"3-(PYRAZOLYL)-1H-PYRROLO[2,3-b]PYRIDINE DERIVATIVES AS KINASE INHIBITORS"

This application claims the benefit of Indian provisional application number 2661/CHE/2012 filed on July 3, 2012 which hereby incorporated by reference.

TECHNICAL FIELD

The invention relates to novel "3-(pyrazolyl)-1H-pyrrolo[2,3-b]pyridine derivatives of formula (I), as protein kinase inhibitors.

BACKGROUND

Protein Kinases are key regulators of cell function that constitute one of the largest and most functionally diverse gene families. Protein kinases participate in the signalling events that control the activation, growth and differentiation of cells in response to extracellular mediators and to changes in the environment. In general, these protein kinases fall into several groups; those which preferentially phosphorylate serine and/ or threonine residues and those which preferentially phosphorylate tyrosine residues.

Protein kinases play crucial role in regulating the different cell processes which include, but are not limited to, proliferation, differentiation, apoptosis, motility, transcription, translation, signalling process and various regulatory mechanisms, by adding phosphate groups to the target protein residues. This phosphorylation event acts as molecular on/off switches that can modulate or regulate the target position biological function. Phosphorylation of targeted proteins occurs in response to a variety of extracellular signals. The appropriate protein kinase functions in signaling pathways to activate or deactivate. Uncontrolled signaling due to defective control of protein phosphorylation is known to contribute to various diseases. In the case of cancer, kinases are known to regulate many aspects of the cell growth, invasion that intrudes upon and destroys adjacent tissues and sometimes metastasis, or spreading to other locations in the body via lymph or blood.

The protein kinase family members include enzymes that control cell growth, migration, activation, proliferation, differentiation, signaling, survival and regulation of the cell cycle. Many diseases and/or disorders are associated with aberrant, abnormal or deregulated activity of one or more kinases. These diseases and/or disorders include, but are not limited to cancers, allergic diseases and/or disorders, autoimmune diseases and/or disorders, inflammatory diseases and/or disorder and/or conditions associated with inflammation and pain, proliferative diseases, hematopoietic disorders, hematological

malignancies, bone disorders, fibrosis diseases and/or disorders, metabolic disorders, muscle diseases and/or disorders respiratory diseases and/or disorders, pulmonary disorders, genetic developmental diseases, neurological and neurodegenerative diseases/or disorders, chronic inflammatory demyelinating neuropathies, cardiovascular, vascular or heart diseases and/or disorders, ophthalmic/ocular diseases and/or disorders, wound repair, infection and viral diseases. Therefore, inhibition of one or more of kinases would have multiple therapeutic indications.

Anaplastic lymphoma kinase (ALK) is a member of the receptor tyrosine kinase superfamily. Anaplastic lymphoma kinase (ALK) also known as ALK tyrosine kinase receptor or CD246 (cluster of differentiation 246) is an enzyme that in humans is encoded by the *ALK* gene. The most abundant expression of ALK occurs in the neonatal brain, suggesting a possible role for ALK in brain development (Duyster, J. et al., Oncogene, 2001, 20, 5623-5637).

ALK is implicated in oncogenesis in hematopoietic and non-hematopoietic tumors. Approximately sixty percent of anaplastic large cell lymphomas (ALCL) are associated with a chromosome mutation that generates a fusion protein consisting of nucleophosmin (NPM) and the intracellular domain of ALK. This mutant protein, NPM-ALK, possesses a constitutively active tyrosine kinase domain that is responsible for its oncogenic property through activation of downstream effectors. In addition, the transforming EML4-ALK fusion gene has been identified in non-small-cell lung cancer (NSCLC) patients (Soda, M., et al., Nature, 2007, 448,561-566) and represents another in a list of ALK fusion proteins that are promising targets for ALK inhibitor therapy. Experimental data have demonstrated that the aberrant expression of constitutively active ALK is directly implicated in the pathogenesis of ALCL and that inhibition of ALK can markedly impair the growth of ALK+ lymphoma cells. The constitutively activated chimeric ALK has also been demonstrated in about 60% of inflammatory myofibroblastic tumors (IMTs), a slow-growing sarcoma that mainly affects children and young adults.

Furthermore, the aberrant expression of full-length ALK receptor proteins has been reported in neuroblastomas and extremely virulent glioblastomas (brain cancer). ALK and its putative ligand, pleiotrophin, are overexpressed in human glioblastomas (Stoica, G. et al., J. Biol. Chem., 2001, 276, 16772-16779). In mouse studies, depletion of ALK reduced glioblastoma tumor growth and prolonged animal survival (Powers, C. et al., J. Biol. Chem., 2002, 277, 14153-14158).

More recently, a novel oncogenic ALK fusion, EML4-ALK, comprising portions of the echinoderm microtubule-associated protein-like 4 (EML4) gene and the anaplastic lymphoma kinase (ALK) gene, has been implicated in a subset of non-small cell lung cancer (NSCLC). Mouse 3T3 fibroblast cells forced to express this fusion tyrosine kinase generated transformed foci in culture and subcutaneous tumors in nude mice. The EML4-ALK fusion transcript was detected in 6.7% of the 75 NSCLC patients examined; these individuals were distinct from those harboring mutations in the epidermal growth factor receptor gene. These findings strongly suggest that EML4-ALK and TPM4-ALK fusions are promising candidates for a therapeutic target in a sizable subset of NSCLC and possibly in some esophageal carcinomas.

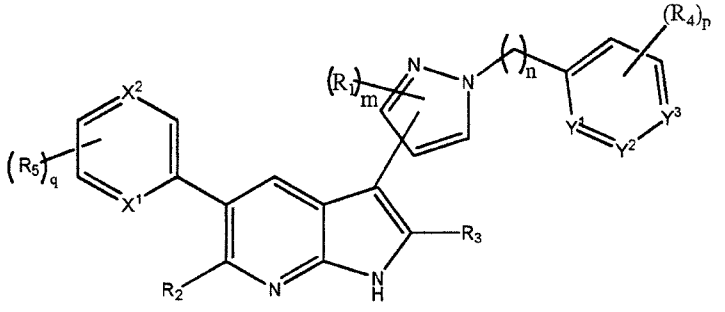
An ALK inhibitor would either permit durable cures when combined with current chemotherapy for ALCL, IMT, or glioblastoma, or be used as a single therapeutic agent in a maintenance role to prevent cancer recurrence in those patients. Various ALK inhibitors have been reported, including amino substituted pyrimidines (WO/2009/032703A1), triazine and pyrimidine compounds (WO/2009/126514), and pyrimidine compounds (WO/2011/143033A1).

Accordingly, a need exists for the identification of small-molecule compounds that specifically inhibit, regulate and/or modulate the signal transduction of kinases, particularly ALK, as a means to treat or prevent associated diseases.

SUMMARY OF THE INVENTION

The invention relates to novel 3-(pyrazolyl)-1H-pyrrolo[2,3-b]pyridine derivatives of formula (I), as protein kinase inhibitors.

In one aspect of the present invention, it relates to compound of formula (I):



(I)

or a pharmaceutically acceptable salts or stereoisomers thereof;

wherein,

X^1 and X^2 are independently selected from CH or N;

$-Y^1-Y^2-Y^3-$ is:

a) –N=CH-CH=

b) –CH=N-CH=

c) –CH=CH-N= or

d) –CH=CH-CH=

each R_1 represents alkyl;

R_2 and R_3 are independently selected from hydrogen, alkyl or cycloalkyl;

each R_4 is independently selected from alkyl, halo, haloalkyl, hydroxyl, alkoxy, haloalkoxy, $-N(R_a)R_b$, nitro, cyano or -NHC(O)alkyl;

each R_5 is independently selected from alkyl, $-OR_a$, $-O(CH_2)_qN(R_a)R_b$, $-O(CH_2)_qOR_a$, $-N(H)SO_2R_a$, $-SO_2NHR_a$, $-N(R_a)R_b$, halo, optionally substituted heterocyclylalkyl, optionally substituted heterocyclyl; wherein the optional substituent at each occurrence is independently selected from alkyl, cyanoalkyl, hydroxyl, hydroxyalkyl, $-C(O)OR_a$, $-C(O)R_a$, $-(CH_2)_nN(R_a)R_b$, $-(CH_2)_nC(O)N(R_a)R_b$, $-C(O)N(R_a)R_b$, $-C(O)(CH_2)_nR_a$, $-SO_2R_a$, $-C(O)(CH_2)_nN(R_a)R_b$, $-C(O)(CH_2)_nOR_a$, or $-(CH_2)_nOR_a$;

R_a and R_b are independently selected from hydrogen, alkyl, cycloalkyl or heterocyclyl;

'm' and 'p' are integers selected from 0 to 2, both inclusive;

'n' is an integer selected from 1 to 2, both inclusive;

'q' is an integer selected from 1 to 3 both inclusive.

In another aspect the present invention provides a pharmaceutical composition comprising the compound of formula (I), and atleast one pharmaceutically acceptable excipient (such as a pharmaceutically acceptable carrier or diluent).

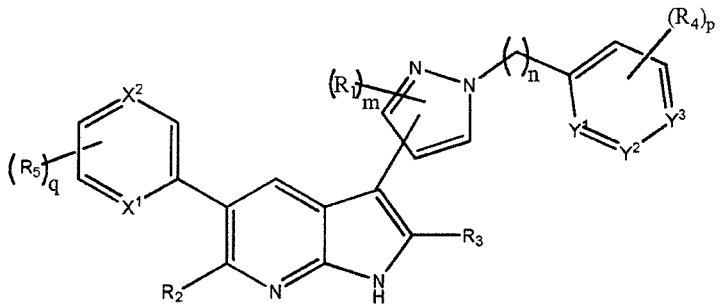
In yet another aspect the present invention relates to the preparation of the compounds of formula (I).

In further yet another aspect of the present invention, it provides 3-(pyrazolyl)-1H-pyrrolo[2,3-b]pyridine derivatives of formula (I), which are used for the treatment and prevention in diseases or disorder, in particular their use in diseases or disorder where there is an advantage in inhibiting protein kinases enzymes- particularly receptor tyrosine kinase, more particularly Anaplastic lymphoma kinase (ALK).

DETAILED DESCRIPTION OF THE INVENTION

Embodiments of the present application provides novel 3-(pyrazolyl)-1H-pyrrolo[2,3-b]pyridine derivatives of formula (I), as protein kinase inhibitors.

One of the embodiment of the present invention provides compound of formula (I):



(I)

or a pharmaceutically acceptable salts or stereoisomers thereof;

wherein,

X^1 and X^2 are independently selected from CH or N;

$-Y^1-Y^2-Y^3-$ is:

a) –N=CH-CH=

b) –CH=N-CH=

c) –CH=CH-N= or

d) –CH=CH-CH=

R_1 represents alkyl;

R_2 and R_3 are independently selected from hydrogen, alkyl or cycloalkyl;

each R_4 is independently selected from alkyl, halo, haloalkyl, hydroxyl, alkoxy, haloalkoxy, $-N(R_a)R_b$, nitro, cyano or –N(H)C(O)alkyl;

each R_5 is independently selected from alkyl, $-OR_a$, $-O(CH_2)_qN(R_a)R_b$, $-O(CH_2)_qOR_a$, $-N(H)SO_2R_a$, $-SO_2NHR_a$, $-N(R_a)R_b$, halo, optionally substituted heterocyclylalkyl, optionally substituted heterocyclyl; wherein the optional substituent at each occurrence is independently selected from alkyl, cyanoalkyl, hydroxyl, hydroxyalkyl, $-C(O)OR_a$, $-C(O)R_a$, $-(CH_2)_nN(R_a)R_b$, $-(CH_2)_nC(O)N(R_a)R_b$, $-C(O)N(R_a)R_b$, $-C(O)(CH_2)_nR_a$, $-SO_2R_a$, $-C(O)(CH_2)_nN(R_a)R_b$, $-C(O)(CH_2)_nOR_a$, or $-(CH_2)_nOR_a$;

R_a and R_b are independently selected from hydrogen, alkyl, cycloalkyl or heterocyclyl;

'm' and 'p' are integers selected from 0 to 2, both inclusive;

'n' is an integer selected from 1 to 2, both inclusive;

'q' is an integer selected from 1 to 3 both inclusive.

The embodiment below are illustrative of the present invention and are not intended to limit the claims to the specific embodiments exemplified.

According to one embodiment, specifically provided are compounds of formula (I), in which R_1 is methyl.

According to yet another embodiment, specifically provided are compounds of formula (I), in which R_2 and R_3 are independently selected from hydrogen or cyclopropyl.

According to yet another embodiment, specifically provided are compounds of formula (I), in which each R_4 is independently selected from alkyl, halo, haloalkyl, hydroxyl, alkoxy, haloalkoxy, $-N(R_a)R_b$, nitro, cyano or -NHC(O)alkyl; and p is 0, 1, or 2.

According to yet another embodiment, specifically provided are compounds of formula (I), in which R_4 is halogen; wherein halogen is fluoro or chloro.

According to yet another embodiment, specifically provided are compounds of formula (I), in which R_4 is independently selected from methyl, –OH, methoxy, ethoxy, $-CF_3$, $-OCF_3$, $-NO_2$, $-NH_2$, –CN or $-NH(CO)CH_3$.

According to yet another embodiment, specifically provided are compounds of formula (I), in which R_5 is independently selected from alkyl, $-OR_a$, $-O(CH_2)_qN(R_a)R_b$, $-O(CH_2)_qOR_a$, $-N(H)SO_2R_a$, $-SO_2N(H)R_a$, $-N(R_a)R_b$, halo, optionally substituted heterocyclylalkyl, optionally substituted heterocyclyl; wherein the optional substituent at each occurrence is independently selected from alkyl, cyanoalkyl, hydroxyl, hydroxyalkyl, -

$C(O)OR_a$, $-C(O)R_a$, $-(CH_2)_nN(R_a)R_b$, $-(CH_2)_nC(O)N(R_a)R_b$, $-C(O)N(R_a)R_b$, $-C(O)(CH_2)_nR_a$, $-SO_2R_a$, $-C(O)(CH_2)_nN(R_a)R_b$, $-C(O)(CH_2)_nOR_a$, or $-(CH_2)_nOR_a$.

According to yet another embodiment, specifically provided are compounds of formula (I), in which R_5 is halo; wherein halo is fluoro.

According to yet another embodiment, specifically provided are compounds of formula (I), in which R_5 is $-OR_a$; wherein R_a is methyl or piperidine.

According to yet another embodiment, specifically provided are compounds of formula (I), in which R_5 is $-N(R_a)R_b$; wherein R_a is hydrogen and R_b piperidine.

According to yet another embodiment, specifically provided are compounds of formula (I), in which R_5 is $-N(H)SO_2R_a$, $-SO_2NHR_a$; wherein R_a is methyl, ethyl or cyclopropyl.

According to yet another embodiment, specifically provided are compounds of formula (I), in which R_5 is alkyl; where alkyl is methyl.

According to yet another embodiment, specifically provided are compounds of formula (I), in which R_5 is heterocyclyl; wherein heterocyclyl is saturated heterocyclyl or unsaturated heterocyclyl.

According to yet another embodiment, specifically provided are compounds of formula (I), in which R_5 is saturated heterocyclyl; wherein saturated heterocyclyl is piperazine, piperidine, morpholine, and 1,4-diazepane.

According to yet another embodiment, specifically provided are compounds of formula (I), in which R_5 is unsaturated heterocyclyl; wherein unsaturated heterocyclyl is pyridine.

According to yet another embodiment, specifically provided are compounds of formula (I), in which R_5 is piperazine optionally substituted with alkyl, cyanoalkyl, hydroxyalkyl, $-C(O)OR_a$, $-C(O)R_a$, $-(CH_2)_nN(R_a)R_b$, $-(CH_2)_nC(O)N(R_a)R_b$, $-C(O)N(R_a)R_b$, $-C(O)(CH_2)_nR_a$.

According to yet another embodiment, specifically provided are compounds of formula (I), in which R_5 is piperazine optionally substituted with methyl and isopropyl.

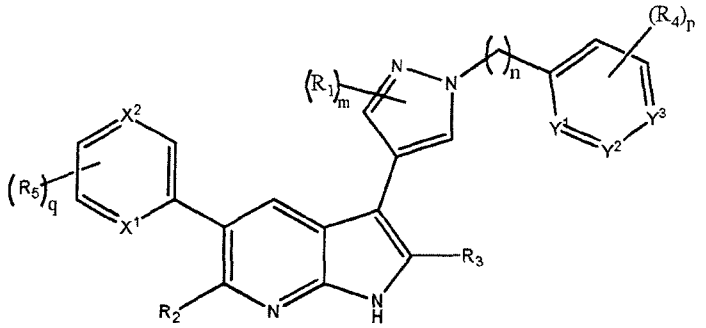
According to yet another embodiment, specifically provided are compounds of formula (I), in which R_5 is piperazine optionally substituted hydroxyalkyl; wherein hydroxyalkyl is selected from $-CH_2-CH_2-OH$, $-CH_2-CH(OH)-CH_3$.

According to yet another embodiment, specifically provided are compounds of formula (I), in which R_5 is piperidine substituted with alkyl and hydroxyl group; wherein alkyl is methyl.

According to yet another embodiment, specifically provided are compounds of formula (I), in which R_5 is optionally substituted heterocyclylalkyl.

According to yet another embodiment, specifically provided are compounds of formula (I), in which R_5 is piperidin-4-ylmethyl.

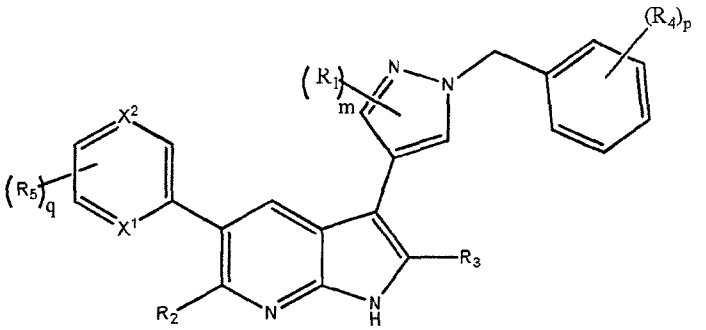
In a particular embodiment of the compounds of formula (I), the invention comprises a particular series of compounds of formula (IA):



(IA)

wherein, R_1, R_2, R_3, R_4, R_5, X^1, X^2, Y^1, Y^2, Y^3, m, n, p and q are same as defined in formula (I); or pharmaceutically acceptable salts or stereoisomers thereof.

In another particular embodiment of the compounds of formula (I), the invention comprises another particular series of compounds of formula (IB):



(IB)

wherein, R_1, R_2, R_3, R_4, R_5, X^1, X^2, m, p and q are same as defined in formula (I); or pharmaceutically acceptable salts or stereoisomers thereof.

According to yet another embodiment, specifically provided are compounds of formula (IB) in which X^1 is CH or N.

According to yet another embodiment, specifically provided are compounds of formula (IB) in which X^2 is CH.

According to yet another embodiment, specifically provided are compounds of formula (IB) in which X^2 is N.

According to yet another embodiment, specifically provided are compounds of formula (IB) in which R_1 is Alkyl; wherein the alkyl is methyl.

According to yet another embodiment, specifically provided are compounds of formula (IB) in which R_4 is halo; wherein the halo is fluorine.

According to yet another embodiment, specifically provided are compounds of formula (IB), in which R_5 is saturated heterocyclyl; wherein saturated heterocyclyl is selected from piperazine, piperidine and morpholine.

According to yet another embodiment, specifically provided are compounds of formula (IB), in which R_5 is piperazine optionally substituted with hydroxyalkyl; wherein hydroxylalkyl is $-CH_2(CH)OHCH_3$.

According to yet another embodiment, specifically provided are compounds of formula (IB), in which R_5 is piperidine optionally substituted with hydroxyl and alkyl; wherein alkyl is methyl.

According to yet another embodiment, specifically provided are compounds of formula (IB) in which m is 0.

According to yet another embodiment, specifically provided are compounds of formula (IB) in which m is 1.

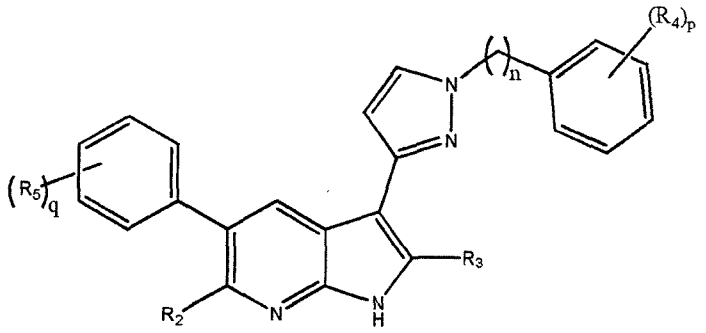
According to yet another embodiment, specifically provided are compounds of formula (IB) in which m is 2.

According to yet another embodiment, specifically provided are compounds of formula (IB) R_5 is $-OR_a$; wherein R_a is hydrogen or alkyl (methyl).

According to yet another embodiment, specifically provided are compounds of formula (IB) R_5 is $-N(R_a)R_b$, $-N(H)SO_2R_a$, $-C(O)(CH_2)_nN(R_a)R_b$, $-C(O)(CH_2)_nOR_a$ - or

$(CH_2)_nC(O)N(R_a)R_b$; wherein each R_a and R_b are independently selected from hydrogen or alkyl.

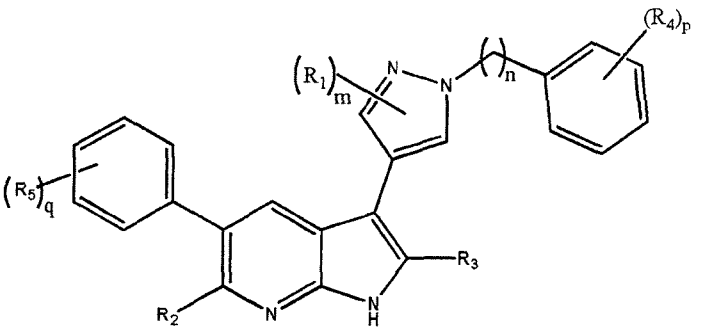
In another particular embodiment of the compounds of formula (I), the invention comprises another particular series of compounds of formula (IC):



(IC)

wherein, R_2, R_3, R_4, R_5, n, p and q are same as defined in formula (I); or pharmaceutically acceptable salts or stereoisomers thereof.

In another particular embodiment of the compounds of formula (I), the invention comprises another particular series of compounds of formula (ID):



(ID)

wherein, R_1, R_2, R_3, R_4, R_5, m, n, p and q are same as defined in formula (I); or pharmaceutically acceptable salts or stereoisomers thereof.

Another embodiment of the present invention provided a pharmaceutical composition comprising the compound as disclosed, and a pharmaceutically acceptable carrier or diluent.

The compounds as disclosed in the present invention are formulated for pharmaceutical administration.

Yet another embodiment of the present invention provides use of the compounds as disclosed in the present invention for the preparation of a medicament for the treatment of cancer.

Yet another embodiment of the present invention provides a method of treatment of cancer, wherein the method comprises administration of an effective amount of the compound of the present invention to the subject in need thereof.

Yet another embodiment of the present invention provides a method for inhibiting growth of tumour cells and/or metastasis by administering an effective amount of the compound of the present invention to the subject in need thereof.

The compounds and pharmaceutically compositions of the present invention are used in the treatment and/or prevention of diseases and/or disorders in which aberrant, abnormal or deregulated activity of ALK; tyrosine kinases evolutionary and structurally related to ALK is Ret, Ros, Axl, and kinases that are members of Trk family (Trk A, B and C) kinase contribute to the pathology and/or symptomology of such diseases and/or disorders. Such diseases and/or disorders mediated by one or more of these kinases are provided herein.

The said tumour cells include cancer such as but not limited to melanoma, renal cancer, prostate cancer, breast cancer, colon cancer and lung cancer, bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, testicular cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, Hodgkin's Disease, non-Hodgkin's lymphoma, cancer of the esophagus, cancer of the small intestine, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, chronic or acute leukemias including acute myeloid leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, solid tumours of childhood, lymphocytic lymphoma, cancer of the bladder, cancer of the kidney or ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), primary CNS lymphoma, tumour angiogenesis, spinal axis tumour, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, T-cell lymphoma, environmentally induced cancers including those induced by asbestos, and combinations of said cancers.

Still yet another embodiment of the present invention provides a method of treatment of cancer, by inhibiting ALK (Anaplastic lymphoma kinase), wherein the method comprises administration of an effective amount of the compound of the present invention to the subject in need thereof.

The compounds of the present invention may be used as single drugs or as a pharmaceutical composition in which the compound is mixed with various pharmacologically acceptable materials.

The pharmaceutical composition is usually administered by a parenteral administration route, but can be administered by oral or inhalation routes. Examples of the parenteral administration include administration by injection, and percutaneous, transmucosal, transnasal and trans pulmonary administrations.

The injectable materials include a solution, a suspension, and a solid injection that is dissolved or suspended in a solvent before use.

The injection is used after one or more active ingredients are dissolved, suspended or emulsified in a solvent. Examples of the solvent include water-soluble solvents (e.g., distilled water, physiological saline and Ringer's solution), oil solvents (e.g., vegetable oils such as olive oil, sesame oil, cotton oil and corn oil, and alcohols such as propylene glycol, polyethylene glycol and ethanol), and combinations thereof.

The dosage of the compounds of the present invention varies depending on age, weight, symptom, therapeutic efficacy, dosing regimen and/or treatment time. Generally, they may be administered by a parenteral route (preferably intravenous administration) in an amount of 1 mg to 100 mg per time, from once a couple of days, once 3 days, once 2 days, once a day to a couple of times a day, in the case of an adult, or continuously administered by intravenous administration from 1 to 24 hours a day. Since the dosage is affected by various conditions, an amount less than the above dosage may sometimes work well enough, or higher dosage may be required in some cases.

Parenteral administration by injection includes all forms of injections, and also includes intravenous fluids. For example, it includes intramuscular injections, subcutaneous injections, intradermal injections, intra-arterial injections, intravenous injections, intraperitoneal injections, injections to spinal cavity, and intravenous drops.

The compounds of the present invention may be administered in combination with other drugs for (1) complementation and/or enhancement of prevention and/or therapeutic

efficacy of the preventive and/or therapeutic drug of the present invention, (2) dynamics, absorption improvement, dosage reduction of the preventive and/or therapeutic drug of the present invention, and/or (3) reduction of the side effects of the preventive and/or therapeutic drug of the present invention.

A concomitant medicine comprising the compounds of the present invention and other drug may be administered as a combination preparation in which both components are contained in a single formulation, or administered as separate formulations. The administration by separate formulations includes simultaneous administration and administration with some time intervals. In the case of the administration with some time intervals, the compound of the present invention can be administered first, followed by another drug or another drug can be administered first, followed by the compound of the present invention. The administration method of the respective drugs may be the same or different.

The dosage of the other drug can be properly selected, based on a dosage that has been clinically used. The compounding ratio of the compound of the present invention and the other drug can be properly selected according to age and weight of a subject to be administered, administration method, administration time, disorder to be treated, symptom and combination thereof. For example, the other drug may be used in an amount of 0.01 to 100 parts by mass, based on 1 part by mass of the compound of the present invention. The other drug may be a combination of two or more kind of arbitrary drugs in a proper proportion. The other drug that complements and/or enhances the preventive and/or therapeutic efficacy of the compound of the present invention includes not only those that have already been discovered, but those that will be discovered in future, based on the above mechanism.

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly understood by one of skill in art to which the subject matter herein belongs. As used in the specification and the appended claims, unless specified to the contrary, the following terms have the meaning indicated in order to facilitate the understanding of the present invention.

As used herein, the term 'compound(s)' comprises the compounds disclosed in the present invention.

As used herein, the term "comprise" or "comprising" is generally used in the sense of include, that is to say permitting the presence of one or more features or components.

As used herein, the term "or" means "and/or" unless stated otherwise.

As used herein, the term "including" as well as other forms, such as "include", "includes" and "included" is not limiting.

As used herein, the term "optionally substituted" refers to the replacement of one or more hydrogen radicals in a given structure with the radical of a specified substituent including, but not limited to: halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, thiol, alkylthio, arylthio, alkylthioalkyl, arylthioalkyl, alkylsulfonyl, alkylsulfonylalkyl, arylsulfonylalkyl, alkoxy, aryloxy, aralkoxy, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, trifluoromethyl, cyano, nitro, alkylamino, arylamino, alkylaminoalkyl, arylaminoalkyl, aminoalkylamino, hydroxy, alkoxyalkyl, carboxyalkyl, alkoxycarbonylalkyl, aminocarbonylalkyl, acyl, aralkoxycarbonyl, carboxylic acid, sulfonic acid, sulfonyl, phosphonic acid, aryl, heteroaryl, heterocyclic, and aliphatic. It is understood that the substituent may be further substituted.

"Alkyl" refers to a hydrocarbon chain that may be a straight chain or branched chain, containing the indicated number of carbon atoms, for example, a C_1-C_{10} alkyl group may have from 1 to 10 (inclusive) carbon atoms in it. Examples of C_1-C_4 and C_1-C_6 alkyl groups include, but are not limited to methyl, ethyl, propyl, butyl, pentyl, hexyl, isopropyl, isobutyl, sec-butyl, tert-butyl, isopentyl, neopentyl, and isohexyl.

As used herein the term "cycloalkyl" alone or in combination with other term(s) means -C_3-C_{10} saturated cyclic hydrocarbyl ring. A cycloalkyl may be a single ring, which typically contains from 3 to 7 carbon ring atoms and more typically from 3 to 6 ring atoms. Examples of single-ring cycloalkyls include cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl. A cycloalkyl may alternatively be polycyclic or contain more than one ring. Examples of polycyclic cycloalkyls include bridged, fused, and spirocyclic carbocyclyls.

As used herein, the term "halo" or "halogen" alone or in combination with other term(s) means fluorine, chlorine, bromine and Iodine.

As used herein, the term "haloalkyl" means alkyl substituted with one or more halogen atoms, where alkyl groups are as defined above. The term "halo" is used herein interchangeably with the term "halogen" means F, Cl, Br or I. Examples of "haloalkyl"

include but are not limited to trifluoromethyl, difluoromethyl, 2,2,2-trifluoroethyl and the like. A haloalkyl group can be unsubstituted or substituted with one or more suitable groups;

As used herein the term "hydroxyl" means –OH group;

"Cyano" refers to –CN group;

As used herein, the term "alkoxy" refers to a straight or branched, saturated aliphatic hydrocarbon radical bonded to an oxygen atom that is attached to a core structure. Examples of alkoxy groups include but are not limited to methoxy, ethoxy, propoxy, isopropoxy, butoxy, isobutoxy, tert-butoxy, pentoxy, 3-methyl butoxy and the like.

"Haloalkoxy" refers to an alkoxy group, as defined above, wherein one or more of the alkoxy group's hydrogen atoms has been replaced with - F,- Cl,- Br or -I. A haloalkoxy group can be unsubstituted or substituted with one or more suitable groups;

As used herein, the term "nitro" alone or in combination with other term(s) means –NO_2, In one embodiment –NO_2 can be further modified to –NH_2.

As used herein the terms "cyanoalkyl" means alkyl substituted with one CN group, where alkyl groups are as defined above. Examples of "cyanoalkyl" include but are not limited to cyanomethyl, cyanoethyl, cyanopropyl, cyanobutyl and the like.

"Hydroxylalkyl-"or "Hydroxyalkyl" refers to an alkyl group, as defined above, wherein one or more of the alkyl group's hydrogen atoms have been replaced with hydroxyl groups. Examples of hydroxylalkyl moieties include but are not limited to -CH_2OH, -CH_2CH_2OH, -$CH_2CH_2CH_2OH$, -$CH_2CH(OH)CH_2OH$, -$CH_2CH(OH)$ CH_3, -$CH(CH_3)CH_2OH$.

As used herein, the term "heterocyclyl" alone or in combination with other term(s) means a saturated {i.e., "heterocycloalkyl"}, partially saturated {i.e., "heterocycloalkenyl"}, or completely unsaturated {i.e., "heteroaryl"} ring structure containing a total of 3 to 14 ring atoms. At least one of the ring atoms is a heteroatom {i.e., oxygen, nitrogen, or sulfur}, with the remaining ring atoms being independently selected from the group consisting of carbon, oxygen, nitrogen, and sulfur. A heterocyclyl may be a single-ring (monocyclic) or polycyclic ring structure. Heterocyclyl moieties include but are not limited to piperazine, piperidine morpholine, 1,4-diazepane and pyridine. A heterocyclyl group can be unsubstituted or substituted with one or more suitable groups.

"Heterocyclylalkyl" refers to an alkyl group, as defined above, wherein one or more of the alkyl group's hydrogen atoms have been replaced with a heterocyclyl as defined above. Heterocyclylalkyl moieties include but are not limited to piperidin-4-ylmethyl, pyrrolidin-1-

ylmethyl. A hetreocyclylalkyl group can be unsubstituted or substituted with one or more suitable groups.

As used herein the term "substituted" refers to a non-hydrogen radical is in the place of hydrogen radical on a carbon or nitrogen of the substituent. Thus, for example, a substituted alkyl substituent is an alkyl substituent in which at least one non-hydrogen radical is in the place of a hydrogen radical on the alkyl substituent. It should be recognized that if there are more than one substitution on a substituent, each non-hydrogen radical may be identical or different, unless otherwise stated.

As used herein, the term "composition" is intended to encompass a product comprising the specified ingredients in the specified amounts, as well as any product which results, directly or indirectly, from combination of the specified ingredients in the specified amounts. By "pharmaceutically acceptable" it is meant the carrier, diluent or excipient must be compatible with the other ingredients of the formulation and not deleterious to the recipient thereof.

As used herein, the term "treat", "treating" and "treatment" refer to a method of alleviating or abrogating a disease and/or its attendant symptoms.

As used herein, the term "prevent", "preventing" and "prevention" refer to a method of preventing the onset of a disease and/or its attendant symptoms or barring a subject from acquiring a disease. As used herein, "prevent", "preventing" and "prevention" also include delaying the onset of a disease and/or its attendant symptoms and reducing a subject's risk of acquiring a disease.

As used herein, the term "therapeutically effective amount" refers to that amount of the compound being administered sufficient to prevent development of or alleviate to some extent one or more of the symptoms of the condition or disorder being treated.

As used herein the term "modulate" refers to the ability of a compound to increase or decrease the function, or activity, of a kinase. "Modulation", as used herein in its various forms, is intended to encompass antagonism, agonism, partial antagonism and/or partial agonism of the activity associated with kinase. Kinase inhibitors are compounds that, e.g., bind to, partially or totally block stimulation, decrease, prevent, delay activation, inactivate, desensitize, or down regulate signal transduction. Kinase activators are compounds that, e.g., bind to, stimulate, increase, open, activate, facilitate, enhance activation, sensitize or up regulate signal transduction.

In a further aspect, the present invention relates to a process for preparing substituted pyridine derivatives of formula (I).

An embodiment of the present invention provides the ALK inhibitor compounds according to of formula (I) may be prepared from readily available starting materials using the following general methods and procedures. It will be appreciated that where typical or preferred experimental conditions (i.e. reaction temperatures, time, moles of reagents, solvents etc.) are given, other experimental conditions can also be used unless otherwise stated. Optimum reaction conditions may vary with the particular reactants or solvents used but such conditions can be determined by the person skilled in the art, using routine optimisation procedures. Moreover, by utilizing the procedures described in detail, one of ordinary skill in the art can prepare additional compounds of the present invention claimed herein. All temperatures are in degrees Celsius (°C) unless otherwise noted.

In a further aspect, the compounds of the present invention can also contain unnatural proportions of atomic isotopes at one or more of the atoms that constitute such compounds. For example the present invention also embraces isotopically-labeled variants of the present invention which are identical to those recited herein, but for the fact that one or more atoms of the compound are replaced by an atom having the atomic mass or mass number different from the predominant atomic mass or mass number usually found in nature for the atom. All isotopes of any particular atom or element as specified are contemplated within the scope of the compounds of the invention and their uses. Exemplary isotopes that can be incorporated in to compounds of the invention include isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorous, sulfur, fluorine, chlorine and iodine, such as ^{2}H ("D"), ^{3}H, ^{11}C, ^{13}C, ^{14}C, ^{13}N, ^{15}N, ^{15}O, ^{17}O, ^{18}O, ^{32}P, ^{33}P, ^{35}S, ^{18}F, ^{36}Cl, ^{123}I and ^{125}I. Isotopically labeled compounds of the present inventions can generally be prepared by following procedures analogous to those disclosed in the Schemes and/or in the Examples herein below, by substituting an isotopically labeled reagent for a non-isotopically labeled reagent.

The **abbreviations** used in the entire specification may be summarized hereinbelow with their particular meaning.

°C (degree Celsius); δ (delta); % (percentage); ACN (Acetonitrile); BnBr (Benzyl bromide); $(BoC)_2O$ (Di tert-butyl dicarbonate); $CDCl_3$ (Deuteriated chloroform); CH_2Cl_2/DCM (Dichloromethane); CH_3SO_2Cl/$MeSO_2Cl$ (Methanesulfonyl chloride); $CuNO_2$ DMF (Dimethyl formamide); DMA (Dimethyl acetamide); DMSO (Dimethyl sulphoxide) ; DME(Dimethoxy ethane); DIPEA/DIEA (N, N- Diisopropyl ethylamine); DMAP (Dimethyl

amino pyridine); DMSO-d_6 (Deuteriated DMSO); d (Doublet); dd (Doublet of doublet); dt (Doublet of triplet); EtOH (Ethanol); Et_2O (Diethyl ether); EtOAc (Ethyl acetate); g or gr (gram); H or H_2 (Hydrogen); H_2O (Water); HOBt (1-Hydroxy benzotriazole); HCl (Hydrochloric acid); h or hr (Hours); HATU (2-(1H-7-Azabenzotriazol-1-yl)-1,1,3,3-tetramethyl uranium hexafluoro phosphate methanaminium); Hz (Hertz); HPLC (High-performance liquid chromatography); $LiOH.H_2O$ (Lithium hydroxide mono hydrate); MeOH/CH_3OH (Methanol); MP (Melting point); mmol (Millimol); M (Molar); µl (Micro litre); ml (Millilitre); mg (Milli gram); m (Multiplet); mm (Millimeter); MHz (Megahertz); MS (ES) (Mass spectroscopy-electro spray); min (Minutes); mM (milli molar); NaOH (Sodium hydroxide); Na_2SO_4 (Sodium sulphate); N_2 (Nitrogen); NMR (Nuclear magnetic resonance spectroscopy); $Na(OAc)_3BH$ (Sodium triacetoxy borohydride), NH_4Cl (Ammonium chloride); Na_2CO_3 (Sodium carbonate); $NH_2OH.HCl$ (Hydroxylamine hydrochloride; 10% Pd/C (10% palladium activated carbon); $Pd(PPh_3)_2Cl_2$ (Bis(triphenylphosphine)palladium(II) dichloride); $Pd(dppf)_2Cl_2$(1,1'-Bis(diphenylphosphino)ferrocene) palladium(II) dichloride; Pd_2 $(dba)_3$ (Trisdibenzylidene acetone) dipalladium; $Pd(pph_3)_4$ [Tetrakistriphenylphosphine palladium(0)]; P (o-tolyl)$_3$ (Tri-o-tolyl phosphine); RT (Room temperature), SiO_2 (Silicon Dioxide), S (Singlet); TEA (Triethyl amine); TFA (Trifluoroaceticacid); TLC (Thin Layer Chromatography); THF (Tetrahydrofuran); tert (Tertiary), TFA/CF_3COOH (Trifluoro acetic acid); t (Triplet); Xantphos (4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene); Zn (Zinc), MHz (Mega Hertz), RM (Reaction mass), pH (Pouvoir hydrogen), TR-FRET (Time resolved fluorescence resonance energy transfer), IC (Inhibitory concentration), nM (Nano molar).

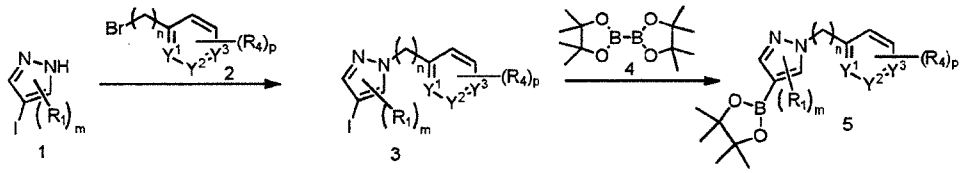
General modes of preparation:

Compounds of this invention may be made by synthetic chemical processes, examples of which are shown herein. It is meant to be understood that the order of the steps in the processes may be varied, that reagents, solvents and reaction conditions may be substituted for those specifically mentioned, and that vulnerable moieties may be protected and deprotected, as necessary.

A general approach for the synthesis of compounds of general formula (I) is depicted in below schemes. As used herein the below schemes the terms R_1, R_2, R_3, R_4, R_5, X^1, X^2, Y^1, Y^2, Y^3, m, n, p and q represents all the possible substitutions as disclosed in formula (I). The term "PG" in below schemes means protecting groups, which include but are not limited to acetyl, benzoyl, benzyl (phenylmethyl), benzylidene, benzyloxycarbonyl (Cbz), tert-

butoxycarbonyl (Boc), 3,4-dimethoxybenzyloxy carbonyl, diphenylmethyl, diphenylphosphoryl, formyl, methanesulfonyl, para-methoxy benzyloxycarbonyl, phenylacetyl, phthaloyl, succinyl, trichloroethoxycarbonyl, triethylsilyl, trifluoroacetyl, trimethylsilyl, triphenylmethyl, triphenylsilyl, para-toluenesulfonyl and the like.

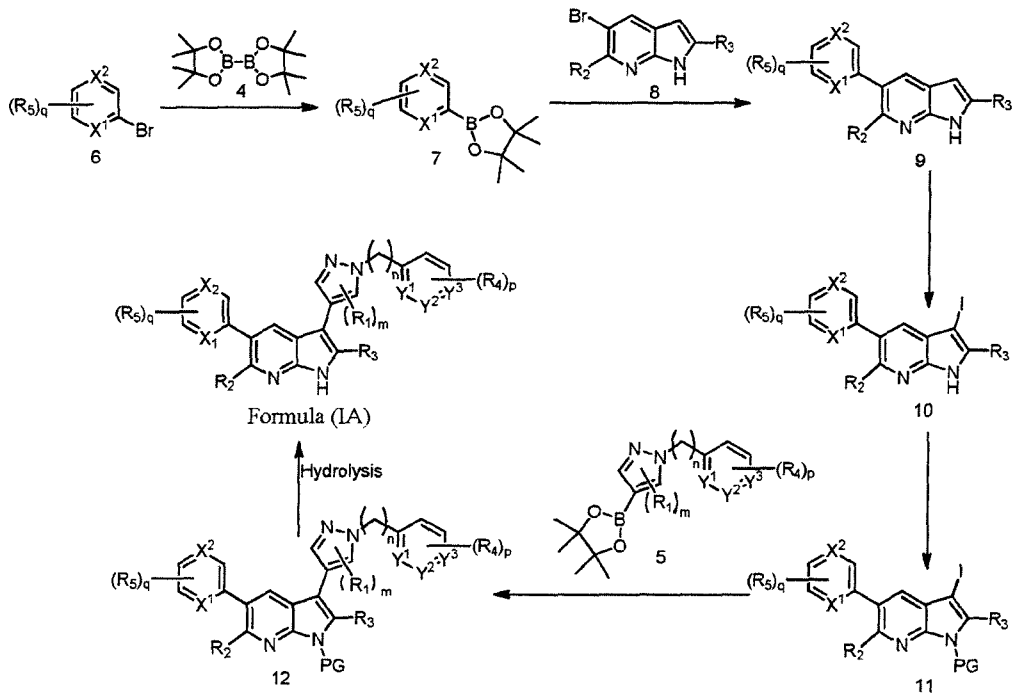
Scheme-1A:



A general method for synthesis of compounds of formula 5 is depicted in scheme-1A; wherein the compounds of formula 1 was treated with compounds of formula 2 in presence of suitable base (K_2CO_3, Na_2CO_3 or NaH) and suitable solvent (DMF) to give compounds of formula 3, which on reacting with compound 4 in presence of suitable base (CH_3COO^- K^+) and catalyst (such as bis(triphenylphosphine)palladium(II) dichloride, 1,1'-bis(diphenylphosphino)ferrocene palladium (II) chloride) in presence of suitable solvent (DMSO) under inert conditions to affords boronate compounds of formula 5, which is e used for the preparation of compounds of formula (I).

