	0.0058		0.0064	0.8690	
277		-3.7	0.0234		0.0946	1.9187	
278		-19.5	0.0126		0.0072	0.0923	
279		-16.9	0.0115		0.0086	0.4385	
280		3.4	0.0631		0.5675	1.2331	

281		-1.9	0.0023		0.0031	0.1633	
282		-5.5	0.0158		0.0029	0.0191	
283		-6.3	0.0063		0.0047	0.1923	
284		18.2	0.3162		0.2404	0.6730	
285		-2.6			0.6714	1.6827	
286		5.8			6.9024	0.1442	
287		-4.1	0.0141		0.0070	0.0028	
288		4.4	0.0059		0.0068	0.0063	
289		-27.6			1.1885	2.4099	
290		-11.2	0.0079		0.0130	0.0067	
291		-7.1	0.0219		0.0991	1.6218	
292		36.7			10.4472	>10	
293		-11.3	0.0437		0.1791	0.4285	
294		-8.1	0.0126		0.0108	0.0028	
295		10.1			>10	>10	
296		3.6	0.1000		0.0624	0.0923	
297		2.6	0.0100		0.0050	0.0056	
298							
299		1.5	0.0200		0.0081	0.0127	
300		-1.8	0.3981		0.1710	20.2302	
301		-2.2	0.1000		0.0776	0.1629	
302		-2.8	0.0316		0.0116	0.0143	
303		-1.6			6.9183	5.1880	
304		3.2	0.0224		0.1127	5.6494	
305		0.9	0.0457		0.0155	0.0197	
306		2.5			6.8707	5.9841	
307		2.2			>10	10.6660	
308		22.9			>10	>10	
309		1.4			1.3062	1.2647	
310		12.2	0.0050		0.0092	0.0026	
311		63.6	0.0158		0.0179	0.0352	
312		9.5	0.0398		0.1574	8.6696	
313		-5.4			1.1117	24.7172	
314		18.7			2.8314	>10	
315		8.8	0.0158		0.0398	2.4889	
316		-9.6	0.0316		0.0723	2.2080	
317		4.8			>10	>10	
318							
319		-6.8			10.0000	4.5709	
320		-19.7			0.6324	0.8337	
321		14.1	0.1000		0.0374	0.5888	
322	100.4						
323	102.4						
324	100.4						
325	99.7						
326	92.0						
327	93.1				>10	>10	
328	88.0				>10	>10	

329	99.5				>10	>10	
330		33.8			>10	>10	
331		-11.0	0.1778		0.1479	4.2954	
332		-9.5	0.6310		0.2168	3.7239	
333		6.9	0.0631		0.1014	>10	
334		101.8			>10	>10	
336		-0.5	0.3715		0.2891	2.1627	

The following compounds were tested in additional runs for the assays described above and the data is provided in Table 3.

Table 3: P2X7 activity of the compounds of Formula (I, Ia, IIa or IIb) in a panel of in-vitro assays

Example	PBMC 1 µM (% control)	PBMC 10 µM (% control)	P2X7 human K_i (µM)	P2X7 rat K_i (µM)	FLIPR (human) IC_{50} (µM)	FLIPR (rat) IC_{50} (µM)	Human whole blood IC_{50} (µM)
1	11.5		0.0759		0.0041	0.6091	
2	7.9		0.0871		0.0121	2.9087	
3	23.0		0.0603		0.0890	4.0059	
4		-3.7	0.0251		0.0465	2.5704	
5		11.6	0.0316		0.0124	0.3236	
6	14.3		0.0427		0.0094	1.7824	
7	98.7						
8	83.1						
9	83.7						
10	76.5						
11		3.7	0.1259		0.0142	0.5922	1.585
12	11.2		0.0851	0.1349	0.0049	0.7661	0.631
13	27.9		0.0794		0.0126	0.1259	
14	12.8		0.0794		0.0767	0.1225	
15	9.1		0.1585		0.0814	0.1354	
16	8.5		0.2512		0.0937	0.2566	
17	6.5		0.0501		0.0339	0.2949	
18	5.3		0.1000		0.0777	1.1822	
19		11.6	0.1000		0.0352	0.4539	
20		8.6	0.5012		0.9311	2.3714	
21		1.6	0.1259		0.0900	2.3190	
22		-15.9	0.1259		0.0096	3.8283	
23		6.4	0.0398		0.0300	0.1131	
24	2.9		0.0912		0.0233	0.0262	
25	9.7		0.0741		0.1415	3.4080	
26	14.0		0.0851		0.0077	0.0549	
27	39.2		1.3804		0.1636	2.8054	
28	4.8		0.0794		0.0065	0.0362	

29	34.7		0.0380		0.0620	2.4963	
30	87.0		0.3981		1.1306	3.6249	
31	50.8		0.3162		0.1490	0.3334	
32		1.9	0.0372		0.0111	0.0475	0.251
33	100.7						
34	29.8		0.6310		0.1582	0.2788	
35	31.6		0.3162		0.3483	0.2351	
36	16.6				3.3884	10.0693	
37		-9.1	0.0794		0.0993	1.5311	
38		-0.3	0.2512		0.0143	0.1265	
39		112.0					
40		36.5	0.0071	0.0078	0.0040	0.1152	0.092
41		40.5			2.5954	10.0000	
42		5.8	0.0398	0.0141	0.0488	0.1709	2.512
43		77.8		1.9953	4.3621	>10	
44		44.7	0.0316		0.0150	0.1164	
45		29.4			1.6106	14.9969	
46		2.1	0.0398		0.0665	0.3034	3.981
47		-1.1	0.3162		0.1470	4.1716	
48	90.1						
49	93.5						
50	96.0						
51	97.6						
52	98.9						
53	99.0		0.7413		1.0163	3.1499	
54	8.6		0.0437		0.1984	4.1115	
55	11.3		0.1259		0.0167	0.2594	
56	10.1		0.0794		0.0251	0.3981	
57		46.7	0.7943		0.7178	0.2198	
58		-2.0	0.1259		0.0107	0.7656	
59		10.2	0.5012		0.3784	0.5272	
60		8.4	0.1000		0.0557	1.6482	
61	-0.1		0.0389		0.0027	1.8737	
62	5.2		0.0437		0.0762	4.2756	
63	12.6		0.0117		0.0038	1.4521	
64		-9.2	0.0316	0.0216	0.0228	2.8820	0.251
65		5.8	0.0158	0.0028	0.0041	0.0063	0.079
66		2.7	0.0158		0.0224	0.2575	0.363
67		6.5	0.0079		0.0020	0.0530	0.158
68		12.9	0.0182		0.0394	0.2096	
69		6.8	0.0141		0.1058	1.4571	
70		10.6	0.0126		0.0075	1.3274	0.501
71		11.1	0.2512		0.0490	0.3972	
72	-5.7		0.0295		0.0042	0.1687	0.126
73	4.3		0.2512	0.0191	0.0145	0.0408	0.016
74	102.6		13.1826	2.2387	13.3660	19.2309	5.012
75	5.2	-0.3	0.0447	0.0062	0.0034	0.0091	0.013
76	1.6		0.3631		0.0244	0.0324	
77	31.7		0.3981		0.1259	0.0063	
78	57.7		0.1000		0.0631	0.5012	