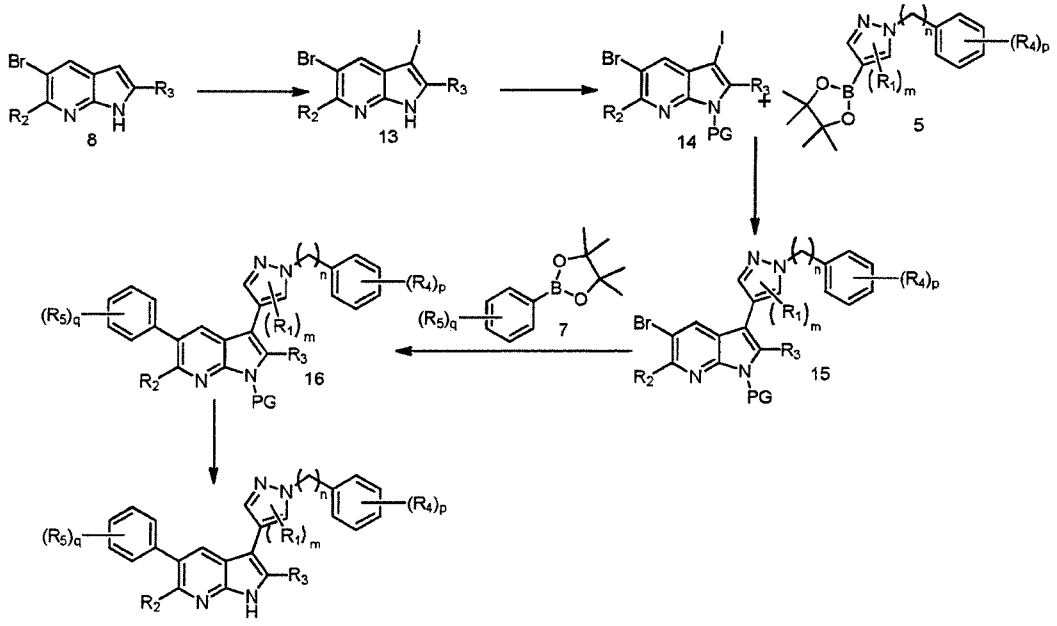
A general approach for the synthesis of compounds of the present invention is depicted in scheme-1, scheme-2 and scheme-3.

Scheme -1:



The first general approach for the synthesis of compounds of formula (IA) is depicted in scheme-1. The compound of formula 6 reacts with Bis(pinacolato)diboron of formula 4 in presence of suitable palladium catalyst to give boronic ester of formula 7. The compound of formula 7 couples with compound of formula 8 under standard coupling condition to give compound of formula 9 which on iodination with suitable reagent (for example N-iodo succinimide) and N-protection with suitable protecting group (for example t-BOC or p-toluene sulfonyl chloride) gives compound of formula 11. Coupling of compound of formula 11 with compound of formula 5 under standard coupling condition gives compound of formula 12 which on hydrolysis give compounds of formula (IA).

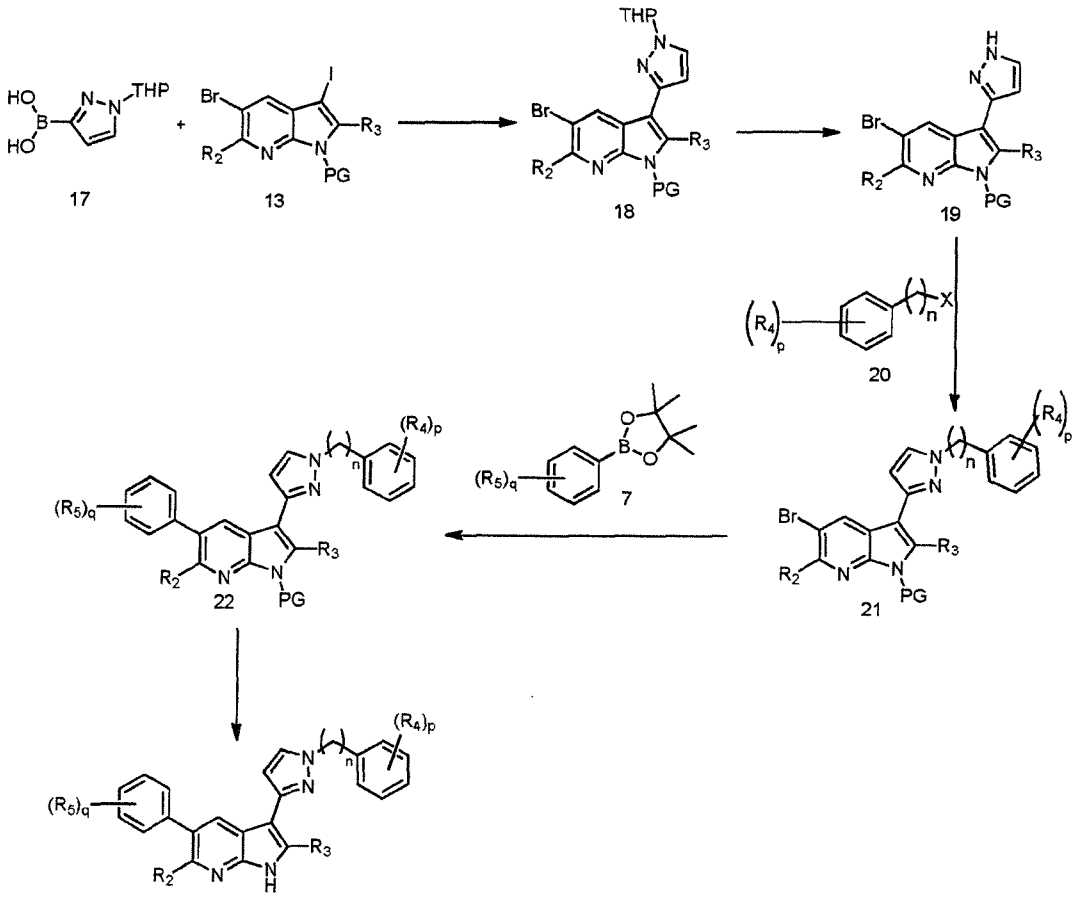
Scheme-2:



Formula (ID)

Alternatively compounds of formula (ID) can also be prepared by following general synthetic approach as depicted in scheme-2. Compound of formula 13 can be obtained by iodination of compound 8 followed by N-protection with appropriate protecting group. Coupling of compound 14 with compound 5 under standard coupling condition affords compound 15. Compound of formula 15 further couples with compound of formula 7 to give compound of formula 16 which on hydrolysis affords compounds of formula (ID).

Scheme-3:



The first general approach for the synthesis of compounds of formula (IC) is depicted in scheme-3. The THP protected pyrazole boronic acid of formula 17 reacts with compound formula 13 in presence of suitable palladium catalyst to give compound of formula 18. THP deprotection of formula 18 with suitable deprotecting agent gives compound formula 19. The compound of formula 19 is alkylated with compound of formula 20 with suitable solvent like DMF and base gives compound of formula 21. The compound of formula 21 couples with formula 7 boronic ester to give compound of formula 22 which on hydrolysis give compounds of formula (IC).

The specifics of the process for preparing compounds of the present invention are detailed in the experimental section.

In the following, the present invention shall be illustrated by means of some examples, which are not construed to be viewed as limiting the scope of the invention.

The commercially available starting materials used in the following experimental description were purchased from Aldrich or Fluka unless otherwise reported.

EXPERIMENTAL

Unless otherwise stated, work-up includes distribution of the reaction mixture between the organic and aqueous phase indicated within parentheses, separation of layers and drying the organic layer over sodium sulphate, filtration and evaporation of the solvent. Purification, unless otherwise mentioned, includes purification by silica gel chromatographic techniques, generally using ethyl acetate/petroleum ether mixture of a suitable polarity as the mobile phase. Use of a different eluent system is indicated within parentheses.

Analysis for the compounds of the present invention unless mentioned, was conducted in the general methods well known to the person skilled in the art. Having described the invention with reference to certain preferred embodiments, other embodiments will become apparent to one skilled in the art from consideration of the specification. The invention is further defined by reference to the following examples, describing in detail the analysis of the compounds of the invention.

It will be apparent to those skilled in the art that many modifications, both to materials and methods, may be practiced without departing from the scope of the invention.

HPLC Methods for Measuring Chemical Purity of the compounds of the invention was conducted by the following methods. Unless otherwise mentioned the method of HPLC, the HPLC is conducted in method D.

Column: Agilent Eclipse XDB-C18 (150mm X4.6mm X5µ)

Method A: A = 0.01% TFA in water, B= ACN: MeOH (1:1); gradient: 95:05

Method B: A = 0.01% TFA in water, B= ACN: MeOH (1:1); gradient: 70:30

Method C: A = 5mM Ammonium acetate in water, B = ACN; gradient: 70:30

Method D: A = water, B = ACN; gradient: 95:05

If required some of the compounds of the present invention were purified by preparative HPLC by using the methods either method 1 or method 2.

COLUMN: WATERS XBRIDGE OBD C18 (19mm x 150mm x 5µ)

Or AGILENT ZORBAX XDB C18 (21.2mm x 150mm x 5µ)

FLOW: 15to 20 ML/MIN

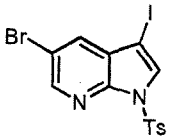
Method 1: Mobile phase A : 0.01% TFA IN WATER

Mobile phase B : ACETONITRILE: METHANOL (1:1)

Method 2: Mobile phase A : 10mM ammonium acetate
Mobile phase B : ACETONITRILE

INTERMEDIATES

Intermediate 1: 5-Bromo-3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridine



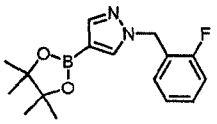
Step-i: 5-Bromo-3-iodo-1H-pyrrolo[2,3-b]pyridine

5-Bromo-1H-pyrrolo[2,3-b]pyridine (5 g, 25 mmol) was dissolved in anhydrous acetone (75 ml) and added N-iodo succinimide (6.18 g, 27.5 mmol) under nitrogen atmosphere and stirred at RT for 2 h. The reaction was monitored by TLC (10% Ethyl acetate in hexane). The reaction mixture was cooled to RT and filtered, washed with cold acetone (50 ml) and dried under vacuum to afford 7.05 g (87% yield) of 5-bromo-3-iodo-1H-pyrrolo[2,3-b]pyridine. MS: m/z = 324.6 (M+1); HPLC: 91.11% in method B.

Step-ii: 5-Bromo-3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridine

5-Bromo-3-iodo-1H-pyrrolo[2,3-b]pyridine (7 g, 21.6 mmol) dissolved in dry DMF (50 ml) was added drop wise to a stirred slurry of sodium hydride (1.73 g, 43.2 mmol) in dry DMF (20 ml) at 0°C and stirred for 30 min. Tosyl chloride (6.15 g, 32.4 mmol) dissolved in dry DMF (14 ml) and added slowly to the above reaction mixture and the reaction temperature was brought to RT and stirred for 30 min. The reaction was monitored by TLC (15% Ethyl acetate in hexane). The reaction mixture was quenched with ice water (500ml) at 0°C and filtered the solid precipitated and dried under vacuum to afford 9.92 g (96.3% yield) of 5-bromo-3-iodo-1-tosyl-1H- pyrrolo[2,3-b]pyridine MS: m/z = 476.8 (M+1).

Intermediate 2: 1-(2-fluorobenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole



Step-i: 1-(2-fluorobenzyl)-4-iodo-1H-pyrazole

To a stirred solution 4-iodo-1H-pyrazole (1.5 g, 7.7 mmol) in DMF (15 ml) was added potassium carbonate (3.2 g, 23.2 mmol) followed by drop wise addition of 2-fluoro benzyl

bromide (2.56 g, 8.5 mmol) and stirred the reaction at RT for 15 h. The reaction was monitored by TLC (50% ethyl acetate in hexane). The reaction mixture was diluted with ice water (150 ml) and extracted with ethyl acetate (2x50 ml). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to afford 2.25 g (96.56% yield) of 1-(2-fluorobenzyl)-4-iodo-1H-pyrazole.

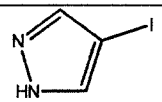
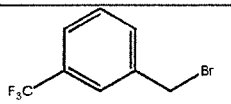
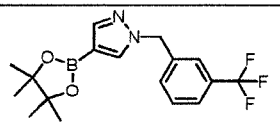
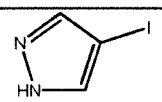
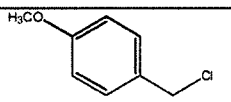
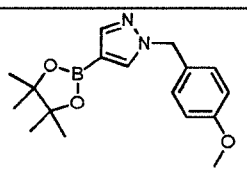
Step-ii: 1-(2-fluorobenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole

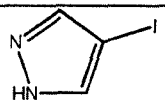
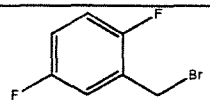
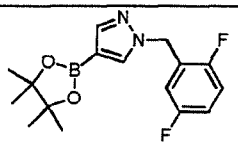
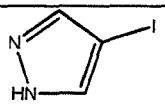
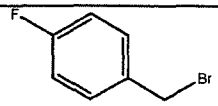
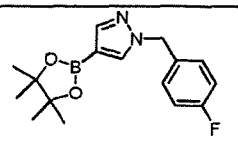
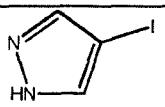
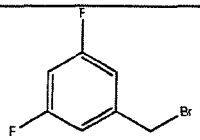
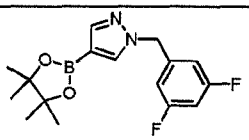
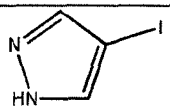
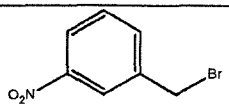
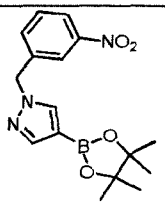
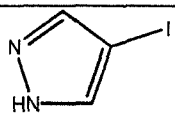
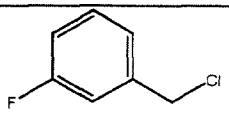
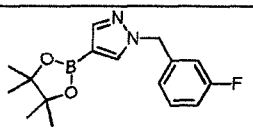
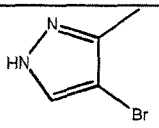
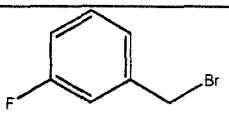
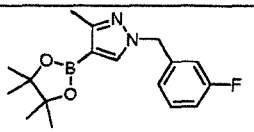
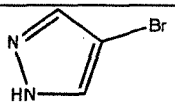
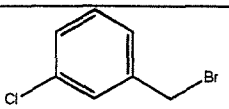
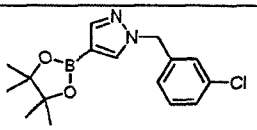
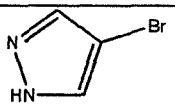
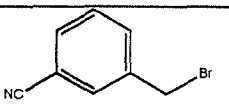
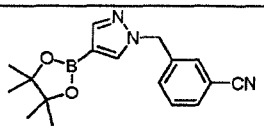
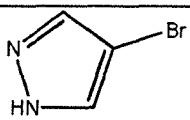
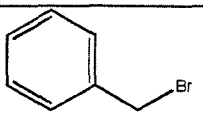
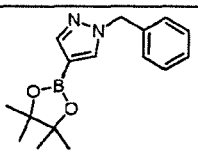
1-(2-fluorobenzyl)-4-iodo-1H-pyrazole (2.25 g, 7.4 mmol) and bispinocalatodiboron (2.07 g, 8.2 mmol) were added to a solution of DMSO (20 ml) previously purged with argon (10 min). The reaction mixture was purged with argon for a further 15mins, followed by the addition of potassium acetate (2.19 g, 22.3 mmol) and bis(triphenylphosphine)palladium(II)dichloride (261 mg, 0.3725 mmol). The resulting mixture was heated to reflux at 80 °C overnight. The reaction was monitored by TLC (40% ethyl acetate in hexane). The reaction mixture was cooled and diluted with ethyl acetate (100 ml) and filtered over celite bed and the filtrate was washed with cold water (2x100 ml). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to afford 2.3 g of the crude product which was taken as such for next reaction.

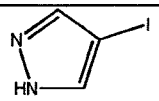
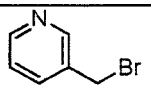
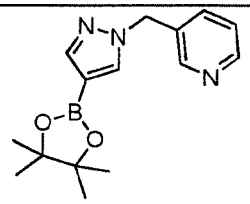
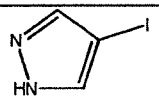
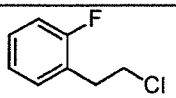
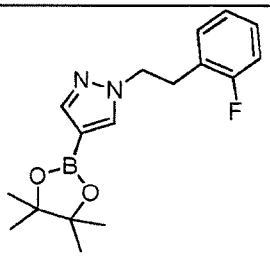
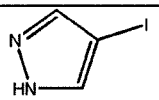
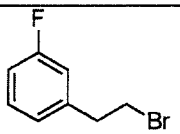
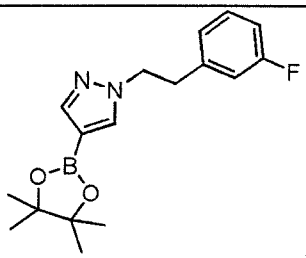
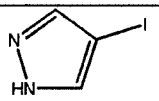
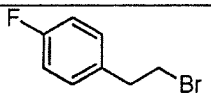
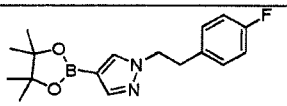
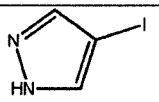
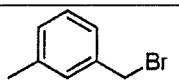
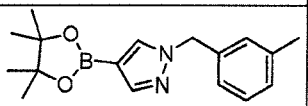
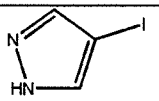
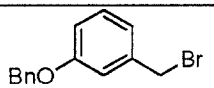
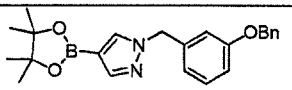
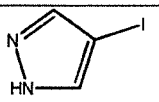
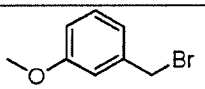
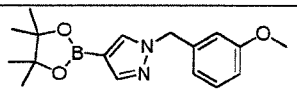
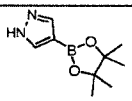
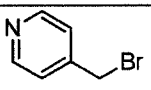
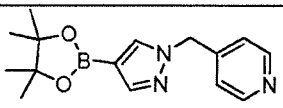
^{1}H NMR (DMSO-d_6, 300MHz): δ 8.01 (s, 1H), 7.95 (s, 1H), 7.37 (m, 2H), 7.19-7.17 (m, 2H), 5.40 (s, 2H), 1.2 (m, 12H).

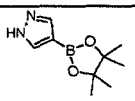
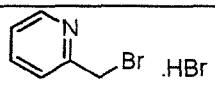
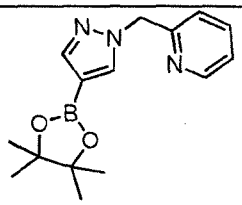
All the substituted 1-benzyl-1H-pyrazole boronic ester listed in Table 1 were prepared by using appropriate 4-halo-1H-pyrazole (reactant A) and substituted benzyl bromide (reactant B) by following similar procedure as depicted in intermediate-2. Most of these intermediates were used in the next step without further purification. Structure information and characterization data for some of the intermediates are given in table-1.

Table 1: Intermediates prepared using similar procedure of Intermediate 2

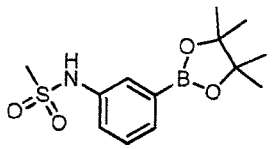
Intermediate	Reactant A	Reactant B	Product	MS (m/z)
4.				-
5.				-

6.				320.9 (M+1).
7.				-
8.				-
10.				330.3(M+1)
11.				303.3(M+1)
12.				-
13.				-
14.				310.3(M+1)
15.				285.3(M+1)

64				-
64A				-
64B				-
64C				-
64D				-
64E				-
64F				-
64G				-

64H				-

Intermediate 3: N-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methane sulfonamide



Step-i: N-(3-Bromophenyl)methanesulfonamide

To a stirred solution of 3-bromo aniline (6 g, 34.87 mmol) in dry DCM (200 ml) at 10°C was added pyridine (4.13 mg, 52.31 mmol) followed by methane sulfonyl chloride (5.194g, 45.34 mmol) and stirred at RT for 15 h. The reaction was monitored by TLC (35% Ethyl acetate in hexane). The reaction mixture was diluted with DCM (50ml) and washed with 1N HCl (25 ml). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to afford 8.45 g (96.3% yield) of N-(3-bromophenyl) methanesulfonamide.

^{1}H NMR (DMSO-d_6, 300MHz): δ 10.01 (s, 1H), 7.368 (s, 1H), 7.365-7.19 (m, 3H), 3.03 (s, 1H). MS: m/z = 251.8 (M+1).

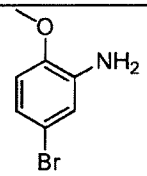
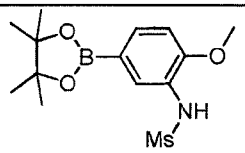
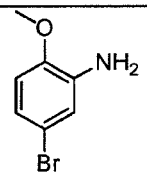
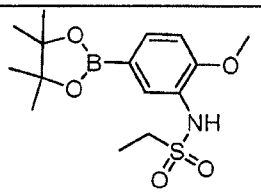
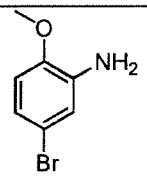
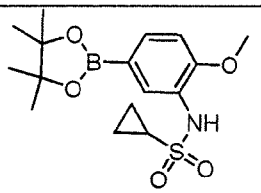
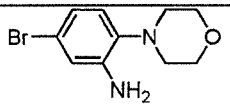
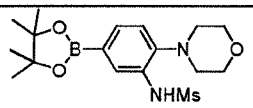
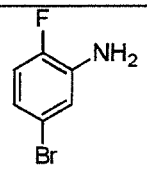
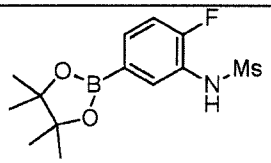
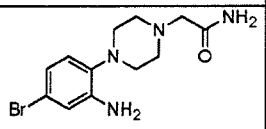
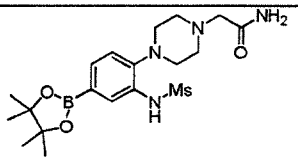
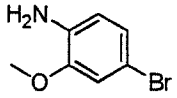
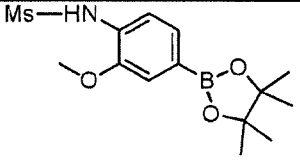
Step-ii: N-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methanesulfonamide

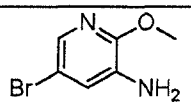
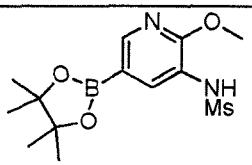
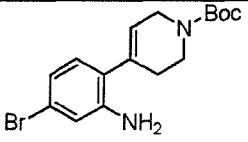
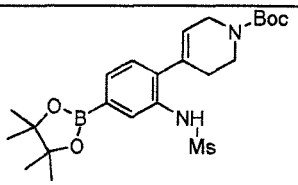
N-(3-bromophenyl) methane sulfonamide (8.3 g, 33 mmol) and bispinocalatodiboron (10.11 g, 39.8 mmol) were added to a solution of DME (80 ml) previously purged with argon (10 min). The reaction mixture was purged with argon for a further 15mins, followed by the addition of potassium acetate (9.77 g, 94.6 mmol) and $PdCl_2$(dppf) (813 mg, 0.99 mmol). The resulting mixture was heated to reflux at 80 °C overnight. The reaction was monitored by TLC (15% ethyl acetate in hexane). The reaction mixture was cooled and diluted with ethyl acetate (100 ml) and filtered over celite bed and the filtrate was washed with water (2x100 ml). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to afford the crude product. Purification by column chromatography on silica gel (15% ethyl acetate in hexane) afforded 9.3 g (94.8% yield) of N-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl) methane sulfonamide. MS: m/z = 298.1 (M+1)

All the substituted N-phenylmethanesulfonamide boronic esters listed in Table 3 were prepared by using appropriate bromo anilines (Reactant A) and alkylsulfonylchloride

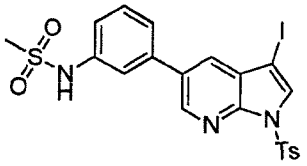
(Reactant B) by following similar procedure as depicted in intermediate-3. Most of the intermediate were used in the next step of reaction without purification. Structure information and characterization data for selected intermediates are given in table-2.

Table 2: Intermediates prepared using similar procedure of intermediate 3

Intermediate	Reactant A	Reactant B	Product	MS (m/z)
17.		Methane sulfonyl chloride		-
18.		Ethane sulfonyl chloride		-
19.		Cyclopropyl sulfonyl chloride		-
20.		Methane sulfonyl chloride		383.3(M+1) .
65		Methane sulfonyl chloride		-
65A		Methane sulfonyl chloride		-
65C		Methane sulfonyl chloride		-

65D		Methane sulfonyl chloride		-
65E		Methane sulfonyl chloride		-

Intermediate 9: N-(3-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methane sulfonamide



Step-i: N-(3-(1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide

5-bromo-1H-pyrrolo[2,3-b]pyridine (1 g, 5 mmol) and N-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methanesulfonamide (intermediate 3) (1.6 g, 5 mmol) were added to a solution of toluene/ethanol/water (6/6/5 ml) previously purged with argon (10 min). The reaction mixture was purged with argon for a further 15mins, followed by the addition of sodium carbonate (1.64 g, 15 mmol) and $PdCl_2(dppf)$ (181 mg, 0.2 mmol) and DME/water (10/5 ml) . The resulting mixture was heated to reflux at 80 °C overnight. The reaction was monitored by TLC (50% ethylacetate in hexane). The reaction mixture was cooled and diluted with ethyl acetate (50 ml) and washed with water (2x50 ml). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to afford crude product. Purification by column chromatography on silica gel (40% ethyl acetate in hexane) afforded 800 mg (57% yield) MS: m/z = 287.9 (M+1),

Step-ii: N-(3-(3-iodo-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide

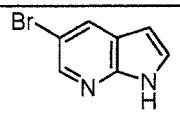
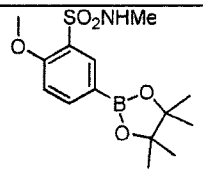
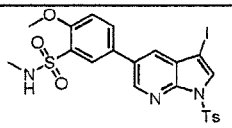
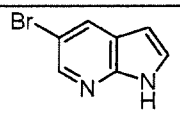
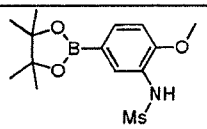
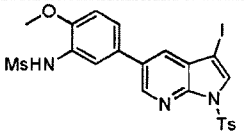
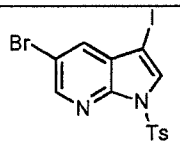
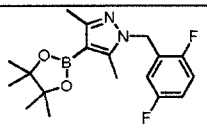
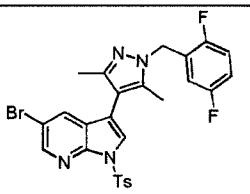
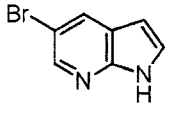
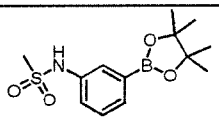
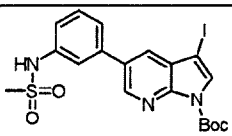
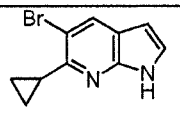
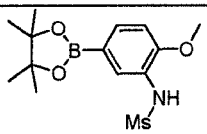
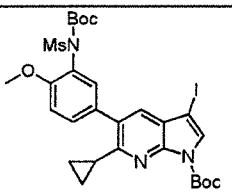
Using similar reaction conditions as described in step i of intermediate 1, N-(3-(1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide (800 mg, 3 mmol) was iodinated with N-iodo succinimide (764 mg, 3 mmol) in acetone (5 ml) to afford 600 mg (50% yield) of the pure product. LCMS: m/z = 413.4 (M+1).

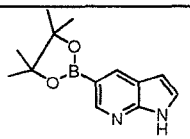
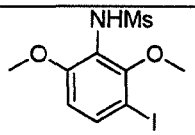
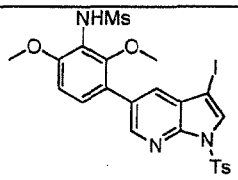
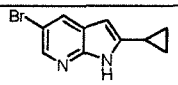
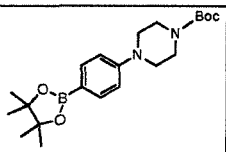
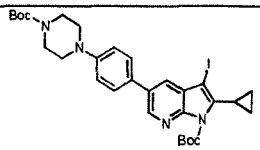
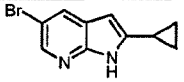
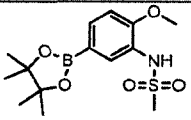
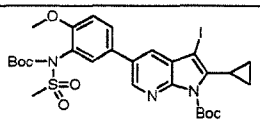
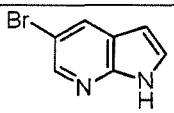
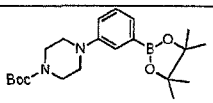
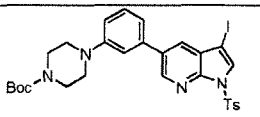
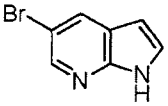
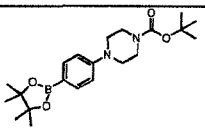
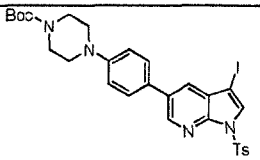
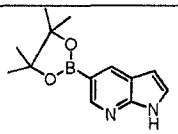
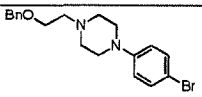
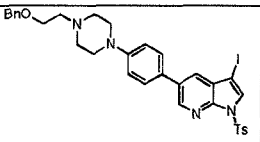
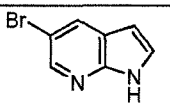
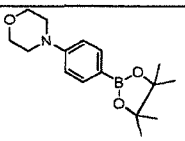
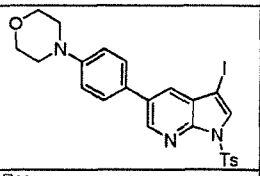
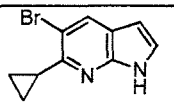
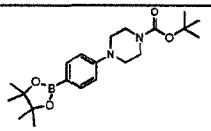
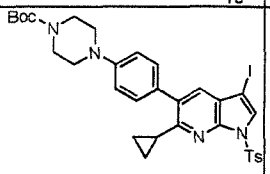
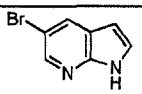
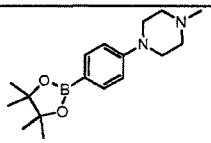
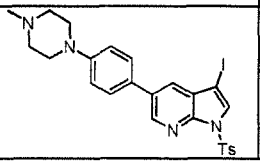
Step –iii: N-(3-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide

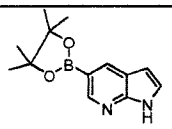
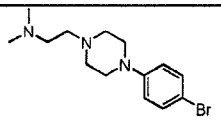
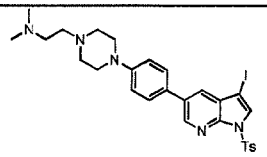
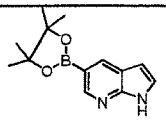
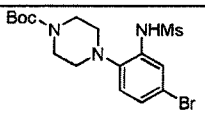
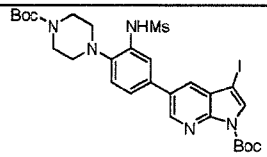
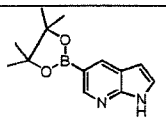
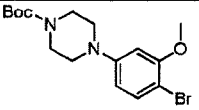
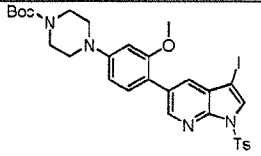
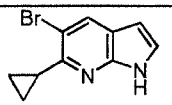
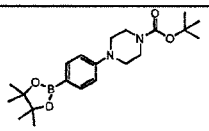
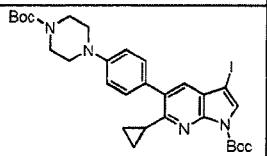
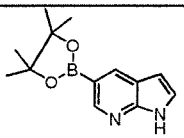
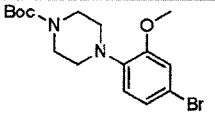
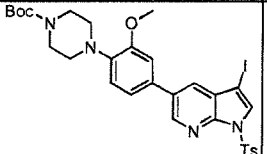
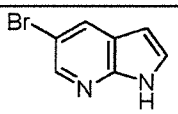
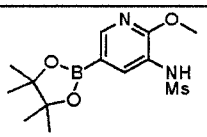
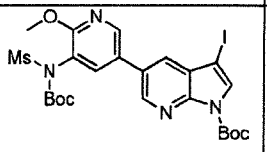
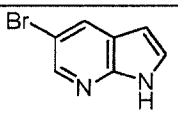
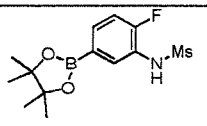
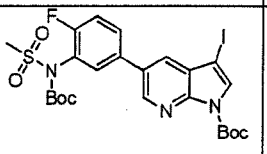
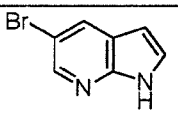
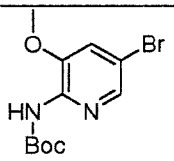
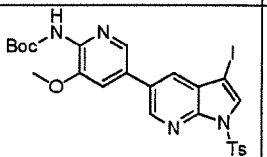
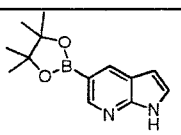
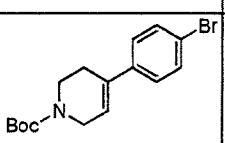
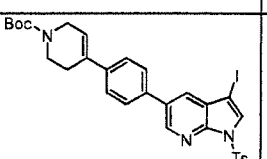
Using similar reaction conditions as described in, step ii of Intermediate 1, N-(3-(3-iodo-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide (800mg, 1.93mmol) was tosylated with p-toluene sulfonylchloride (100mg, 2.09mmol) and 60% suspension of sodium hydride in paraffin (193mg, 4.82mmol) in DMF (10mL) to afford 800mg of the titled compound.

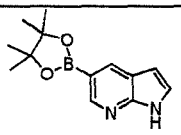
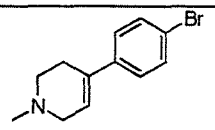
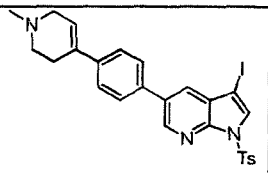
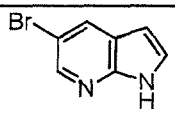
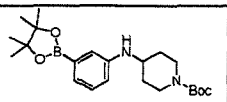
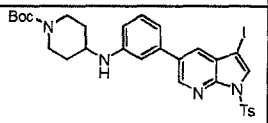
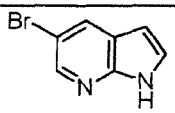
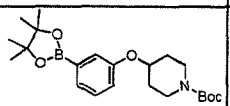
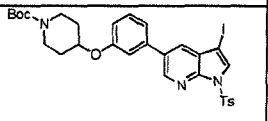
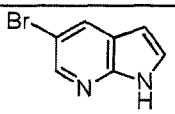
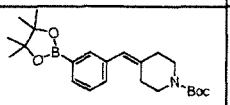
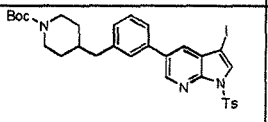
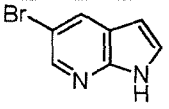
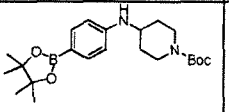
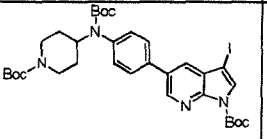
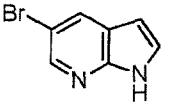
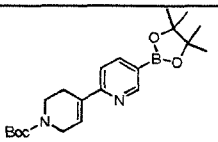
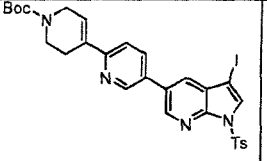
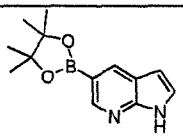
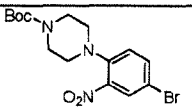
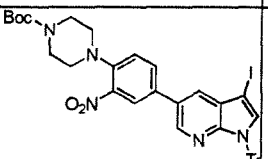
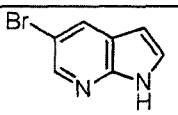
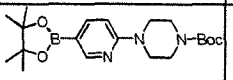
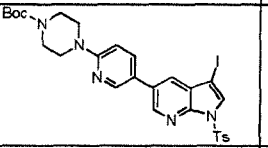
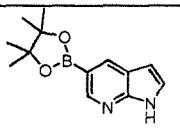
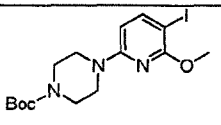
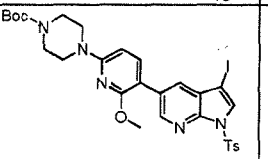
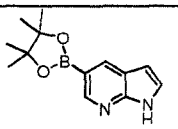
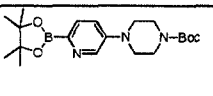
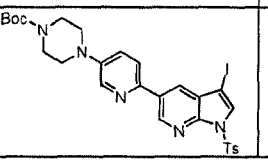
All the substituted 5-phenyl pyrrolo[2,3-b]pyridine derivatives listed in table 5 were prepared by reacting Reactant A with Reactant B by following similar reaction procedure as described in intermediate-9. $(Boc)_2O$ also used as a protecting group for some intermediates prepared using General procedure of intermediate 9. Most of the intermediate were used in the next step of reaction without purification. Structure information and characterization data for selected intermediates are given in table-3.

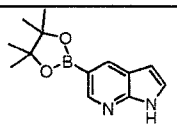
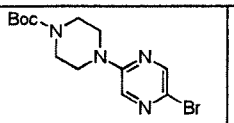
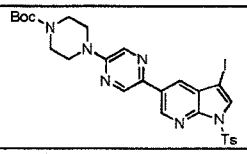
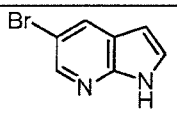
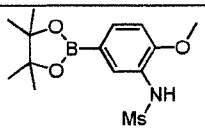
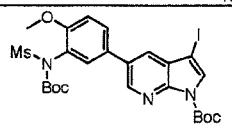
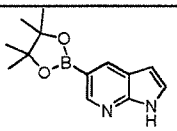
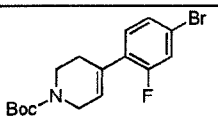
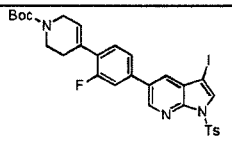
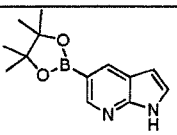
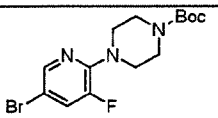
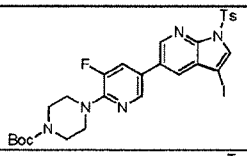
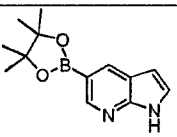
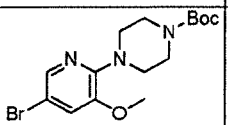
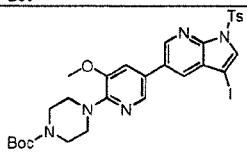
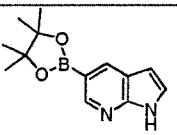
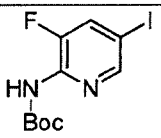
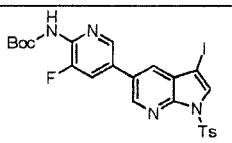
Table 3: Intermediates Prepared Using General procedure of intermediate 9

Intermediate	Reactant A	Reactant B	Product	MS (m/z)
22.				598.0(M+1)
23.				-
26.				-
32				514.1 (M+1).
33.				-

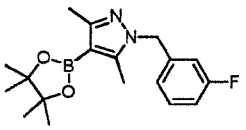
34.				627.8(M+1)
35.				645.1(M+1)
36.				683.8(M+1).
39.				659.0(M+1)
41				658.9(M+1)
42.				693.0(M+1).
43.				560.0 (M+1)
47.				699.0 (M+1)
48.				573.0 (M+1)

49.				630.1 (M+1)
50.				-
52				689.1(M+1).
57				588.8(M+1).
58				689.1(M+1).
66				-
66A				-
66B				-
66C				

66D				-
66E				-
66F				-
66G				-
66H				-
66I				-
66J				-
66K				-
66L				-
66M				-

66N				-
66P				-
66Q				-
66R				-
66S				-
66T				-

Intermediate 16: 1-(3-fluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxa borolan-2-yl)-1H-pyrazole



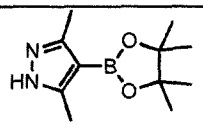
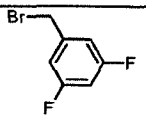
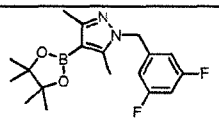
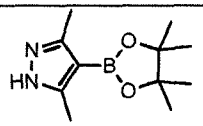
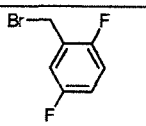
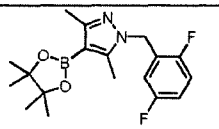
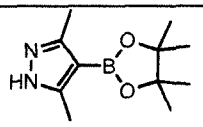
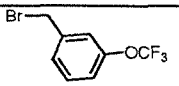
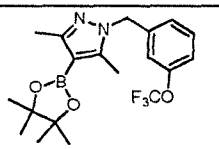
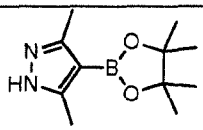
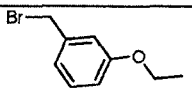
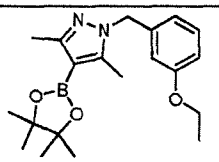
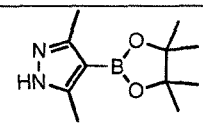
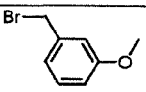
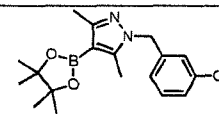
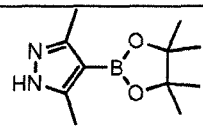
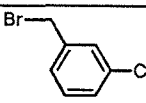
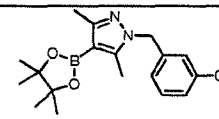
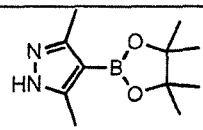
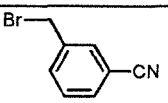
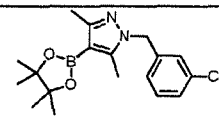
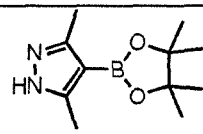
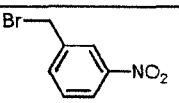
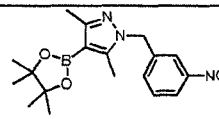
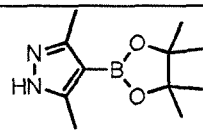
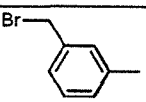
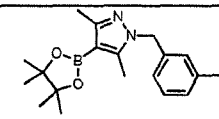
Using similar reaction conditions as described in (step i of Intermediate-2), 3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (1 g, 4.5 mmol) was reacted with 3-fluoro benzyl bromide (1.02 g, 5.4 mmol) in DMF (10 ml) and potassium carbonate (1.86 g, 13.5 mmol) to afford 1.4 g (94.59% yield) of the pure product.

MS: m/z = 331.2 (M+1).

All the substituted 1-(benzyl)-3,5-dimethyl-1H-pyrazole boronic ester listed in Table 2 were prepared by using appropriate 3,5-dimethyl-1H-pyrazole boronic ester (reactant A) and substituted benzyl bromide (Reactant B) by following similar procedure as depicted in intermediate-16. Most of the intermediate were used in the next step of reaction without

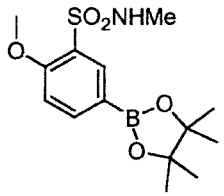
purification. Structure information and characterization data for selected intermediates are given in table-4.