79	23.2		0.0316		0.0062	0.0865	
80		4.6	0.0398		0.0207	0.0187	0.016
81		5.9	0.0631		0.0735	0.1076	
82		7.9	0.0575		0.0173	0.1545	
83		4.5	0.1585		0.0169	0.3972	
84		8.5	0.0398		0.0177	0.1871	0.200
85		24.7	0.0398		0.0141	0.0146	
86		13.0	0.0398		0.0129	0.1361	
87		3.3	1.2589	0.7943	2.5050	5.2180	3.311
88		18.2	0.0126	0.0022	0.0022	0.0020	0.002
89	-1.5		0.0158		0.0055	0.9078	
90	13.3		0.0295		0.0103	0.9727	
91	6.1		0.0234	0.0068	0.0027	2.5119	0.316
92	2.7		0.0263		0.0054	0.4395	
93	9.0		0.0398		0.0079	0.2512	
94		10.8	0.0316		0.0124	0.1230	
95		14.4	0.3162		0.2042	>10	
96		3.6	0.0148		0.0025	0.1786	
97		12.7	0.0200		0.0045	2.2909	
98		32.5	0.0141		0.0066	0.5483	
99	7.0		0.0813	0.7413	0.0115	0.1948	
100	9.2		0.0759		0.0062	1.6387	
101	7.6		0.0851		0.1285	3.4594	
102	18.0		0.1096		0.2299	5.9361	
103	56.0		0.2754		0.3917	8.3560	
104	8.9		0.0501		0.2046	1.6088	
105	51.0		0.1995		0.0794	1.2589	
106	64.4		0.2512		0.1585	1.5849	
107	24.7		0.0794		0.0158	0.7943	
108	1.1		0.1000		0.0126	0.7943	
109	94.1				0.2512	3.1623	
110	-15.1		0.1820		0.0100	1.2589	
111	15.7		0.0794		0.1585	1.5849	
112	51.9		0.2512		0.1259	3.9811	
113		42.6	0.3981		0.8551	>10	
114	20.4		0.2512		0.0631	1.2589	
115		-3.3			1.0691	>10	
116		45.3	0.0063		0.0088	0.0041	
117		4.3			2.2182	>10	
118		12.6	0.7943		1.1858	1.7378	
119		20.0	0.0063	0.0025	0.0013	0.0015	0.013
120		-3.8	0.0063		0.0059	0.0556	
121		-0.2	0.0112		0.0032	0.0065	
122		0.2	0.0200		0.0048	0.0120	
123	22.0		0.0631		0.0501	1.0000	
124	94.7						
125	83.4		0.2512		0.1585	1.2589	
126	71.7		0.0933		0.0855	1.4109	
127		9.2	0.0398		0.0221	0.0891	
128		23.1			2.1086	>10	

129		8.4			0.3664	3.3497	
130		3.7	0.0501		0.0036	0.1545	0.501
131		8.3	0.0501		0.0021	0.0304	0.316
132		3.8	0.0501		0.0783	4.4259	
133		-0.2	0.0100	0.0016	0.0022	0.0093	
134		12.3	3.9811		6.6989	10.8643	
135		1.7	0.1000		0.0482	1.3804	
136		5.3	0.0158		0.0093	0.1327	0.063
137							
138							
139							
140							
141		40.5			9.5940	>10	
142		33.8	0.0100		0.0020	0.1432	
143		58.0			>10	>10	
144		19.6	0.0032		0.0097	0.0552	
145		15.2			2.3068	13.7721	
146		30.9			2.7040	>10	
147		-8.9	0.0398		0.0113	0.5070	
148		-9.6	0.0316		0.0085	0.0118	
149		3.5			2.4917	17.2783	
150							
151		19.5	0.0501		0.0057	0.0216	
152		15.4			0.9795	1.9770	
153		28.9	0.0631		0.0051	0.0303	
154		-0.6	0.0079		0.0165	0.0102	
155		111.6					
156		1.8	0.0063		0.0144	0.6039	
157		-1.4	3.1623		1.5346	3.2961	
158		1.1	0.0094	0.0055	0.0030	0.0188	0.008
159		54.1			>10	>10	
160		101.5			>10	>10	
161		-0.9	0.0158		0.0181	0.1791	
162							
163							
164		98.1					
165		60.7			9.7949	>10	
166		0.6	0.0025		0.0024	0.0185	
167		4.2			10.4713	>10	
168		-4.2	0.0032		0.0036	0.0049	
169		95.0					
170		-5.7	0.0200	0.0032	0.0089	0.0102	
171		28.7			2.0277	>10	
172		-6.0	0.0316	0.0050	0.0117	0.0054	
173		8.8	0.0158		0.0089	0.0102	
174		4.2	0.0501		0.0033	1.6827	
175		4.5	0.0398		0.0181	2.8774	
176		7.3	0.0316		0.0080	0.0072	
177		8.6	0.0794		0.2270	>10	
178		-4.7	0.0035	0.0115	0.0051	0.1180	