Table 4: Intermediates prepared using similar procedure of Intermediate 16

Intermediate	Reactant A	Reactant B	Product	MS (m/z)
24.				-
25.				-
44.				-
46.				357.2(M+1)
53.				492.3 (M+1)
54.				347.1 (M+1)
55.				-
56.				-
56A.				-

5

Intermediate 21: 2-methoxy-N-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzene sulfonamide



Step-i: 5-bromo-2-methoxy-N-methylbenzenesulfonamide

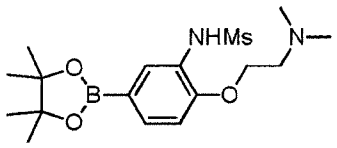
To a stirred ice cold mixture of methylamine hydrochloride (231.1mg, 3.5mmol), triethylamine (1.26mL, 8.755mmol) in DCM was added a solution of 5-bromo-2-methoxybenzene-1-sulfonyl chloride (500mg, 1.751mmol) in DCM at 0°C. This was stirred at RT for three hours. This mixture was then poured on to ice cold water and extracted with DCM, dried over sodium sulfate and concentrated to get 400mg (81.63% yield) of titled compound.

Step-ii: 2-methoxy-N-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzene sulfonamide

Using similar reaction conditions as described in step ii of intermediate-3 , 5-bromo-2-methoxy-N-methylbenzenesulfonamide (400mg, 0.716mmol) was coupled with 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (466mg, 0.917mmol) in potassium acetate (420mg, 2.14mmol), $PdCl_2$(dppf).DCM complex (52.2mg, 0.0358mmol), 1,4-Dioxane (10mL) to give 250mg (53.53% yield) of the pure product after purification by chromatographic column (Silicagel-60/120) using 20% ethyl acetate as eluent.

^{1}H NMR ($CDCl_3$, 300MHz): δ 8.35 (s, 1H), 7.98-7.95 (dd, 1H), 7.03-7.00 (d, 1H), 4.77-4.75 (d, 1H), 4.00 (s, 3H), 2.59-2.58 (d, 3H) 1.33 (s, 12H). MS: m/z= 328.0 (M+1)

Intermediate 27: N-(2-(2-(dimethylamino)ethoxy)-5-(4,4,5,5-tetramethyl-1,3,2-dioxa borolan-2-yl)phenyl)methanesulfonamide



Step-i: 2-(4-bromo-2-nitrophenoxy)-N, N-dimethylethanamine

A solution of 2-(dimethylamino)ethanol (2.2g, 24.9mmol), DMF was added slowly to a stirred suspension of sodium hydride (2.17g, 56.7mmol), DMF at 0°C. This was then added a solution of 4-bromo-2-fluoro-1-nitrobenzene (5g, 22.7mmol) in DMF dropwise at the same temperature. The reaction completed in half an hour. Reaction mass was quenched by ice and

this was extracted into ethyl acetate (150ml). Organic portion was dried and concentrated to afford 4.1g (62.5%yield) of the title compound.

^{1}H NMR (CDCl3, 300MHz): δ7.958-7.95 (d, 1H), 7.63-7.59 (dd, 1H), 7.00-6.97 (d, 1H), 4.19-4.16 (t,2H), 2.79-2.76 (t, 2H), 2.33 (s, 6H). LCMS: m/z = 288.9 (M+1)

Step-ii: 5-bromo-2-(2-(dimethylamino)ethoxy)aniline

Zinc dust (4.52g, 69.2mmol) was added to a stirred solution of 2-(4-bromo-2-nitrophenoxy)-N,N-dimethylethanamine (4g, 13.8mmol), ammonium chloride (3.7g, 69.2mmol), THF/Water (40/40mL) at RT. Reaction completed in 4 hours. The RM was filtered and the filtrate was concentrated. The residue was dissolved in ethyl acetate and washed with water, dried over sodium sulfate, concentrated to get the crude mass which was washed with hexanes to afford titled compound 1.85g (51.67% yield) as solid.

^{1}H NMR (DMSO-d_6, 300MHz): δ 6.74-6.70 (m, 2H), 6.59-6.56 (m, 1H), 4.99 (s, 2H), 3.97-3.93 (t, 2H), 2.59-2.56 (t, 2H), 2.18 (s, 6H). LCMS: m/z = 260.8 (M+2)

Step-iii: N-(5-bromo-2-(2-(dimethylamino)ethoxy)phenyl)methanesulfonamide

Using similar reaction conditions as described in step i of intermediate 17, 5-bromo-2-(2-(dimethylamino)ethoxy)aniline (1.8g, 6.94mmol) was mesylated with methanesulfonyl chloride (875mg, 7.63mol), pyridine (822mg, 10.4mmol), DCM (20mL) to afford 1.97g (83.12% yield) of the titled compound.

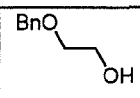
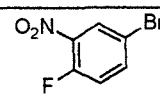
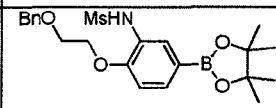
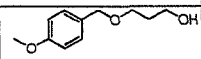
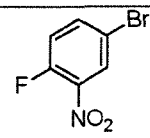
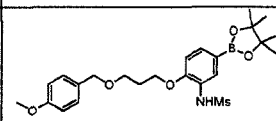
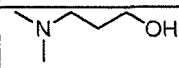
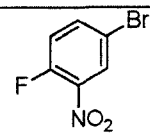
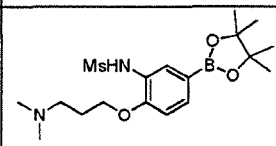
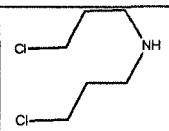
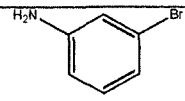
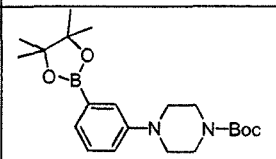
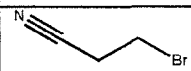
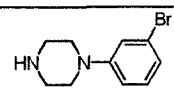
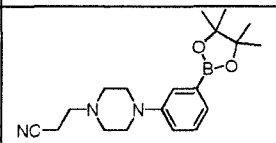
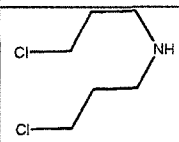
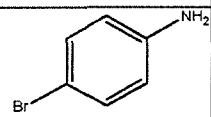
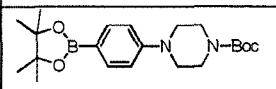
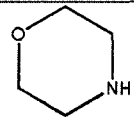
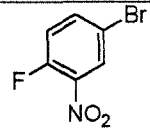
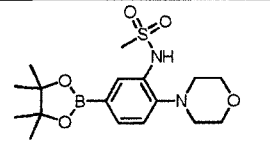
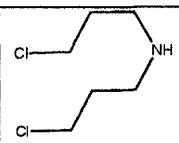
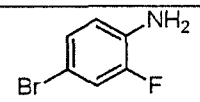
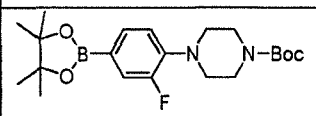
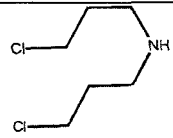
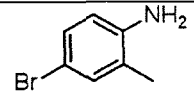
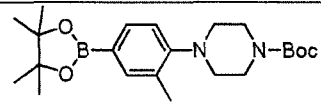
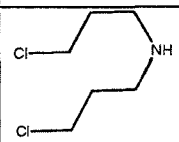
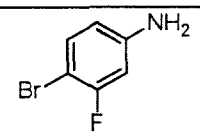
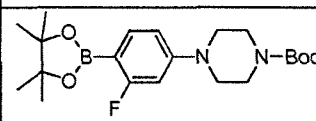
^{1}H NMR ($CDCl_3$, 300MHz): δ 7.71-7.0 (d, 1H), 7.2-7.16 (dd, 1H), 6.92-6.89 (d, 1H), 4.07-4.04 (t, 2H), 2.92 (s,3H), 2.56-2.53 (t, 2H), 2.35 (s,6H).

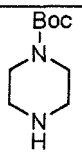
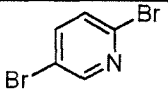
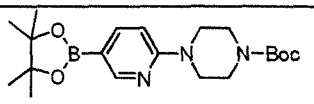
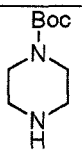
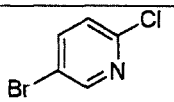
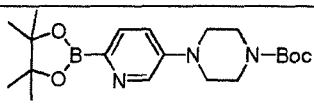
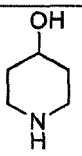
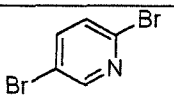
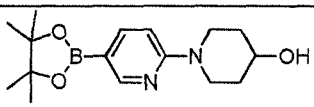
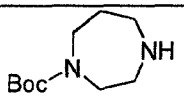
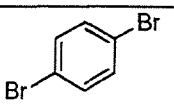
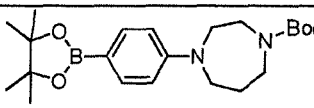
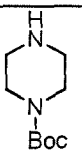
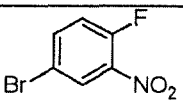
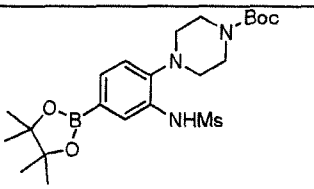
Step-iv: N-(2-(2-(dimethylamino)ethoxy)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl) methanesulfonamide

Using similar reaction conditions as described in step ii of intermediate 2, N-(5-bromo-2-(2-(dimethylamino)ethoxy)phenyl)methanesulfonamide (1.9g, 5.6mmol) was coupled with 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (2.13g, 8.45mmol) in potassium acetate (1.65g, 16.8mmol), PdCl2(dppf) (204.68mg, 0.28mmol), DMSO (40mL) to give 250mg (11.57%yield) of the title compound. LCMS: m/z = 385.1 (M+1)

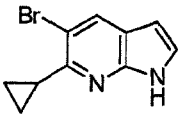
All the substituted N-(alkoxyphenyl)methanesulfonamide boronic esters listed in Table 4 were prepared by reacting Reactant A with Reactant B by following similar procedure as depicted in intermediate-27. Most of the intermediate were used in the next step of reaction without purification. Structure information and characterization data for selected intermediates are given in table 5.

Table 5: Intermediates Prepared Using General procedure of intermediate 27

Intermediate	Reactant A	Reactant B	Product	MS (m/z)
28				448.3(M+1)
29.				492.3 (M+1).
30				-
37				-
38.				342.5(M+1)
40.				243(M+2)
51.				383.1(M+1)
69				-
69A				-
69B				-

69C				-
69D				-
69E				-
69F				-
69G				-

Intermediate 31: 5-bromo-6-cyclopropyl-1H-pyrrolo[2,3-b]pyridine



Step-i: N-(6-bromopyridin-2-yl)pivalamide

To an ice cold solution of 6-bromopyridine-2-amine (7g, 40.5mmol) in DCM was added pivaloyl chloride (5.23mL, 42.48mmol), N-ethyl-N-isopropylpropan-2-amine (13.6mL, 82.9mmol) sequentially. The solution was stirred for an hour then diluted with 50mL of ether. The mixture was washed with saturated sodium bicarbonate. The organic layer was dried over sodium sulfate, filtered concentrated. The residue was slowly solidified after scratching in ethyl acetate-hexane mixture to afford 7.2gm (69.2% yield) of the titled compound. LCMS: m/z = 257.0 (M+1).

Step-ii: N-(6-cyclopropylpyridin-2-yl)pivalamide

A mixture of N-(6-bromopyridin-2-yl)pivalamide (2g, 7.77mmol), cyclopropylboronic acid (935mg, 10.88mmol), potassium phosphate (toluene/water(10/3mL) taken in screw cap tube

was purged with argon for 15 minutes and then added palladium(II)acetate (174mg, 0.77mmol), tricyclohexylphosphine (435.7mg, 1.55mmol) sequentially, purged argon for another 5 min. The resultant mixture was stirred at 100°c under closed argon atmosphere. Reaction completed in 14h, reaction mass was cooled to room temperature, extracted into ethyl acetate, (100ml) organic portion was washed with water, dried over sodium sulfate and concentrated to afford 4g of the titled compound. LCMS: m/z = 219.0 (M+1).

Step-iii: 6-cyclopropylpyridin-2-amine

To a solution of N-(6-cyclopropylpyridin-2-yl)pivalamide (4.25gm, 19.49 mmol) in dioxane (34 ml) was added 9N HCl (34 ml). The mixture was stirred for 18 hours at 90°C. After cooling to 25°C, the pH of the reaction was adjusted with to achieve pH-9. The solution was diluted with ethyl acetate (200ml) quantity and washed with saturated sodium bicarbonate. Next, the organic portion was dried over sodium sulfate and concentrated to get 2gm (77.5% yield) clear oil.

Step-iv: 5-bromo-6-cyclopropylpyridin-2-amine

A solution of 6-cyclopropylpyridin-2-amine (2g, 14.93mmol), methanol (25mL) was added N-bromosuccinimide (2.64g, 14.93mmol) portionwise. After stirring at room temperature for 30minutes, mixture was evaporated and the residue obtained was purified on column (SiO_2) using 10% ethyl acetate in hexanes as eluent. This afforded 2.1gm (68.5% yield) of title compound.

^{1}H NMR ($CDCl_3$, 300MHz): δ 7.45-7.43 (d,1H), 6.16-6.13 (d, 1H), 4.30-4.20 (bs, 2H), 2.40-2.30 (m, 1H), 1.00-0.90 (m, 2H), 0.85-0.80 (m, 2H). MS: m/z = 215.0 (M+1).

Step-v: 5-bromo-6-cyclopropyl-3-iodopyridin-2-amine

A solution of 5-bromo-6-cyclopropylpyridin-2-amine (2.1g, 9.81mmol), trifluoroaceticacid (170mg, 1.47mmol), N-iodosuccinimide (2.2g, 9.81mmol) stirred at room temperature for 30minutes. Reaction mass was quenched with water, basified with ammonium hydroxide solution. Solid separated was filtered and dried to get 3.3g (100% yield) of titled compound. 1H NMR ($CDCl_3$, 300MHz): δ 7.85 (s, 1H), 4.80-4.65 (bs, 2H), 2.39-2.25 (m, 1H), 1.0-0.90 (m, 4H).MS: m/z = 338.9 (M+1).

Step-vi: 5-bromo-6-cyclopropyl-3-((trimethylsilyl)ethynyl)pyridin-2-amine

Cuprous iodide (11.23mg, 0.059mmol) was added to a mixture of 5-bromo-6-cyclopropyl-3-iodopyridin-2-amine (1g, 2.95mmol), triethylamine (13.4g, 132.75mmol) and THF (4mL) and the resultant mixture was purged with nitrogen gas. Ethynyltrimethylsilane (347.7mg, 3.54mmol) and $Pd(PPh_3)_2Cl_2$ (41.36 mg, 0.059 mmol) were added and purged with argon. The resultant mixture was stirred under argon atmosphere for 5 hours. The mixture was

concentrated to residue. Residue was dissolved in ethyl acetate, washed with water, brine and dried over sodium sulfate and concentrated to get solid which was further purified on column (SiO_2) using 15% ethyl acetate in hexane as eluent. This afforded 1.2g (crude) of the pure compound.

Step-vii: 5-bromo-6-cyclopropyl-2-(trimethylsilyl)-1H-pyrrolo[2,3-b]pyridine

A stirred solution of 5-bromo-6-cyclopropyl-3-((trimethylsilyl)ethynyl)pyridin-2-amine(1g, 3.2mmol), tert-butanol (10mL) was added potassium tert-butoxide (1.45g, 12.9mmol) and stirred at ambient temperature for 15 min. RM was quenched with water and extracted with ethyl acetate, organic portion was dried over sodium sulfate and concentrated to give 1.2g of the titled compound.

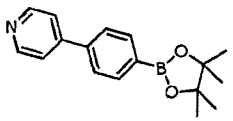
^{1}H NMR ($CDCl_3$, 300MHz): δ 7.86-7.85 (m, 1H), 6.45-6.42 (m, 1H), 4.98-4.96 (m, 1H), 4.88-4.7 (m, 1H), 4.55 (s, 2H), 2.35-2.31 (m, 1H), 2.0 (s, 9H), 1.04-0.86 (m, 4H). LCMS: m/z = 311.1 (M+1).

Step-viii: 5-bromo-6-cyclopropyl-1H-pyrrolo[2,3-b]pyridine

A stirred solution of 5-bromo-6-cyclopropyl-2-(trimethylsilyl)-1H-pyrrolo[2,3-b]pyridine (1.5g, 4.84mmol), tert-butanol (15mL), 9N-hydrochloric acid (15mL) was heated to reflux for 8 hours. Reaction mixture was cooled and basified with 50% sodium hydroxide to pH 8, extracted with ethyl acetate. Organic portion was in turn washed with brine, dried over sodium sulfate and concentrated to give 910mg (79.13% yield) of the title compound.

^{1}H NMR ($CDCl_3$, 300MHz) δ 9.43 (bs, 1H), 8.06 (s, 1H), 6.39-6.38 (m, 1H), 2.647-2.603 (m, 1H), 1.09-1 (m, 4H). LCMS: m/z = 237.0 (M+1).

Intermediate 45: 4-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)pyridine



Step-i: 4-(4-bromophenyl)pyridine

Using similar reaction conditions as described in step i of intermediate 9, 4-bromo pyridine (2 g, 8.44 mmol) was coupled with (4-bromophenyl) boronic acid (1 g, 9.2 mmol) in sodium carbonate (3.57 g, 33.7 mmol), $Pd(PPh_3)_4$ (487 mg, 0.422 mmol) and toluene/ethanol/water (50/50/20 ml) to afford 2.2 g of the crude product which was taken as such for next reaction. LCMS: 235.9 m/z = (M+2).

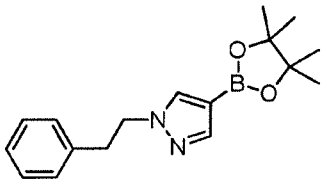
Step-ii: 4-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)pyridine.

Using similar reaction conditions as described in step ii of intermediate 2, 4-(4-bromophenyl) pyridine (1 g, 4.27 mmol) was reacted with bispinocalatodiboron (1.3 g, 5.12 mmol) in

potassium acetate (2 g, 20.62 mmol), bis(triphenylphosphine)palladium(II)dichloride (156 mg, 0.21 mmol) and 1,4-dioxane (30 ml) to afford 720 mg (60% yield) of the crude product which was taken as such for next reaction.

^{1}H NMR (DMSO-d_6, 300MHz): δ 8.66-8.64 (m, 1H), 7.94-7.91 (m, 1H), 7.71 (m, 1H), 7.67-7.63 (m, 2H), 7.59-7.54 (m, 2H), 7.45-7.3 (m, 1H), 1.38-1.22 (m, 12H)

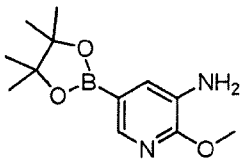
Intermediate 59: 1-phenethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole



To a stirred solution 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (300mg, 1.5463 mmol) in DMF (2 ml) cooled at 0° C was added sodium hydride (124 mg, 3.0927 mmol) and stirred at 0° C for further 20 min. Phenethyl bromide (344mg, 1.8556 mmol) was then added drop wise and stirred the reaction at RT for 3 hrs. The reaction mixture was diluted with ice water (150 ml) and extracted with dichloromethane (2x50 ml). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to afford 300 mg (43.47% yield) of the titled compound. MS: m/z = 299.4 (M+1)

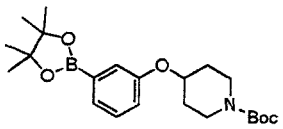
^{1}H NMR ($CDCl_3$, 300MHz): δ 7.81 (s, 1H), 7.54(s, 1H), 7.29-7.21 (m, 2H), 7.10-7.08 (d, 1H), 4.35-4.30 (t, 2H), 3.19-3.14 (t, 2H), 1.28 (s, 12H).

Intermediate 60 : 2-methoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-amine



Using similar reaction conditions as described in step ii of intermediate-3 , 5-bromo-2-methoxypyridin-3-amine (891mg, 4.39 mmol) was coupled with 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (1.86g, 5.27mmol) using potassium acetate(1.46g, 14.92 mmol) and $PdCl_2$(dppf) (160mg, 0.21mmol) in 1,4-dioxane (30mL) to give 1g (91.1% yield) of the pure product after purification by chromatographic column (Silicagel-60/120) using 20% ethyl acetate as eluent.

Intermediate 61: tert-butyl 4-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy)piperidine-1-carboxylate



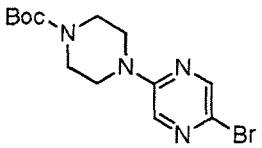
Step-i tert-butyl 4-(3-bromophenoxy)piperidine-1-carboxylate

The mixture of 3-bromophenol (2.0g, 11.56mmol), tert-butyl 4-((methylsulfonyl)oxy)piperidine-1-carboxylate (3.87g, 13.872mmol) and caesium carbonate (11.27g, 34.68mmol) in DMF (25ml) was heated at 65°C for 14hours. Cooled to RT and diluted with ether. Ether layer was washed with water and brine, dried over sodium sulphate and distilled off the solvent to afford 3.5g (85.3% yield) of the titled product after purification with (60/120 silica gel) column chromatography using 5% ethyl acetate in hexane as eluent. MS: m/z = 356.0 (M+1).

Step-ii: tert-butyl 4-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy)piperidine-1-carboxylate

Using similar reaction conditions as described in step ii of intermediate-3 , tert-butyl 4-(3-bromophenoxy)piperidine-1-carboxylate (2.0g, 5.71 mmol) was coupled with 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (1.73g, 6.85mmol) using potassium acetate (1.67g, 17.13 mmol) and $PdCl_2$(dppf) (208mg, 0.285mmol) in dioxane (20mL) to give 2.1g (91.3% yield) of the titled product after purification by chromatographic column (Silicagel-60/120) using 5% ethyl acetate as eluent. MS: m/z = 304.0 (M-Boc+1).

Intermediate 62: tert-butyl 4-(5-bromopyrazin-2-yl)piperazine-1-carboxylate



Step-i tert-butyl 4-(pyrazin-2-yl)piperazine-1-carboxylate

A mixture of 2-chloropyrazine (2.13g, 18.7mmol), tert-butyl piperazine-1-carboxylate(3.16g, 17mmol) and caesium carbonate (7.7g, 23.7mmol) in DMF (35ml) was heated at 100°C for 16 hours. Cooled to RT and diluted with ether. Ether layer was washed with water and brine, dried over sodium sulphate and distilled off the solvent to afford 2g (40.7% yield) of the titled product after purification with (60/120 silica gel) column chromatography using 40% ethyl acetate in hexane as eluent.

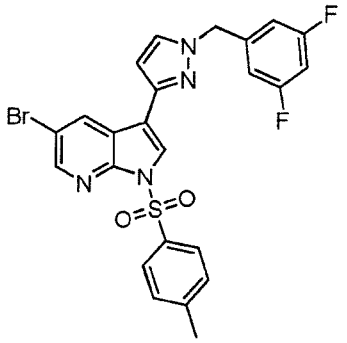
Step-ii tert-butyl 4-(5-bromopyrazin-2-yl)piperazine-1-carboxylate

Using similar reaction conditions as described in step i of intermediate 1, tert-butyl 4-(pyrazin-2-yl)piperazine-1-carboxylate (2g, 7.5 mmol) was brominated with N-

bromosuccinimide (1.46 g, 8.25 mmol) in chloroform (20 ml) to afford 1.4 g (54% yield) of the pure product. MS: m/z = 343.1 (M+1).

Intermediate 63

5-bromo-3-(1-(2, 5-difluorobenzyl)-1H-pyrazol-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine



Step-i: 5-bromo-3-(1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazol-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using the same reaction conditions as described in step-i of example 1, 5-bromo-3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridine (Intermediate 1) (100mg, 0.209 mmol) was coupled with (1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazol-3-yl)boronic acid (103mg, 0.524mmol) using sodium carbonate (66 mg, 0.627 mmol) and $Pd(PPh_3)_2Cl_2$ (7mg, 0.0104 mmol) in DME/water (3/0.7 ml) to afford 60mg (crude) product.MS: m/z = 501.1 (M+1)

Step-ii: 5-bromo-3-(1H-pyrazol-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride

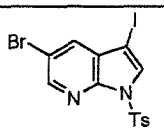
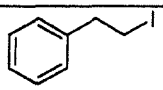
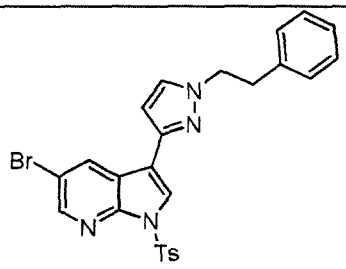
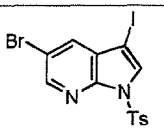
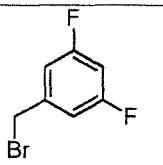
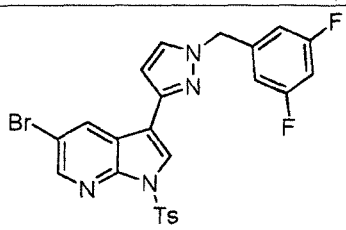
Using the same reaction conditions as described in Step-ii of example-7, (1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazol-3-yl)boronic acid (100mg, 0.198mmol) was deprotected in chloroform/ HCl in ether (1/1ml) to afford 60mg (66.8%) of the titled compound.

Step-iii: 5-bromo-3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

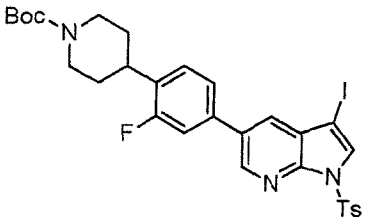
Using similar reaction conditions as described in, step ii of Intermediate 1, 5-bromo-3-(1H-pyrazol-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride (100mg, 0.239mmol) was alkylated with 1-(bromomethyl)-3,5-difluorobenzene (45mg, 0.239mmol) and 60% suspension of sodium hydride in paraffin (28mg, 0.717mmol) in DMF (5mL) to afford 100mg (crude) of the titled compound.

Table 6: Intermediates prepared using similar procedure of Intermediate 63

Intermediate	Reactant A	Reactant B	Product

63A			
63B			

Intermediate 67: tert-butyl 4-(2-fluoro-4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine -1-carboxylate



Step-i tert-butyl 4-(4-chloro-2-fluorophenyl)-5,6-dihydropyridine-1(2H)-carboxylate

Using similar reaction conditions as described in step i of intermediate 9, 4-chloro-2-fluoro-1-iodobenzene (681mg, 2.657 mmol) was coupled with tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydropyridine-1(2H)-carboxylate (1 g, 3.322 mmol) using sodium carbonate (1.056 g, 9.966 mmol) and $PdCl_2(dppf)$ (122 mg, 0.166 mmol) in THF/water (10/2 ml) at 75°C for 2 hours to afford 450mg (44.64%) of the crude product after purification with (60/120 silica gel) column chromatography using 10% ethyl acetate in hexane as eluent. MS: m/z = 212.0 (M-Boc+1).

^1H NMR ($CDCl_3$, 300MHz): δ 7.16-7.04 (m, 3H), 5.92 (s, 1H), 4.06-4.05 (d, 2H), 3.62-3.58 (t, 2H), 2.46 (s, 2H), 1.488 (s, 9H).

Step-ii tert-butyl 4-(2-fluoro-4-(1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5,6-dihydropyridine-1(2H)-carboxylate

Using similar reaction conditions as described in step i of intermediate 9, tert-butyl 4-(4-chloro-2-fluorophenyl)-5,6-dihydropyridine-1(2H)-carboxylate (320 mg, 1.025 mmol) was coupled with 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrrolo[2,3-b]pyridine

(375mg, 1.538mmol) using potassium carbonate (653mg, 3.076 mmol), $Pd(PPh_3)_2Cl_2$ (94mg, 0.102mmol) and tricyclohexylphosphine (43 mg, 0.153 mmol) in dioxane/water (10/2 ml) to afford 320mg of the product after purification with (60/120 silica gel) column chromatography using 2% methanol in DCM as eluent.

Step-iii: tert-butyl 4-(2-fluoro-4-(1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

To a solution of tert-butyl 4-(2-fluoro-4-(1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5,6-dihydropyridine-1(2H)-carboxylate (320mg, 0.814mmol) in ethyl acetate/ methanol 20/20 mL was added palladium hydroxide (160mg) and stirred under hydrogen atmosphere for 7 days. The catalyst was filtered through celite and the solvent was distilled off to get 320mg (99.37% yield) of the titled compound. MS: m/z = 396.3 (M+1)

Step-iv: tert-butyl 4-(2-fluoro-4-(3-iodo-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step i of intermediate 1, tert-butyl 4-(2-fluoro-4-(1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (320 mg, 0.810 mmol) was iodinated with N-iodosuccinimide (219 mg, 0.972 mmol) in DCM (20 ml) to afford 400 mg (94.7% yield) of the pure product. MS: m/z = 522.1 (M+1).

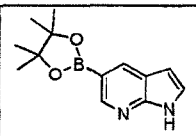
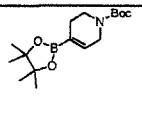
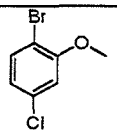
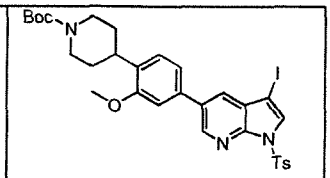
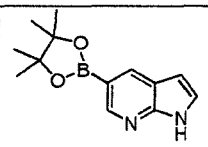
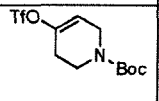
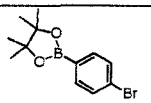
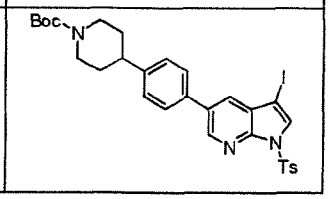
Step–v: tert-butyl 4-(2-fluoro-4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in, step ii of Intermediate 1, tert-butyl 4-(2-fluoro-4-(3-iodo-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (400mg, 0.767mmol) was tosylated with p-toluene sulfonylchloride (220mg, 1.151mmol) and DMAP (282mg, 2.303mmol) in DCM (20mL) to afford 250mg (48.26% yield) of the titled compound after purification with (60/120 silica gel) column chromatography using 1% methanol in DCM as eluent. MS: m/z = 676.3(M+1)

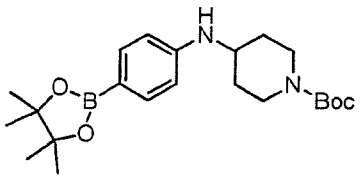
^{1}H NMR ($CDCl_3$, 300MHz): δ 8.619-8.611 (d, 1H), 8.12-8.09 (d, 2H), 7.89 (s, 1H), 7.767-7.760 (d, 1H), 7.31-7.23 (m, 5H), 4.26 (s, 2H), 3.08-3.00 (m, 1H), 2.95-2.75 (m, 2H), 2.38 (s, 3H), 1.86-1.64 (m, 4H), 1.489 (s, 9H).

Table 7: Intermediates Prepared Using General procedure of intermediate 67

Intermediate	Reactant A	Reactant B	Reactant C	Product

67A				
67B				

Intermediate 68: tert-butyl 4-((4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)amino)piperidine-1-carboxylate



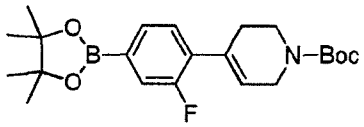
Step-i: tert-butyl 4-((4-bromophenyl)amino)piperidine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-133, tert-butyl 4-oxopiperidine-1-carboxylate (3gm, 15.0mmol) and 4-bromoaniline (2.59gm, 15.0mmol) were reacted using $Na(OAc)_3BH$ (105mg, 0.494mmol) and 3 drops of acetic acid in dichloroethane (80mL) to afford 6.7gm (crude) of the titled compound. MS: m/z = 256.8 (M-Boc+1).

Step-ii: tert-butyl 4-((4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)amino)piperidine -1-carboxylate

Using similar reaction conditions as described in step ii of intermediate-3 , tert-butyl 4-((4-bromophenyl)amino)piperidine-1-carboxylate (6.7g, 18.8mmol) was coupled with 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (7.19g, 28.3mmol) using potassium acetate (6.45g, 65.8mmol) and $Pd(dppf)Cl_2.DCM$ (410mg, 0.5mmol) in 1,4-Dioxane (150mL) to give 5.0g (65.8% yield) of the pure product after purification by chromatographic column (Silicagel-60/120) using 75% ethyl acetate as eluent. MS: m/z = 402.9 (M+1)

Intermediate 70: tert-butyl 4-(2-fluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-5,6-dihydropyridine-1(2H)-carboxylate



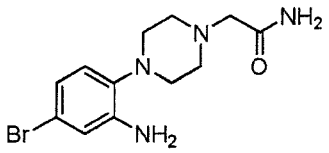
Step-i: tert-butyl 4-(4-bromo-2-fluorophenyl)-5,6-dihydropyridine-1(2H)-carboxylate

Using similar reaction conditions as described in step i of intermediate 9, 4-bromo-2-fluoro-1-iodobenzene (500mg, 1.95 mmol) was coupled with tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydropyridine-1(2H)-carboxylate (660mg, 2.14 mmol) using sodium carbonate (620mg, 5.85mmol) and $PdCl_2(PPh_3)_2$ (69mg, 0.097 mmol) in DME/water (10/2 ml) at 85°C for 2 hours to afford 300mg (50.5%) of the crude product after purification with (60/120 silica gel) column chromatography using 20% ethyl acetate in hexane as eluent. MS: m/z = 300.0 (M+1) (t-butyl cleaved mass was observed)

Step-ii: tert-butyl 4-(2-fluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-5,6-dihydropyridine-1(2H)-carboxylate

Using similar reaction conditions as described in step ii of intermediate-3 , tert-butyl 4-(4-bromo-2-fluorophenyl)-5,6-dihydropyridine-1(2H)-carboxylate (250mg, 0.698 mmol) was coupled with 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (265mg, 1.047mmol) using potassium acetate (205mg, 2.09 mmol) and $Pd(dppf)Cl_2$ (26mg, 0.035mmol) in 1,4-dioxane (10mL) to give 270mg (96.42% yield) of the pure product after purification by chromatographic column (silicagel-60/120) using 15% ethyl acetate as eluent. MS: m/z = 404.4 (M+1).

Intermediate 71: 2-(4-(2-amino-4-bromophenyl)piperazin-1-yl)acetamide



Step-i: 1-(4-bromo-2-nitrophenyl)piperazine hydrochloride

Using similar reaction conditions as described in (step i of Intermediate-2), tert-butyl piperazine-1-carboxylate (1.5 g, 6.81mmol) was reacted with 4-bromo-1-fluoro-2-nitrobenzene (1.28g, 6.81mmol) in DMF (25 ml) and potassium carbonate (2.35g, 17.02mmol) to afford crude product. Using similar reaction conditions as described in Step-ii of example-7, above crude was deprotected in HCl in ether/methanol (10/10ml). This afforded 2.0g (99% yield).

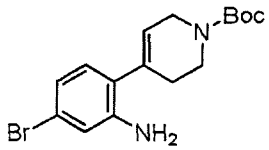
Step-ii: 2-(4-(4-bromo-2-nitrophenyl)piperazin-1-yl)acetamide

Using the same reaction conditions as described in step-i of example-82A, 1-(4-bromo-2-nitrophenyl)piperazine hydrochloride (1.2g 3.69mmol) was alkylated using 2-chloroacetamide (517mg, 5.53mmol) and sodium carbonate (930mg, 11.07mmol) in toluene/ethanol (15/15mL) to get 510mg (40.3% yield) of the titled compound. MS: m/z = 343.0 (M+1)

Step-iii: 2-(4-(2-amino-4-bromophenyl)piperazin-1-yl)acetamide

Using similar reaction conditions as described in step ii of Intermediate-27, 2-(4-(4-bromo-2-nitrophenyl)piperazin-1-yl)acetamide (600mg, 1.74mmol) was reduced using zinc dust (568mg, 8.74mmol) and ammonium chloride (461mg, 8.74mmol) in THF/water 10/10 ml to afford 508mg (93% yield) of the titled product.

Intermediate 72: tert-butyl 4-(2-amino-4-bromophenyl)-5,6-dihydropyridine-1(2H)-carboxylate



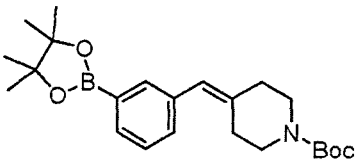
Step-i: tert-butyl 4-(4-bromo-2-nitrophenyl)-5,6-dihydropyridine-1(2H)-carboxylate

Using similar reaction conditions as described in step i of intermediate 9, 4-bromo-1-iodo-2-nitrobenzene (500mg, 1.53 mmol) was coupled with tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydropyridine-1(2H)-carboxylate (475mg, 1.53 mmol) using sodium carbonate (486mg, 4.59mmol) and $Pd(PPh_3)_2Cl_2$ (53mg, 0.07 mmol) in DME/water (10/2 ml) at 80°C for 3 hours to afford 400mg (68.9%) of the product after purification with (60/120 silica gel) column chromatography using 30% ethyl acetate in hexane as eluent.

Step-ii: tert-butyl 4-(2-amino-4-bromophenyl)-5,6-dihydropyridine-1(2H)-carboxylate

Using similar reaction conditions as described in step ii of Intermediate-27, tert-butyl 4-(4-bromo-2-nitrophenyl)-5,6-dihydropyridine-1(2H)-carboxylate (450mg, 1.17mmol) was reduced using zinc dust (610mg, 9.39mmol) and ammonium chloride (1.0g, 18.72mmol) in THF/water 10/5 ml to afford 300mg (72.4% yield) of the titled product after purification with (60/120 silica gel) column chromatography using 30% ethyl acetate in hexane as eluent. MS: m/z = 295.1 (M-Boc+1)

Intermediate 73: tert-butyl 4-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzylidene)piperidine-1-carboxylate



Step-i: tert-butyl 4-(3-bromobenzylidene)piperidine-1-carboxylate

The mixture of 1-bromo-3-(bromomethyl)benzene (6.2g, 24.8mmol) and triethyl phosphite (4.53g, 27.28mmol) was heated at 90°C for 12 hours, cooled to 0°C, added DME (40ml) and tert-butyl 4-oxopiperidine-1-carboxylate (5.73g, 28.8mmol) and sodium hydride (1.19g,

49.6mmol) and stirred at RT for 2-3 hours. Diluted with water and extracted with ether to afford 4.5g (51.5% yield) of the titled product after purification with (60/120 silica gel) column chromatography using 10% ethyl acetate in hexane as eluent. MS: m/z = 353.2 (M+1).

Step-ii: tert-butyl 4-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzylidene)piperidine-1-carboxylate

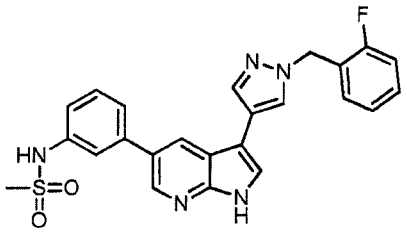
Using similar reaction conditions as described in step ii of intermediate-3 , tert-butyl 4-(3-bromobenzylidene)piperidine-1-carboxylate (4.5g, 12.7 mmol) was coupled with 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (3.87g, 15.2mmol) using potassium acetate (3.73g, 38.1 mmol) and $PdCl_2$(dppf) (460mg, 0.63mmol) in DME (100mL) to give 6g(crude) of the titled product after purification by chromatographic column (Silicagel-60/120) using 15% ethyl acetate as eluent. MS: m/z = 344.1 (M-Boc+1)

EXAMPLES

The present invention is further exemplified, but not limited, by the following examples that illustrate the preparation of compounds according to the invention.

Example 1

N-(3-(3-(1-(2-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl) phenyl)methanesulfonamide



Step-i: 5-Bromo-3-(1-(2-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

5-Bromo-3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridine (Intermediate-1) (350 mg, 0.83 mmol) and 1-(2-fluorobenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (Intermediate-2) (301 mg, 0.99 mmol) were added to a solution of toluene/ethanol/water (5/5/2.5 ml) previously purged with argon (10 min). The reaction mixture was purged with argon for a further 15mins, followed by the addition of potassium carbonate (230 mg, 1.6 mmol) and $Pd(PPh_3)_4$ (48 mg, 0.0415 mmol). The resulting mixture was heated to reflux at 80 °C overnight. The reaction was monitored by TLC (50% ethylacetate in hexane). The reaction mixture was cooled and diluted with ethyl acetate (50 ml) and washed with water (2x50 ml). The organic layer was dried over Na_2SO_4, and concentrated under reduced

pressure to afford crude product. Purification by column chromatography on silica gel (20% ethyl acetate in hexane) afforded 285 mg (43.64% yield) of titled compound. MS: m/z = 527.0 (M+1),

Step-ii: N-(3-(3-(1-(2-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl) phenyl)methanesulfonamide

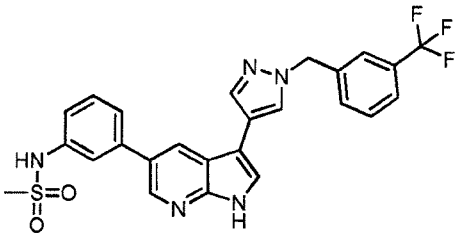
5-Bromo-3-(1-(2-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (140 mg, 0.267 mmol) and N-(3-(4,4,5,5-tetramethyl-1,3,2- dioxaborolan-2-yl)phenyl) methane sulfonamide (Intermediate 3) (95 mg, 0.32 mmol) were added to a solution of toluene/ethanol/water (5/5/2.5 ml) previously purged with argon (10 min). The reaction mixture was purged with argon for a further 15mins, followed by the addition of potassium carbonate (74 mg, 0.534 mmol) and $Pd(PPh_3)_4$ (15 mg, 0.0133 mmol). The resulting mixture was heated to reflux at 80 °C for 2 h. The reaction was monitored by TLC (50% ethyl acetate in hexane). The reaction mixture was cooled and diluted with ethyl acetate (50 ml) and washed with water (2x50 ml). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to afford 205mg of crude product which was taken as such for next reaction. MS: m/z = 616.1 (M+1).

Step-iii: N-(3-(3-(1-(2-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl) methanesulfonamide

N-(3-(3-(1-(2-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl) methanesulfonamide (200 mg) dissolved in 12.5 ml of THF-water-methanol (1:1:0.5) mixture and added lithium hydroxide (40.8mg, 0.97mmol) at 0 °C and stirred at room temperature for 15 h. The reaction was monitored by TLC (100% ethyl acetate in hexane) until TLC indicated that reaction was complete. The reaction mixture was diluted with ethyl acetate (25 ml) and washed with water (2x25 ml). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to afford crude product. Purification by preparative TLC (5% methanol in DCM) afforded 17 mg (14.99% yield) of tilted compound. ^1H NMR (DMSO-d_6, 300MHz): δ 9.83 (s, 1H), 8.479-8.472 (d, 1H), 8.38 (s, 1H), 8.33-8.32 (d, 1H), 7.95-7.78 (m, 2H), 7.53-7.43 (m, 4H), 7.27-7.18 (m, 3H), 5.44 (s, 2H), 3.05 (s, 1H). MS: m/z = 462.1 (M+1), HPLC: 95.83% in method A.

Example 2

N-(3-(3-(1-(3-(trifluoromethyl)benzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b] pyridin-5-yl)phenyl)methanesulfonamide



Step-i: 5-bromo-1-tosyl-3-(1-(3-(trifluoromethyl)benzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b] pyridine

Using similar reaction conditions as described in step-i of example-1, 5-bromo-3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridine (Intermediate 1) (300 mg, 0.629 mmol) was coupled with 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(3-(trifluoromethyl)benzyl)-1H-pyrazole (Intermediate 4) (310 mg, 0.88 mmol) in sodium carbonate (200 mg, 1.88 mmol), bis(triphenyl phosphine)palladium(ii) dichloride (22 mg, 0.0314 mmol) and toluene/ethanol/water (30/10/2.5 ml) to afford 167 mg (46.2% yield) of the pure product after column purification using 30% ethyl acetate in hexane as eluent.

MS: m/z = 577.00 (M+2).