179		-4.3			1.0568	>10	
180		-3.7			0.5916	>10	
181		-0.1	0.1000		0.0944	>10	
182		62.5					
183		-1.2	0.0316		0.0204	0.0083	
184		-0.7	0.3715		0.1059	1.6406	
185		-3.7	0.0251		0.0195	0.0398	
186		-0.5			>10	>10	
187		-0.6	0.0224		0.0446	6.4714	
188		-0.7	0.0079	0.0025	0.0027	0.0085	
189		0.5	0.0135		0.0039	0.0063	
190		7.1			1.5560	1.2912	
191		5.2	0.0251		0.0122	1.3002	
192		-6.3			3.2681	10.0000	
193		1.4	0.0224		0.0344	0.3007	
194		-12.8	1.3804		4.5154	>10	
195		14.4	0.0100		0.0034	0.0108	
196		-3.1	0.5012		0.3908	2.6182	
197		2.1			0.6622	0.6714	
198		1.3	0.6310		0.1803	4.9774	
199		0.0	0.0398		0.0086	0.0025	
200		3.2	0.0251		0.0370	0.0173	
201		20.4			1.2503	7.6208	
202		24.1	0.0100	0.0025	0.0017	0.0037	
203		0.6	0.0079		0.0105	0.1132	
204		180.6					
205		17.1	0.0040		0.0010	0.1084	
206		-1.0	0.0282		0.0159	0.0800	
207		45.0			8.5507	>10	
208		20.9	0.0100	0.0020	0.0126	0.0200	0.015
209		-1.0	0.0158		0.0142	0.0021	
210		0.8	0.0050		0.0102	0.0077	
211		28.5			6.3096	5.0119	
212		17.4	0.0050		0.0050	0.0016	
213		0.3	0.0251		0.0133	0.0106	
214		8.2			8.4918	46.2381	
215		2.7	0.0100		0.0020	0.0019	
216		0.6	0.0126		0.0126	0.0834	
217		60.8					
218		6.1	0.0025		0.0124	0.0180	
219		76.5			7.4131	>10	
220		15.1	0.0061	0.0010	0.0048	0.0059	0.036
221		17.8			0.5058	6.6834	
222		11.8	0.0251		0.0011	0.0010	
223		1.8	0.0447		0.0250	0.5636	
224		103.3					
225		-1.0	0.0091		0.0062	0.0423	
226		58.0					
227		-0.4	0.0200		0.0072	0.0102	
228		-1.1	0.0075	0.0028	0.0099	0.0145	0.021

229		116.4					
230		2.9	0.0589		0.0139	0.0895	
231		-4.8			0.4989	38.1944	
232		7.5			5.5976	>10	
233		-0.1	0.1000		0.0060	0.1324	
234		-40.9	0.0794		0.1995	1.9953	
235		-3.7	0.0141	0.0031	0.0054	0.0066	0.017
236		9.3			1.1858	>10	
237		-5.1	0.0363		0.0032	0.1276	
238		-4.1	0.0794		0.0271	0.7244	
239		86.9					
240		-8.9	2.5119		0.1002	0.0226	
241		6.5	1.9953		2.5823	>10	
242		-3.4	0.0251		0.0815	0.0604	
243		1.0	0.0631		0.0160	0.0150	
244		-2.3			1.1429	13.5207	
245		-7.3	0.1000		0.1607	2.0701	
246		-3.1	0.1738		0.2296	6.5313	
247		-0.8			2.3281	8.2035	
248		74.3					
249		5.1	0.0200	0.0022	0.0127	0.0038	
250		-1.3	0.0398		0.0086	0.6699	
251		11.6	0.1445		0.1237	9.1096	
252		-0.8	0.0282		0.0188	0.0223	
253		-2.6	0.1950		0.1849	12.6911	
254		0.9	0.0447		0.0223	4.2560	
255		-5.5	0.0724		0.0160	0.2113	
256		7.1			4.3652	>10	
257		7.1	0.0158		0.3873	4.3551	
258		-3.2	0.0631		0.0855	4.8417	
259		-3.5	0.0575		0.0406	10.0925	
260		1.4	0.0355		0.0270	6.9343	
261		-3.1	0.0363		0.0293	2.6164	
262		-3.6	0.0398		0.1252	3.4674	
263		-1.6	0.0550		0.0175	2.7083	
264		89.5			>10	>10	
265		76.5					
266		5.8	0.0200		0.0127	0.0126	
267		-50.8	0.0100		0.0081	0.0095	
268		-59.9			0.5998	1.2190	
269		16.3	0.0200		0.0131	0.0206	
270		47.9					
271		14.3	0.0059	0.0016	0.0017	0.0200	
272		-7.6	0.1000		0.6223	3.0200	
273		-2.1	0.0182		0.0076	0.0832	
274		-4.8	0.0417		0.0745	1.8793	
275		-8.3	0.0245		0.0469	0.6730	
276		-0.9	0.0058		0.0064	0.8690	
277		-3.7	0.0234		0.0946	1.9187	
278		-19.5	0.0126		0.0072	0.0923	