Step-ii: N-(3-(1-tosyl-3-(1-(3-(trifluoromethyl)benzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b] pyridin-5-yl)phenyl)methanesulfonamide

Using similar reaction conditions as described in step 2 of example 1, 5-bromo-1-tosyl-3-(1-(3-(trifluoromethyl)benzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine (165 mg, 0.28 mmol) was coupled with N-(3-(4,4,5,5-tetramethyl-1,3,2- dioxaborolan-2-yl)phenyl) methane sulfonamide (Intermediate 3) (119 mg, 0.401 mmol) in sodium carbonate (91 mg, 0.86 mmol), bis(triphenyl phosphine)palladium(ii) dichloride(10 mg, 0.014 mmol) and toluene/ethanol/water (15/6/2 ml) to afford 188 mg (98.4% yield) of the pure product after column purification using 60% ethyl acetate in hexane as eluent. MS: m/z = 666.10 (M+1).

Step-iii: N-(3-(3-(1-(3-(trifluoromethyl)benzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b] pyridin -5-yl)phenyl)methanesulfonamide:

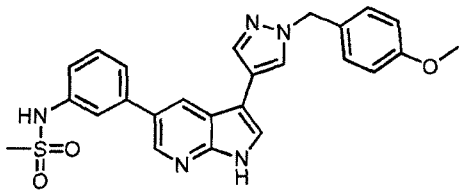
Using similar reaction conditions as described in step-iii in example 1, 5 N-(3-(1-tosyl-3-(1-(3-(trifluoromethyl)benzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methane sulfonamide (188 mg, 0.28 mmol) was hydrolyzed with lithium hydroxide (35.5 mg, 0.847 mmol) in THF/water/methanol (12/6/3 ml) mixture to afford 20 mg (14% yield) of the pure product.

1H NMR ($CDCl_3$, 300MHz): δ 11.07 (s, 1H), 10.27 (s, 1H), 8.79 (s, 1H), 8.31 (s, 1H), 7.89 (s, 1H), 7.72 (s, 1H), 7.7-7.649 (m, 1H), 7.6-7.447 (m, 7H), 5.46 (s, 2H), 3.12 (s, 3H).

MS: m/z = 512.1 (M+1), HPLC: 98.88% in method A.

Example 3

N-(3-(3-(1-(4-methoxybenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo [2,3-b]pyridin-5-yl)phenyl)n methane sulfonamide



Step-i: 5-bromo-3-(1-(4-methoxybenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine:

Using similar reaction conditions as described in step-i of example-1, 5-bromo-3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridine (Intermediate 1) (750 mg, 1.78 mmol) was coupled with 1-(4-methoxybenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (Intermediate 5) (671 mg, 2.13 mmol) in sodium carbonate (614 mg,4.4 mol), bis(triphenyl phosphine)palladium(ii) dichloride (62 mg, 2.13 mmol) and toluene/ethanol/water (10/10/5 ml) to afford 550.0mg (57.95% yield) of the pure product after column purification using 30% ethyl acetate in hexane as eluent.

^{1}H NMR (DMSO-d_6, 300MHz): δ 8.56-8.50 (m, 3H), 8.25 (s,1H), 8.08 (s, 1H), 7.97-7.94 (d, 2H), 7.41-7.39 (d, 2H), 7.27-7.24 (d, 2H), 6.91-6.89 (d, 2H), 5.27 (s, 2H), 3.72 (s, 3H), 2.32 (s, 3H). MS: m/z = 539.0 (M+2).

Step-ii: N-(3-(3-(1-(4-methoxybenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide:

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(4-methoxybenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (240 mg, 0.44 mmol) was coupled with N-(3-(4,4,5,5-tetramethyl-1,3,2- dioxaborolan-2-yl)phenyl) methane sulfonamide (intermediate 3) (160 mg, 0.53 mmol) in sodium carbonate (142 mg, 1.34 mmol), bis(triphenyl phosphine)palladium(ii) dichloride (16 mg, 0.022 mmol) and toluene/ethanol/water (7/7/4 ml) to afford 250mg (89.28% yield) of the pure product after column purification using 35% ethyl acetate in hexane as eluent. MS: m/z = 628.3(M+1).

Step-iii: N-(3-(3-(1-(4-methoxybenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl) phenyl) methanesulfonamide:

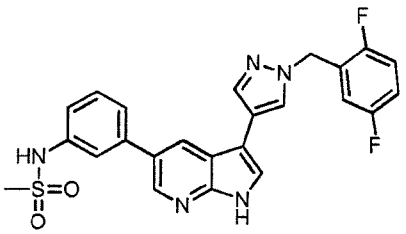
Using similar reaction conditions as described in step-iii of example-1, N-(3-(3-(1-(4-methoxybenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methane

sulfonamide (250 mg, 0.39 mmol) was hydrolyzed with lithium hydroxide (66 mg, 1.6 mmol) in THF/water/methanol (4/3/1 ml) mixture to afford 15mg (9.57% yield) of the pure product after purification by prep TLC using 2% methanol in DCM as eluent.

^{1}H NMR (DMSO-d_6, 300MHz): δ 11.79 (s, 1H), 9.83 (s, 1H), 8.469 (s, 1H), 8.33-8.31 (d, 2H), 7.91 (s, 1H), 7.75 (s, 1H), 7.52-7.43 (m, 3H), 7.27-7.22 (t, 3H), 6.91-6.89 (d, 2H), 5.28 (s, 2H), 3.72 (s, 3H), 3.05 (s, 3H). MS: m/z = 474.2 (M+1), HPLC: 94.18% in Method-C.

Example 4

N-(3-(3-(1-(2,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methane sulfonamide



Step-i: 5-bromo-3-(1-(2,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine:

Using similar reaction conditions as described in step-i of example 1, 5-bromo-3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridine (Intermediate 1) (1 g, 2.37 mmol) was coupled with 1-(2,5-difluorobenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (Intermediate 6) (688 mg, 3.3 mmol) in sodium carbonate (749 mg, 7.07 mmol), bis(triphenyl phosphine)palladium(ii) dichloride (83 mg, 0.11 mmol) and toluene/ethanol/water (10/10/5 ml) to afford 550mg (42.63% yield) of the pure product after column purification using 30% ethyl acetate in hexane as eluent.

^{1}H NMR (DMSO-d_6, 300MHz): δ 8.59-8.51 (m, 3H), 8.29 (s, 1H), 8.13 (s, 1H), 7.98-7.95 (d, 2H), 7.42-7.40 (d, 2H), 7.35-7.10 (m, 4H), 5.52 (s, 2H), 2.33 (s, 3H).

MS: m/z = 542.6 (M-1).

Step-ii: N-(3-(3-(1-(2,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b] pyridin-5-yl)phenyl)methanesulfonamide

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(2,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (250 mg, 0.46 mmol) was coupled with N-(3-(4,4,5,5-tetramethyl-1,3,2- dioxaborolan-2-yl)phenyl) methane sulfonamide (intermediate 3) (150 mg, 0.506 mol) in sodium carbonate (146 mg, 1.38 mol), bis(triphenyl phosphine)palladium(ii) dichloride (16 mg, 0.023 mmol) and

toluene/ethanol/water (7/7/4 ml) to afford 250.0mg (85.91% yield) of the pure product after column purification using 40% ethyl acetate in hexane as eluent.

Step-iii: N-(3-(3-(1-(2,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl) methanesulfonamide

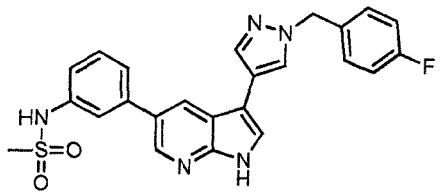
Using similar reaction conditions as described in step-iii of example-1, N-(3-(3-(1-(2,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl) methanesulfonamide (250 mg, 0.39 mmol) was hydrolyzed with lithium hydroxide (66 mg, 1.57 mmol) in THF/water/methanol (5/4/3 ml) mixture to afford 170mg (89.94% yield) of the pure product.

^{1}H NMR (DMSO-d_6, 300MHz): δ 11.83 (s, 1H), 8.47-8.32 (m, 3H), 7.97 (s, 1H), 7.799-7.794 (d, 1H), 7.64-7.55 (m, 3H), 7.49-7.44 (m, 3H), 7.32-7.21 (m, 2H), 5.44 (s, 2H), 3.03 (s, 3H)

MS: m/z = 479.8 (M+1), HPLC: 73.14% in method A.

Example 5

N-(3-(3-(1-(4-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl) methanesulfonamide



Step-i: 5-bromo-3-(1-(4-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-i of example-1, 5-bromo-3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridine (Intermediate 1) (700 mg, 1.46 mmol) was coupled with 1-(4-fluorobenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 7) (554 mg, 1.83 mmol) in sodium carbonate (466 mg, 4.4 mmol), bis(triphenylphosphine) palladium(ii)dichloride (51mg, 0.073mmol) and toluene/ethanol/water (20/8/2 ml) to afford 300 mg (38.9% yield) of the pure product after column purification using 20% ethyl acetate in hexane as eluent. MS: m/z = 526.7(M+1)

Step-ii: N-(3-(3-(1-(4-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl) phenyl)methanesulfonamide

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(4-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (150 mg, 0.285 mmol) was coupled with N-(3-(4,4,5,5-tetramethyl-1,3,2- dioxaborolan-2-yl)phenyl) methane

sulfonamide (intermediate 3) (127 mg, 0.427 mmol) in sodium carbonate (90.6 mg, 0.855 mmol), bis(triphenyl phosphine)palladium(ii) dichloride (39.8 mg, 0.057 mmol) and toluene/ethanol/water (20/8/2 ml) to afford 138 mg (79% yield) of the pure product after column purification using 40% ethyl acetate in hexane as eluent. MS: m/z = 616.3 (M+1).

Step-iii: N-(3-(3-(1-(4-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl) methane sulfonamide

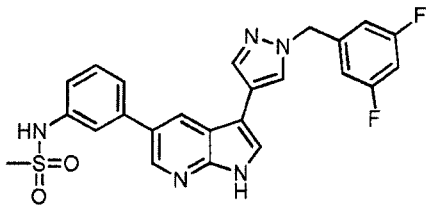
Using similar reaction conditions as described in step-iii of example-1, N-(3-(3-(1-(4-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methane sulfonamide (137 mg, 0.222 mmol) was hydrolyzed with lithium hydroxide (47 mg, 1.111 mmol) in THF/water/methanol (12/6/3 ml) mixture to afford 1 mg (1% yield) of the title compound.

^{1}H NMR (CD_3OD, 600MHz): δ 8.48 (br, 1H), 8.365-8.361 (d, 1H), 8.183 (s, 1H), 7.922 (s, 1H), 7.64 (s, 1H), 7.568 (m, 1H), 7.52-7.50 (m, 2H), 7.48-7.44 (m, 1H), 7.37-7.34 (m, 2H), 7.31-7.29 (m, 1H), 7.127-7.083 (m, 2H), 5.411 (s, 2H), 3.025 (s, 3H)

MS: m/z = 462.4 (M+1), HPLC: 90.99% in method B

Example 6

N-(3-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl) methane sulfonamide



Step-i: N-(3-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl) phenyl)methanesulfonamide:

Using similar reaction conditions as described in step-i of example-1, N-(3-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide (intermediate 9) (200 mg, 0.352 mmol) was coupled with 1-(3,5-difluorobenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxa borolan-2-yl)-1H-pyrazole (Intermediate 8) (159 mg, 0.528 mmol) in sodium carbonate (112 mg, 1.05 mmol), $PdCl_2$(dppf) (13 mg, 0.017 mmol) and toluene/ethanol/water (18/12/8 ml) to afford 300 mg of the crude product.

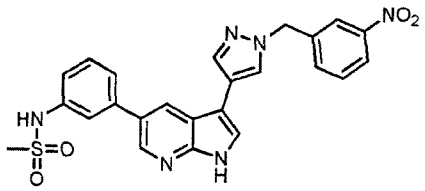
Step-ii: N-(3-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl) methane sulfonamide:

Using similar reaction conditions as described in step-iii of example-1, N-(3-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methane sulfonamide (300 mg, 0.473 mmol) was hydrolyzed with lithium hydroxide (40 mg, 0.946 mmol) in THF/water/methanol (15/10/5 ml) mixture to afford 20 mg (8.8% yield) of the desired compound.

^{1}H NMR (DMSO-d_6, 400MHz): δ 11.82 (s, 1H), 9.82 (s, 1H), 8.48-8.47 (d, 1H), 8.43 (s,1H), 8.355-8.350 (d,1H), 8.00 (s, 1H), 7.71-7.80 (d, 1H), 7.53-7.46 (m, 3H), 7.25-7.23 (m, 2H), 6.98-6.97 (d, 2H), 5.42 (s, 2H), 3.05 (s, 3H). MS: m/z = 479.8 (M+1), HPLC: 94.78% (Method-B).

Example 7

N-(3-(3-(1-(3-nitrobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methane sulfonamide



Step-i: tert-butyl 5-(3-(methylsulfonamido)phenyl)-3-(1-(3-nitrobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo [2,3-b]pyridine-1-carboxylate

Using similar reaction conditions as described in step-i of example 1, tert-butyl 3-iodo-5-(3-(methylsulfonamido)phenyl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (intermediate-32) (300 mg, 0.5 mmol) was coupled with 1-(3-nitrobenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 10) (211 mg, 0.6 mmol) in sodium carbonate (189 mg, 1.7 mmol), $PdCl_2$(dppf) (20 mg, 0.02 mmol) and DME/water (3/3 ml) to afford 200 mg (59% yield) of the pure product after column purification using 30% ethyl acetate in hexane as eluent.

Step-ii: N-(3-(3-(1-(3-nitrobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl) methanesulfonamide

tert-butyl 5-(3-(methylsulfonamido)phenyl)-3-(1-(3-nitrobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo [2,3-b] pyridine-1-carboxylate (200 mg, 0.409 mmol) dissolved in 10 ml of methanol and added 1,4-dioxane/HCl (2 ml) at 0 °C and stirred at room temperature for 15 h. The reaction was monitored by TLC (30% ethyl acetate in hexane). The reaction mixture was concentrated under reduced pressure to afford crude product. The residue was basified with saturated sodium bicarbonate solution and extracted with ethyl acetate (2x25 ml). The

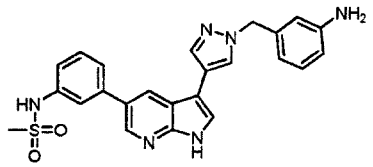
organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to afford 100 mg (62% yield) of the pure required product.

^{1}H NMR (DMSO-d_6, 400MHz): δ11.82 (s, 1H), 9.85 (s, 1H), 8.47(s, 2H), 8.33 (s, 1H), 8.18-8.15 (d, 2H), 8.00 (s, 1H), 7.806-7.7.800 (d, 1H), 7.75-7.34 (d, 1H), 7.69-7.65 (t, 1H), 7.52-7.44 (m, 3H), 7.24-7.22 (d, 1H), 5.55 (s, 2H), 3.05 (s, 3H).

MS: m/z = 489.3 (M+1), HPLC: 93.67 % (method B)

Example 8

N-(3-(3-(1-(3-aminobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl) methane sulfonamide



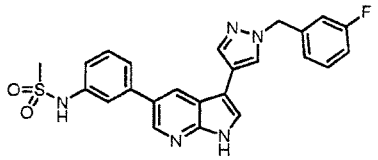
N-(3-(3-(1-(3-nitrobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methane sulfonamide (Example-7) (80mg, 0.163mmol), was reduced by palladium on carbon(8mg, 10% W/W) in THF/MeOH (2/2 mL) under positive pressure of hydrogen using a bladder. The catalyst filtered off and concentrated to get crude compound. This was then purified by preparative TLC using 10% ethyl acetate in hexanes as eluent yielded 12mg (16% yield) of pure titled compound.

^{1}H NMR (DMSO-d_6, 400MHz): δ11.85 (s, 1H), 9.83(s, 1H), 8.47-8.46 (d, 1H), 8.33-8.32 (m, 2H), 7.92 (s, 1H), 7.775-7.770 (d, 1H), 7.53-7.44 (m, 3H), 7.24-7.22 (d, 1H), 6.96-6.94 (t, 1H), 6.46-6.42 (m, 2H), 5.20 (s, 2H), 5.10 (b, 2H), 3.05 (s, 3H).

MS: m/z = 459.3 (M+1), HPLC: 92.06 % (method B)

Example 9

N-(3-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl) phenyl)methanesulfonamide



Step-i: 5-bromo-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b] pyridine

Using similar reaction conditions as described in step-i of example-1, 5-bromo-3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridine (intermediate 1) (700 mg, 1.46 mmol) was coupled with 1-(3-fluorobenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate

11) (554 mg, 1.83 mmol) in sodium carbonate (466 mg, 4.4 mmol), bis(triphenyl phosphine)palladium(ii) dichloride (51 mg, 0.073 mmol) and toluene/ethanol/water (30/10/4 ml) to afford 422 mg (54.8% yield) of the pure product after column purification using 20% ethyl acetate in hexane as eluent.

Step-ii: N-(3-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl) phenyl) methanesulfonamide:

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (100 mg, 0.19 mmol) was coupled with N-(3-(4,4,5,5-tetramethyl-1,3,2- dioxaborolan-2-yl)phenyl) methane sulfonamide (intermediate 3) (84.8 mg, 0.285 mmol) in sodium carbonate (60.5 mg, 0.57 mmol), bis(triphenyl phosphine)palladium(ii) dichloride (13.3 mg, 0.019 mmol) and toluene/ethanol/water (12/6/2 ml) to afford 106 mg of the crude product which was taken as such for next step. MS: m/z = 615.7(M+1).

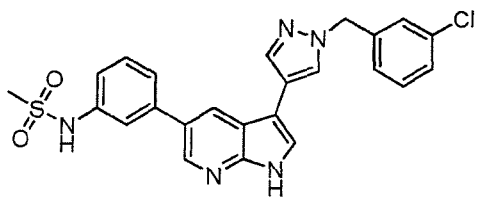
Step-iii: N-(3-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl) phenyl) methane sulfonamide

Using similar reaction conditions as described in step-iii of example-1, N-(3-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methane sulfonamide (106 mg, 0.17 mmol) was hydrolyzed with lithium hydroxide (36 mg, 0.861 mmol) in THF/water/methanol (12/6/2 ml) mixture to afford 10 mg (12.6% yield) of the pure product.

^{1}H NMR (CD_3OD, 300MHz): δ 8.464-8.458 (d, 1H), 8.352-8.347 (d, 1H), 8.185 (s, 1H), 7.923 (s, 1H), 7.64 (s, 1H), 7.544-7.538 (m, 1H), 7.514-7.431 (m, 2H), 7.37-7.26 (m, 2H), 7.115-6.997 (m, 2H), 5.426 (s, 2H), 3.002 (s, 3H). MS: m/z = 461.8 (M+1), HPLC: 96.947% in method A.

Example 10

N-(3-(3-(1-(3-chlorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo [2,3-b]pyridin-5-yl) phenyl)methanesulfonamide



Step-i: N-(3-(3-(1-(3-chlorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl) phenyl)methanesulfonamide

Using similar reaction conditions as described in step-i of example-1, N-(3-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide (intermediate 9) (200mg, 0.35mmol), was coupled with 1-(3-chlorobenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 13) (123mg, 0.385mmol), in sodium carbonate (111mg, 1.05mmol), $PdCl_2$(dppf) (12.8mg, 0.017mmol) and DME/water (2/1 ml) to afford 90 mg (41% yield) of the pure product after column purification using 40% ethyl acetate in hexane as eluent.

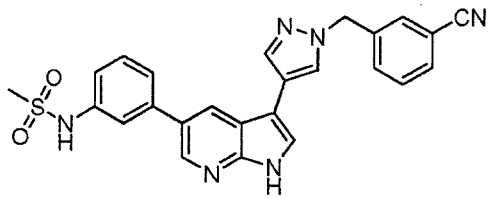
Step-ii: N-(3-(3-(1-(3-chlorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl) methanesulfonamide:

Using similar reaction conditions as described in step-iii of example-1, N-(3-(3-(1-(3-chlorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methane sulfonamide (90 mg, 0.14 mmol) was hydrolyzed with lithium hydroxide (18 mg, 0.42 mmol) in THF/water/methanol (1/0.5/1 ml) mixture to afford 12 mg (18% yield) of the pure product after purification by preparative TLC (Silicagel-1000micron) using 10% ethyl acetate in hexane as eluent.

^{1}H NMR (DMSO-d_6, 400MHz): δ 11.83 (s, 1H), 9.85 (s, 1H), 8.48-8.47 (d, 1H), 8.43 (s, 1H), 8.346-8.342 (d, 1H), 7.90 (s, 1H), 7.80-7.79 (d, 1H), 7.51-7.25 (m, 8H), 5.40 (s, 2H), 3.06 (s, 3H). MS: m/z = 478.2 (M+1), HPLC: 92.01% (method B)

Example 11

N-(3-(3-(1-(3-cyanobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl) phenyl)methanesulfonamide



Step-i: N-(3-(3-(1-(3-cyanobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl) methanesulfonamide

Using similar reaction conditions as described in step-ii of example-1, N-(3-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide (Intermediate 9) (200mg, 0.35mmol) was coupled with 3-((4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-yl)methyl) benzonitrile (Intermediate 14) (119.8 mg, 0.38mmol) in sodium carbonate (111mg, 1.05mmol), $PdCl_2$(dppf) (12.8mg, 0.017mmol) and DME/water (2/1 ml)

to afford 90 mg (30% yield) of the pure product after column purification using 50% ethyl acetate in hexane as eluent.

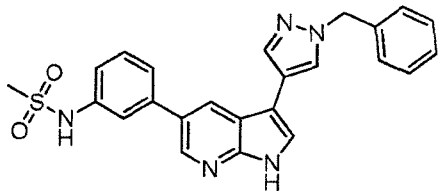
Step-ii: N-(3-(3-(1-(3-cyanobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl) methanesulfonamide

Using similar reaction conditions as described in step-iii of example-1, N-(3-(3-(1-(3-cyanobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl) methane sulfonamide (90 mg, 0.14 mmol) was hydrolyzed with lithium hydroxide (18 mg, 0.43 mmol) in THF/water/methanol (1/0.5/1 ml) mixture to afford 10 mg (15% yield) of the pure product after purification by preparative TLC (Silicagel-1000micron) using 10% ethyl acetate in hexane as eluent.

^{1}H NMR (DMSO-d_6, 400MHz): δ11.88 (s, 1H), 9.85 (b, 1H), 8.478-8.475 (d, 1H), 8.43 (s, 1H), 8.34 (s, 1H), 7.986 (s, 1H), 7.80-7.75 (m, 3H), 7.60-7.45 (m, 5H), 7.26-7.24 (d, 1H) 5.46 (s, 2H), 3.05 (s, 3H) MS: m/z = 469.4 (M+1), HPLC 93.92%, (method – A).

Example 12

N-(3-(3-(1-benzyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl) methanesulfonamide



Step-i: 3-(1-benzyl-1H-pyrazol-4-yl)-5-bromo-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-i of example-1, 5-Bromo-3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridine (intermediate 1) (400mg, 0.83mmol), 1-benzyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 15) (262.05mg, 0.92mmol) in sodium carbonate (263.9 mg, 105.99 mmol), bis(triphenylphosphine) palladium (ii) dichloride (29 mg, 0.04 mmol) and toluene/ethanol/water (6/6/2 ml) to afford 220 mg (51.7% yield) of the pure product after column purification using 30% ethyl acetate in hexane as eluent.

Step-ii: N-(3-(3-(1-benzyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl) methanesulfonamide

Using similar reaction conditions as described in step-ii of example-1, 3-(1-benzyl-1H-pyrazol-4-yl)-5-bromo-1-tosyl-1H-pyrrolo[2,3-b]pyridine (220mg, 0.433mmol) was coupled with N-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methanesulfonamide

(intermediate 3) in Sodium carbonate (137.68mg, 1.29mmol), $PdCl_2(dppf)$ (15.8mg, 0.02mmol), toluene/ethanol/water (5/5/2 ml). This on purification by preparative TLC using methanol/chloroform as eluent afforded 120mg (46.3% yield) of the pure compound.

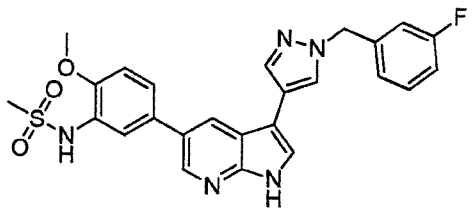
Step-iii: N-(3-(3-(1-benzyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl) methane sulfonamide

Using similar reaction conditions as described in step-iii of example-1, N-(3-(3-(1-benzyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide (60mg, 0.1mmol) was hydrolyzed by lithium hydroxide (9mg, 0.2mmol) in methanol/water/THF (1/1/1 ml) which afforded 4mg (9% yield) after purification by preparative TLC (silicagel-1000micron) using 5% methanol in chloroform as eluent.

^1H NMR (DMSO-d_6, 300MHz): δ 8.46-8.45 (d, 1H), 8.34-8.33 (d, 1H), 8.14 (s, 1H), 7.9 (s, 1H), 7.62 (s, 1H), 7.54 (m, 1H), 7.5-7.43 (m, 2H), 7.37-7.33 (m, 2H), 7.3-7.27 (m, 3H), 5.4 (s, 2H), 3.0 (s, 3H). MS: m/z = 443.6 (M+1), HPLC: 88.2%, Method A.

Example 13

N-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl) methane sulfonamide



Step-i: N-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl) methanesulfonamide

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (compound of step-i of example 9) (200mg, 0.380mmol) was coupled with N-(2-methoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methanesulfonamide (Intermediate 17) (185mg, 0.58mmol) in sodium carbonate (121mg, 1.14mmol), $Pd(PPh_3)_2Cl_2$ (26.6mg, 0.038mmol), toluene/ethanol/water (20/7/3 mL). This afforded 153mg (62.4% yield) after purification by column (Silica gel 6/120) using 3% methanol in chloroform as eluent. MS: m/z = 645.7(M+1)

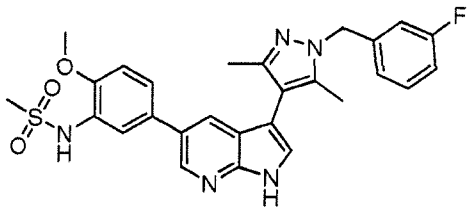
Step-ii: N-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxy phenyl) methanesulfonamide.

Using similar reaction conditions as described in step-iii of example-1, N-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl) methane sulfonamide (150mg, 0.232mmol) was hydrolyzed with lithium hydroxide (49mg, 1.162mmol) in THF/Methanol/Water (15/6/4mL) to yield 17 mg (15% yield) after purification by preparative TLC (Silicagel-1000micron) using 2% methanol in chloroform as eluent.

^{1}H NMR (CD_3OD, 400MHz): δ 8.446-8.441 (d, 1H), 8.327-8.322 (d, 1H), 8.215 (s, 1H), 7.936 (s, 1H), 7.746-7.741 (d, 1H), 7.643 (s, 1H). 7.577-7.551 (m, 1H), 7.398-7.364 (m, 1H), 7.21-7.188 (d, 1H), 7.210-7.188 (d, 1H), 7.137-7.118 (d, 1H), 7.067-7.026 (m, 2H), 5.426 (s, 2H), 3.98 (s, 3H), 3.002 (s, 3H). MS: m/z = 491.8 (M+1), HPLC: 97.01% in method A.

Example 14

N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b] pyridin-5-yl)-2-methoxy phenyl)methanesulfonamide



Step-i: 5-bromo-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-i of example-1, 5-bromo-3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridine (intermediate 1) (711mg, 1.46mmol) was coupled with 1-(3-fluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 16) (581mg, 1.76mmol) in 2 molar sodium carbonate (5 mL), $Pd(PPh_3)_2Cl_2$ (51mg, 0.073mmol), acetonitrile (25mL). This afforded 300 mg yield 48.5 % of titled compound after purification by column using 25% ethyl acetate in hexane.

Step-ii: N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b] pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide:

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (300mg, 0.542mmol) was coupled with N-(2-methoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methanesulfonamide (intermediate-17) (212mg, 0.650mmol) in sodium carbonate

(172mg, 1.62mmol), 1,2-methoxyethane (15mL). This afforded 350mg of the crude titled compound.

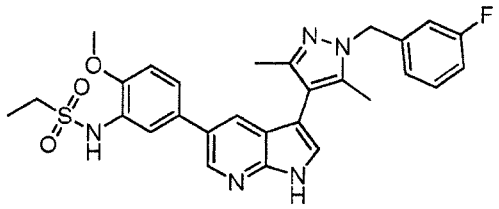
Step-iii: N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b] pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide:

Using similar reaction conditions as described in step-iii of example-1, N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide was hydrolyzed with lithium hydroxide(65mg, 1.56mmol) in THF/Methanol/water (10/3/2 mL). This yielded 22mg (8.4% yield) of pure compound after purification by flash chromatography.

^{1}H NMR (DMSO-d_6, 300MHz): δ 11.9 (s, 1H), 9.07 (s, 1H), 8.519-8.515 (d, 2H), 7.827-8.23 (d, 2H), 7.56-7.43 (m, 3H), 7.21-7.04 (m, 4H), 5.36 (s, 2H), 3.90 (s, 3H), 3.03 (s, 3H), 2.21-2.17 (d, 6H). MS: m/z = 520.1 (M+1), HPLC: 95.74% (Method-B).

Example 15

N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b] pyridin-5-yl)-2-methoxy phenyl)ethanesulfonamide



Step-i: N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b] pyridin-5-yl)-2-methoxyphenyl)ethanesulfonamide

Using similar reaction conditions as described in step-i of example-1, 5-bromo-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (compound of step-iof example 14) (170mg, 0.307 mmol) was coupled with N-(2-methoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)ethanesulfonamide (intermediate 18) (125mg, 0.368mmol) using $PdCl_2$(dppf) (50mg, 0.0614 mmol) in sodium carbonate (97mg, 0.920 mmol), DME/water (10/2 mL) to afford 200mg of the crude titled compound.

Step-ii: N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)ethanesulfonamide

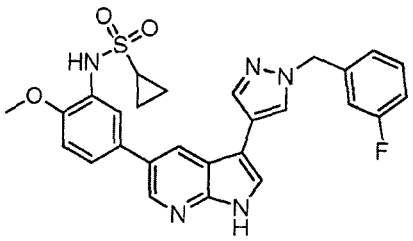
Using similar reaction conditions as described in step-iii of example-1, N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin -5-yl)-2-methoxyphenyl) ethanesulfonamide (200mg, 0.291mmol) was hydrolyzed by lithium

hydroxide(36mg, 0.87mmol) in THF/Methanol/Water(10/3/2 ml) to give 25mg (16.5%yield) after purification by flash chromatography.

^{1}H NMR (DMSO-d_6, 300MHz): δ 11.9 (s,1H), 9.02 (s, 1H), 8.45 (s,1H), 7.79 (s, 1H), 7.54-7.49 (m, 3H), 7.19-7.0 (m, 4H), 5.33 (s, 2H), 3.86 (s, 3H), 3.06-3.04 (m, 2H0, 2.17-2.13 (d, 6H), 1.27-1.23 (t, 3H). MS: m/z = 534.8 (M+1), HPLC: 90.27% (Method-B)

Example 16

N-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)cyclopropanesulfonamide



Step-i: N-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo [2,3-b]pyridin-5-yl)-2-methoxyphenyl) cyclopropanesulfonamide

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (Compound of step-i of -9) (150mg, 2.85mmol) was coupled with N-(2-methoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)cyclopropane sulfonamide (intermediate 19) (131mg, 0.371mmol), $Pd(PPh_3)_2Cl_2$ (10mg, 0.0142 mmol), Toluene/ethanol/water (15/10/5 ml) to afford 120mg (62.82% yield) of the titled compound. MS: m/z = 672.2 (M+1)

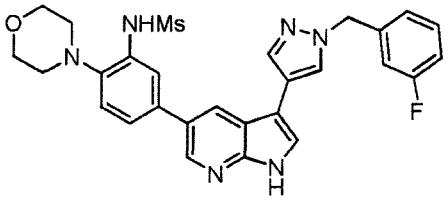
Step-ii: N-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)cyclopropanesulfonamide

Using similar reaction conditions as described in step-iii of example-1, N-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl) cyclopropanesulfonamide (80mg, 0.119mmol) was hydrolyzed by lithium hydroxide (0.0109g, 0.238mmol), THF/Methanol/water (12/8/4 mL) to afford 5mg (8.19% yield) of the titled compound.

^{1}H NMR (DMSO-d_6, 300MHz): δ 11.8 (s, 1H), 9.04 (s, 1H), 8.44-8.42 (d, 2H), 8.29 (s, 1H), 7.96 (s, 1H), 7.77 (s, 1H), 7.61-7.58 (m, 2H0, 7.20-7.10 (m, 4H), 5.41 (s, 2H), 3.88 (s, 3H), 0.92-0.88 (m, 4H). MS: m/z = 517.8 (M+1), HPLC: 84.12% Method B.

Example 17

N-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-morpholinophenyl) methanesulfonamide



Step-i: N-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-morpholinophenyl)methanesulfonamide

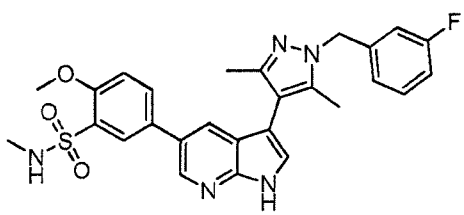
Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine Compound of step-I in Example 9) (200mg, 0.3809mmol) was coupled with N-(2-morpholino-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methane sulfonamide (Intermediate 20) (220mg, 0.5714mmol), $Pd(PPh_3)_2Cl_2$ (13.5mg,0.01904mmol), Toluene/ethanol/water (20/10/4 ml) to afford 240mg (90.2% yield) of the titled compound.

Step-ii: N-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-morpholinophenyl)methanesulfonamide

Using similar reaction conditions as described in step-iii of example-1, N-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-morpholinophenyl) methanesulfonamide (240mg, 0.342mmol) was hydrolyzed by lithium hydroxide (143mg, 3.42mmol), THF/Methanol/water (20/8/8 mL) to yield 34mg (18%) of the titled compound. ^{1}H NMR (DMSO-D_6, 400MHz): δ 11.8 (s, 1H), 8.618 (s, 1H), 8.469-8.464 (m, 1H), 8.421 (s, 1H), 8.317-8.313 (d, 1H), 7.963 (s, 1H), 7.782-7.777 (d, 1H), 7.649-7.645 (d, 1H), 7.58-7.52 (m, 1H), 7.44-7.366 (m, 2H), 7.16-7.08 (m, 3H), 5.402 (s, 2H), 3.80.3-3.791 (m, 4H), 3.197 (s, 3H), 2.898-2.887 (m, 4H). MS: m/z = 546.8(M+1); HPLC: 96.04% in method B.

Example 18

5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b] pyridin-5-yl)-2-methoxy-N-methylbenzenesulfonamide



Step-i: 5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b] pyridin-5-yl)-2-methoxy-N-methylbenzenesulfonamide

Using similar reaction conditions as described in step-i of example-1, 5-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxy-N-methylbenzenesulfonamide (intermediate 22) (140mg, 0.234mmol) was coupled with 1-(3-fluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 16) (154mg, 0.469mmol), $Pd(PPh_3)_2Cl_2$ (3.22mg, 0.011mmol), sodium carbonate (75mg, 0.702mmol), Toluene/ethanol(3/5 ml) to afford 80mg (51% yield) of the titled compound.

^1H NMR ($CDCl_3$, 300MHz): δ 8.63 (s, 1H), 8.14-8.12 (d, 2H), 8.04 (s, 1H), 7.73-7.64 (m, 3H), 7.49-7.46 (m, 1H), 7.33-7.30 (m, 3H), 7.15-7.12 (d, 1H), 7.01-6.95 (m, 2H), 6.86-6.83 (d, 1H), 5.31 (s, 2H), 4.84-4.83 (m, 1H), 4.03 (s, 3H), 2.63-2.61 (d, 3H), 2.39 (s, 3H), 2.20 (s, 3H), 2.13 (s, 3H). MS: m/z = 674.2 (M+1)

Step-ii: 5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxy-N-methylbenzenesulfonamide

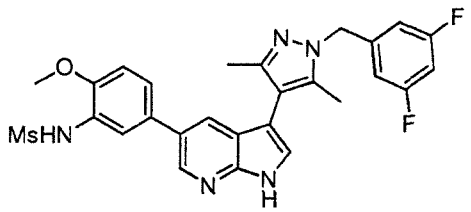
Using similar reaction conditions as described in step-iii of example-1, 5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxy-N-methylbenzenesulfonamide (80mg, 0.118mmol) was hydrolyzed by lithium hydroxide (143mg, 0.593mmol), THF/Methanol/water(1/1/0.5 mL) to afford 22mg (36.06% yield) of the titled compound.

^1H NMR (CD_3OD , 400MHz): δ 8.47-8.46 (d, 1H), 8.029-8.024 (d, 1H), 7.89-7.86 (m, 2H), 7.41 (s, 1H), 7.38-7.30 (m, 2H), 7.05-6.96 (m, 2H), 6.90-6.85 (m, 1H), 5.36 (s, 2H), 4.00 (s, 3H), 2.53 (s, 3H), 2.21 (s, 3H), 2.18 (s, 3H).

MS: m/z = 520.1 (M+1), HPLC Purity: 93.81% (Method B).

Example 19

N-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide



Step-i: N-(5-(3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide

Using similar reaction conditions as described in step-ii of example-1, N-(5-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide (Intermediate 23) (160mg, 0.267mmol) was coupled with 1-(3,5-difluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-

tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 24) (111.89mg, 0.321mmol) in sodium carbonate (84.89 mg, 0.801mmol) $Pd(PPh_3)_2Cl_2$ (9.7mg, 0.013), Toluene/ethanol/water (7/7/2 mL) to afford 210 mg of the crude compound.

MS: m/z = 692.1 (M+1)

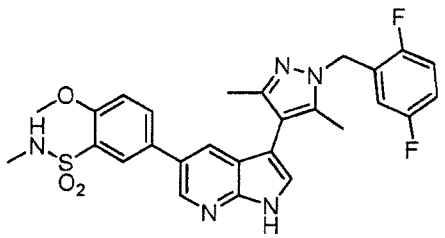
Step-ii: N-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide

Using similar reaction conditions as described in step-iii of example-1, N-(5-(3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl) methanesulfonamide (210mg, 0.3mmol) was hydrolyzed by lithium hydroxide (34.2mg, 0.91mmol), THF/Methanol/water (4/6/1 mL) to afford 1.6mg of the titled compound after purification by preparative TLC (SiO_2-1000micron) eluted by 3% MeOH in $CHCl_3$).

^1H NMR ($CDCl_3$, 300MHz): δ 8.9 (b, 1H), 8.5 (s, 1H), 7.84 (m, 1H), 7.78 (m, 1H), 7.0 (m, 1H), 6.85 (m, 1H), 6.78-6.7 (m, 3H), 5.29 (s, 2H), 3.93 (s, 3H), 2.98 (s, 3H), 2.51 (s, 3H), 2.17 (s, 3H). MS: m/z = 538.1 (M+1), HPLC: 86.27% in method B

Example 20

5-(3-(1-(2,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxy-N-methylbenzenesulfonamide



Step-i: 5-(3-(1-(2,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxy-N-methylbenzenesulfonamide

Using similar reaction conditions as described in step-ii of example 15-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxy-N-methylbenzenesulfonamide (intermediate 22) (200mg, 0.335 mmol) was coupled with 1-(2,5-difluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (Intermediate 25) (146mg,0.418mmol) in sodium carbonate (106mg, 1.0mmol), $Pd(PPh_3)_2Cl_2$ (11.7mg, 0.011mmol), Toluene/ethanol/water (20/10/2 ml) to afford 142mg (61.4%yield) of the titled compound after purification by column (SiO_2-eluted by 0.4 to 1.2% MeOH in $CHCl_3$).

MS: m/z = 692.1 (M+1).

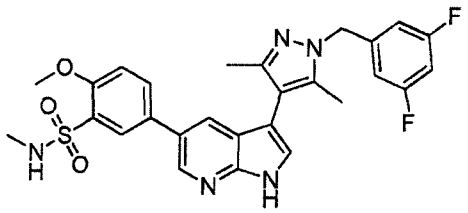
Step-ii: 5-(3-(1-(2,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxy-N-methylbenzenesulfonamide

Using similar reaction conditions as described in Step-iii of example 1, 15-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxy-N-methylbenzenesulfonamide (140mg, 0.202mmol)was hydrolyzed by lithium hydroxide (81mg, 2.02mmol), THF/Methanol/water (24/12/6 ml) to yield 9mg (8.3% yield) of the titled compound after purification by preparative TLC (SiO_2-1000micron eluted by 3% MeOH in $CHCl_3$).

^{1}H NMR (CD_3OD, 300MHz): δ 8.382 (b, 1H), 7.942-7.935 (d,1H), 7.815-7.808 (m, 2H), 7.334 (s, 1H), 7.241-7.213 (d, 1H), 7.08-6.96 (m, 1H), 6.66-6.56 (m, 1H), 5.289 (s, 2H), 3.914 (s, 3H), 2.444 (s, 3H), 2.138-2.110 (d, 6H). MS: m/z = 538.2 (M+1); HPLC: 95.57% in method B.

Example 21

(3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b] pyridin-5-yl)-2-methoxy-N-methylbenzenesulfonamide



Step-i: 5-(3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b] pyridin-5-yl)-2-methoxy-N-methylbenzenesulfonamide

Using similar reaction conditions as described in step-ii of example 1, 5-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxy-N-methylbenzenesulfonamide (intermediate 22) (200mg, 0.335 mmol) was coupled with 1-(3,5-difluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 24) (146mg,0.418mmol) in sodium carbonate (100mg, 1.0mmol) $Pd(PPh_3)_2Cl_2$(11.7mg, 0.011mmol), Toluene/ethanol/water (20/10/2 ml) to afford 180mg (77.9% yield) of the titled compound after purification by column (SiO_2-eluted by 0.4 to 1.2% MeOH in $CHCl_3$).

MS: m/z = 692.0 (M+1).

Step-ii: 5-(3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxy-N-methylbenzenesulfonamide

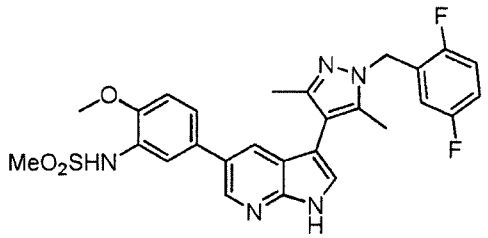
Using similar reaction conditions as described in step-iii of example 1, 5-(3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-

methoxy-N-methylbenzenesulfonamide (180mg, 0.2604mmol) was hydrolyzed by lithium hydroxide (109mg, 2.604mmol), THF/Methanol/water (24/12/6 ml) to yield 16mg (11.4% yield) of the titled compound after purification by preparative TLC (SiO2-1000micron eluted by 3% MeOH in $CHCl_3$).

^1H NMR (CD_3OD, 300MHz): δ 8.382 (m, 1H), 7.940-7.935 (d, 1H), 7.816-7.779 (m, 2H), 7.342 (s, 1H), 7.241-7.213 (d, 1H), 6.68-6.64 (m, 1H), 5.275 (s, 2H), 3.914 (s, 3H), 2.441 (s, 3H), 2.128-2.101 (d, 6H). MS: m/z = 538.1 (M+1); HPLC: 95.69% in method B.

Example 22

N-(5-(3-(1-(2,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide



Step-i: N-(5-(3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(2,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b] pyridine (Intermediate 26) (125mg, 0.218mmol) was coupled with N-(2-methoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methanesulfonamide (intermediate 17) (107.2mg,0.327mmol) in sodium carbonate (69.3mg, 0.654mmol) $Pd(PPh_3)_2Cl_2$ (7.65mg, 0.01mmol), Toluene/ethanol/water(5/3/2 ml) to afford 100 mg (66.6% yield) of the titled compound after purification by column (SiO_2-eluted by 80% EtOAc in hexanes).