279		-16.9	0.0115		0.0086	0.4385	
280		3.4	0.0631		0.2553	1.3480	
281		-1.9	0.0023		0.0022	0.3486	
282		-5.5	0.0158		0.0029	0.0191	
283		-6.3	0.0063		0.0047	0.1923	
284		18.2	0.3162		0.2404	0.6730	
285		-2.6			0.6714	1.6827	
286		5.8			6.9024	0.1442	
287		-4.1	0.0141		0.0070	0.0028	
288		4.4	0.0059		0.0068	0.0063	
289		-27.6			1.1885	2.4099	
290		-11.2	0.0079		0.0130	0.0067	
291		-7.1	0.0219		0.0991	1.6218	
292		36.7			10.4472	>10	
293		-11.3	0.0437		0.1791	0.4285	
294		-8.1	0.0126		0.0108	0.0028	
295		10.1			>10	>10	
296		3.6	0.1000		0.0624	0.0923	
297		2.6	0.0100		0.0050	0.0056	
298							
299		1.5	0.0398		0.0133	0.0311	
300		-1.8	0.3981		0.1710	20.2302	
301		-2.2	0.1000		0.0776	0.1629	
302		-2.8	0.0316		0.0116	0.0143	
303		-1.6			6.9183	5.1880	
304		3.2	0.0224		0.1127	5.6494	
305		0.9	0.0457		0.0155	0.0197	
306		2.5			6.8707	5.9841	
307		2.2			>10	10.6660	
308		22.9			>10	>10	
309		1.4			1.3062	1.2647	
310		12.2	0.0050		0.0092	0.0026	
311		63.6	0.0158		0.0179	0.0352	
312		9.5	0.0398		0.1136	4.8719	
313		-5.4			0.8804	24.7172	
314		18.7			3.5375	>10	
315		8.8	0.0158		0.0281	2.4757	
316		-9.6	0.0316		0.0723	2.2080	
317		4.8			>10	>10	
318							
319		-6.8			10.0000	4.5709	
320		-19.7			0.6324	0.8337	
321		14.1	0.1000		0.0374	0.5888	
322	100.4						
323	102.4						
324	100.4						
325	99.7						
326	92.0						
327	93.1				>10	>10	
328	88.0				>10	>10	