MS: m/z = 692.1(M+1)

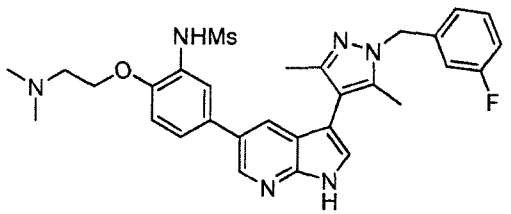
Step-ii: N-(5-(3-(1-(2,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b] pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide

Using similar reaction conditions as described in step-iii of example-1, N-(5-(3-(1-(2,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b] pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide (100mg, 0.14mmol)was hydrolyzed by lithium hydroxide(30.3mg, 0.722mmol), THF/Methanol/water (3/3/1 ml) to afford 13mg (28.2% yield) of the titled compound after purification by column (SiO_2-eluted by 2% MeOH in CHCl3).

^{1}H NMR ($CDCl_3$, 300MHz): δ 9.37 (s, 1H), 8.54 (s, 1H), 7.84-7.78 (m, 2H), 7.37-7.35 (m, 1H), 7.02-6.99 (m, 1H), 6.95-6.85 (m, 1H), 6.80-6.60 (m, 2H), 5.29 (s, 2H), 3.94 (s, 3H), 2.99 (s, 3H), 2.25 (s, 3H), 2.17 (s, 3H). MS: m/z = 538.1 (M+1), HPLC Purity: 91.44%, (Method: B).

Example 23

N-(2-(2-(dimethylamino)ethoxy)-5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide



Step-i: 2-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b] pyridin-5-yl)phenoxy)-N,N-dimethylethanamine

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b] pyridine (compound of step 1 of Example 14) (100mg, 0.18mmol) was coupled with N-(2-(2-(dimethylamino)ethoxy)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methane sulfonamide (Intermediate 27) (229mg,0.596mmol) in sodium carbonate (57mg, 0.54mmol) $Pd(PPh_3)_2Cl_2$ (6mg, 0.009mmol), Toluene/ethanol/water (5/2.5/1 ml) to afford 52mg (39.39% yield) of the titled compound after purification by preparative TLC (SiO2-eluted by 5% methanolic ammonia in DCM). MS: m/z = 731.4 (M+1)

Step-ii: N-(2-(2-(dimethylamino)ethoxy)-5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide

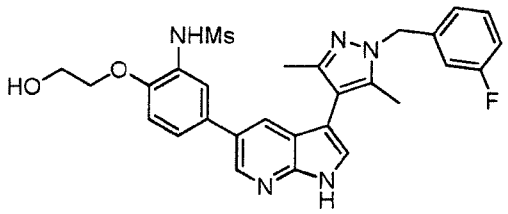
Using similar reaction conditions as described in step-iii of example-1, N-(5-(3-(1-(2,6-dichloro-3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl) methanesulfonamide (200mg, 0.264mmol) was hydrolyzed by lithium hydroxide (55.5mg, 1.32mmol), THF/Methanol/water (4/3/1 ml) to afford 6mg (15.2% yield) of the titled compound after purification by recrystallization in 7:3 ether-Chloroform.

^{1}H NMR ($CDCl_3$, 300MHz): δ 9.36 (s, 1H), 8.56-8.55 (d, 1H), 7.87-7.79 (m, 2H), 7.35-7.31 (m, 2H), 7.14-7.11 (d, 1H), 6.99-6.96 (d, 1H), 6.72 s, 1H), 5.31 (s, 2H), 4.17-4.13 (t, 2H), 2.94 (s, 3H), 2.61-2.57 (t, 3H), 2.39 (s, 6H), 2.25 (s, 3H), 2.17 (s, 4H).

MS: m/z = 577.2 (M+1), HPLC: 92.87% in Method B.

Example 24

N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(2-hydroxyethoxy)phenyl)methanesulfonamide



Step-i: N-(2-(2-(benzyloxy)ethoxy)-5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (compound of step-i of example-14) (150mg, 0.271mmol) was coupled with N-(2-(2-(benzyloxy)ethoxy)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methanesulfonamide (intermediate 28) (242mg,0.542mmol) in sodium carbonate (86mg,0.813mmol) $Pd(PPh_3)_2Cl_2$ (10mg, 0.0135mmol), Toluene/ethanol/water(5/2.5/1 ml) to afford 120mg (55.8% yield) of the titled compound after purification by column (SiO_2-eluted by 30% EA in hexanes).

MS: m/z = 794.1 (M+1)

Step-ii: N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(2-hydroxyethoxy)phenyl)methanesulfonamide

A stirred solution of N-(2-(2-(benzyloxy)ethoxy)-5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide (120mg, 0.151mmol), toluene/TFA (5/5 ml) was heated to 70°C for overnight. TLC showed reaction completion. Reaction mass was cooled to RT and solvents evaporated under reduced pressure. This afforded 152mg of the crude titled compound.

MS: m/z = 704.2 (M+1)

Step-iii: N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(2-hydroxyethoxy)phenyl)methanesulfonamide

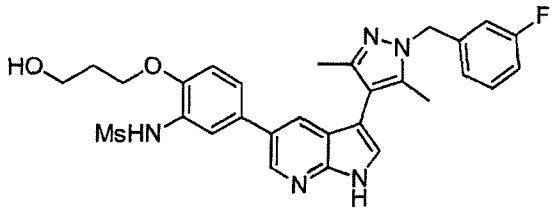
Using similar reaction conditions as described in step-iii of example-1, N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(2-hydroxyethoxy)phenyl)methanesulfonamide (150mg, 0.208mmol) was hydrolyzed by lithium hydroxide (88mg, 2.08mmol), THF/Methanol/water(3/3/1.5 ml) to afford 15mg (15.38% yield) of the title compound.

^{1}H NMR (DMSO-d_6, 300MHz): δ11.9 (s, 1H), 9.00 (s, 1H), 8.49 (s, 1H), 7.81 (s, 1H), 7.59 (s, 1H), 7.51-7.41 (m, 3H), 7.15-7.12 (d, 1H), 7.05-7.03 (m, 1H), 6.87 (s, 1H), 4.06 (m, 2H), 3.78 (m, 2H), 3.00 (s, 3H), 2.18-2.14 (d, 6H),

MS: m/z= 550.1(M+1), HPLC: 87.11% in Method B

Example 25

N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(3-hydroxypropoxy)phenyl)methanesulfonamide



Step-i: N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b] pyridin-5-yl)-2-(3-((4-methoxybenzyl)oxy)propoxy)phenyl)methanesulfonamide

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b] pyridine (step-i of example-14) (200mg, 0.3mmol) was coupled with N-(2-(3-(4-methoxyphenoxy)propoxy)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methanesulfonamide (intermediate 29) (160mg, 0.3mmol) in sodium carbonate(120mg, 1mmol) PdCl2(dppf) (14mg, 0.001mmol), 1,2-dimethoxy ethane/water (2/2 mL) to afford 120mg (41%yield) of the titled compound after purification by column (SiO_2-eluted by 30% EA in hexanes).

Step-ii: N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b] pyridin-5-yl)-2-(3-hydroxypropoxy)phenyl)methanesulfonamide

A stirred solution of N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo [2,3-b]pyridin-5-yl)-2-(3-((4-methoxybenzyl)oxy)propoxy)phenyl)methanesulfonamide (120mg, 0.1mmol), TFA/toluene (169mg/3 mL) was heated to 80°C for overnight. TLC showed reaction completion. Reaction mass was cooled to RT and solvents evaporated under reduced pressure. This afforded 60mg of the crude titled compound.

MS: m/z = 718.2 (M+1).

Step-iii: N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(3-hydroxypropoxy)phenyl)methanesulfonamide

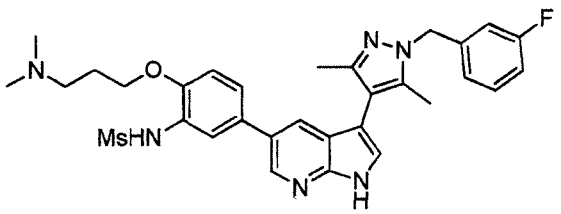
Using similar reaction conditions as described in step-iii of example-1, N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(3-

hydroxypropoxy)phenyl) methanesulfonamide (60mg, 0.08mmol)was hydrolyzed by lithium hydroxide (6mg, 0.25mmol), THF/methanol/water (1/1/0.5 ml) to afford 5mg (1.1% yield) of the titled compound.

^{1}H NMR (DMSO-d_6, 400MHz): δ 11.85 (s, 1H), 8.90 (s, 1H), 8.47 (s, 1H), 7.77 (s, 1H), 7.52-7.41 (m, 4H), 7.15-7.00 (m, 4H), 5.32 (s, 2H), 4.60 (b, 1H), 4.13 (t, 2H), 3.63-3.61 (t, 2H), 2.97 (s, 3H), 2.17-2.13 (d, 6H), 1.93 (m, 2H). MS: m/z = 564.1 (M+1), HPLC: 98.85 % (method – B).

Examlpe 26

N-(2-(3-(dimethylamino)propoxy)-5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo [2,3-b]pyridin-5-yl)phenyl)methanesulfonamide



Step-i: N-(2-(3-(dimethylamino)propoxy)-5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide

Using similar reaction conditions as described in step-ii of example 1, 5-bromo-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b] pyridine (step-i of example-14) (250mg, 0.4mmol) was coupled with N-(2-(3-(dimethylamino)propoxy)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methanesulfonamide (intermediate-30) (200mg, 0.5 mmol) in sodium carbonate (154mg, 1.4mmol) $PdCl_2$(dppf) (18mg, 0.05mmol), 1,2-dimethoxyethane/water (2/2 mL) to afford 40mg (12% yield) of the titled compound after purification by preparative TLC (SiO_2)-eluted by 30% ethyl acetate in hexane.

Step-ii: N-(2-(3-(dimethylamino)propoxy)-5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide

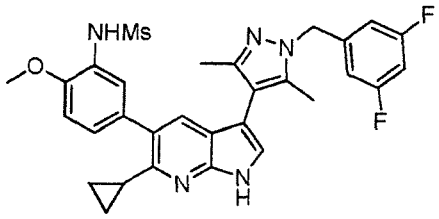
Using similar reaction conditions as described in step-iii of example-1, N-(2-(3-(dimethylamino) propoxy)-5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide (40mg, 0.05mmol)was hydrolyzed by lithium hydroxide(4mg, 0.16mmol), THF/methanol/water (1/1/0.5 ml) to afford 5mg (16% yield) of the titled compound after purification by preparative TLC (SiO_2)-eluted by 5% methanol in DCM.

^{1}H NMR ($CDCl_3$, 400MHz): δ 8.88 (s, 1H), 8.54-8.53 (d, 1H), 7.84 (s, 1H), 7.808-7.803 (d, 1H), 7.33-7.23 (m, 3H), 7.05-7.03 (d, 1H), 6.99-6.90 (m, 2H), 6.87-6.852 (d, 1H), 5.31 (s,

2H), 4.16-4.13 (t, 2H), 2.96 (s, 3H), 2.52-2.49 (t, 2H), 2.31 (s, 6H), 2.25 (s, 3H), 2.17 (s, 3H), 2.00-1.97 (m, 2H). MS: m/z = 591.4 (M+1), HPLC: 91.28 % in method B.

Example 27

N-(5-(6-cyclopropyl-3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b] pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide



Step-i: tert-butyl 5-(3-(N-(tert-butoxycarbonyl) methylsulfonamido)-4-methoxyphenyl)-6-cyclopropyl-3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 5-(3-(N-(tert-butoxycarbonyl)methylsulfonamido)-4-methoxyphenyl)-6-cyclopropyl-3-iodo-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (intermediate 33) (150mg, 0.21mmol) was coupled with 1-(3,5-difluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 24) (91.69mg, 0.24mmol) in sodium carbonate(66.77mg, 0.483mmol), $Pd(PPh_3)_2Cl_2$(7.36mg, 0.01mmol), 1,2-dimethoxyethane/water (10/2ml) to give 70mg (41% yield) of titled compound. MS: m/z = 778.0(M+1)

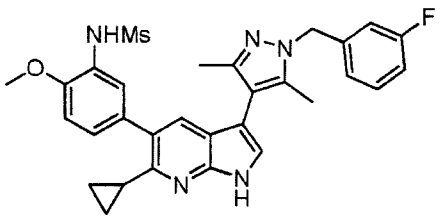
Step-ii: N-(5-(6-cyclopropyl-3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo [2,3-b] pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 6-cyclopropyl-3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-methoxy-3-(methyl sulfonamido)phenyl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (70mg, 0.103 mmol) was deprotected in HCl in 1,4-dioxane (2ml). This afforded 5mg (9.1% yield) of the titled compound.

^{1}H NMR (CD3OD, 300MHz): δ 8.24 (s, 1H), 7.66 (s, 1H), 7.59-7.58 (m, 1H), 7.38-7.34 (dd, 1H), 7.22-7.19 (m, 1H), 6.93-6.90 (m, 1H), 6.82-6.76 (m, 1H), 5.45-5.39 (t, 2H), 3.96 (s, 3H), 2.94 (s, 3H), 2.5-2.4 (m, 1H), 2.25 (s, 3H), 1.4-1.0 (m, 4H). MS: m/z = 538.1 (M+1), HPLC: 81% method B

Example 28

N-(5-(6-cyclopropyl-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide



Step-i: tert-butyl 5-(3-(N-(tert-butoxycarbonyl)methylsulfonamido)-4-methoxyphenyl)-6-cyclopropyl-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 5-(3-(N-(tert-butoxycarbonyl)methylsulfonamido)-4-methoxyphenyl)-6-cyclopropyl-3-iodo-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (intermediate 33) (200mg, 0.31mmol) was coupled with 1-(3-fluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 16) (123.15mg, 0.37mmol) in sodiumcarbonate (98.57mg, 0.93mmol), $Pd(PPh_3)_2Cl_2$ (10.8mg, 0.01mmol), 1,2-dimethoxyethane/water (10/2ml) to give 60mg (25.4% yield) of titled compound.

MS: m/z = 760.1 (M+1)

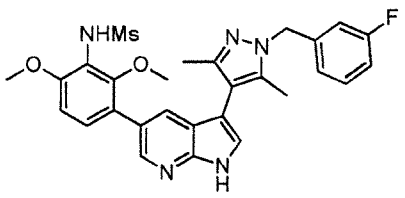
Step-ii: N-(5-(6-cyclopropyl-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo [2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 5-(3-(N-(tert-butoxycarbonyl)methylsulfonamido)-4-methoxyphenyl)-6-cyclopropyl-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (60mg, 0.078 mmol) was deprotected in HCl in 1,4-dioxane (2ml).This afforded 8mg (18.1% yield) of the titled compound.

^{1}H NMR (CDCl3, 300MHz): δ 9.1-9.0 (b, 1H), 7.679-7.673 (d, 1H), 7.52 (s, 1H), 7.14-7.13 (d, 1H), 6.99-6.96 (m, 3H), 6.85 (m, 2H), 5.28 (s, 3H), 3.93 (s, 3H), 2.99 (s, 3H), 2.23 (s, 3H), 2.14 (s, 3H), 0.89-0.85 (m, 4H). MS: m/z = 559.9 (M+1), HPLC: 85.5% in method B.

Example 29

N-(3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b] pyridin-5-yl)-2,6-dimethoxy phenyl)methanesulfonamide



Step-i: N-(3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b] pyridin-5-yl)-2,6-dimethoxyphenyl)methanesulfonamide

Using similar reaction conditions as described in step-ii of example-1, N-(3-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2,6-dimethoxyphenyl) methane sulfonamide (intermediate 34) (55mg, 0.485mmol) was coupled with 1-(3-fluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate-16) (57.8mg, 0.175 mmol) in sodium carbonate (28mg, 0.263 mmol), $Pd(PPh_3)_2Cl_2$ (3.0mg, 0.0043mmol), Toluene/ethanol/water (10/5/2ml) to give 40mg (64.5% yield) of titled compound.

MS: m/z = 704.2 (M+1).

Step-ii: N-(3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2,6-dimethoxyphenyl)methanesulfonamide

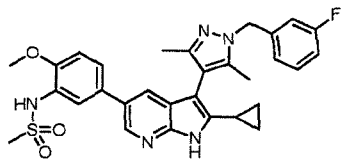
Using similar reaction conditions as described in step-iii of example-1, N-(3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2,6-dimethoxy phenyl)methanesulfonamide (40mg, 0.05mmol) was hydrolyzed by lithium hydroxide (23.8mg, 0.5mmol), THF/Methanol/water (12/4/4 ml) to afford 7mg (25.9% yield) of the titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ 8.5 (b, 1H), 8.181-8.177 (d, 1H), 7.525 (s, 1H), 7.356-7.334 (m, 2H), 6.991-6.957 (m, 3H), 6.9-6.85 (m, 1H), 5.363 (s, 2H), 3.930 (s, 3H), 3.499 (s, 3H), 3.184 (s, 1H), 2.231-2.204 (d, 6H).

MS: m/z = 550.0 (M+1); HPLC: 94.463% in method A.

Example 30

N-(5-(2-cyclopropyl-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide



Step-i: tert-butyl 5-(3-(N-(tert-butoxycarbonyl) methylsulfonamido)-4-methoxyphenyl)-2-cyclopropyl-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 5-(3-(N-(tert-butoxycarbonyl)methylsulfonamido)-4-methoxyphenyl)-2-cyclopropyl-3-iodo-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (intermediate 36) (110 mg, 0.1610 mmol) was coupled with 1-(3-fluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-

pyrazole (intermediate 16) (61 mg, 0.1771 mmol) in sodium carbonate (51 mg, 0.4831 mmol), $Pd(PPh_3)_4$ (10 mg, 0.0080 mmol) and DME/water (3/1 ml) to afford 150 mg of the crude product which was taken as such for next reaction.

Step-ii: N-(5-(2-cyclopropyl-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo [2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide

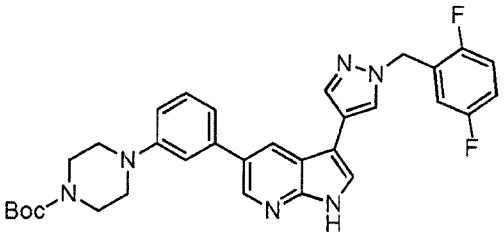
tert-butyl5-(3-(N-(tert-butoxycarbonyl)methylsulfonamido)-4-methoxyphenyl)-2-cyclopropyl-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (150 mg) was hydrolyzed with methanol/HCl (5 ml) at 0 °C and purified by prep HPLC to afford 9 mg (8.18% yield) of the pure required product.

^1H NMR (CD_3OD , 400MHz): δ 8.32-8.31 (s, 1H), 7.65-7.64 (d, 1H), 7.54-7.7.53 (d, 1H), 7.42-7.37 (q, 1H), 7.06-6.94 (m, 3H), 6.88-6.86 (d, 1H), 5.39 (s, 2H), 3.85 (s, 3H), 3.82 (s, 3H), 2.14 (s, 3H), 2.04 (s, 3H), 1.94-1.93 (m, 1H), 1.04-0.90 (m, 4H).

MS: m/z = 560.0 (M+1), HPLC Purity: 78.69% Method: B.

Example 31

tert-butyl 4-(3-(3-(1-(2,5-difluorobenzyl)-1h-pyrazol-4-yl)-1h-pyrrolo[2,3-b] pyridin-5-yl)phenyl) piperazine-1-carboxylate



Step-i: tert-butyl 4-(3-(3-(1-(2,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo [2,3-b]pyridin -5-yl) phenyl) piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(2,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (step-i of example-4) (380mg, 0.552mmol) was coupled with tert-butyl 4-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl) piperazine-1-carboxylate (intermediate 37) (428mg, 1.104mmol) in sodium carbonate (176mg, 1.657mmol), $Pd(PPh_3)_2Cl_2$ (38.7mg, 0.0552mmol), toluene/ethanol/water (30/15/6 ml). This afforded 454mg (89.7% yield) after purification by column (Silica gel 60/120) using 35%ethyl acetate in hexane as eluent.

MS: m/z = 725.6 (M+2)

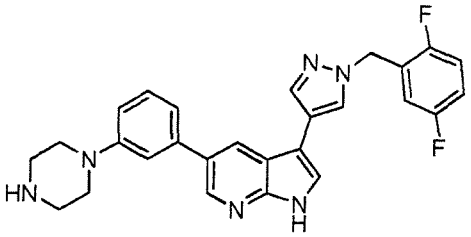
Step-ii tert-butyl 4-(3-(3-(1-(2,5-difluorobenzyl)-1h-pyrazol-4-yl)-1h-pyrrolo[2,3-b] pyridin-5-yl)phenyl) piperazine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(3-(3-(1-(2,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl) piperazine-1-carboxylate (450mg, 0.621mmol) was hydrolyzed by lithium hydroxide (130mg, 3.107mmol), THF/Methanol/water (20/10/4 ml) to yield 300.0mg yield 84% of the titled compound after purification by preparative TLC (SiO2-using 2% methanol in chloroform as eluent)

^{1}H NMR (CD_3OD, 300MHz): δ 9.05 (b, 1H), 8.559-8.552 (d, 1H), 8.187-8.180 (m, 1H), 7.866 (s, 1H), 7.760 (s, 1H), 7.449-7.370 (m, 1H), 7.164-7.150 (m, 1H), 7.1-6.85 (m, 3H), 5.423 (s, 2H), 3.645-3.611 (m, 4H), 3.241-3.224 (m, 4H), 1.496 (s, 9H). MS: m/z = 571.1 (M+1); HPLC: 90.45% in method B.

Example 32

3-(1-(2,5-difluorobenzyl)-1H-pyrazol-4-yl)-5-(3-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b] pyridine



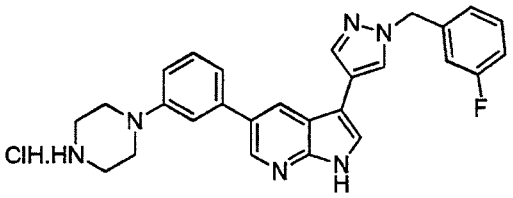
To a stirred solution of tert-butyl 4-(3-(3-(1-(2,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (Example-31) (200mg, 0.351mmol) in methanol (5ml) added saturated HCl in methanol at 0°C. This gradually brought to RT and stirred for four hours. Reaction mass was cooled and added ether to get solids. Solvents decanted and solids washed by ethyl acetate and dried. This residue was made free base using saturated sodium carbonate. This afforded 16.0mg (9.75% yield) of titled compound after purification by preparative TLC (SiO2 using 3% methanol in chloroform as eluent)

^{1}H NMR (CD_3OD, 300MHz): δ 8.557-8.550 (d, 1H), 8.192-8.184 (d, 1H), 7.866 (s, 1H), 7.762 (s, 1H), 7.446-7.360 (m, 2H), 7.160-7.10 (m, 2H), 7.05-6.85 (m, 3H), 5.420 (s, 2H), 3.276-3.242 (m, 4H), 3.119-3.086 (m, 4H).

MS: m/z = 470.9(M+1); HPLC: 97.41% in method A.

Example 33

3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(3-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b] pyridine hydrochloride



Step-i: tert-butyl 4-(3-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b] pyridin-5-yl) phenyl) piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (compound of step-i of example-9) (225 mg, 0.428mmol) was coupled with tert-butyl 4-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) phenyl) piperazine-1-carboxylate (intermediate 37) (332mg, 0.857mmol) in sodium carbonate (182mg, 1.714mmol), $Pd(PPh_3)_2Cl_2$ (34mg, 0.0285mmol), toluene/ethanol/water (22/11/5.5 ml). This afforded 147mg (48.6% yield) after purification by column (Silica gel 60/120) using 35%ethyl acetate in hexane as eluent.

MS: m/z = 706.8 (M+1)

Step-ii: tert-butyl 4-(3-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl) phenyl) piperazine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(3-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl) phenyl) piperazine-1-carboxylate (142mg, 0.2mmol) was hydrolyzed by lithium hydroxide (84mg, 2mmol), THF/Methanol/water (20/8/5 ml) to yield 77mg (70% yield) of the titled compound.

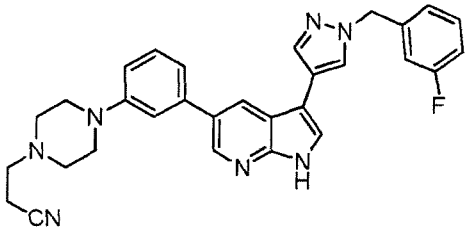
Step-iii: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(3-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b] pyridine hydrochloride

To a stirred solution of tert-butyl 4-(3-(3-(1-(2,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (76mg, 0.137mmol) in methanol (5ml) added saturated HCl in dioxane at 0°C. This gradually brought to RT and stirred for four hours. Reaction mass was cooled and added ether to get solids. Solvents decanted and solids washed by ethyl acetate and dried. This afforded 20mg (29.8% yield) titled compound.

^1H NMR (CD_3OD, 400MHz): δ 9.071-9.067 (d, 1H), 8.778-8.774 (d, 1H), 8.605 (s, 1H), 8.215 (s, 1H), 8.009 (s, 1H), 7.618-7.614 (m, 1H), 7.535-7.496 (t, 1H), 7.460-7.441 (m, 1H), 7.405-7.351 (m, 1H), 7.272-7.248 (m, 1H), 7.174-7.155 (m, 1H), 7.086-7.030 (m, 2H), 5.530 (s, 2H), 3.682-3.656 (m, 4H), 3.497-3.471 (m, 4H), 3.339 (s, 3H). MS: m/z = 453.4 (M+1); HPLC: 89.28% in method A.

Example 34

3-(4-(3-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl) propanenitrile



Step-i: 3-(4-(3-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl) phenyl piperazin-1-yl)propanenitrile

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (compound of step-i of example-9) (165mg, 0.314mmol) was coupled with 3-(4-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) phenyl) piperazin-1-yl)propanenitrile (intermediate 38) (160mg, 0.471mmol) in sodium carbonate (100mg, 0.942mmol), $Pd(PPh_3)_2Cl_2$(22mg, 0.0314mmol), toluene/ethanol/water (20/10/5 ml). This afforded 88mg (42.5% yield) after purification by column (Silica gel 60/120) using 1.5% methanol in chloroform as eluent.

MS: m/z = 660.4 (M+1)

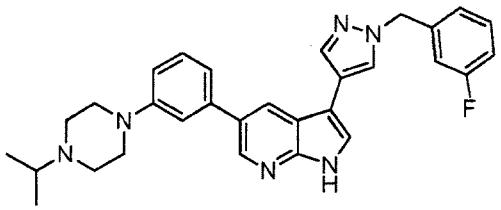
Step-ii: 3-(4-(3-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl) piperazin-1-yl)propanenitrile

Using similar reaction conditions as described in step-iii of example-1, 3-(4-(3-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl) phenyl) piperazin-1-yl)propanenitrile (86mg, 0.13mmol) was hydrolyzed by lithium hydroxide (27mg, 6.525mmol), THF/Methanol/water (15/4/4 ml) to yield 5mg (5.6% yield) of the titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ 8.481 (s, 1H), 8.407-8.402 (d, 1H), 8.198 (s, 1H), 7.955 (s, 1H), 7.674 (s, 1H), 7.48-7.292 (m, 4H), 7.123-6.98 (m, 4H), 5.439 (s, 2H), 3.8-3.4 (m, 4H), 3.2-3.0 (t, 2H). MS: m/z = 506.4 (M+1); HPLC: 98.91% in method A.

Example 35

3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(3-(4-isopropylpiperazin-1-yl) phenyl) -1H-pyrrolo [2,3-b]pyridine



Step-i: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(3-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo [2,3-b]pyridine hydrochloride

Using similar reaction conditions as described in step-iii of example-33, tert-butyl 4-(3-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl) phenyl) piperazine-1-carboxylate (compound of step-i of example-33) (130mg, 0.184mmol) was deprotected using methanol/HCl in dioxane (5/5mL) to give 86mg, (72.8%) of the titled compound.

Step-ii: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(3-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo [2,3-b]pyridine hydrochloride

To a stirred solution of 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(3-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride (85mg, 1.132mmol), potassium carbonate (54.7mg, 0.396mmol), DMF (5ml) added 2-bromopropane (18mg, 0.145mmol) and the mixture was heated to 50°C for overnight. Then reaction mass was cooled to room temperature and water was added, this was then extracted into ethyl acetate, organic portion was dried over sodium sulfate and concentrated to give 80mg (93% yield) of the titled compound.

MS: m/z = 649.4(M+1)

Step-iii: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(3-(4-isopropylpiperazin-1-yl)phenyl)-1H-pyrrolo [2,3-b]pyridine

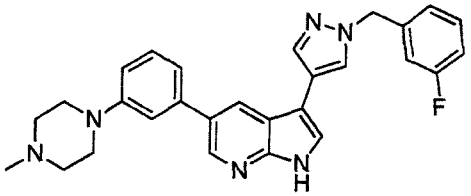
Using similar reaction conditions as described in step-iii of example-1, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(3-(4-isopropylpiperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (79mg, 0.121mmol) was hydrolyzed by lithium hydroxide (55mg, 1.21mmol), THF/Methanol/water (15/5/5 ml) to yield 8mg (13.3% yield) of the titled compound.

^{1}H NMR ($CDCl_3$, 300MHz): δ 9.0 (b, 1H), 8.55 (s, 1H), 8.15 (s, 1H), 7.88 (s, 1H), 7.7 (s, 1H), 7.46-7.3 (m, 3H), 7.2-6.9 (m, 3H), 5.389 (s, 2H), 3.4 (m, 4H), 2.7 (m, 4H), 1.4-1.0 (m, 7H).

MS: m/z = 495.4 (M+1); HPLC: 89.22% in method B.

Example 36

3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(3-(4-methylpiperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine



Step-i: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(3-(4-methylpiperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

A mixture of 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(3-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (step-i of example-35) (87mg, 0.143mmol), HCHO(13mg, 0.43mmol), 1,2-dichloroethane (2ml) was stirred at RT under nitrogen for 30 minutes. Sodium triacetoxy borohydride (91mg, 0.43mmol) was then added and stirred at the same temperature for overnight. Reaction mass quenched water, basified by saturated sodium bicarbonate and extracted into ethyl acetate. Organic layer dried over sodium sulfate and concentrated to give 74mg (84% yield) of the titled compound. MS: m/z = 621.0 (M+1)

Step-ii: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(3-(4-methylpiperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b] pyridine

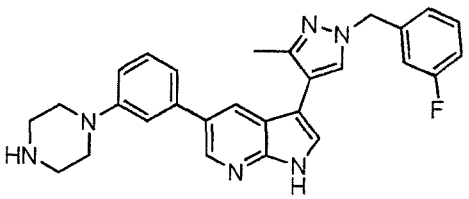
Using similar reaction conditions as described in step-iii of example-1, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(3-(4-methylpiperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (74mg, 0.119mmol) was hydrolyzed by lithium hydroxide (50mg, 1.19mmol), THF/Methanol/water (12/6/3 ml) to yield 8mg (30mg 53.9% yield) of the titled compound.

^{1}H NMR ($CDCl_3$, 300MHz): δ 9.4 (b, 1H), 8.566-8.559 (d, 1H), 8.185-8.178 (d, 1H), 7.874 (s, 1H), 7.706 (s, 1H), 7.451-7.443 (d, 1H), 7.413-7.3 (m, 2H), 7.2-6.956 (m, 5H), 5.392 (s, 2H), 3.340-3.307 (m, 4H), 2.669-2.636 (m, 4H), 2.401(s, 3H).

MS: m/z = 467.4 (M+1); HPLC: 98.239% in method B.

Example 37

3-(1-(3-fluorobenzyl)-3-methyl-1H-pyrazol-4-yl)-5-(3-(piperazin-1-yl)phenyl)-1H-pyrrolo [2,3-b] pyridine



Step-i: tert-butyl 4-(3-(3-(1-(3-fluorobenzyl)-3-methyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo [2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 4-(3-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (intermediate 39) (200mg, 0.308mmol) was coupled with 1-(3-fluorobenzyl)-3-methyl-4-(4,4,5,5-tetramethyl-1,3-dioxolan-2-yl)-1H-pyrazole (intermediate 12) (244mg, 0.772mmol) in sodium carbonate (98mg, 0.926mmol), $Pd(PPh_3)_2Cl_2$ (11mg, 0.015mmol), toluene/ethanol//water (3/3/3ml). This afforded 130g (59.6% yield) after purification by column (Silica gel 60/120) using 1.5% of methanol in chloroform as eluent.

MS: m/z = 710.3(M+1)

Step-ii: tert-butyl 4-(3-(3-(1-(3-fluorobenzyl)-3-methyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b] pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(3-(3-(1-(3-fluorobenzyl)-3-methyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b] pyridin-5-yl)phenyl)piperazine-1-carboxylate (130mg, 0.183mmol) was hydrolyzed by lithium hydroxide (77mg, 1.83mmol), THF/Methanol/water (12/6/3 ml) to yield 8mg (102mg 96% yield) of the titled compound.

MS: m/z = 557.3(M+2)

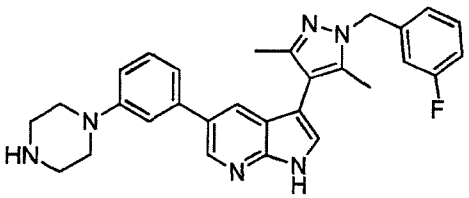
Step-iii: 3-(1-(3-fluorobenzyl)-3-methyl-1H-pyrazol-4-yl)-5-(3-(piperazin-1-yl)phenyl)-1H-pyrrolo [2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(3-(3-(1-(3-fluorobenzyl)-3-methyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl) phenyl)piperazine-1-carboxylate (83mg, 0.146mmol) was deprotected in methanol (5ml), HCl in dioxane (5ml). This afforded 20mg (27.1% yield) of the titled compound.

^1H NMR (CD_3OD, 400MHz): δ 8.852-8.818 (m, 1H), 8.726-8.723 (d, 1H), 8.272 (s, 1H), 7.951 (s, 1H), 7.832-7.798 (d, 1H), 7.499-7.459 (t, 1H), 7.407-7.317 (m, 3H), 7.160-7.129 (m, 2H), 7.070-7.048 (m, 2H), 5.404 (s, 2H), 3.549-3.523 (m, 4H), 3.418-3.393 (m, 4H), 2.392 (s, 3H). MS: m/z = 467.2 (M+1); HPLC: 94.845% in method A

Example 38

3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(3-(piperazin-1-yl) phenyl)-1H-pyrrolo [2,3-b] pyridine



Step-i: tert-butyl 4-(3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo [2,3-b] pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 4-(3-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (intermediate 39) (250mg, 0.379mmol) was coupled with 1-(3-fluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 16) (220mg, 0.666mmol) in sodium carbonate (121mg, 1.139mmol), $Pd(PPh_3)_2Cl_2$ (13.3mg, 0.0189mmol), toluene/ethanol//water (25/12.5/6ml). This afforded 267g (60% yield) after purification by column (Silica gel 60/120) using 1.5% of methanol in chloroform as eluent. MS: m/z = 735.3 (M+1).

Step-ii: tert-butyl 4-(3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b] pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (160mg, 0.363mmol) was hydrolyzed by lithium hydroxide (152mg, 3.633mmol), THF/Methanol/water (20/10/5 ml) to yield 8mg (96.7mg 79.5% yield) of the titled compound.

MS: m/z = 581.2(M+2)

Step-iii: 3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(3-(piperazin-1-yl)phenyl)-1H-pyrrolo [2,3-b]pyridine

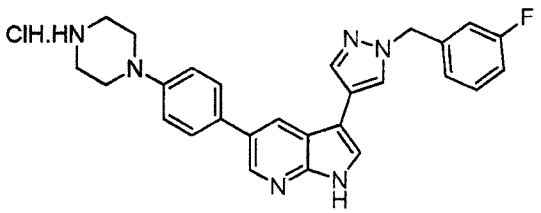
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl) phenyl)piperazine-1-carboxylate (96mg, 0.165mmol) was deprotected in methanol (5ml), HCl in dioaxane (5ml). This afforded 20mg (23.5% yield) of the titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ 8.759-8.755 (d, 1H), 8.639-8.635 (d, 1H), 7.818 (s, 1H), 7.482-7.370 (m, 3H), 7.284-7.265 (d, 1H), 7.154-7.087 (m, 3H), 6.995-6.971 (m, 1H), 5.489 (s, 2H), 3.530-3.516 (m, 4H), 3.413-3.387 (m, 4H), 2.288 (s, 6H).

MS: m/z = 481.1 (M+1); HPLC: 85.59% in method A.

Example 39

3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo [2,3-b]pyridine hydrochloride



Step-i: tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (compound of step-i of example-9) (200mg, 0.53mmol) was coupled with tert-butyl 4-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)piperazine-1-carboxylate (intermediate 40) (251mg,0.64mmol) in sodium carbonate (168mg, 1.59mmol) PdCl2(dppf) (19mg, 0.0265mmol), 1,2-Dimethoxyethane/water (25/3 ml) to afford 160mg (59.47% yield) of the titled compound.

MS: m/z = 707.1 (M+1)

Step-ii: tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl) phenyl) piperazine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl) phenyl) piperazine-1-carboxylate (160mg, 0.22mmol) was hydrolyzed by lithium hydroxide (28.5mg, 0.67mmol), THF/Methanol/water (3/2/1 ml) to afford 90mg (72% yield) of the titled compound. MS: 553.2 m/z = (M+1)

Step-iii: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b] pyridine hydrochloride

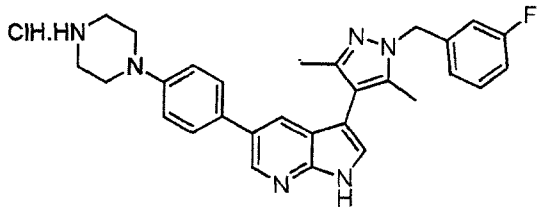
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl) phenyl) piperazine-1-carboxylate (96mg, 0.165mmol) was deprotected in dioxane (1ml), HCl in dioxane (3ml). This afforded 20mg (23.7% yield) of the titled compound.

^{1}H NMR (DMSO-d_6, 300MHz): δ 9.1-9.0 (b, 1H), 8.54-8.53 (d, 1H), 8.46 (s, 1H), 8.42 (m, 1H), 8.0 (s, 1H), 7.81 (d, 1H), 7.73-7.70 (m,, 2H), 7.4 (m, 1H), 7.14-7.11 (m, 4H), 5.41 (s, 2H), 3.43-3.41 (m, 6H), 3.3-3.2 (b, 4H).

MS: 453.2 m/z = (M+1), HPLC: 96.3% in method B.

Example 40

3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl) -1H-pyrrolo [2,3-b]pyridine hydrochloride



Step-i: tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 4-(4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (intermediate 41) (130mg, 0.19mmol) was coupled with 1-(3-fluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 16) (71mg, 0.21mmol) in sodium carbonate (40mg, 0.38mmol), $PdCl_2$(dppf) (6.94mg, 0.0095mmol), 1,2-Dimethoxyethane/water (15/1.5 ml) to give titled compound quantity and yield as off white solid. MS: m/z = 735.2 (M+1).

Step-ii: tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b] pyridin -5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b] pyridin-5-yl)phenyl)piperazine-1-carboxylate (200mg, 0.270mmol) was hydrolyzed by lithium hydroxide(34.2mg, 081mmol), THF/Methanol/water(10/5/1 ml) to yield 80mg (50.6% yield) of the titled compound.

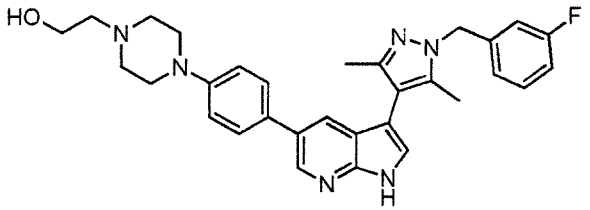
Step-iii: 3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo [2,3-b]pyridine hydrochloride

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl) phenyl)piperazine-1-carboxylate (80mg, 0.137mmol) was deprotected in dioxane (1ml), HCl in dioxane (3ml). This afforded 5mg (23.5% yield) of the titled compound.

^{1}H NMR (DMSO-d_6, 300MHz): δ 9.14-9.0 (b, 1H), 8.54 (d, 1H), 7.92 (s, 1H), 7.63-7.60 (s 2H), 7.54-7.53 (s, 1H), 7.5 (m, 1H), 7.10-7.04 (m, 5H), 5.34 (s, 2H), 3.41 (m, 4H), 3.25 (m, 4H), 2.17-2.14 (d, 4H). MS: m/z = 481.2 (M+1), HPLC: 90.3% in Method B.

Example 41

2-(4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)ethanol



Step-i: 5-(4-(4-(2-(benzyloxy)ethyl)piperazin-1-yl)phenyl)-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-1, 5-(4-(4-(2-(benzyloxy) ethyl)piperazin-1-yl)phenyl)-3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridine (intermediate 42) (130mg, 0.203mmol) was coupled with 1-(3-fluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 16) (101mg, 0.305mmol) in sodium carbonate (65mg, 0.602mmol), $Pd(PPh_3)_2Cl_2$ (7mg, 0.0101mmol), Toluene/ethanol/water (5/2.5/1ml) to give 155mg of the crude titled compound.

MS: m/z = 769.3 (M+1)

Step-ii: 2-(4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b] pyridin-5-yl)phenyl)piperazin-1-yl)ethanol

5-(4-(4-(2-(benzyloxy)ethyl)piperazin-1-yl)phenyl)-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (150mg, 0.195mmol) was dissolved in trifluoroacetic acid/toluene (5/5 ml) and heated to 70°C for overnight. Solvents evaporated off to yield 208mg of the crude titled compound.

Step-iii: 2-(4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)ethanol

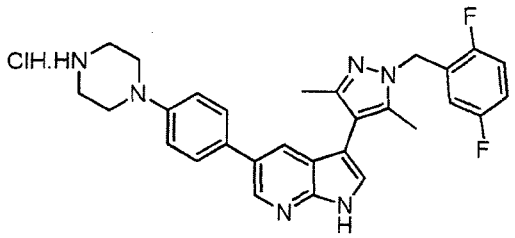
Using similar reaction conditions as described in step-iii of example-1, 2-(4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl) phenyl)piperazin-1-yl)ethanol (200mg, 0.259mmol) was hydrolyzed by lithium hydroxide (108mg, 2.59mmol), THF/Methanol/water (5/5/2.5 ml) to yield 3mg (2.2% yield) of the titled compound.

^{1}H NMR (CD_3OD, 300MHz): δ 8.34 (s, 1H), 7.75-7.74 (d, 1H), 7.44-7.41 (m, 2H), 7.28-7.27 (m, 2H), 7.00-6.7 (m, 4H), 6.52-6.51 (d, 1H), 5.26 (s, 2H), 3.73-3.69 (t, 2H), 3.26 (m, 4H), 2.91 (m, 4H), 2.79-2.77 (t, 2H), 2.12-2.08 (m, 6H).

MS: m/z = 525.2(M+1), HPLC: 80.69% in method A.

Example 42

3-(1-(2,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine hydrochloride



Step-i: tert-butyl 4-(4-(3-(1-(2,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo [2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 4-(4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (intermediate 41) (160mg, 0.243mmol) was coupled with 1-(2,5-difluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 25) (85mg, 0.243mmol) in sodium carbonate (77mg, 0.729mmol), $Pd(PPh_3)_2Cl_2$ (17mg, 0.0243mmol), Toluene/ethanol/water (15/7.5/1ml) to give 230mg of titled compound.

MS: m/z = 753.1 (M+1).

Step-ii: tert-butyl 4-(4-(3-(1-(2,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b] pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(3-(1-(2,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (230mg, 0.305mmol) was hydrolyzed by lithium hydroxide (129mg, 3.05mmol), THF/Methanol/water (12/4/4 ml) to afford 46mg (25.2% yield) of the titled compound. MS: m/z = 599.3 (M+1).

Step-iii: 3-(1-(2,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine hydrochloride

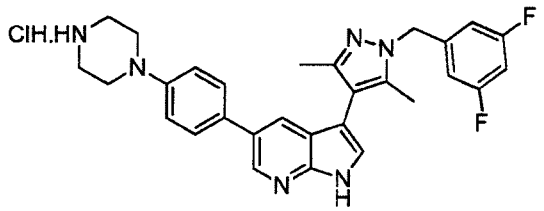
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(2,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl) phenyl)piperazine-1-carboxylate (45mg, 0.07mmol) was deprotected in methanol (5ml), HCl in 1,4-dioaxane (5ml).This afforded 5mg (14.7% yield) of the titled compound.

^{1}H NMR (CD_3OD, 300MHz): δ 8.351-8.345 (d, 1H), 7.763-7.756 (d, 1H), 7.440-7.412 (m, 2H), 7.293 (s, 1H), 7.095-7.081 (m,1H), 6.996-6.967 (m, 3H), 6.584 (m, 1H), 5.287 (s, 2H),

3.146-3.114 (m, 4H), 2.972-2.940 (m, 4H), 2.132-2.109 (d, 6H). MS: m/z = 499.2 (M+1); HPLC: 85.79% in method B.

Example 43

3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine hydrochloride



Step-i: tert-butyl 4-(4-(3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo [2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 4-(4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (intermediate 41) (200mg, 0.303mmol) was coupled with 1-(3,5-difluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 24)(126mg, 0.364mmol) in sodium carbonate (96.3mg, 0.909mmol), $Pd(PPh_3)_2Cl_2$ (10.63mg, 0.015mmol), toluene/ethanol/water (3/5/1ml) to give 160 mg (72.7% yield) of titled compound. MS: m/z = 753.1 (M+1)

Step-ii: tert-butyl 4-(4-(3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b] pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (160mg, 0.212mmol) was hydrolyzed by lithium hydroxide (44.6mg, 1.063mmol), THF/Methanol/water (2/3/1 ml) to yield 100mg (63.3% yield) of the titled compound.

Step-iii: 3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine hydrochloride

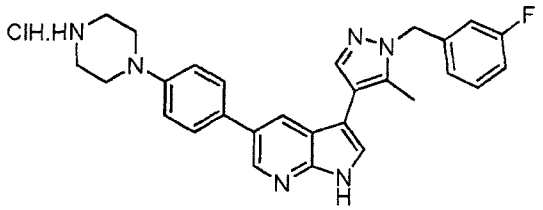
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (100mg, 0.167mmol) was deprotected in methanol(5ml), HCl in 1,4-dioaxane (5ml).This afforded 100mg (63.3% yield) of the titled compound.

^{1}H NMR ($CDCl_3$, 300MHz): δ 8.56 (s, 1H), 7.858-7.853 (d, 1H), 7.54-7.51 (d, 2H), 7.03-7.01 (d, 2H), 6.69-6.67 (m, 2H), 5.29 (s, 2H), 3.65-3.59 (t, 4H), 3.21-3.19 (t, 4H), 2.26 (s, 3H), 2.15 (s, 3H), 1.49 (s, 9H).

MS: m/z = 599.2 (M+1).

Example 44

3-(1-(3-fluorobenzyl)-5-methyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo [2,3-b]pyridine hydrochloride



Step-i: tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-5-methyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 4-(4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (intermediate 41) (300mg, 0.455mmol) was coupled with 1-(3-fluorobenzyl)-5-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 12) (187mg, 0.592mmol) in sodium carbonate (145mg, 1.365mmol), $Pd(PPh_3)_2Cl_2$ (16mg, 0.0227mmol), Toluene/ethanol/water (5/10/1ml) to give 250mg (76.2% yield) of titled compound after purification by column (SiO2) using 20% ethyl acetate in hexane as eluent.

^{1}H NMR ($CDCl_3$, 300MHz): δ 8.64 (s, 1H), 8.12-8.09 (d, 2H), 7.87 (s, 1H), 7.70 (s, 1H), 7.56 (s, 1H), 7.49-7.44 (m, 2H), 7.34-7.25 (m, 2H), 7.01-6.99 (m, 3H), 5.31 (s, 2H), 3.62-3.60 (t, 4H), 3.25-3.19 (t, 4H), 2.39 (s, 3H), 2.37 (s, 3H), 1.49 (s, 9H).

MS: m/z = 721.1 (M+1).

Step-ii: tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-5-methyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b] pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-5-methyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b] pyridin-5-yl)phenyl)piperazine-1-carboxylate (250mg, 0.346mmol) was hydrolyzed by lithium hydroxide (72.8mg, 1.734mmol), THF/Methanol/water(2/3/1 ml) to yield 100mg (52% yield) of the titled compound.

^{1}H NMR ($CDCl_3$, 400MHz): δ 9.28 (S, 1H), 8.54 (s, 1H), 8.01 (s, 1H), 7.59-7.52 (m, 3H), 7.34-7.27 (m, 2H), 7.05-6.94 (m, 4H), 5.32 (s, 2H), 3.61-3.60 (m, 4H), 3.19 (s, 4H), 2.40 (s, 3H), 1.49 (s, 9H). MS: m/z = 657.2 (M+1)

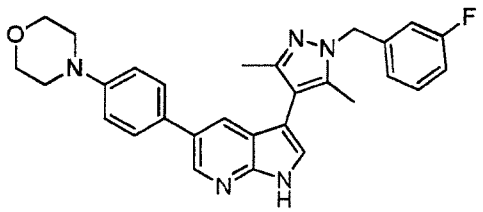
Step-iii: 3-(1-(3-fluorobenzyl)-5-methyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo [2,3-b]pyridine hydrochloride

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-5-methyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl) phenyl) piperazine-1-carboxylate (100mg, 0.176mmol) was deprotected with HCl in 1,4-dioaxane (5ml). This afforded 50mg (60.9% yield) of the titled compound.

^{1}H NMR ($CDCl_3$, 300MHz): δ 9.08 (s, 1H), 8.55-8.54 (d, 1H), 8.02-8.01 (d, 1H), 7.60 (s, 1H), 7.54-7.51 (d, 2H), 7.34-7.31 (m, 2H), 7.10-6.95 (m, 4H), 5.32 (s, 2H), 3.23-3.19 (m, 4H), 3.09-3.05 (m, 4H), 2.41 (s, 3H). MS: m/z = 467.4 (M+1), HPLC Purity: 96.37% Method: A.

Example 45

4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl) morpholine



Step-i: 4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b] pyridin-5-yl)phenyl) morpholine

Using similar reaction conditions as described in step-ii of example-1, 4-(4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)morpholine (intermediate 43) (150mg, 0.268mmol) was coupled with 1-(3-fluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 16) (133mg, 0.402mmol) in sodium carbonate (86mg, 0.805mmol), $Pd(PPh_3)_2Cl_2$ (10mg, 0.0134mmol), Toluene/ethanol/water (5/5/5ml) to afford 100mg (58.82% yield) of titled compound.

MS: m/z = 636.1 (M+1)

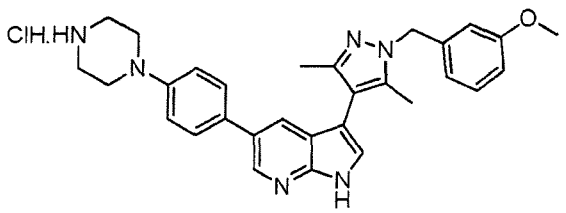
Step-ii: 4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)morpholine

Using similar reaction conditions as described in step-iii of example-1, 4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl) morpholine (100mg, 0.157mmol) was hydrolyzed by lithium hydroxide (33mg, 0.786mmol), THF/Methanol/water (5/5/3 ml) to afford 24mg (32% yield) of the titled compound.

^{1}H NMR ($CDCl_3$, 300MHz): δ 9.36 (s, 1H), 8.56 (s, 1H), 7.87 (s, 1H), 7.75-7.52 (d, 2H), 7.40-7.30 (m, 1H), 7.10-6.95 (m, 3H), 6.90-6.80 (d, 1H), 5.32 (s, 2H), 3.91-3.88 (m, 4H), 3.23-3.20 (m, 4H), 2.26 (s, 3H), 2.15 (s, 3H). MS: m/z = 482.3 (M+1), HPLC Purity: 99.13% Method: B.

Example 46

3-(1-(3-methoxybenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl) phenyl)-1H-pyrrolo[2,3-b]pyridine hydrochloride



Step-i: tert-butyl 4-(4-(3-(1-(3-methoxybenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 4-(4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (intermediate 41) (250mg, 0.3mmol) was coupled with 1-(3-methoxybenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 53) (131mg, 0.4mmol) in sodium carbonate (123mg, 1mmol), $PdCl_2$(dppf)(140mg, 0.18mmol), Toluene/ethanol/water (2/2/1ml) to give 40mg (14% yield)of titled compound.

MS: m/z = 747.3 (M+1).

Step-ii: tert-butyl 4-(4-(3-(1-(3-methoxybenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(3-(1-(3-methoxybenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (70mg, 0.9mmol) was hydrolyzed by lithium hydroxide (7mg, 0.22mmol), THF/Methanol/water(2/2/1 ml) to afford 17mg(31% yield) of the titled compound after purification by column (SiO2) using 70% ethyl acetate in hexane as eluent.

MS: m/z = 593.3 (M+1).

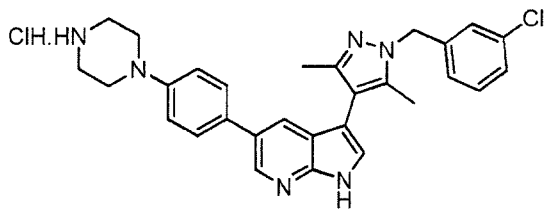
Step-iii: 3-(1-(3-methoxybenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H -pyrrolo [2,3-b]pyridine hydrochloride

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(3-methoxybenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl) phenyl)piperazine-1-carboxylate (17mg, 0.023 mmol) was deprotected in methanol/1,4-dioxane in (0.5/2ml).This afforded 5mg (36% yield) of the titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ 8.75 (s, 2H), 7.90 (s, 1H), 7.72 (m, 2H), 7.35-7.34 (d, 1H), 7.20 (m, 2H), 6.97-6.86 (m, 3H), 5.57 (s, 2H), 3.81 (s, 3H), 3.53 (m, 4H), 3.40 (m, 4H), 2.39-2.38 (d, 6H). MS: m/z = 493.1 (M+1), HPLC – 91.06% (method A).

Example 47

3-(1-(3-chlorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl) phenyl)-1H-pyrrolo[2,3-b]pyridine hydrochloride



Step-i: tert-butyl 4-(4-(3-(1-(3-chlorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 4-(4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (intermediate 41) (200mg, 0.3mmol) was coupled with 1-(3-chlorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 54) (107mg, 0.33mmol) in sodium carbonate (99mg, 0.9 mmol), $Pd(dppf)Cl_2$ (12mg, 0.01mmol), toluene/ethanol/water (2/2/1ml) to give 70 mg (31% yield) of titled compound.

Step-ii: tert-butyl 4-(4-(3-(1-(3-chlorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo [2,3-b] pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(3-(1-(3-chlorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (70mg, 0.9mmol) was hydrolyzed by lithium hydroxide(7mg, 0.27mmol), THF/Methanol/water(1/1/0.5 ml) to afford 12mg (22% yield) of the titled compound after purification by column (SiO_2) using 70% ethyl acetate in hexane as eluent.

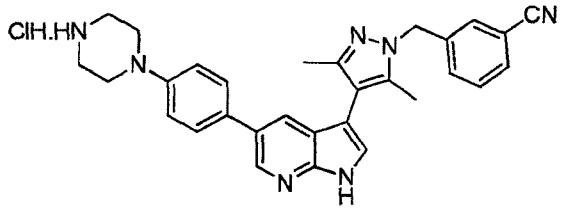
Step-iii: 3-(1-(3-chlorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo [2,3-b]pyridine hydrochloride

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(3-chlorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (12mg, 0.02 mmol) was deprotected in methanol/1,4-dioxane in (0.3/2ml).This afforded 5mg (55% yield)of the titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ 8.72 (s, 1H), 8.669 (s, 1H), 7.85 (s, 1H), 7.71-7.69 (d, 2H), 7.42-7.39 (m, 2H), 7.32 (s, 1H), 7.24-7.18 (m, 3H), 5.52 (s, 2H), 3.53-3.50 (m, 4H), 3.41-3.38 (m, 4H), 2.33-2.32 (d, 6H). MS: m/z = 497.2 (M+1), HPLC – 95.77 % (method – B).

Example 48

3-((3,5-dimethyl-4-(5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridin-3-yl)-1H-pyrazol -1-yl)methyl)benzonitrile hydrochloride



Step-i: tert-butyl 4-(4-(3-(1-(3-cyanobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 4-(4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (intermediate 41) (200mg, 0.3mmol) was coupled with 3-((3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-yl)methyl)benzonitrile (intermediate 55) (103mg, 0.3mmol) in sodium carbonate (98mg, 0.9mmol), $PdCl_2$(dppf) (11mg, 0.01mmol), toluene/ethanol/water (2/2/1ml) to give 80mg (36% yield) of titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ8.44-8.43 (d, 1H), 7.85 -7.84 (d, 1H), 7.55-7.49 (m, 5H), 7.38 (s, 1H), 7.09 -7.07 (d, 2H), 6.60 (s, 1H), 5.41 (s, 2H), 3.27-3.24 (m, 4H), 3.11-3.09 (m, 4H), 2.21-2.17 (m, 6H).

MS: m/z = 488.1 (M+1), HPLC – 92.75% (method - B).

Step-ii: 3-((3,5-dimethyl-4-(5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridin-3-yl)-1H-pyrazol -1-yl)methyl)benzonitrile hydrochloride

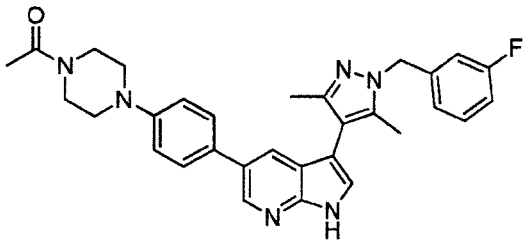
Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(3-(1-(3-cyanobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b] pyridin-5-yl)phenyl)piperazine-1-carboxylate (80mg, 0.1mmol) was hydrolyzed by lithium hydroxide

(6mg, 0.2mmol), THF/Methanol/water(1/1/0.5 ml) to give tert-butyl 4-(4-(3-(1-(3-cyanobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate, which was then deprotected Using similar reaction conditions as described in Step-ii example 7, in methanol/1,4-dioxane (0.3/2ml). This afforded 3mg (5% yield) of the titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ8.44-8.43 (d, 1H), 7.85 -7.84 (d, 1H), 7.55-7.49 (m, 5H), 7.38 (s, 1H), 7.09 -7.07 (d, 2H), 6.60 (s, 1H), 5.41 (s, 2H), 3.27-3.24 (m, 4H), 3.11-3.09 (m, 4H), 2.21-2.17 (m, 6H). MS: m/z = 488.1 (M+1), HPLC – 92.75% (method B).

Example 49

1-(4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b] pyridin-5-yl) phenyl) piperazin-1-yl)ethanone



Step-i: 3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-iii of example-38, tert-butyl 4-(3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (compound of step-i of example-40) (190mg, 0.258mmol) was deprotected using methanol/HCl in dioxane (7/7mL) to give 110mg, (64.2%) of the titled compound.

Step-ii: 1-(4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b] pyridin-5-yl)phenyl)piperazin-1-yl) ethanone

A stirred solution of 3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (100mg, 0.157mmol), triethylamine (47.8mg, 0.473 mmol), DCM (3ml) was added acetyl chloride (18.5mg, 0.236mmol) drop wise at 0°C. Reaction mass was gradually warmed to room temperature, reaction completed in an hour. Reaction mass was diluted with DCM and washed with water, dried over sodium sulfate and concentrated to give 98mg (92.4% yield) of the titled compound.

MS: m/z = 677.2 (M+1).

Step-iii: 1-(4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl) phenyl) piperazin-1-yl)ethanone

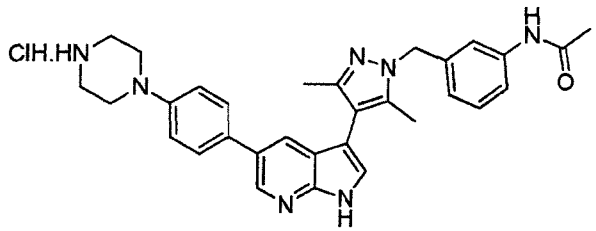
Using similar reaction conditions as described in step-iii of example-1, 1-(4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)ethanone (98mg, 0.144mmol) was hydrolyzed by lithium hydroxide (61mg, 1.44mmol), THF/Methanol/water (12/6/3 ml) to afford 16mg (21.3% yield) of the titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ 8.545 (b, 1H), 8.270-8.264 (m, 1H), 7.577-7.549 (m, 3H), 7.379-7.306 (m, 1H), 7.115-7.086 (d, 2H), 7.022-6.966 (m,1H), 6.875-6.843 (m, 1H), 5.344 (s, 2H), 3.735-3.663 (m, 4H), 3.231-3.196 (m, 4H), 2.185-2.165 (d, 2H), 2.115 (s, 3H).

MS: m/z = 523.1 (M+1); HPLC: 97.70% in method B.

Example 50

N-(3-((3,5-dimethyl-4-(5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridin-3-yl)-1H-pyrazol-1-yl) methyl)phenyl)acetamide



Step-i: tert-butyl 4-(4-(3-(3,5-dimethyl-1-(3-nitrobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo [2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of intermediate 1, tert-butyl 4-(4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (intermediate 41) (400mg, 0.6mmol) was coupled with 3,5-dimethyl-1-(3-nitrobenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 56) (240mg, 0.66mmol) in sodium carbonate (196mg, 1mmol), $PdCl_2$(dppf) (22mg, 0.03mmol), toluene/ethanol/water (2/2/2ml) to give 200mg (43% yield) of titled compound after purification by column (SiO_2) using 30% ethyl acetate in hexane as eluent.

MS: m/z = 762.3 (M+1).

Step-ii: tert-butyl 4-(4-(3-(1-(3-aminobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo [2,3-b] pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in example-8, tert-butyl 4-(4-(3-(3,5-dimethyl-1-(3-nitrobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-

1-carboxylate (200mg, 0.262mmol) was reduced by 10% palladium on carbon (20mg, 10%W/W), ethanol (3 mL) to yield 150mg (yield 78.08%) of the titled compound. MS: m/z = 7 32.3 (M+1).

Step-iii: tert-butyl 4-(4-(3-(1-(3-acetamidobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo [2,3-b] pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-i of example-49, tert-butyl 4-(4-(3-(1-(3-aminobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b] pyridin-5-yl)phenyl)piperazine-1-carboxylate (150mg, 2mmol) was acylated with acetyl chloride (21mg, 0.26mmol) in triethylamine (0.088ml, 6mmol) and DCM (3ml) to afford 70mg (44% yield) of the titled compound. MS: m/z = 774.1 (M+1).

Step-iv: tert-butyl 4-(4-(3-(1-(3-acetamidobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo [2,3-b] pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(3-(1-(3-acetamidobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo [2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (90mg, 0.1mmol) was hydrolyzed by lithium hydroxide (9mg, 0.3mmol), THF/Methanol/water (1/1/0.5 ml) to yield 20mg (29% yield) of the titled compound.

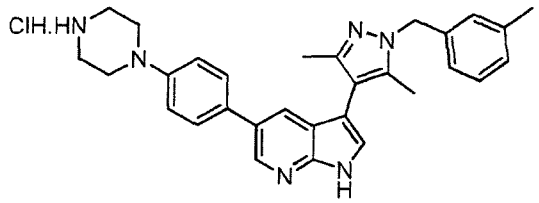
Step-v: N-(3-((3,5-dimethyl-4-(5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridin-3-yl)-1H-pyrazol-1-yl)methyl)phenyl)acetamide

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(3-acetamidobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl) phenyl)piperazine-1-carboxylate (20mg, mmol) was deprotected in methanol/1,4-dioxane HCl in (0.2/2ml) to afford 6mg (38% yield) of the titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ 8.78-8.72 (d, 2H), 7.93 (s, 1H), 7.73-7.69 (m, 3H), 7.39 – 7.36 (m, 2H), 7.21 -7.19 (d, 2H), 7.11-7.10 (d, 1H), 5.61 (s, 2H), 3.54-3.51 (m, 4H), 3.41-3.40 (m, 4H), 2.40-2.38 (d, 6H) 2.05 (s, 3H). MS: m/z = 520.2 (M+1), HPLC – 88.65% (method – A).

Example 51

3-(3,5-dimethyl-1-(3-methylbenzyl)-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl) phenyl)-1H-pyrrolo[2,3-b] pyridine hydrochloride



Step-i: tert-butyl 4-(4-(3-(3,5-dimethyl-1-(3-methylbenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo [2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 4-(4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (intermediate 41) (300mg, 0.4mmol) was coupled with (Intermediate 56A) 3,5-dimethyl-1-(3-methylbenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (163mg, 0.5mmol) in sodium carbonate (147mg, 1.0mmol), $PdCl_2(dppf)$ (17mg, 0.02mmol), toluene/ethanol/water (2/2/3ml) to give 90mg (28% yield) of titled compound.

Step-ii: tert-butyl 4-(4-(3-(3,5-dimethyl-1-(3-methylbenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b] pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(3-(3,5-dimethyl-1-(3-methylbenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (90mg, 0.1mmol) was hydrolyzed by lithium hydroxide (9mg, 0.3mmol), THF/Methanol/water (1/1/0.5 ml) to afford 20mg (29% yield) of the titled compound. MS: m/z = 577.2 (M+1)

Step-iii: 3-(3,5-dimethyl-1-(3-methylbenzyl)-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo [2,3-b]pyridine hydrochloride

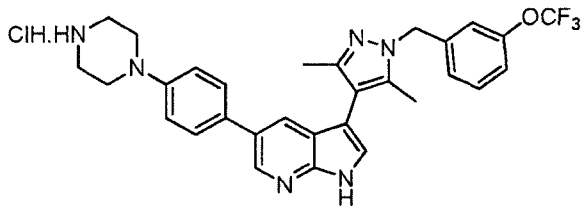
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(3,5-dimethyl-1-(3-methylbenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl) phenyl)piperazine-1-carboxylate (20mg, 0.034 mmol) was deprotected in methanol/1,4-dioxane HCl in (0.3/1ml). This afforded 10mg (63% yield) of the titled compound.

^1H NMR (CD_3OD, 400MHz): δ 8.74 (s, 1H), 8.65 (s, 1H), 7.86 (s, 1H), 7.71 – 7.69 (d, 2H), 7.32 -7.29 (t, 1H), 7.20-7.15 (m, 4H), 7.09-7.07 (d, 1H), 5.51(s, 2H), 3.53-3.50 (m, 4H), 3.41-3.38 (m, 4H), 2.36-2.34 (m, 9H).

MS: m/z = 477.2 (M+1) HPLC – 98.14% (method – B).

Example 52

3-(3,5-dimethyl-1-(3-(trifluoromethoxy)benzyl)-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine hydrochloride



Step-i: tert-butyl 4-(4-(3-(3,5-dimethyl-1-(3-(trifluoromethoxy)benzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 4-(4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (intermediate 41) (150mg, 0.227mmol) was coupled with 3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(3-(trifluoromethoxy)benzyl)-1H-pyrazole (Intermediate 44) (135.6mg, 0.34mmol) in sodium carbonate (72.4mg, 0.68mmol), $PdCl_2(dppf)Cl_2$ (8mg, 0.011mmol), toluene/ethanol/water (3/5/1ml) to give 140mg (76.9% yield) of titled compound. MS: m/z = 801.3(M+1)

Step-ii: tert-butyl 4-(4-(3-(3,5-dimethyl-1-(3-(trifluoromethoxy)benzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(3-(3,5-dimethyl-1-(3-(trifluoromethoxy)benzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (140mg, 0.174mmol) was hydrolyzed by lithium hydroxide (36.7mg, 0.27mmol), THF/Methanol/water (2/3/1 ml) to afford 90mg (80.3% yield) of the titled compound. LCMS: m/z= 647.2 (M+1)

Step-iii: 3-(3,5-dimethyl-1-(3-(trifluoromethoxy)benzyl)-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl) phenyl) -1H-pyrrolo[2,3-b]pyridine hydrochloride

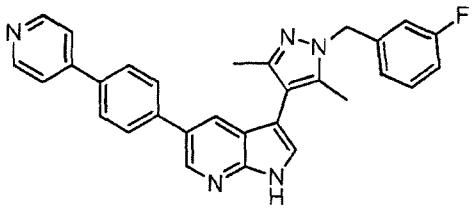
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(3,5-dimethyl-1-(3-(trifluoromethoxy)benzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (90mg, 0.139mmol) was deprotected with HCl in methanol (5ml). This afforded 18mg (23.6% yield) of the titled compound.

^1H NMR ($CDCl_3$, 400MHz): δ 9.12 (s, 1H), 8.56-8.55 (d, 1H), 7.846-7.841 (d, 1H), 7.52-7.50 (d, 2H), 7.40-7.36 (t, 1H), 7.22 (s, 1H), 7.13-7.09 (m, 2H), 7.03-7.00 (m, 3H), 5.33 (s, 2H), 4.40-4.25 (bs, 1H), 3.22-3.19 (m, 4H), 3.08-3.05 (m, 4H), 2.25 (s, 3H), 2.14 (s, 3H).

MS: m/z = 547.2 (M+1), HPLC Purity: 87.04% Method: B

Example 53

3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(pyridin-4-yl) phenyl)-1H-pyrrolo[2,3-b]pyridine



Step-i: 3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(pyridin-4-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b] pyridine (step-i of example-14) (150mg, 0.27mmol) was coupled with 4-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)pyridine (intermediate 45) (91.44mh, 0.32mmol) in sodium carbonate (85.86, 0.81mmol), toluene/ethanol/water (5/5/2ml). This afforded 120mg (70.5% yield) of the titled compound.

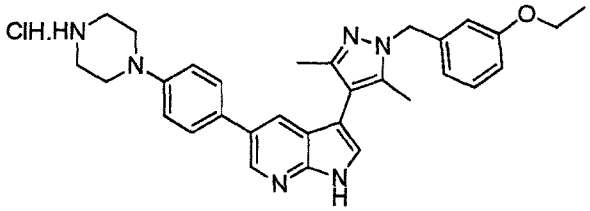
Step-ii: 3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(pyridin-4-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-iii of example-1, 3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(pyridin-4-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (120mg, 0.19mmol) was hydrolyzed by lithium hydroxide (36.7mg, 0.27mmol), in THF/Methanol/water (2/2/1 ml) to afford 22mg 24.3%yield of pure compound after purification by preparative TLC (SiO_2) using 5% methanol in chloroform as eluent.

^{1}H NMR (DMSO-d_6, 300MHz): δ 8.44-8.3 (b, 1H), 7.899-7.877 (d, 1H), 7.767-7.743 (s, 1H), 7.44 (m, 1H), 7.34-7.30 (m, 1H), 7.02-6.99 (m, 1H), 6.87-6.84 (m, 1H), 5.32 (s, 1H), 2.16 (s, 6H). MS: 453.2 m/z = (M+1), HPLC: 93.5% in method A.

Example 54

3-(1-(3-ethoxybenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl) phenyl)-1H-pyrrolo[2,3-b] pyridine hydrochloride



Step-i: tert-butyl 4-(4-(3-(1-(3-ethoxybenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo [2,3-b] pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 4-(4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (intermediate 41) (125mg, 0.189mmol) was coupled with 1-(3-ethoxybenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 46) (81.13mg, 0.227mmol) in sodium carbonate (60.1mg, 0.567mmol), $Pd(PPh_3)_2Cl_2$(6.6mg, 0.0095mmol), toluene/ethanol/water (3/5/1ml) to give 140mg of titled compound.

MS: m/z = 761.0 (M+1)

Step-ii: tert-butyl 4-(4-(3-(1-(3-ethoxybenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b] pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(3-(1-(3-ethoxybenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b] pyridin-5-yl)phenyl)piperazine-1-carboxylate (140mg, 0.183mmol) was hydrolyzed by lithium hydroxide(38.6mg, 0.919mmol), THF/Methanol/water (2/3/1 mL) to afford 100mg (90% yield) of the titled compound.

MS: m/z = 607.3 (M+1)

Step-iii: 3-(1-(3-ethoxybenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine hydrochloride

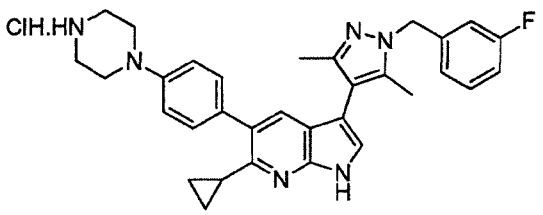
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(3-ethoxybenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (100mg, 0.139mmol) was deprotected with HCl in methanol (5ml) to afford 4mg (4.8% yield) of the titled compound.

^{1}H NMR (CD_3OD , 300MHz): δ 8.39-8.38 (d, 1H), 7.79-7.78 (d, 1H), 7.48-7.45 (m, 2H), 7.32 (s, 1H), 7.22-7.17 (t, 1H), 7.05-7.02 (d, 2H), 6.78-6.76 (dd, 1H), 6.69-6.67 (d, 1H), 6.59 (s, 1H), 5.27 (s, 2H), 3.95-3.93 (q, 2H), 3.95-3.57 (d, 2H), 3.26-3.19 (m, 4H), 3.05-3.02 (m, 2H), 2.16 (s, 3H), 2.12 (s, 3H), 1.30-1.26 (t, 3H).

MS: m/z = 507.3 (M+1), HPLC Purity: 92.87% Method: B

Example 55

6-cyclopropyl-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine hydrochloride



Step-i: tert-butyl 4-(4-(6-cyclopropyl-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 4-(4-(6-cyclopropyl-3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl) piperazine-1-carboxylate (intermediate 47) (115mg, 0.161mmol) was coupled with 1-(3-fluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 16) (81.53mg, 0.24mmol) in sodium carbonate (51.9mg, 0.483mmol), $Pd(PPh_3)_2Cl_2$(5.6mg, 0.008mmol), 1,2-dimethoxyethane/water (10/2ml) to afford 113mg (89% yield) of titled compound.

Step-ii: tert-butyl 4-(4-(6-cyclopropyl-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(6-cyclopropyl-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (111mg, 0.14mmol) was hydrolyzed by lithium hydroxide (17.6mg, 0.42mmol), in methanol/water (3/2 ml) to afford 14mg of the titled compound.

^{1}H NMR (CDCl3, 300MHz):): δ 8.7 (b, 1H), 7.52 (s, 1H), 7.40-7.37 (m, 2H), 7.107-7.099 (d, 1H), 7.002-6.9 (m, 3H), 6.9-6.8 (m, 1H), 5.26 (s, 2H), 3.62-3.59 (t, 3H), 3.209-3.117 (t, 3H), 2.22 (s, 1H), 3.12 (s, 3H), 1.496 (s, 9H), 1.16-1.15 (m, 2H), 0.91-0.87 (m, 2H).

MS: m/z = 621.3 (M+1).

Step-iii: 6-cyclopropyl-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine hydrochloride

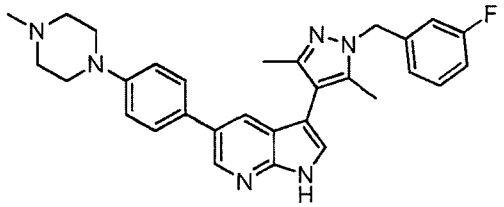
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(6-cyclopropyl-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (14mg, 0.022 mmol) was deprotected in HCl in 1,4-dioxane (2ml) to afford 8mg (64% yield) of the titled compound.

^{1}H NMR (CDCl3, 300MHz):): δ 8.21 (s, 1H), 7.69 (s, 1H), 7.48-7.38 (m, 3H), 7.19-7.7.16 (d, 2H), 7.08-7.05 (d, 1H), 7.001-6.96 (m, 1H), 5.49 (s, 2H), 3.53-3.49 (t, 3H), 3.41-3.38 (t, 3H), 2.5-2.4 (m, 1H), 2.29-2.28 (d, 6H), 1.4-1.25 (m, 2H), 1.21-1.12 (m, 4H).

MS: 521.2 m/z = (M+1), HPLC: 93.079% in Method A.

Example 56

3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(4-methylpiperazin-1-yl)phenyl) -1H –pyrrolo [2,3-b]pyridine



Step-i: 3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(4-methylpiperazin-1-yl) phenyl) -1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-1, 3-iodo-5-(4-(4-methylpiperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (intermediate 48) (200mg, 0.349 mmol) was coupled with 1-(3-fluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 16) (231mg, 0.699mmol) in sodium carbonate(111mg, 1.048mmol), $PdCl_2$(dppf) (12.7mg, 0.017mmol), Toluene/ethanol/water (20/10/2ml) to afford 262mg of the crude titled compound.

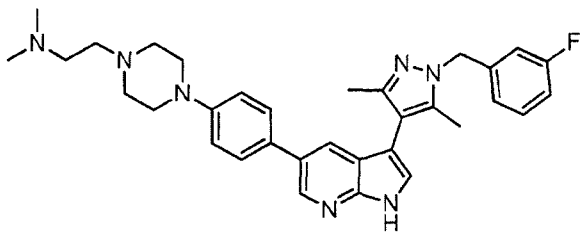
MS: m/z = 649 (M+1)

Step-ii: 3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(4-methylpiperazin-1-yl) phenyl) -1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-iii of example-1, 4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)morpholine (260mg, 0.4mmol) was hydrolyzed by lithium hydroxide (160mg, 4mmol), THF/Methanol/water(12/6/3 ml) to afford 16mg(8.1% yield) of the titled compound. ^{1}H NMR (CD_3OD, 300MHz): δ 8.535 (s, 1H), 8.135-8.130 (d, 1H), 7.623-7.595 (d, 1H), 7.535 (s, 1H), 7.390-7.340 (m, 1H), 7.167-7.138 (d, 3H), 7.028-7.001 (m, 2H), 6.899-6.85 (m, 1H), 5.378 (s, 2H), 3.964-3.919 (m, 2H), 3.649-3.610 (m, 2H), 3.15-3.02 (m, 2H), 2.983 (s, 3H), 2.218-2.196 (d, 6H). MS: m/z = 495.1 (M+1); HPLC: 82.46% in method B.

Example 57

2-(4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl) piperazin-1-yl)-N,N-dimethylethanamine



Step-i: 2-(4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)-N,N-dimethylethanamine

Using similar reaction conditions as described in step-ii of intermediate 1, 2-(4-(4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)-N,N-dimethylethanamine (intermediate 49) (150mg, 0.485mmol) was coupled with 1-(3-fluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 16) (157mg, 0.477mmol) in sodium carbonate (76mg, 0.716mmol), $PdCl_2$(dppf) (8.7mg, 0.011mmol), Toluene/ethanol/water (15/7.5/1.5ml) to afford 192mg yield % of the crude titled compound.
MS: m/z = 706.0 (M+1)

Step-ii: 2-(4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl) phenyl)piperazin-1-yl)-N,N-dimethylethanamine

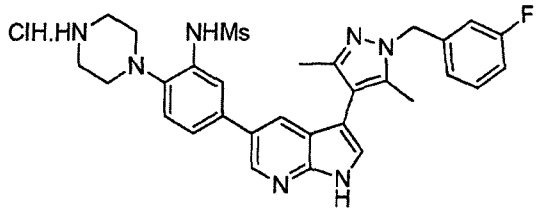
Using similar reaction conditions as described in step-iii of intermediate 1, 2-(4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)-N,N-dimethylethanamine (190mg, 0.269mmol) was hydrolyzed by lithium hydroxide (113mg, 2.69mmol), THF/Methanol/water (12/6/3 ml) to afford 34mg (23% yield) of the titled compound.

^{1}H NMR (CD_3OD, 300MHz): δ 8.432-8.426 (d, 1H), 7.835-7.829 (d, 1H), 7.512-7.475 (m, 2H), 7.367-7.324 (m, 1H), 7.069-6.968 (m, 3H), 6.878-6.845 (m, 1H), 5.349 (s, 2H), 3.68-3.48 (m, 2H), 3.162-3.12 (t, 2H), 2.967 (t, 1H), 2.82-2.715 (m, 8H), 2.206-2.166 (d, 6H), 1.923 (s, 1H).

MS: m/z = 552.2(M+1); HPLC: 94.87% in method B.

Example 58

N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b] pyridin-5-yl)-2-(piperazin-1-yl)phenyl)methanesulfonamide hydrochloride



Step-i: tert-butyl 5-(4-(4-(tert-butoxycarbonyl)piperazin-1-yl)-3-(methylsulfonamido)phenyl)-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 5-(4-(4-(tert-butoxycarbonyl)piperazin-1-yl)-3-(methylsulfonamido)phenyl)-3-iodo-1H-pyrrolo [2,3-b]pyridine-1-carboxylate (intermediate 50) (200mg, 0.286mmol) was coupled with 1-(3-fluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole

(intermediate 16) (123mg, 0.373mmol) in sodium carbonate (90mg, 0.858mmol), $Pd(PPh_3)_2Cl_2$ (10mg, 0.0143mmol), Toluene/ethanol/water (5/5/2.5ml) to afford 6mg (2.7% yield) of titled compound. MS: m/z = 774.2(M+1)

Step-ii: N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(piperazin-1-yl)phenyl)methanesulfonamide hydrochloride

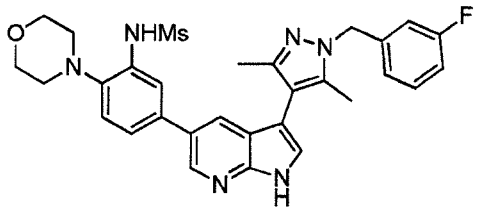
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-1H-pyrazol-1-yl) piperidine-1-carboxylate (187mg, 0.334mmol) was deprotected in methanol/HCl in diethyl ether (0.5/2ml) to afford 3mg (63.42% yield) of the titled compound.

^{1}H NMR (CD3OD), 300MHz): δ8.77-8.71 (d, 2H), 7.92-7.83 (m, 2H), 7.59-7.44 (m, 3H), 7.15-7.06 (m, 2H), 5.59 (s 2H), 3.49-3.45 (m, 4H), 3.23-3.20 (m, 7H), 2.39-2.37 (d, 6H).

MS: m/z = 574.1 (M+1), HPLC: 95.99% Method A.

Example 59

N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b] pyridin-5-yl)-2-morpholino phenyl)methanesulfonamide



Step-i: N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b] pyridin-5-yl)-2-morpholinophenyl)methanesulfonamide

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b] pyridine (compound of step-i of example-14) (250mg, 0.451mmol) was coupled with N-(2-morpholino-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methane sulfonamide (intermediate 51) (259mg, 0.677mmol) in sodium carbonate (143.4mg, 1.353mmol), Toluene/ethanol/water(3/8/1ml). This afforded 150mg (45.59% yield) of the titled compound.

MS: m/z = 728.9(M+1)

Step-ii: N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-morpholinophenyl)methanesulfonamide

Using similar reaction conditions as described in step-iii of example-1, N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-morpholinophenyl)methanesulfonamide (150mg, 0.205mmol) was hydrolyzed with lithium

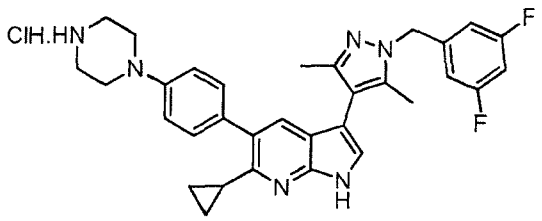
hydroxide (43.2mg, 1.02mmol) in THF/Methanol/water (2/3/1 ml). This yielded 23mg (19.49% yield) of pure compound.

^{1}H NMR ($CDCl_3$, 300MHz): δ 9.17 (s, 1H), 8.55 (s, 1H), 7.86 (s, 2H), 7.75 (s, 1H), 7.32 (s, 3H), 6.99-6.97 (m, 2H), 6.90-6.80 (d, 1H), 5.31 (s, 2H), 3.91-3.88 (m, 4H), 3.10 (s, 3H), 2.92-2.89 (m, 4H), 2.26 (s, 3H), 2.17 (s, 3H).

MS: m/z = 575.1 (M+1), HPLC Purity: 98.92% Method: B.

Example 60

6-cyclopropyl-3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo [2,3-b]pyridine hydrochloride



Step-i: tert-butyl 5-(4-(4-(tert-butoxycarbonyl)piperazin-1-yl)phenyl)-6-cyclopropyl-3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 5-(4-(4-(tert-butoxycarbonyl)piperazin-1-yl)phenyl)-6-cyclopropyl-3-iodo-1H-pyrrolo [2,3-b]pyridine-1-carboxylate (intermediate 57) (120mg, 0.186mmol) was coupled with 1-(3,5-difluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 24) (97.24mg, 0.27mmol) in sodium carbonate (59.1mg, 0.483mmol), $Pd(PPh_3)_2Cl_2$ (6.5mg, 0.009mmol), 1,2-dimethoxyethane/water (15/2ml) to afford 62mg (45% yield) of titled compound. MS: m/z = 739.2 (M+1).

Step-ii: 6-cyclopropyl-3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine hydrochloride

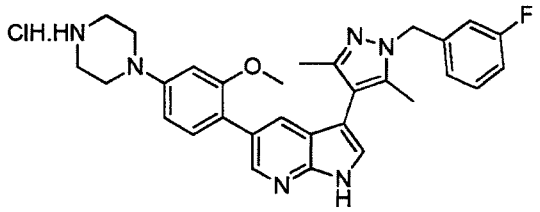
Using similar reaction conditions as described in Step-ii of example-7, tert-butyl 5-(4-(4-(tert-butoxycarbonyl)piperazin-1-yl)phenyl)-6-cyclopropyl-3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (62mg, 0.022 mmol) was deprotected in HCl in methanol (2ml).This afforded 4 mg(5% yield) of the titled compound.

^{1}H NMR (CDCl3, 300MHz): δ 8.44 (b, 1H), 7.68 (s, 1H), 7.42-7.39 (d, 2H), 7.02-7.00 (d, 2H), 6.661-6.641 (m, 1H), 6.311-6.305 (d, 1H), 5.26 (s, 2H), 3.25-3.21 (m, 3H), 3.10-3.07 (t, 3H), 2.41 (s, 3H), 2.32 (s, 3H), 1.13-1.10 (m, 2H), 0.88-0.85 (m, 4H).

MS: m/z = 539.2 (M+1).

Example 61

3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(2-methoxy-4-(piperazin -1-yl)phenyl)-1H-pyrrolo [2,3-b]pyridine hydrochloride



Step-i: tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo [2,3-b]pyridin-5-yl)-3-methoxyphenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 4-(4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxyphenyl)piperazine-1-carboxylate (intermediate 52) (30mg, 0.043mmol) was coupled with 1-(3-fluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 16) (17mg, 0.052mmol) in sodium carbonate (14mg, 0.13mmol), $Pd(PPh_3)_2Cl_2$(1.5mg, 0.00218mmol), Toluene/ethanol/water (2/1/0.5ml) to afford 156.0mg (crude) of titled compound.

MS: m/z = 766.3 (M+1).

Step-ii: tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b] pyridin-5-yl)-3-methoxyphenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxyphenyl) piperazine-1-carboxylate (150mg, 0.196mmol) was hydrolyzed by lithium hydroxide (25mg, 0.588mmol), THF/Methanol/water(2/2/1 ml) to yield 16mg of the titled compound after purification by preparative TLC(SiO_2) using 50% ethyl acetate in hexane as eluent. MS: m/z = 611.3 (M+1).

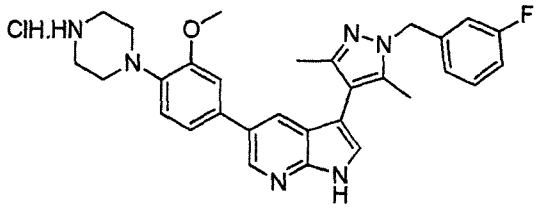
Step-iii: 3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(2-methoxy-4-(piperazin-1-yl) phenyl)-1H-pyrrolo[2,3-b]pyridine hydrochloride

Using similar reaction conditions as described in step-iii of example-7, tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxyphenyl)piperazine-1-carboxylate (16mg, 0.026 mmol) was deprotected in HCl in ether/ methanol (2/0.5ml).This afforded 13.0mg (97.23% yield) of the titled compound.

^{1}H NMR (CD3OD, 300MHz): δ 8.60 (s, 2H), 7.85 (s, 1H), 7.41-7.38 (m, 2H), 7.12 (m, 3H), 6.79-6.78 (m, 2H), 5.55 (s, 2H), 3.85 (s, 3H), 3.56-3.53 (m, 4H), 3.41-3.38 (m, 4H), 2.35 (s, 6H). MS: m/z = 511.3 (M+1), HPLC: 99.2% in method B.