329	99.5				>10	>10	
330		33.8			>10	>10	
331		-11.0	0.1778		0.1479	4.2954	
332		-9.5	0.6310		0.2168	3.7239	
333		6.9	0.0631		0.1014	>10	
334		101.8			>10	>10	
336		-0.5	0.3715		0.2891	2.1627	
346		-2.3	0.0100		0.0065	0.0022	
347		2.0			1.2050	0.3236	
348		77.7					
349		0.7	0.0079		0.0027	0.0022	
350		16.2			6.9024	2.5882	
351		0.6	0.0100		0.0012	0.0013	
352		98.2			>10	>10	
353		107.5					
354		83.4					
355		-2.0	0.0603		0.0887	0.3936	
356		-5.9			0.0214	0.1197	
357		42.4			14.3880	16.2181	
358		-0.7	0.0380		0.0152	0.0607	
359		-8.2	0.0200		0.0140	0.0158	
360		-7.1			>10	>10	
361		75.3			>10	>10	
362		90.2			>10	>10	
363		63.9			>10	>10	
364		4.8			1.2445	5.7943	
365		108.2					
366		2.0					
367		0.9	0.1148		0.0757	2.1478	
368		-2.3	0.0398		0.0226	0.2350	
369		74.5					
370		-2.2	0.0631		0.0597	0.2564	
371		-2.3	0.0176	0.0473	0.0043	0.0425	
372		1.3			1.6256	8.7297	
373		17.2			1.6558	10.1391	
374		104.3			>10	>10	
375		63.3			>10	>10	
376		96.3					
377		8.1			5.5081	15.5597	
378		-0.1	0.1585		0.0789	0.1371	
379		3.8	0.1995		0.1125	0.0474	
380		113.7					
381		4.1	0.1202		0.0385	0.2339	
382		-2.7	0.0200		0.0065	0.0566	
383		87.3					
384		-6.3			1.3804	>10	
385		12.4	0.1000		0.0461	0.0578	
386		107.5					
387		8.4	0.0891		0.0244	0.1607	
388		-18.8	0.0759		0.0219	2.2751	

389		88.9					
390		6.5	0.0138		0.0106	0.2109	
391		112.1					
392		14.4	0.0040		0.0036	0.0473	
393		8.5	0.0891		0.0512	11.0535	
394		6.2	0.0178		0.0108	0.3459	
395		14.7	0.6310		1.4723	2.5763	
396		23.0			9.7724	>10	
397		64.7					
398		0.2			0.5383	>10	
399		1.1			1.7219	>10	
400		32.0			16.9434	>10	
401		82.0					
402		0.3			0.8790	14.6893	
403		-0.2			0.4355	12.4738	
404		-3.1	0.0063		0.0024	0.0016	
405		-0.4			1.6033	2.2962	
406		-3.6	0.0229		0.0348	0.6026	
407		77.4					
408		53.6					
409		0.5			0.0289	0.0184	
410		-1.5			0.0142	0.0135	
411		69.6					
412		-12.6			0.0283	0.0041	
413		68.5					
414		22.4			>10	36.6438	
415		1.5			0.1459	0.0129	
416		1.9			0.0473	0.0081	
417		112.2					
418		97.6					
419		-0.4			0.0920	0.0157	
420		0.0	0.0044		0.0018	0.0069	
421		-1.4			1.0328	>10	
422		-9.6			0.0144	0.0031	
423		70.7			35.5631	22.1309	
424		-11.2			0.0140	0.0046	
425		83.5			33.3426	5.3211	
426		113.2			>10	>10	
427		-0.8			0.2618	8.2794	
428		1.4			0.0166	0.0212	
429		2.3			0.0171	0.0416	
430		-4.0	0.0363		0.0708	0.1578	
431		-6.4	0.0123		0.0060	0.3199	
432		0.3	0.0158		0.0126	0.0328	
433		-3.6	0.0158		0.0189	2.5527	
434		3.1	0.0479		0.0435	0.4315	
435		-11.3	0.1000		0.0586	2.7797	
436		-3.4			1.1298	>10	
437		-11.7	0.1445		0.2399	14.5546	
438		-10.8			0.0137	0.4819	

439		1.2					

CLAIMS

1. The use of at least one compound of formula I or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of inflammation, pain, Alzheimer's disease or depression.

2. The use of at least one compound of formula (IIa or IIb) or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of inflammation, pain, Alzheimer's disease or depression.

3. The use of claim 1 wherein the disease, disorder or medical condition is treatment resistant depression.

4. The use of claim 2, wherein the disease, disorder or medical condition is treatment resistant depression.