Example 62

3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(3-methoxy-4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine hydrochloride



Step-i: tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 4-(4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)piperazine-1-carboxylate (intermediate 58) (200mg, 0.3mmol) was coupled with 1-(3-fluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 16) (130mg, 0.13mmol) in sodium carbonate (95mg, 0.9mmol), Pd(PPh3)2Cl2(15mg, 0.015mmol), Toluene/ethanol/water (10/2/2.5ml) to give 150mg (64.65% yield) of titled compound. MS: m/z = 765.3 (M+1).

Step-ii: tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)piperazine-1-carboxylate (140mg, 0.18mmol) was hydrolyzed by lithium hydroxide(23mg, 0.554mmol), THF/Methanol/water(5/5/2 ml) to afford 70mg of the titled compound. MS: m/z = 610.9 (M+1)

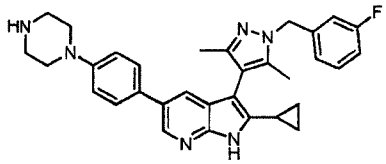
Step-iii: 3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(3-methoxy-4-(piperazin-1-yl) phenyl)-1H-pyrrolo[2,3-b]pyridine hydrochloride

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)piperazine-1-carboxylate (70mg, 0.114 mmol) was deprotected in HCl in 1,4-dioxane / 1,4-dioxane (5/5m).This afforded 3mg (4.54% yield) of the titled compound.

^{1}H NMR (DMSO-d_6, 400MHz): δ 11.82 (s, 1H), 8.55 (s, 1H), 7.84 (s, 1H), 7.50-7.43 (m, 2H), 7.19-6.94 (m, 6H), 5.35 (s, 1H), 3.88 (s, 3H), 2.93-2.86 (d, 8H), 2.19-2.16 (d, 6H)
MS: m/z = 511 (M+1), HPLC: 94.29% in Method-B.

Example 63

2-cyclopropyl-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl) -1H-pyrrolo[2,3-b]pyridine



Step-i: tert-butyl 5-(4-(4-(tert-butoxycarbonyl)piperazin-1-yl)phenyl)-2-cyclopropyl-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate

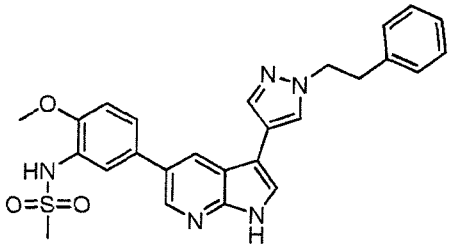
Using similar reaction conditions as described in step-ii of example-1, tert-butyl 5-(4-(4-(tert-butoxycarbonyl)piperazin-1-yl)phenyl)-2-cyclopropyl-3-iodo-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (Intermediate 35) (50 mg, 0.07763 mmol) was coupled with 1-(3-fluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 16) (30 mg, 0.08540 mmol) in sodium carbonate (25 mg, 0.2329 mmol), $Pd(PPh_3)_4$ (5 mg, 0.00388 mmol) and DME/water (5/1 ml) to afford 100 mg of the crude product which was taken as such for next reaction.
MS: m/z = 721.0 (M+1).

Step-ii: 2-cyclopropyl-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine

tert-butyl 5-(4-(4-(tert-butoxycarbonyl)piperazin-1-yl)phenyl)-2-cyclopropyl-3-(1-(3-fluoro benzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b] pyridine-1-carboxylate (100 mg) dissolved in 2 ml of methanol and added methanol/HCl (3 ml) at 0 °C and stirred at room temperature for 30 min. The reaction was monitored by TLC (10% methanol in chloroform). The reaction mixture was concentrated under reduced pressure to afford crude product. The residue was basified with saturated sodium bicarbonate solution and extracted with DCM (2x25 ml). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to afford 7 mg (9.72% yield) of the pure required product.
^{1}H NMR (DMSO-d_6 , 400MHz): δ 11.30 (s, 1H), 8.34 (s, 1H), 7.64-7.39 (m, 5H), 7.15-7.11 (t, 1H), 7.01-6.95 (m, 4H), 5.34 (s, 2H), 4.20-4.00 (m, 4H), 3.10-3.00 (m, 4H), 2.09 (s, 3H), 2.08 (s, 3H), 1.82-1.79 (m, 1H), 0.96-0.95 (m, 4H).
MS: m/z = 521.4 (M+1), HPLC Purity: 80.32% Method: A

Example 64

N-(2-methoxy-5-(3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide



Step-i: N-(2-methoxy-5-(3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide

Using similar reaction conditions as described in step-ii of example-1, N-(5-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide (Intermediate 23) (90mg, 0.1506mmol) was coupled with 1-phenethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 59) (67mg, 0.225mmol) using $Pd(PPh_3)_2Cl_2$(6mg, 0.05mmol) and sodium carbonate (40mg, 0.376mmol) in toluene/ethanol/water(3/2/1 ml) to afford 100mg of the crude compound. MS: m/z = 642.7 (M+1).

Step-ii: N-(2-methoxy-5-(3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide

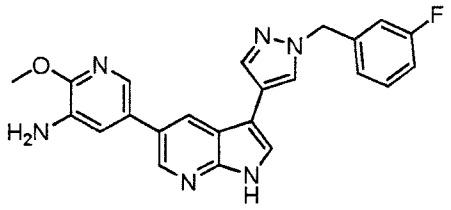
Using similar reaction conditions as described in step-iii of example-1, N-(2-methoxy-5-(3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide (100mg, 0.155mmol) was hydrolyzed by lithium hydroxide (13mg, 0.311mmol) in THF/methanol/water (5/1/2 mL) to afford 13mg of the titled compound.

^{1}H NMR (DMSO-d_6, 400MHz): δ 9.07 (s, 1H), 8.45-8.44 (d, 1H), 8.186-8.182 (d, 1H), 8.13 (,s 1H), 7.89 (s, 1H), 7.716-7.710 (d, 1H), 7.60-7.59 (m, 2H), 7.31-7.28 (m, 2H), 7.24-7.19 (m, 4H), 4.43-4.39 (t, 2H), 3.91 (s, 3H), 3.20-3.16 (t, 2H), 3.02 (s, 3H).

MS: m/z = 487.8 (M+1), HPLC: 95.48% in method A.

Example 65

5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxypyridin-3-amine



Step-i: 5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxypyridin-3-amine

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (compound of Step-iof example 9) (150mg, 0.280mmol) was coupled with 2-methoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-amine (Intermediate 60) (86mg, 0.34mmol) using sodium carbonate (89mg, 0.84mmol) and $Pd(PPh_3)_2Cl_2$ (10mg, 0.014mmol) in DME/water (10/1 mL) to afford 80mg (49.2% yield) after purification by column (Silica gel 6/120) using 4/1/5 EtOAc/methanol/hexane as eluent.

Step-ii: 5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxypyridin-3-amine

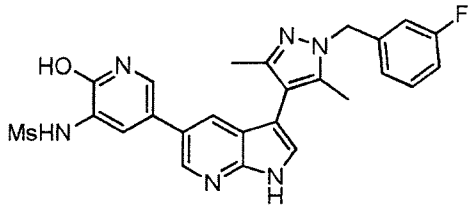
Using similar reaction conditions as described in step-iii of example-1, 5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxypyridin-3-amine (80mg, 0.14mmol) was hydrolyzed with lithium hydroxide (12mg, 0.28mmol) in THF/methanol/water (2/2/1mL) to yield 10 mg (17.1% yield) after purification by preparative TLC(Silicagel-1000micron) using 5% methanol in chloroform as eluent.

^{1}H NMR (CD_3OD, 300MHz): δ 8.37 (s, 1H), 8.27 (s, 1H), 8.17 (s, 1H), 7.91 (s, 1H), 7.717-7.712 (d, 1H), 7.61 (s, 1H), 7.36-7.29 (m, 2H), 7.10-6.98 (m, 3H), 5.41 (s, 2H), 4.00 (s, 3H).

MS: m/z = 415.2(M+1), HPLC: 88.73% in method B.

Example 66

N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-hydroxypyridin-3-yl)methanesulfonamide



Step-i: tert-butyl 3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(6-methoxy-5-(methylsulfonamido)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 5-(5-(N-(tert-butoxycarbonyl)methylsulfonamido)-6-methoxypyridin-3-yl)-3-iodo-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (intermediate 66) (100mg, 0.155mmol) was coupled with 1-(3-fluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 16) (61mg, 0.186mmol) using $Pd(PPh_3)_2Cl_2$ (5mg, 0.0077mol) and sodium carbonate (49mg, 0.465mmol) in DME/water(10/1 ml) to afford 61mg (54.5% yield) of the titled compound. MS: m/z = 621.2 (M+1).

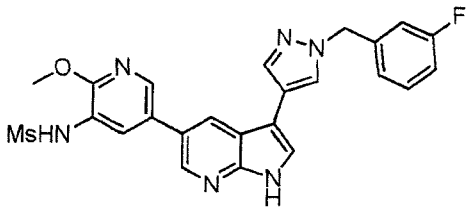
Step-ii: N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-hydroxypyridin-3-yl)methanesulfonamide

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(6-methoxy-5-(methylsulfonamido)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (61mg, 0.098 mmol) was deprotected in HCl in MeOH (3ml) to afford 5mg (11.3% yield) of the titled compound.

^{1}H NMR (CD_3OD, 300MHz): δ 8.71-8.62 (d, 2H), 7.91-7.88 (d, 2H), 7.68 (s, 1H), 7.47-7.42 (m, 1H), 7.15-7.02 (m, 3H), 6.60 (s, 1H), 5.57 (s, 2H), 3.09 (s, 3H), 2.36 (s, 3H), 2.35 (s, 3H). MS: m/z = 506.8(M+1), HPLC: 90.22% in method B.

Example 67

N-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxypyridin-3-yl)methanesulfonamide



Step-i: N-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxypyridin-3-yl)methanesulfonamide

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (compound of step-iof example 9) (100mg, 0.19mmol) was coupled with N-(2-methoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-3-yl)methanesulfonamide (Intermediate 65D) (69mg, 0.20mmol) using sodium carbonate (61mg, 0.57mmol) and $Pd(PPh_3)_2Cl_2$ (7mg, 0.009mmol) in DME/water (5/0.5 mL). This afforded 72mg (58.5% yield) of the titled compound.

Step-ii: N-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxypyridin-3-yl)methanesulfonamide.

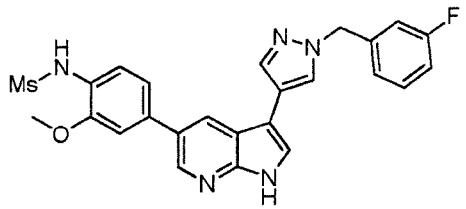
Using similar reaction conditions as described in step-iii of example-1, N-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxypyridin-3-yl)methanesulfonamide (70mg, 0.108mmol) was hydrolyzed with lithium hydroxide (14mg, 0.324mmol) in THF/methanol/water (3.5/3.5/0.5mL) to yield 17 mg (31.8% yield) after purification by preparative TLC (Silicagel-1000micron) using 5%methanol in chloroform as eluent.

^{1}H NMR (CD_3OD, 300MHz): δ 8.42 (s, 1H), 8.34-8.33 (s, 1H), 8.288-8.280 (d, 1H), 8.22 (s, 1H), 8.04-8.03 (d, 1H), 7.934-7.931 (d, 1H), 8.04-8.03 (d, 1H), 7.934-7.931 (d, 1H), 7.65 (s, 1H), 7.38-7.35 (q, 1H), 7.12-7.09 (d, 1H), 7.03-6.99 (m, 2H), 5.42 (s, 2H), 4.06 (s, 3H), 3.03 (s, 3H).

MS: m/z = 492.8(M+1), HPLC: 96.33% in method B.

Example 68

N-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide



Step-i: N-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl) methanesulfonamide

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (compound of step-i of example 9) (100mg, 0.19mmol) was coupled with N-(2-methoxy-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methanesulfonamide (Intermediate 65C) (62mg, 0.19mmol) using potassium carbonate (60mg, 0.57mmol) and $Pd(PPh_3)_4$ (11mg, 0.0095mmol) in toluene/ethanol/water (2/2/1 mL). This afforded 63mg (51.4% yield) after purification by preparative TLC (silicagel-1000micron) using 40% ethyl acetate in hexane as eluent. MS: m/z = 646.2 (M+1).

Step-ii: N-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide.

Using similar reaction conditions as described in step-iii of example-1, N-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl) methanesulfonamide (60mg, 0.093mmol) was hydrolyzed with lithium hydroxide(12mg,

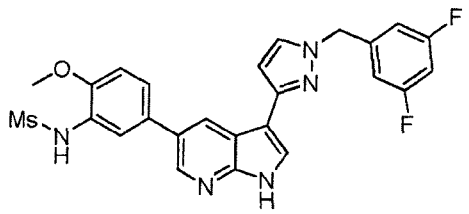
0.279mmol) in THF/methanol/water (2/2/1mL) to yield 20 mg (43.8% yield) of title compound.

^{1}H NMR (DMSO-d_6, 300MHz): δ 11.8 (s, 1H), 8.99 (s, 1H), 8.578-8.571 (d, 1H), 8.43 (s, 1H), 8.386-8.380 (d, 2H), 7.99 (s, 1H), 7.78-7.77 (d, 1H), 7.41-7.34 (m, 4H), 7.15-7.08 (m, 3H), 5.40 (s, 2H), 3.95 (s, 3H), 2.97 (s, 3H).

MS: m/z = 492.2 (M+1), HPLC: 91.15% in method B.

Example 69

N-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide



Step-i: N-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (Intermediate 63) (100mg, 0.184mmol) was coupled with N-(2-methoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methanesulfonamide (Intermediate 17) (65mg, 0.22mmol) using sodium carbonate (58mg, 0.552mmol) and $Pd(PPh_3)_4$ (10mg, 0.0092mmol) in toluene/ethanol/water (2/2/1 ml) to afford 46mg (37.7% yield) after purification by preparative TLC (silicagel-1000micron) using 40%ethyl acetate in hexane as eluent. MS: m/z = 664.1 (M+1)

Step-ii: N-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide

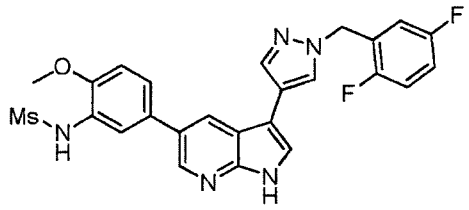
Using similar reaction conditions as described in step-iii of example-1, N-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide (53mg, 0.0799mmol) was hydrolyzed by lithium hydroxide (17mg, 0.399mmol) in THF/methanol/water (2/2/1 ml) to yield 20mg of the titled compound.

^{1}H NMR (DMSO-d_6, 300MHz): δ 11.8 (s, 1H), 9.00 (s, 1H), 8.538-8.530 (d, 1H), 8.45-8.44 (d, 1H), 7.89-7.88 (d, 2H), 7.55-7.54 (d, 1H), 7.50-7.46 (dd,1 H), 7.19-7.15 (m, 2H), 7.00-6.98 (m, 2H), 6.699-6.692 (d, 1H), 5.40 (s, 2H), 3.86 (s, 3H), 2.97 (s, 3H).

MS: m/z = 510.1(M+1), HPLC: 96.47% in method B.

Example 70

N-(5-(3-(1-(2,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide



Step-i: N-(5-(3-(1-(2,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(2,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (step-i of example-4) (200mg, 0.368mmol) was coupled with N-(2-methoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methanesulfonamide (Intermediate 17) (120mg, 0.368mmol) using sodium carbonate (117mg, 1.1049mmol) and $Pd(PPh_3)_2Cl_2$ (14mg, 0.018mmol) in DME/water (15/2 ml) to afford 121mg (49.5% yield) after purification by column chromatography (Silica gel 230/400) using 50% ethyl acetate in hexane as eluent. MS: m/z = 664.2 (M+1)

Step-ii: N-(5-(3-(1-(2,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide

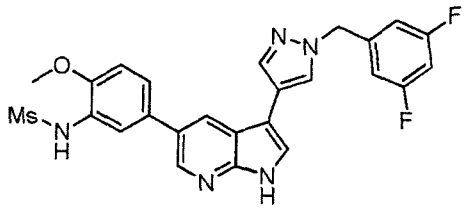
Using similar reaction conditions as described in step-iii of example-1, N-(5-(3-(1-(2,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide (120mg, 0.180mmol) was hydrolyzed by lithium hydroxide 38mg, 0.904mmol) in THF/methanol/water (15/7.5/4 ml) to yield 21mg of the titled compound.

^{1}H NMR ($CDCl_3$, 400MHz): δ 10.3 (s, 1H), 8.49-8.48 (d, 1H), 8.256-8.252 (d, 1H), 7.85 (s, 1H), 7.81-7.80 (d, 1H), 7.77 (s, 1H), 7.48-7.47 (d, 1H), 7.39-7.37 (dd, 1H), 7.26-6.91 (m, 5H), 5.42 (s, 2H), 3.96 (s, 3H), 3.01 (s, 3H).

MS: m/z = 510.1 (M+1), HPLC: 96.37% in method B.

Example 71

N-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide



Step-i: 5-bromo-1-tosyl-3-(1-(3-(trifluoromethyl)benzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b] pyridine

Using similar reaction conditions as described in step-i of example-1, 5-bromo-3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridine (Intermediate 1) (1 g, 2.09 mmol) was coupled with 1-(3,5-difluorobenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (Intermediate 8) (805 mg, 2.51 mmol) using sodium carbonate (645 mg, 6.27 mmol) and $Pd(PPh_3)_2Cl_2$ (77 mg, 0.1047 mmol) in toluene/ethanol/water (10/10/2 ml) to afford 680 mg (60.1% yield) of the pure product after column purification using 30% ethyl acetate in hexane as eluent.

Step-ii: N-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (200mg, 0.3683mmol) was coupled with N-(2-methoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methanesulfonamide (Intermediate 17), (120mg, 0.368mmol) using sodium carbonate (117mg, 1.1049mmol) and $Pd(PPh_3)_2Cl_2$ (14mg, 0.0184mmol) in DME/water (15/2 ml). This afforded 107mg (43.8% yield) after purification by column (Silica gel 230/400) using 65% ethyl acetate in hexane as eluent. MS: m/z = 664.1 (M+1).

Step-iii: N-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide

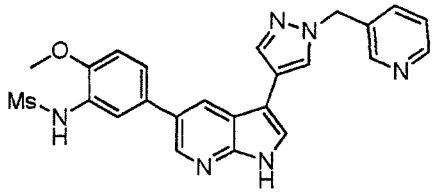
Using similar reaction conditions as described in step-iii of example-1, N-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide (105mg, 0.1582mmol) was hydrolyzed by lithium hydroxide (34mg, 0.791mmol) in THF/methanol/water (15/7.5/4 ml) to yield 13mg of the titled compound.

^{1}H NMR (CD_3OD, 300MHz): δ 8.556-8.551 (d, 2H), 8.51-8.50 (d, 1H), 8.28 (s, 1H), 7.98 (s, 1H), 7.76-7.75 (m, 2H), 7.64-7.76 (dd, 1H), 7.22-7.20 (d, 1H), 6.94-6.84 (m, 2H), 5.44 (s, 2H), 3.99 (s, 3H), 2.99 (s, 3H).

MS: m/z = 510.1 (M+1), HPLC: 98.06% in method B

Example 72

N-(2-methoxy-5-(3-(1-(pyridin-3-ylmethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide



Step-i: tert-butyl 5-(3-(N-(tert-butoxycarbonyl)methylsulfonamido)-4-methoxyphenyl)-3-(1-(pyridin-3-ylmethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 5-(5-(N-(tert-butoxycarbonyl)methylsulfonamido)-6-methoxypyridin-3-yl)-3-iodo-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (intermediate 66P) (150mg, 0.233mmol) was coupled with 3-((4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-yl)methyl)pyridine (intermediate 64) (73mg, 0.256mmol) using $Pd(PPh_3)_2Cl_2$ (9mg, 0.0116mol) and sodium carbonate (74mg, 0.699mmol) in toluene/ethanol/water (3/3/2 ml) to afford 60mg (38% yield) of the titled compound after purification by column (Silica gel 60/120) using 30%ethyl acetate in hexane as eluent. MS: m/z = 675.1 (M+1).

Step-ii: N-(2-methoxy-5-(3-(1-(pyridin-3-ylmethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide

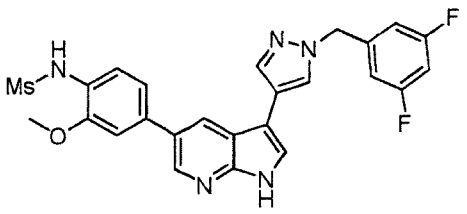
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 5-(3-(N-(tert-butoxycarbonyl)methylsulfonamido)-4-methoxyphenyl)-3-(1-(pyridin-3-ylmethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (60mg, 0.219 mmol) was deprotected in HCl in ether/MeOH (1/3ml) to afford 13mg (29% yield) of the titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ 8.78 (s, 2H), 8.53 (s, 2H), 8.42-8.37 (m, 2H), 8.02 (s, 1H), 8.00-7.94 (m, 1H), 7.77-7.76 (m, 2H), 7.62-7.59 (dd, 1H), 7.24-7.21 (d, 1H), 5.66 (s, 2H), 3.98 (s, 3H), 2.99 (s, 3H).

MS: m/z = 475.1 (M+1), HPLC: 97.36% in method A.

Example 73

N-(4-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide



Step-i: N-(4-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (step 1 example 71) (150mg, 0.38mmol) was coupled with N-(2-methoxy-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methanesulfonamide (Intermediate 65C) (149mg, 0.45mmol) using sodium carbonate (121mg, 1.14mmol) and $Pd(PPh_3)_2Cl_2$ (2mg, 0.001mmol) in DME/water (10/1 ml) to afford 98mg (26.2% yield) after purification by column (Silica gel 60/120) using 65%ethyl acetate in hexane as eluent.

Step-ii: N-(4-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide

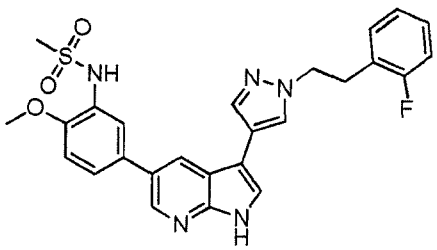
Using similar reaction conditions as described in step-iii of example-1, N-(4-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide (95mg, 0.14mmol) was hydrolyzed by lithium hydroxide (18mg, 0.42mmol) in THF/methanol/water (2/2/1 ml) to yield 38mg (52.1% yield) of the titled compound after purification by preparative TLC (Silicagel-1000micron) using 5%methanol in chloroform as eluent.

^{1}H NMR (DMSO-d_6, 300MHz): δ 11.8 (s, 1H), 8.95 (s, 1H), 8.559-8.552 (d, 1H), 8.42 (s, 1H), 8.367-8.361 (d, 1H), 7.99 (s, 1H), 7.77-7.76 (d, 1H), 7.38 (s, 1H), 7.35-7.32 (m, 2H), 7.20-7.10 (m, 1H), 6.97-6.95 (d, 2H), 5.39 (s, 2H), 3.94 (s, 3H), 2.96 (s, 3H).

MS: m/z = 510.1 (M+1), HPLC: 87.42% in method B

Example 74

N-(5-(3-(1-(2-fluorophenethyl)-1H-pyrazol-4-yl)-1H-pyrrolo [2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide



Step-i: tert-butyl 5-(3-(N-(tert-butoxycarbonyl) methylsulfonamido)-4-methoxyphenyl)-3-(1-(pyridin-3-ylmethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 5-(5-(N-(tert-butoxycarbonyl)methylsulfonamido)-6-methoxypyridin-3-yl)-3-iodo-1H-pyrrolo[2,3-

b]pyridine-1-carboxylate (intermediate 66P) (150mg, 0.233mmol) was coupled with 1-(2-fluorophenethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 64A) (81mg, 0.256mmol) using $Pd(PPh_3)_2Cl_2$ (9mg, 0.0116mol) and sodium carbonate (74mg, 0.699mmol) in toluene/ethanol/water (3/3/2 ml) to afford 40mg (24% yield) of the titled compound after purification by column (Silica gel 60/120) using 30%ethyl acetate in hexane as eluent.

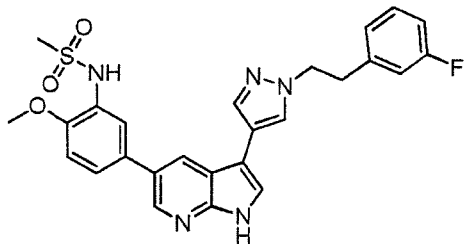
Step-ii: N-(5-(3-(1-(2-fluorophenethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 5-(3-(N-(tert-butoxycarbonyl)methylsulfonamido)-4-methoxyphenyl)-3-(1-(pyridin-3-ylmethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (40mg, mmol) was deprotected in HCl in ether/MeOH (1/3ml). This afforded 5mg (17% yield) of the titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ 8.49 (s, 1H), 8.30 (s, 1H), 7.87-7.86 (d, 2H), 7.747-7.742 (d, 1H), 7.65 (s, 1H), 7.59-7.57 (dd, 1H), 7.26-7.02 (m, 5H), 4.51-4.48 (t, 2H), 4.00 (s, 3H), 3.32-3.25 (t, 2H), 3.00 (s, 3H). MS: m/z = 506.2 (M+1), HPLC: 97.44% in method B.

Example 75

N-(5-(3-(1-(3-fluorophenethyl)-1H-pyrazol-4-yl)-1H-pyrrolo [2, 3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide



Step-i: 5-bromo-3-(1-(3-fluorophenethyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-i of example-1, 5-bromo-3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridine (Intermediate 1) (200mg, 0.41 mmol) was coupled with 1-(3-fluorophenethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (Intermediate 64B) (172 mg, 0.54 mmol) using sodium carbonate (130 mg, 1.23 mmol) and $Pd(PPh_3)_2Cl_2$ (14 mg, 0.020 mmol) in toluene/ethanol/water (20/10/5 ml) to afford 80 mg (35.39% yield) of the pure product after column purification using 30% ethyl acetate in hexane as eluent. MS: m/z = 539.1(M+1)

Step-ii: N-(5-(3-(1-(3-fluorophenethyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3-fluorophenethyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (80mg, 0.148mmol) was coupled with N-(2-methoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methanesulfonamide (Intermediate 17) (58mg, 0.178mmol) using sodium carbonate (47mg, 0.444mmol) and $Pd(PPh_3)_2Cl_2$ (5mg, 0.0074mmol) in DME/water (10/1 ml). This afforded 27mg (43.8% yield) after purification by column (Silica gel 60/120) using 30%ethyl acetate in hexane as eluent.

Step-iii: N-(5-(3-(1-(3-fluorophenethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide

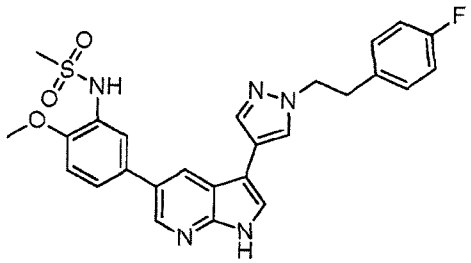
Using similar reaction conditions as described in step-iii of example-1, N-(5-(3-(1-(3-fluorophenethyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide (27mg, 0.0409mmol) was hydrolyzed by lithium hydroxide (34mg, 0.818mmol) in THF/methanol/water (2/2/1 ml) to yield 8mg (40.0% yield) of the titled compound.

^{1}H NMR (DMSO-d_6, 300MHz): δ 11.7 (s, 1H), 9.04 (s, 1H), 8.43-8.42 (d, 1H), 8.176-8.170 (d, 1H), 8.13 (s, 1H), 7.87 (s, 1H), 7.69-7.68 (d, 1H), 7.58-7.57 (m, 2H), 7.32-7.19 (m, 2H), 7.06-7.01 (m, 2H), 4.33-4.38 (t, 2H), 3.89 (s, 3H), 3.21-3.16 (t, 2H), 3.00 (s, 3H).

MS: m/z = 506.1 (M+1), HPLC: 91.31% in method B.

Example 76

N-(5-(3-(1-(4-fluorophenethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide



Step-i: 5-bromo-3-(1-(4-fluorophenethyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-i of example-1, 5-bromo-3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridine (Intermediate 1) (200mg, 0.41 mmol) was coupled with 1-(4-fluorophenethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (Intermediate

64C) (172 mg, 0.54 mmol) using sodium carbonate (130 mg, 1.23 mmol) and $Pd(PPh_3)_2Cl_2$ (14 mg, 0.020 mmol) in toluene/ethanol/water (20/10/5 ml) to afford 70 mg (30.97% yield) of the pure product after column purification using 30% ethyl acetate in hexane as eluent. MS: m/z = 540.9 (M+1).

Step-ii: N-(5-(3-(1-(4-fluorophenethyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(4-fluorophenethyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (70mg, 0.129mmol) was coupled with N-(2-methoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methanesulfonamide (Intermediate 17) (50mg, 0.155mmol) using sodium carbonate (41mg, 0.387mmol) and $Pd(PPh_3)_2Cl_2$ (4mg, 0.0064mmol) in DME/water (10/1 ml). This afforded 25mg (29.41% yield) after purification by column (Silica gel 60/120) using 30% ethyl acetate in hexane as eluent. MS: m/z = 660.1(M+1).

Step-iii: N-(5-(3-(1-(4-fluorophenethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide

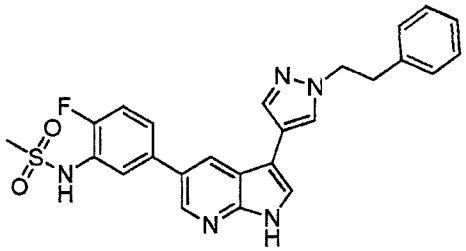
Using similar reaction conditions as described in step-iii of example-1, N-(5-(3-(1-(4-fluorophenethyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide (25mg, 0.0379mmol) was hydrolyzed by lithium hydroxide (15mg, 0.379mmol) in THF/methanol/water (2/2/1 ml) to yield 8mg (40.0% yield) of the titled compound.

^{1}H NMR (DMSO-d_6, 300MHz): δ 11.7 (s, 1H), 9.034-9.035 (d, 1H), 8.43-8.42 (d, 1H), 8.20 (s, 1H), 8.14 (s, 1H), 7.87 (s, 1H), 7.69-7.68 (d, 2H), 7.58-7.56 (m, 2H), 7.26-7.18 (m, 3H), 7.11-7.05 (m, 2H), 4.39-4.35 (t, 2H), 3.89 (s, 3H), 3.18-3.13 (t, 2H), 3.00 (s, 3H).

MS: m/z = 506.5 (M+1), HPLC: 96.65% in method B.

Example 77

N-(2-fluoro-5-(3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide



Step-i: 5-bromo-3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-i of example-1, 5-bromo-3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridine (Intermediate 1) (400mg, 0.838 mmol) was coupled with 1-phenethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (Intermediate 59) (250 mg, 0.838 mmol) using sodium carbonate (266 mg, 2.515 mmol) and $Pd(PPh_3)_2Cl_2$ (30 mg, 0.041 mmol) in toluene/ethanol/water (20/10/5 ml) to afford 191 mg (44% yield) of the pure product after column purification using 20% ethyl acetate in hexane as eluent. MS: m/z = 521.1 (M+1)

Step-ii: N-(2-fluoro-5-(3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (190mg, 0.364mmol) was coupled with N-(2-fluoro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methanesulfonamide (Intermediate 65) (115mg, 0.364 mmol) using sodium carbonate (115mg, 1.093mmol) and $Pd(PPh_3)_2Cl_2$ (14mg, 0.0182mmol) in DME/water (15/2 ml). This afforded 147mg (64.1% yield) after purification by column (Silica gel 60/120) using 25% ethyl acetate in chloroform as eluent. MS: m/z = 630.3 (M+1).

Step-iii: N-(2-fluoro-5-(3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide

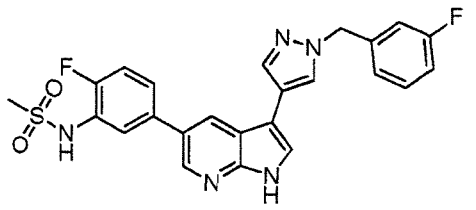
Using similar reaction conditions as described in step-iii of example-1, N-(2-fluoro-5-(3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide (145mg, 0.230mmol) was hydrolyzed by lithium hydroxide (48mg, 1.15mmol) in THF/methanol/water (15/5/5 ml) to yield 41mg (37.6% yield) of the titled compound after purification by preparative TLC(Silicagel-1000micron) using 50% ethyl acetate in hexane as eluent.

^1H NMR (CD_3OD, 300MHz): δ 8.44-8.40 (d, 1H), 8.108-8.101 (d, 1H), 7.83-7.74 (m, 2H), 7.58-7.50 (m, 2H), 7.40-7.10 (m, 5H), 4.46-4.42 (t, 2H), 3.20-3.16 (t, 2H), 3.06 (s, 3H).

MS: m/z = 476.5 (M+1), HPLC: 93.52% in method A.

Example 78

N-(2-fluoro-5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide



Step-i: N-(2-fluoro-5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (compound of Step-i of example 9) (166mg, 0.317mmol) was coupled with N-(2-fluoro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methanesulfonamide (Intermediate 65) (100mg, 0.317 mmol) using sodium carbonate(101mg, 0.952mmol) and $Pd(PPh_3)_2Cl_2$(12mg, 0.015mmol) in DME/water (15/2 mL). This afforded 190mg (94.5% yield) of the titled compound. MS: m/z = 634.0 (M+1).

Step-ii: N-(2-fluoro-5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide

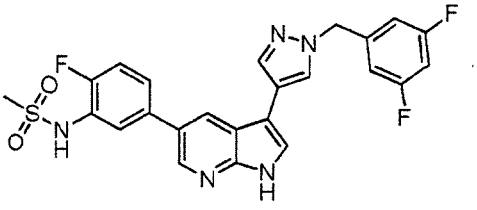
Using similar reaction conditions as described in step-iii of example-1, N-(2-fluoro-5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide (60mg, 0.094mmol) was hydrolyzed with lithium hydroxide(20mg, 0.474mmol) in THF/methanol/water (15/5/5mL) to yield 22 mg (48.8% yield).

^{1}H NMR (CD_3OD, 400MHz): δ 8.467-8.462 (d, 1H), 8.36-8.35 (d, 1H), 8.22 (s, 1H), 7.95 (s, 1H), 7.84-7.80 (dd, 1H), 7.63-7.57 (m, 1H), 7.44-7.32 (m, 2H), 7.16-7.12 (d, 1H), 7.10-7.02 (m, 2H).

MS: m/z = 480.3(M+1), HPLC: 92.50% in method B.

Example 79

N-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-fluorophenyl)methanesulfonamide



Step-i: N-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-fluorophenyl)methanesulfonamide

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (Step 1 example 71) (172mg, 0.317mmol) was coupled with N-(2-fluoro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methanesulfonamide (Intermediate 65) (100mg, 0.317 mmol) using sodium carbonate (101mg, 0.952mmol) and $Pd(PPh_3)_2Cl_2$ (12mg, 0.015mmol) in DME/water (15/2 ml). This afforded 54mg (26.2% yield). MS: m/z = 652.0 (M+1).

Step-ii: N-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-fluorophenyl)methanesulfonamide

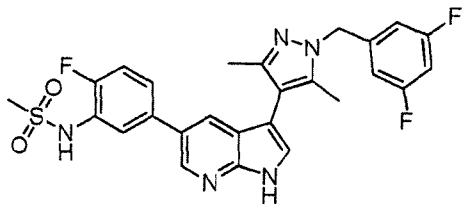
Using similar reaction conditions as described in step-iii of example-1, N-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-fluorophenyl)methanesulfonamide (53mg, 0.184mmol) was hydrolyzed by lithium hydroxide (18mg, 0.407mmol) in THF/methanol/water (15/5/5 ml) to yield 34mg (85% yield) of the titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ 8.44-8.43 (d, 1H), 8.35-8.34 (d, 1H), 8.23 (s, 1H), 7.953-7.951 (d, 1H), 7.80-7.77 (dd, 1H), 7.66 (s, 1H), 7.59-7.55 (m, 1H), 7.34-7.29 (m, 1H), 6.90-6.86 (m, 2H), 5.43 (s, 2H), 305 (s, 3H).

MS: m/z = 498.1 (M+1), HPLC: 93.19% in method B.

Example 80

N-(5-(3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-fluorophenyl)methanesulfonamide



Step-i: tert-butyl 5-(3-(N-(tert-butoxycarbonyl)methylsulfonamido)-4-fluorophenyl)-3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 5-(3-(N-(tert-butoxycarbonyl)methylsulfonamido)-4-fluorophenyl)-3-iodo-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (Intermediate 66A)(85mg, 0.134mmol) was coupled with 1-(3,5-difluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 24) (93mg, 0.269mmol) using sodium carbonate (43mg, 0.404mmol) and

$Pd(PPh_3)_2Cl_2$ (5mg, 0.006) in DME/water (20/4 mL) to afford 89mg of the crude compound. MS: m/z = 670.2 (M+1) (de boc mass observed)

Step-ii: N-(5-(3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-fluorophenyl)methanesulfonamide

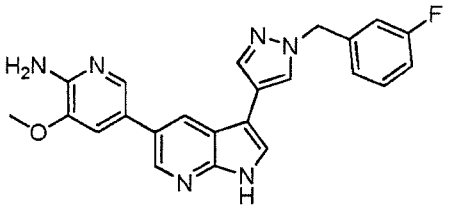
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 5-(3-(N-(tert-butoxycarbonyl)methylsulfonamido)-4-fluorophenyl)-3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (88mg, 0.121mmol)was was deprotected in HCl in dioxane/MeOH (5/2ml). This afforded 27mg (35% yield) of the titled compound.

^1H NMR ($CDCl_3$, 300MHz): δ 13.6 (s, 1H), 8.42 (s, 1H), 8.26 (s, 1H), 7.80-7.77 (d, 1H), 7.50 (s, 1H), 7.33-7.32 (m, 2H), 6.79-6.69 (m, 4H), 5.33 (s, 2H), 3.09 (s, 3H), 2.24 (s, 3H), 2.18 (s, 3H).

MS: m/z = 526.2 (M+1), HPLC: 94.82% in method B.

Example 81

5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxypyridin-2-amine



Step-i: tert-butyl (5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxypyridin-2-yl)carbamate

Using similar reaction conditions as described in step-i of example-1, tert-butyl (5-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxypyridin-2-yl)carbamate (intermediate 66B) (200mg, 0.322mmol) was coupled with 1-(3-fluorobenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 11) (147mg, 0.483mmol) using $Pd(PPh_3)_2Cl_2$ (12mg, 0.016mol) and sodium carbonate (86mg, 0.806mmol) in toluene/ ethanol/water(10/2/2 ml) to afford 200mg (93.2% yield) of the titled compound after column purification using 40% ethyl acetate in hexane as eluent. MS: m/z= 669.1(M+1)

Step-ii: tert-butyl (5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxypyridin-2-yl)carbamate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl (5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxypyridin-2-

yl)carbamate (200mg, 0.299mmol) was hydrolyzed by lithium hydroxide (25mg, 0.598mmol) in THF/methanol/water (5/1/1 ml) to yield 120mg (78.4% yield) of the titled compound. MS: m/z= 515.1(M+1)

Step-iii: 5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxypyridin-2-amine

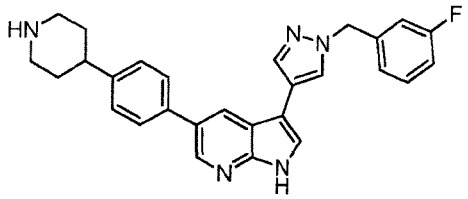
Using similar reaction conditions as described in step-ii of example-7, tert-butyl (5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxypyridin-2-yl)carbamate (120mg, 0.233mmol) was deprotected in TFA/DCM (1/5ml). This afforded 27mg (21.9% yield) of the titled compound.

^{1}H NMR (DMSO-d_6, 400MHz): δ 8.577-8.572 (d, 1H), 8.417-8.413 (d, 1H), 8.37 (s, 1H), 8.03 (s, 2H), 7.956-7.953 (d, 1H), 7.86-7.79 (s, 1H), 7.799-7.793 (d, 1H), 7.40-7.39 (q, 1H), 7.12-7.07 (m, 3H), 5.40 (s, 2H), 4.06 (s, 3H).

MS: m/z = 415.6(M+1), HPLC: 93.86% in method A.

Example 82

3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(piperidin-4-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine



Step-i: tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5,6-dihydropyridine-1(2H)-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 4-(4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5,6-dihydropyridine-1(2H)-carboxylate (intermediate 66C) (250mg, 0.381mmol) was coupled with 1-(3-fluorobenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 11) (172mg, 0..571mmol) using $Pd(PPh_3)_2Cl_2$ (14mg, 0.019mol) and sodium carbonate (121mg, 1.143mmol) in toluene/ethanol/water(20/10/4 ml) to afford 237mg (88% yield) of the titled. MS: m/z = 704.3 (M+1)

Step-ii: tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

To a solution of tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5,6-dihydropyridine-1(2H)-carboxylate (235mg,

0.334mmol) in ethyl acetate/ ethanol 15/15 mL was added palladium hydroxide (60mg) and stirred under hydrogen atmosphere for 18 hours. The catalyst was filtered through celite and the solvent was distilled off to get 191mg (81.0% yield) of the titled compound. MS: m/z = 706.3 (M+1)

Step-iii: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(piperidin-4-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (191mg, 0.270mmol) was deprotected in HCl in dioxane/MeOH (5/5ml). This afforded 173mg (99% yield) of the titled. MS: m/z = 606.8 (M+1).

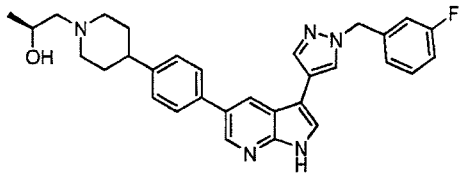
Step-iv: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(piperidin-4-yl) phenyl)-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-iii of example-1, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(piperidin-4-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride (170mg, 0.026mmol) was hydrolyzed by lithium hydroxide (12mg, 0.264mmol) in THF/methanol/water (10/5/2.5 ml) to yield 60mg (40% yield) of the titled compound.

^{1}H NMR (CD_3OD, 300MHz): δ 8.54 (s, 2H), 8.229-8.227 (d, 1H), 7.959-7.957 (d, 1H), 7.73-7.70 (m, 3H), 7.44-7.41 (d, 2H), 7.38-7.23 (m, 1H), 7.12-7.09 (d, 1H), 7.08-7.00 (m, 2H), 5.43 (s, 2H), 3.55-3.50 (d, 2H), 3.21-3.13 (m, 2H), 3.05-2.93 (m, 1H), 2.16-2.11 (d, 2H), 2.02-1.89 (m, 2H). MS: m/z = 452.5 (M+1), HPLC: 96.75% in method A.

Example 82A

(S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo [2,3-b]pyridin-5-yl)phenyl)piperidin-1-yl)propan-2-ol



Step 1 (S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidin-1-yl)propan-2-ol

Seal tube containing 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(piperidin-4-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride (product of step-iii of example 82) (125mg, 0.194mmol), (S)-2-methyloxirane (23mg, 0.389mmol), DIPEA (100mg, 0.778mmol) and

ethanol were heated at 85°C for 3 hours and distilled the solvent on rotavapor to get 128mg (99% yield) of the titled compound. MS: m/z = 664.4 (M+1).

Step-ii: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(piperidin-4-yl) phenyl)-1H-pyrrolo[2,3-b]pyridine

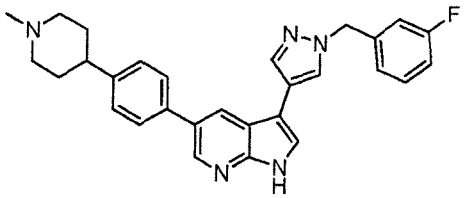
Using similar reaction conditions as described in step-iii of example-1, (S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidin-1-yl)propan-2-ol (127mg, 0.191mmol) was hydrolyzed by lithium hydroxide (80mg, 1.913mmol) in THF/methanol/water (20/10/5 ml) to yield 15mg (5% yield) of the titled.

^{1}H NMR (CD_3OD, 400MHz): δ 7.46-8.45 (d, 1H), 8.33-8.32 (d, 1H), 8.19 (s, 1H), 7.93 (s, 1H), 7.63-7.61 (m, 3H), 7.39-7.34 (m, 3H), 7.11-7.09 (d, 1H), 7.06-7.01 (m, 2H), 5.43 (s, 2H), 4.05-4.00 (m, 1H), 3.25-3.19 (t, 2H), 2.64-2.33 (m, 4H), 1.93-1.85 (m, 4H), 1.30-1.26 (m, 1H), 1.20-1.18 (d, 3H).

MS: m/z = 510.2 (M+1), HPLC: 96.39% in method A.

Example 83

3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(1-methylpiperidin-4-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine



Step-i: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-i of example-1, 3-iodo-5-(4-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (intermediate 66D) (200mg, 0.351mmol) was coupled with 1-(3-fluorobenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 11) (117mg, 0.386mmol) using $Pd(PPh_3)_2Cl_2$ (13mg, 0.017mol) and sodium carbonate (112mg, 1.053mmol) in toluene/ ethanol/water (3/3/2 ml) to afford 180mg (83% yield) of the titled compound after column purification using 10% methanol in DCM as eluent. MS: m/z = 617.9 (M+1)

Step-ii: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-iii of example-1, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)phenyl)-1-tosyl-1H-

pyrrolo[2,3-b]pyridine (180mg, 0.291mmol) was hydrolyzed by lithium hydroxide (37mg, 0.874mmol) in THF/methanol/water (2/2/2 ml) to yield crude 230mg of the titled compound.

Step-iii: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(1-methylpiperidin-4-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine

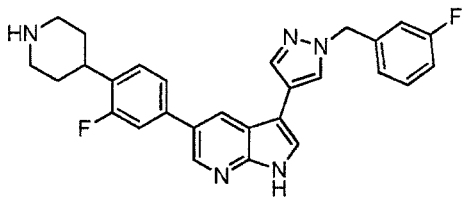
Using similar reaction conditions as described in step-ii of example-82, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine (130mg, 0.280mmol) was reduced with palladium hydroxide (50mg) in ethyl acetate/ethanol 5/5 mL to afford 10mg (6.0% yield) of the titled compound.

^{1}H NMR (CD_3OD, 300MHz): δ 8.627-8.621 (d, 1H), 8.56 (s, 1H), 8.26 (s, 1H), 7.97 (s, 1H), 7.77-7.73 (m, 3H), 7.45-7.42 (d, 2H), 7.38-7.33 (m, 1H), 7.13-7.00 (m, 3H), 5.44 (s, 2H), 3.67-3.63 (d, 2H), 3.22-3.15 (t, 2H), 3.03-2.94 (m, 4H), 2.20-2.00 (m, 4H).

MS: m/z = 466.7 (M+1), HPLC: 95.92% in method B.

Example 84

5-(3-fluoro-4-(piperidin-4-yl) phenyl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine



Step-i: tert-butyl 4-(2-fluoro-4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 4-(2-fluoro-4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (intermediate 67) (250mg, 0.370mmol) was coupled with 1-(3-fluorobenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 11) (168mg, 0.555mmol) using $Pd(DPPF)Cl_2$ (14mg, 0.018mol) and sodium carbonate (118mg, 1.110mmol) in toluene/ ethanol/water (5/5/1 ml) to afford 250mg (93.2% yield) of the titled compound after column purification using 1% methanol in DCM as eluent. MS: m/z = 724.4(M+1)

Step-ii: tert-butyl 4-(2-fluoro-4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(2-fluoro-4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (250mg, 0.345mmol) was hydrolyzed by lithium

hydroxide (73mg, 1.726mmol) in THF/methanol/water (5/2/1 ml) to yield crude 150mg (76.14% yield) of the titled compound. MS: m/z = 570.2(M+1)

Step-iii: 5-(3-fluoro-4-(piperidin-4-yl)phenyl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine

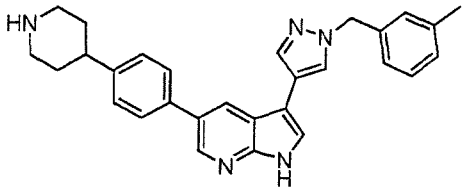
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(2-fluoro-4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo [2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (150mg, 0.263mmol)was was deprotected in TFA/DCM (2/5ml). This afforded 30mg (19.6% yield) of the titled.

^{1}H NMR (CD_3OD, 400MHz): δ 8.67-8.66 (d, 1H), 8.60 (s, 1H), 8.28 (s, 1H), 7.97 (s, 1H), 7.78 (s, 1H), 7.58-7.54 (m, 2H), 7.47-7.43 (t, 1H), 7.39-7.33 (q, 1H), 7.12-7.10 (d, 1H), 7.05-7.00 (m, 2H), 5.43 (s, 2H), 3.55-3.52 (d, 2H), 3.28-3.16 (m, 3H), 2.21-2.03 (m, 4H).

MS: m/z = 470.4(M+1), HPLC: 98.34% in method A.

Example 85

3-(1-(3-methylbenzyl)-1H-pyrazol-4-yl)-5-(4-(piperidin-4-yl) phenyl)-1H-pyrrolo[2,3-b]pyridine



Step-i: tert-butyl 4-(4-(3-(1-(3-methylbenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 4-(2-fluoro-4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (intermediate 67B) (155mg, 0.235mmol) was coupled with 1-(3-methylbenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 64D) (105mg, 0.353mmol) using $Pd(dppf)Cl_2$ (9mg, 0.011mol) and sodium carbonate (75mg, 0.7070mmol) in toluene/ethanol/water(20/10/5 ml) to afford 165mg (crude) of the titled compound. MS: m/z = 702.7 (M+1)

Step-ii: tert-butyl 4-(4-(3-(1-(3-methylbenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(3-(1-(3-methylbenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (164mg, 0.233mmol) was hydrolyzed by lithium hydroxide (98mg, 2.33mmol)

in THF/methanol/water (16/4/4 ml) to yield crude 109mg (86% yield) of the titled compound after column purification using 1.5% methanol in DCM as eluent. MS: m/z = 548.4 (M+1).

Step-iii: 3-(1-(3-methylbenzyl)-1H-pyrazol-4-yl)-5-(4-(piperidin-4-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine

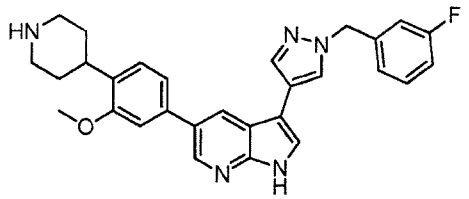
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(3-methylbenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (108mg, 0.197mmol)was was deprotected in TFA/toluene (5/5ml). This afforded 30mg (27% yield) of the titled.

^{1}H NMR (CD_3OD, 300MHz): δ 8.627-8.622 (d, 1H), 8.56 (s, 1H), 8.20 (s, 1H), 7.94 (s, 1H), 7.75-7.71 (m, 3H), 7.44-7.42 (d, 2H), 7.25-7.20 (t, 1H), 7.13-7.07 (m, 3H), 5.37 (s, 2H), 3.55-3.51 (d, 2H), 3.21-3.13 (m, 2H), 3.03-2.94 (m, 1H), 2.31 (s, 3H), 2.14-2.10 (d, 2H), 2.03-1.89 (qd, 2H).

MS: m/z = 448.4 (M+1), HPLC: 98.27% in method A.

Example 86

Tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo [2, 3-b] pyridin-5-yl)-2-methoxyphenyl) piperidine-1-carboxylate



Step-i: tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 4-(4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)piperidine-1-carboxylate (intermediate 67A) (260mg, 0.378mmol) was coupled with 1-(3-fluorobenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 11) (172mg, 0.567mmol) using $Pd(dppf)Cl_2$ (14mg, 0.018mol) and sodium carbonate (121mg, 1.134mmol) in toluene/ethanol/water(6/2/1 ml) to afford 200mg (71.9% yield) of the titled compound after column purification using 2% methanol in DCM as eluent. MS: m/z = 736.4(M+1)

Step-ii: tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-

methoxyphenyl)piperidine-1-carboxylate (200mg, 0.271mmol) was hydrolyzed by lithium hydroxide (57mg, 1.358mmol) in THF/methanol/water (5/2/2 ml) to yield crude 100mg (63.2% yield) of the titled compound. MS: m/z = 582.2(M+1)

Step-iii: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(3-methoxy-4-(piperidin-4-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine

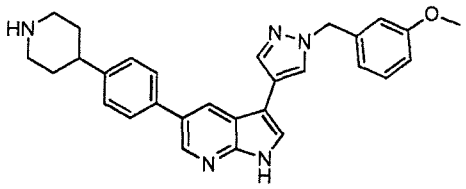
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo [2, 3-b] pyridin-5-yl)-2-methoxyphenyl) piperidine-1-carboxylate (100mg, 0.171mmol) was deprotected in TFA/DCM (2/5ml). This afforded 15mg (14.7% yield) of the titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ 8.06 (s, 2H), 8.24 (s, 1H), 7.96 (s, 1H), 7.75 (s, 1H), 7.38-7.29 (m, 4H), 7.12-7.10 (d, 1H), 7.04-7.00 (m, 2H), 5.42 (s, 2H), 3.95-3.93 (s, 3H), 3.53-3.50 (d, 2H), 3.34-3.30 (m, 1H), 3.19-3.13 (m, 2H), 2.09-1.97 (m, 4H).

MS: m/z = 482.2(M+1), HPLC: 94.26% in method A.

Example 87

3-(1-(3-methoxybenzyl)-1H-pyrazol-4-yl)-5-(4-(piperidin-4-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine



Step-i: tert-butyl 4-(4-(3-(1-(3-methoxybenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 4-(2-fluoro-4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (intermediate 67B) (125mg, 0.190mmol) was coupled with 1-(3-methoxybenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 64F) (90mg, 0.285mmol) using $Pd(dppf)Cl_2$ (7mg, 0.009mol) and sodium carbonate (181mg, 0.578mmol) in toluene/ethanol/water(20/10/5 ml) to afford 121mg (crude) of the titled compound. MS: m/z = 718.3 (M+1).

Step-ii: tert-butyl 4-(4-(3-(1-(3-methoxybenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(3-(1-(3-methoxybenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-

yl)phenyl)piperidine-1-carboxylate (120mg, 0.167mmol) was hydrolyzed by lithium hydroxide (70mg, 1.67mmol) in THF/methanol/water (12/6/3 ml) to yield crude 86mg (91% yield) of the titled compound. MS: m/z = 564.3 (M+1).

Step-iii: 3-(1-(3-methoxybenzyl)-1H-pyrazol-4-yl)-5-(4-(piperidin-4-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine

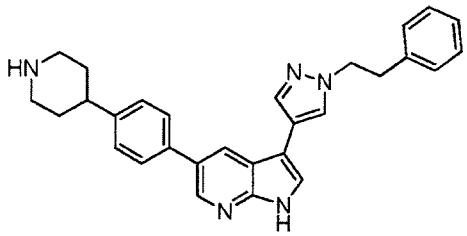
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(3-methoxybenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (85mg, 0.150mmol)was was deprotected in TFA/toluene (2.5/5ml). This afforded 11mg (16.2% yield) of the titled compound.

^{1}H NMR (CD_3OD, 300MHz): δ 8.458-8.451 (d, 1H), 8.327-8.321 (d, 1H), 8.14 (s, 1H), 7.90 (s, 1H), 7.65-7.61 (m, 3H), 7.38-7.35 (d, 2H), 7.29-7.23 (m, 1H), 6.87-6.85 (m, 2H), 5.38 (s, 2H), 3.25-3.76 (s, 3H), 3.25-3.20 (d, 2H), 2.87-2.73 (m, 3H), 1.93-1.72 (m, 4H).

MS: m/z = 464.6 (M+1), HPLC: 90.63% in method A.

Example 88

3-(1-phenethyl-1H-pyrazol-4-yl)-5-(4-(piperidin-4-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine



Step-i: tert-butyl 4-(4-(3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 4-(2-fluoro-4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (intermediate 67B) (125mg, 0.190mmol) was coupled with 1-phenethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 59) (85mg, 0.285mmol) using $Pd(dppf)Cl_2$ (7mg, 0.009mol) and sodium carbonate (181mg, 0.578mmol) in toluene/ ethanol/water (20/10/5 ml) to afford 129mg (crude) of the titled compound. MS: m/z = 702.3 (M+1)

Step-ii: tert-butyl 4-(4-(3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (125mg, 0.178mmol) was hydrolyzed by lithium hydroxide (75mg, 1.78mmol) in

THF/methanol/water (12/6/3 ml) to yield crude 87mg (89% yield) of the titled compound.
MS: m/z = 548.3 (M+1)

Step-iii: 3-(1-phenethyl-1H-pyrazol-4-yl)-5-(4-(piperidin-4-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine

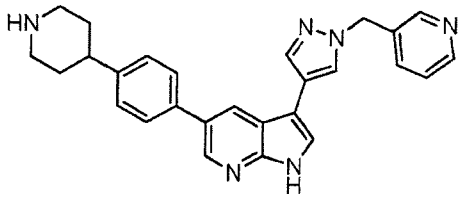
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (85mg, 0.155mmol)was was deprotected in TFA/toluene (2.5/5ml). This afforded 14mg (20.2% yield) of the titled compound.

^{1}H NMR (CD_3OD, 300MHz): δ 8.576-8.571 (d, 1H), 8.46-8.45 (d, 1H), 7.90 (s, 1H), 7.81 (s, 1H), 7.73-7.71 (m, 3H), 7.48-7.46 (d, 2H), 7.25-7.20 (m, 2H), 7.14-7.07 (m, 3H), 7.48-7.43 (t, 2H), 3.56-3.52 (d, 2H), 3.22-3.15 (m, 4H), 3.07-2.98 (dt, 1H), 2.17-2.13 (d, 2H), 2.06-1.91 (m, 2H).

MS: m/z = 448.4 (M+1), HPLC: 91.78% in method B.

Example 89

5-(4-(piperidin-4-yl)phenyl)-3-(1-(pyridin-3-ylmethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine



Step-i: tert-butyl 4-(4-(3-(1-(pyridin-3-ylmethyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 4-(4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (intermediate 67B) (200mg, 0.304mmol) was coupled with 3-((4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-yl)methyl)pyridine (intermediate 64) (104mg, 0.364mmol) using $Pd(dppf)Cl_2$ (11mg, 0.015mol) and sodium carbonate (97mg, 0.912mmol) in acetonitrile/water(3/1 ml) to afford 150mg (72.0% yield) of the titled compound after column purification using 3% methanol in DCM as eluent.

Step-ii: tert-butyl 4-(4-(3-(1-(pyridin-3-ylmethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(3-(1-(pyridin-3-ylmethyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-

yl)phenyl)piperidine-1-carboxylate (150mg, 0.217mmol) was hydrolyzed by lithium hydroxide (27mg, 0.653mmol) in THF/methanol/water (3/3/3 ml) to yield crude 120mg (crude) of the titled compound. MS: m/z = 532.9 (M+1).

Step-iii: 5-(4-(piperidin-4-yl)phenyl)-3-(1-(pyridin-3-ylmethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine

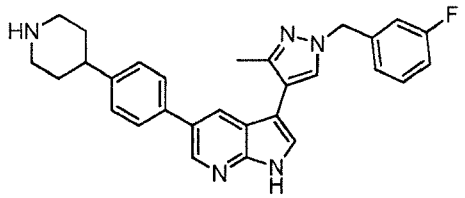
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(pyridin-3-ylmethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (120mg, 0.224mmol) was deprotected in TFA/methnaol (5/5ml). This afforded 15mg (12% yield) of the titled compound.

^{1}H NMR (CD_3OD, 300MHz): δ 8.76 (s, 2H), 8.56-8.55 (d, 2H), 8.36-8.34 (m, 2H), 8.02(s, 1H), 7.95-7.91 (m, 1H), 7.75-7.72 (m, 3H), 7.45-7.42 (m, 2H), 5.66 (s, 2H), 3.56-3.51 (d, 2H), 3.22-3.14 (t, 2H), 3.10-2.99 (m, 1H), 2.16-2.11 (d, 2H), 2.03-1.93 (td, 2H).

MS: m/z = 435.2 (M+1), HPLC: 97.0% in method A.

Example 90

3-(1-(3-fluorobenzyl)-3-methyl-1H-pyrazol-4-yl)-5-(4-(piperidin-4-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine



Step-i: tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-3-methyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 4-(4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (intermediate 67B) (120mg, 0.182mmol) was coupled with 1-(3-fluorobenzyl)-3-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 12) (64mg, 0.200mmol) using $Pd(PPh_3)_2Cl_2$ (6mg, 0.009mol) and sodium carbonate (58mg, 0.547mmol) in acetonitrile /water(3/2 ml) to afford 100mg (76% yield) of the titled compound.

Step-ii: tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-3-methyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-3-methyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (100mg, 0.138mmol) was hydrolyzed by lithium

hydroxide (17mg, 0.416mmol) in THF/methanol/water (2/2/1 ml) to yield 100mg (crude) of the titled compound.

Step-iii 3-(1-(3-fluorobenzyl)-3-methyl-1H-pyrazol-4-yl)-5-(4-(piperidin-4-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine

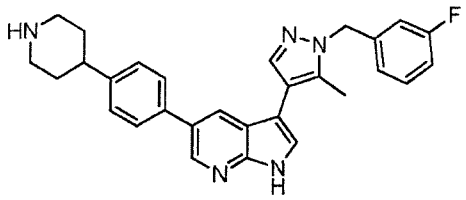
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-3-methyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (100mg, 0.176mmol) was deprotected in TFA/methnaol (3/3ml). This afforded 5mg (152% yield) of the titled compound after purification by preparative HPLC along with one more isomer Example 91.

^{1}H NMR (CD_3OD , 300MHz): δ 8.51 (s, 1H), 8.24 (s, 1H), 7.80 (s, 1H), 7.72-7.67 (m, 2H), 7.51 (s, 1H), 7.42-7.34 (m, 3H), 7.06-6.87 (m, 3H), 5.46 (s, 2H), 3.61-3.51 (m, 2H), 3.21-3.13 (m, 2H), 3.02-2.94 (t, 1H), 2.37 (s, 3H), 2.15-2.11 (m, 2H), 2.02-1.89 (m, 2H).

MS: m/z = 466.2(M+1), HPLC: 89.39% in method B.

Example 91

3-(1-(3-fluorobenzyl)-5-methyl-1H-pyrazol-4-yl)-5-(4-(piperidin-4-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine



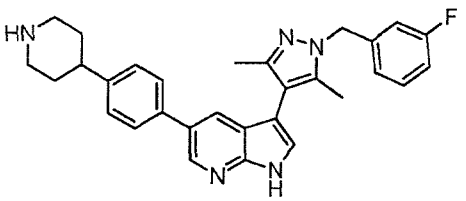
Yield 10mg

^{1}H NMR (CD_3OD, 300MHz): δ 8.55 (s, 1H), 8.41-8.40 (m, 1H), 8.11 (s, 1H), 7.71-7.60 (m, 3H), 7.43-7.43 (m, 3H), 7.12-7.00 (m, 3H), 5.37 (s, 2H), 3.54-3.50 (d, 2H), 3.21-3.13 (t, 2H), 2.98-2.94 (m, 1H), 2.38 (s, 3H), 2.15-2.10 (d, 2H), 2.02-1.94 (m, 2H).

MS: m/z = 466.2 (M+1), HPLC: 92.74% in method A.

Example 92

3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperidin-4-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine



Step-i: tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 4-(4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (intermediate 67B) (150mg, 0.52mmol) was coupled with 1-(3-fluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 16) (208mg, 0.63mmol) using $Pd(PPh_3)_2Cl_2$ (18g, 1.56mol) and sodium carbonate (165mg, 1.56mmol) in toluene/ethanol/water(10/10/2 ml) to afford 140mg (83.6% yield) of the titled compound. MS: m/z = 677.2 (M+1) (de t-butyl).

Step-ii: tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (134mg, 0.182mmol) was hydrolyzed by lithium hydroxide (38mg, 0.91mmol) in THF/methanol/water (4/4/2 ml) to yield 103mg (97.3% yield) of the titled compound. MS: m/z = 580.3(M+1).

Step-iii 3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperidin-4-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine

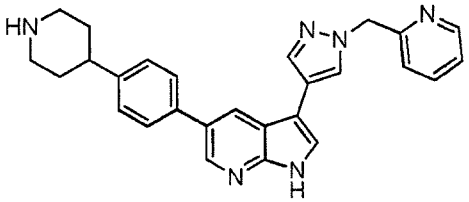
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (113mg, 0.194mmol) was deprotected in TFA/DCM (5/5ml). This afforded 12mg (12.9% yield) of the titled compound.

^1H NMR (CD_3OD, 300MHz): δ 8.55 (s, 1H), 8.09-8.08 (d, 1H), 7.65-7.62 (m, 2H), 7.51 (s, 1H), 7.41-7.34 (m, 3H), 7.06-7.00 (m, 2H), 6.90-6.87 (s, 1H), 5.38 (s, 2H), 3.54-3.47 (m, 2H), 3.20-3.13 (m, 2H), 3.01-2.93 (m, 1H), 2.22 (s, 3H), 2.20 (s, 3H), 2.14-1.88 (m, 4H).

MS: m/z = 480.2 (M+1), HPLC: 98.73% in method B.

Example 93

5-(4-(piperidin-4-yl)phenyl)-3-(1-(pyridin-2-ylmethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine



Step-i: tert-butyl 4-(4-(3-(1-(pyridin-2-ylmethyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 4-(4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (intermediate 67B) (150mg, 0.52mmol) was coupled with 2-((4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-yl)methyl)pyridine (intermediate 64H) (180mg, 0.63mmol) using $Pd(PPh_3)_2Cl_2$ (18mg, 0.026mol) and sodium carbonate (165mg, 1.56mmol) in toluene/ethanol/water(10/10/2 ml) to afford 140mg (97.2% yield) of the titled compound. MS: m/z = 688.4 (M+1).

Step-ii: tert-butyl 4-(4-(3-(1-(pyridin-2-ylmethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(3-(1-(pyridin-2-ylmethyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (140mg, 0.203mmol) was hydrolyzed by lithium hydroxide (44mg, 1.04mmol) in THF/methanol/water (4/4/2 ml) to yield 110mg (98.5% yield) of the titled compound. MS: m/z = 535.3 (M+1).

Step-iii 5-(4-(piperidin-4-yl)phenyl)-3-(1-(pyridin-2-ylmethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine

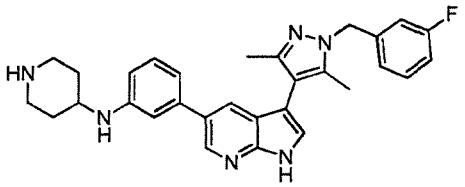
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(pyridin-2-ylmethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (110mg, 0.205mmol) was deprotected in TFA/DCM (5/5ml). This afforded 10mg (11.1% yield) of the titled compound.

^{1}H NMR (CD_3OD, 300MHz): δ 8.73 (s, 1H), 8.68-8.67 (d, 1H), 8.59 (s, 1H), 8.38 (s, 1H), 8.16-8.11 (t, 1H), 8.01 (s, 1H), 7.81 (s, 1H), 7.75-7.72 (d, 2H), 7.66-7.61 (t, 1H), 7.49-7.42 (m, 3H), 5.68 (s, 2H), 3.55-3.51 (d, 2H), 3.21-3.13 (m, 2H), 3.03-2.95 (m, 1H), 2.14-1.90 (m, 4H).

MS: m/z = 434.9 (M+1) , HPLC: 92.12% in method A.

Example 94

N-(3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidin-4-amine



Step-i: tert-butyl 4-((3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)amino)piperidine-1-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 4-((3-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)amino)piperidine-1-carboxylate (intermediate 66E) (200mg, 0.297mmol) was coupled with 1-(3-fluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 16) (141mg, 0.446mmol) using $Pd(PPh_3)_2Cl_2$ (11mg, 0.014mmol) and sodium carbonate (79mg, 0.744mmol) in Toluene/ethanol/water (5/2/1 ml) to afford 150mg (67.5% yield) of the titled compound after column purification using 1% methanol in DCM as eluent. MS: m/z = 749.3 (M+1).

Step-ii: tert-butyl 4-((3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)amino)piperidine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-((3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)amino)piperidine-1-carboxylate (150mg, 0.200mmol) was hydrolyzed by lithium hydroxide (17mg, 0.401mmol) in THF/methanol/water (5/1/1 ml) to yield 80mg (67.2% yield) of the titled compound after column purification using 2% methanol in DCM as eluent. MS: m/z = 594.8 (M+1).

Step-iii: N-(3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidin-4-amine

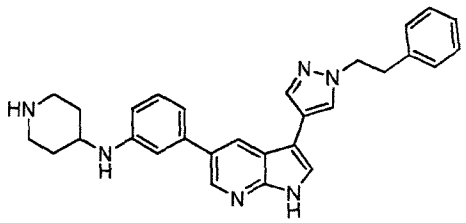
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-((3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)amino)piperidine-1-carboxylate (80mg, 0.134mmol) was deprotected in HCl in methanol (5ml). This afforded 16mg (20.4% yield) of the titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ 8.8-8.6 (bs, 1H), 8.37 (s, 1H), 7.67 (s, 1H), 7.41-7.35 (m, 2H), 7.12-7.10 (m, 2H), 7.06-7.04 (m, 2H), 6.94-6.90 (m, 2H), 5.41 (s, 2H), 3.85-3.70 (m, 1H), 3.50-3.47 (m, 2H), 3.18-3.12 (t, 2H), 2.29-2.24 (m, 8H), 1.79-1.76 (m, 2H).

MS: m/z = 495.3 (M+1) , HPLC: 85.03% in method A.

Example 95

N-(3-(3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidin-4-amine



Step-i: tert-butyl 4-((3-(3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)amino)piperidine-1-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 4-((3-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)amino)piperidine-1-carboxylate (intermediate 66E) (200mg, 0.297mmol) was coupled with 1-phenethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 59) (133mg, 0.446mmol) using $Pd(PPh_3)_2Cl_2$(11mg, 0.014mmol) and sodium carbonate (79mg, 0.744mmol) in toluene/ethanol/water (5/2/1 ml) to afford 150mg (70.4% yield) of the titled compound after column purification using 1% methanol in DCM as eluent. MS: m/z = 717.3 (M+1).

Step-ii: tert-butyl 4-((3-(3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)amino)piperidine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-((3-(3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)amino)piperidine-1-carboxylate (150mg, 0.209mmol) was hydrolyzed by lithium hydroxide (18mg, 0.418mmol) in THF/methanol/water (5/1/1 ml) to yield 80mg (67.7% yield) of the titled compound after column purification using 2% methanol in DCM as eluent. MS: m/z = 562.9 (M+1).

Step-iii: N-(3-(3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidin-4-amine

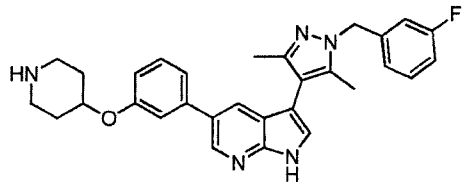
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-((3-(3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)amino)piperidine-1-carboxylate (80mg, 0.142mmol) was deprotected in HCl in methanol (5ml). This afforded 18mg (21.9% yield) of the titled compound.

^{1}H NMR (CD_3OD , 400MHz): δ 8.55 (s, 1H), 8.435-8.431 (d, 1H), 7.91 (s, 1H), 7.81 (s, 1H), 7.71 (s, 1H), 7.39-7.32 (t, 1H), 7.29-7.20 (t, 2H), 7.16-7.13 (m, 2H), 7.04-7.03 (m, 2H), 6.85-6.80 (d, 1H), 4.49-4.46 (t, 2H), 3.85-3.75 (m, 1H), 3.52-3.49 (m, 2H), 3.22-3.19 (m, 4H), 2.35-2.25 (dd, 2H), 1.80-1.65 (m, 2H).

MS: m/z = 463.3 (M+1), HPLC: 90.63% in method A

Example 96

3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(3-(piperidin-4-yloxy)phenyl)-1H-pyrrolo[2,3-b]pyridine



Step-i: tert-butyl 4-(3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenoxy)piperidine-1-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 4-(3-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenoxy)piperidine-1-carboxylate (intermediate 13) (150mg, 0.222mmol) was coupled with 1-(3-fluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 16) (106mg, 0.334mmol) using $Pd(PPh_3)_2Cl_2$ (8mg, 0.011mmol) and sodium carbonate (59mg, 0.557mmol) in toluene/ethanol/water (4/1/1 ml) to afford 120mg (71.8% yield) of the titled compound after column purification using 1% methanol in DCM as eluent. MS: m/z = 750.4 (M+1).

Step-ii: tert-butyl 4-(3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenoxy)piperidine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenoxy)piperidine-1-carboxylate (120mg, 0.160mmol) was hydrolyzed by lithium hydroxide (14mg, 0.320mmol) in THF/methanol/water (5/1/1 ml) to yield 80mg (84.2% yield) of the titled compound after column purification using 2% methanol in DCM as eluent. MS: m/z = 595.8 (M+1).

Step-iii: 3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(3-(piperidin-4-yloxy)phenyl)-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenoxy)piperidine-1-carboxylate (80mg, 0.134mmol) was deprotected in HCl in methanol (5ml). This afforded 33mg (40.2% yield) of the titled compound.

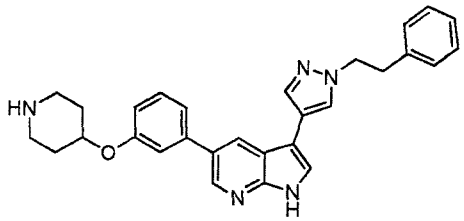
^1H NMR (CD_3OD , 400MHz): δ 8.75-8.60 (bs, 1H), 8.37 (s, 1H), 7.66 (s, 1H), 7.48-7.44 (t, 1H), 7.42-7.37 (q, 1H), 7.33-7.29 (m, 2H), 7.11-7.04 (m, 3H), 6.93-6.91 (d, 1H), 5.41 (s, 2H),

4.85-4.82 (m, 1H), 3.48-3.41 (m, 2H), 3.28-3.23 (m, 2H), 2.25-2.2 8(m, 8H), 2.12-2.06 (m, 2H).

MS: m/z = 496.3(M+1), HPLC: 96.84% in method A.

Example 97

3-(1-phenethyl-1H-pyrazol-4-yl)-5-(3-(piperidin-4-yloxy)phenyl)-1H-pyrrolo[2,3-b]pyridine



Step-i: tert-butyl 4-(3-(3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenoxy)piperidine-1-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 4-(3-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenoxy)piperidine-1-carboxylate (intermediate 13) (150mg, 0.222mmol) was coupled with 1-phenethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 59) (100mg, 0.334mmol) using $Pd(PPh_3)_2Cl_2$(8mg, 0.011mmol) and sodium carbonate (59mg, 0.557mmol) in toluene/ethanol/water (4/1/1 ml) to afford 120mg (75.0% yield) of the titled compound after column purification using 1% methanol in DCM as eluent. MS: m/z = 718.4 (M+1).

Step-ii: tert-butyl 4-(3-(3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenoxy)piperidine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(3-(3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenoxy)piperidine-1-carboxylate (120mg, 0.167mmol) was hydrolyzed by lithium hydroxide (14mg, 0.334mmol) in THF/methanol/water (5/1/1 ml) to yield 80mg (85.1% yield) of the titled compound after column purification using 2% methanol in DCM as eluent. MS: m/z= 563.8(M+1)

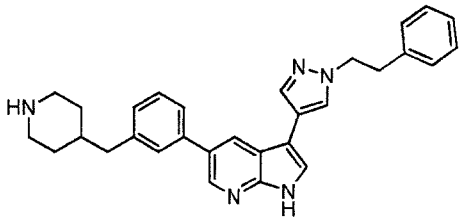
Step-iii: 3-(1-phenethyl-1H-pyrazol-4-yl)-5-(3-(piperidin-4-yloxy)phenyl)-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(3-(3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenoxy)piperidine-1-carboxylate (80mg, 0.142mmol) was deprotected in HCl in methanol(5ml). This afforded 31mg (37.7% yield) of the titled compound after purification by preparative HPLC.

^{1}H NMR (CD_3OD , 400MHz): δ 8.70-8.50 (bs, 1H), 8.32 (s, 1H), 7.89 (s, 1H), 7.79 (s, 1H), 7.65 (s, 1H), 7.52-7.45 (t, 1H), 7.39-7.30 (m, 2H), 7.29-7.20 (t, 2H), 7.19-7.09 (m, 4H), 4.85-4.75 (m, 1H), 4.49-4.45 (t, 2H), 3.51-3.49 (m, 2H), 3.30-3.10 (m, 4H), 2.30-2.10 (m, 4H).
MS: m/z = 464.3 (M+1), HPLC: 95.43% in method A

Example 98

3-(1-phenethyl-1H-pyrazol-4-yl)-5-(3-(piperidin-4-ylmethyl) phenyl)-1H-pyrrolo[2, 3-b] pyridine



Step-i: tert-butyl 4-(3-(3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)benzyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 4-(3-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)benzyl)piperidine-1-carboxylate (intermediate 66G) (100mg, 0.148mmol) was coupled with 1-phenethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 59) (67mg, 0.223mmol) using $Pd(PPh_3)_2Cl_2$ (6mg, 0.007mmol) and sodium carbonate (40mg, 0.372mmol) in toluene/ethanol/water (5/2/1 ml) to afford 90mg (84.1% yield) of the titled compound after column purification using 50% ethyl acetate in hexane as eluent. MS: m/z = 659.8 (M+1) (de t-butyl).

Step-ii: tert-butyl 4-(3-(3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)benzyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(3-(3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)benzyl)piperidine-1-carboxylate (90mg, 0.128mmol) was hydrolyzed by lithium hydroxide (11mg, 0.251mmol) in THF/methanol/water (5/1/1 ml) to yield 60mg (52.3% yield) of the titled compound after column purification using 2% methanol in DCM as eluent. MS: m/z = 561.9 (M+1).

Step-iii: 3-(1-phenethyl-1H-pyrazol-4-yl)-5-(3-(piperidin-4-ylmethyl)phenyl)-1H-pyrrolo[2,3-b]pyridine

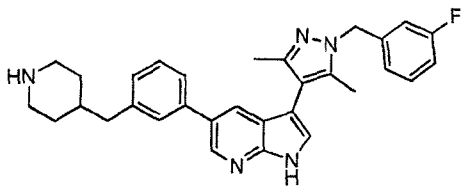
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(3-(3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)benzyl)piperidine-1-carboxylate (60mg, 0.106mmol) was deprotected in HCl in methanol (5ml). This afforded 20mg (32.4% yield) of the titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ 8.65-8.60(bs, 1H), 8.52 (s, 1H), 7.92 (s, 1H), 7.87 (s, 1H), 7.74 (s, 1H), 7.61-7.58 (d, 2H), 7.53-7.41 (t, 1H), 7.33-7.26 (d, 1H), 7.26-7.22 (t, 2H), 7.15-7.09 (m, 3H), 4.49-4.45 (t, 2H), 3.41-3.38 (d, 2H), 3.22-3.18 (t, 2H), 2.99-2.93 (t, 2H), 2.77-2.76 (d, 2H), 2.01-1.90 (m, 3H), 1.56-1.46 (m, 2H).

MS: m/z = 462.7 (M+1), HPLC: 88.14% in method A.

Example 99

3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(3-(piperidin-4-ylmethyl)phenyl)-1H-pyrrolo[2,3-b]pyridine



Step-i: tert-butyl 4-(3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)benzyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 4-(3-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)benzyl)piperidine-1-carboxylate (intermediate 66G) (100mg, 0.148mmol) was coupled with 1-(3-fluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 16) (74mg, 0.223mmol) using $Pd(PPh_3)_2Cl_2$ (6mg, 0.007mmol) and sodium carbonate (40mg, 0.372mmol) in toluene/ethanol/water (6/5/2 ml) to afford 100mg (90.1% yield) of the titled compound after column purification using 50% ethyl acetate in hexane as eluent. MS: m/z = 747.8 (M+1).

Step-ii: tert-butyl 4-(3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)benzyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)benzyl)piperidine-1-carboxylate (100mg, 0.133mmol) was hydrolyzed by lithium hydroxide (12mg, 0.267mmol) in THF/methanol/water (5/1/1 ml) to yield 60mg (75.4% yield) of the titled compound after column purification using 2% methanol in DCM as eluent. MS: m/z = 593.9 (M+1).

Step-iii: 3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(3-(piperidin-4-ylmethyl)phenyl)-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-

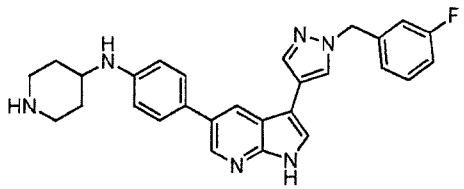
yl)benzyl)piperidine-1-carboxylate (60mg, 0.101mmol) was deprotected in HCl in methanol (5ml). This afforded 25mg (40.6% yield) of the titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ 8.67 (s, 1H), 8.34 (s, 1H), 7.66 (s, 1H), 7.56-7.54 (m, 2H), 7.48-7.38 (m, 2H), 7.30-7.28 (d, 1H), 7.08-7.04 (m, 2H), 6.93-6.91 (d, 1H), 5.42 (s, 2H), 3.40-3.37 (d, 2H), 2.98-2.92 (t, 2H), 2.74-2.72 (d, 2H), 2.25-2.23 (d, 6H), 2.10-1.90 (m, 3H), 1.53-1.47 (m, 2H).

MS: m/z = 494.3 (M+1), HPLC: 95.16% in method A.

Example 100

N-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidin-4-amine



Step-i: tert-butyl 4-((4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)amino)piperidine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (compound of Step-iof example 9) (150mg, 0.280mmol) was coupled with tert-butyl 4-((4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)amino)piperidine-1-carboxylate (Intermediate 68)(137mg, 0.34mmol) using sodium carbonate(79mg, 0.75mmol) and $Pd(PPh_3)_2Cl_2$(10mg, 0.014mmol) in DME/water (20/2 mL). This afforded 130mg (63.4% yield) after purification by column (Silica gel 6/120) using 50% EtOAc/DCM as eluent. MS: m/z = 720.8 (M+1).

Step-ii: tert-butyl 4-((4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)amino)piperidine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-((4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)amino)piperidine-1-carboxylate (130mg, 0.18mmol) was hydrolyzed with lithium hydroxide(37mg, 0.9mmol) in THF/methanol/water (2/2/1mL) to yield 60 mg (58.8% yield) after purification by preparative TLC (Silicagel-1000micron) using 3%methanol in chloroform as eluent. MS: m/z = 566.8 (M+1).

Step-iii: N-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidin-4-amine

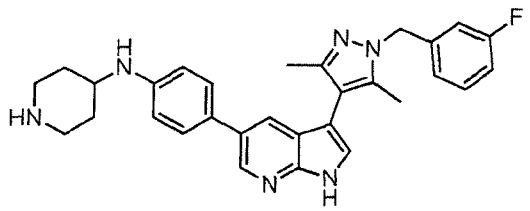
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-((4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)amino)piperidine-1-carboxylate (60mg, 0.10mmol) was deprotected in methanol/ether HCl (3.0/0.3ml). This afforded 40mg (75.4% yield) of the titled.

^{1}H NMR (CD_3OD, 400MHz): δ 9.01-9.00 (d, 1H), 8.71-8.70 (d, 1H), 8.39 (s, 1H), 8.05 (s, 1H), 7.95 (s, 1H), 7.90-7.87 (m, 2H), 7.37-7.34 (m, 3H), 7.14-7.12 (s, 1H), 7.04-7.01 (m, 2H), 5.46 (s, 2H), 3.95-3.85 (m, 1H), 3.54-3.51 (d, 2H), 3.81-3.72 (t, 2H), 3.30-3.26 (d, 2H), 2.00-1.90 (m, 2H).

MS: m/z = 466.9 (M+1), HPLC: 96.60% in method A.

Example 101

N-(4-(3-(1-(3-fluorobenzyl)-3, 5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo [2, 3-b] pyridin-5-yl)phenyl) piperidin-4-amine



Step-i: tert-butyl 5-(4-((tert-butoxycarbonyl)(1-(tert-butoxycarbonyl)piperidin-4-yl)amino)phenyl)-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 5-(4-((tert-butoxycarbonyl)(1-(tert-butoxycarbonyl)piperidin-4-yl)amino)phenyl)-3-iodo-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (intermediate 66H) (150mg, 0.20mmol) was coupled with 1-(3-fluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 16) (89mg, 0.27mmol) using $Pd(dppf)Cl_2$(8mg, 0.01mmol) and sodium carbonate (63mg, 0.6mmol) in toluene/ethanol/water (20/10/5 ml) to afford 40mg (25.3% yield) of the titled compound after column purification using 35% ethyl acetate in hexane as eluent. MS: m/z = 694.9 (M-Boc+1).

Step-ii: N-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidin-4-amine

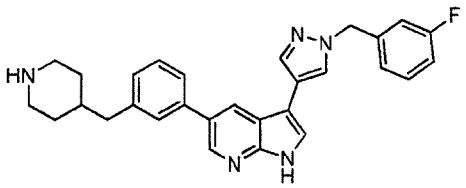
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 5-(4-((tert-butoxycarbonyl)(1-(tert-butoxycarbonyl)piperidin-4-yl)amino)phenyl)-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (25mg, 0.050mmol)

was deprotected in methanol/ether HCl (3/2ml). This afforded 5mg (31.2% yield) of the titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ 8.70 (s, 1H), 8.59 (s, 1H), 7.80 (s, 1H), 7.72-7.70 (d, 2H), 7.46-7.40 (m, 1H), 7.02-7.18 (d, 2H), 7.12-7.09 (m, 2H), 7.02-7.00 (d, 1H), 5.51 (s, 2H), 3.85-3.80 (m, 1H), 3.52-3.47 (d, 2H), 3.20-3.10 (t, 2H), 2.33-2.13 (m, 8H), 2.13-1.83 (m, 2H). MS: m/z = 494.9 (M+1), HPLC: 95.22% in method B.

Example102

3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(3-(piperidin-4-ylmethyl)phenyl)-1H-pyrrolo[2,3-b]pyridine



Step-i: tert-butyl 4-(3-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)benzyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 4-(3-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)benzyl)piperidine-1-carboxylate (intermediate 66G) (300mg, 0.44mmol) was coupled with 1-(3-fluorobenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 11) (170mg, 0.58mmol) using Pd(DPPF)Cl_2(15mg, 0.02mmol) and sodium carbonate (140mg, 1.32mmol) in toluene/ethanol/water (15/8/4 ml) to afford 200mg (62.3% yield) of the titled compound after column purification using 30% ethyl acetate in hexane as eluent. MS: m/z = 720.3 (M+1).

Step-ii: tert-butyl 4-(3-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)benzyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(3-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)benzyl)piperidine-1-carboxylate (200mg, 0.277mmol) was hydrolyzed by lithium hydroxide (116mg, 2.77mmol) in THF/methanol/water (10/10/5 ml) to yield 50mg (31.8% yield) of the titled compound. MS: m/z = 566.2 (M+1)

Step-iii: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(3-(piperidin-4-ylmethyl)phenyl)-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(3-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)benzyl)piperidine-1-

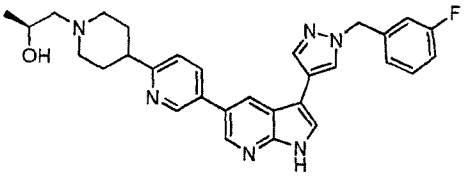
carboxylate (50mg, 0.088mmol) was deprotected in methanol / ether HCl (5/1ml). This afforded 40mg (90.9% yield) of the titled compound.

^{1}H NMR (DMSO-d_6, 300MHz): δ 11.9 (s, 1H), 8.75-8.65 (bs, 1H), 8.53-8.52 (d, 1H), 8.42-8.38 (m, 2H), 7.98 (s, 1H), 7.78-7.77 (d, 2H), 7.62-7.57 (m, 2H), 7.43-7.35 (m, 2H), 7.19-7.05 (m, 4H), 5.40 (s, 2H), 3.23-3.18 (d, 2H), 2.80-2.54 (m, 5H), 2.25-2.15 (bs, 1H), 1.76-1.71 (d, 2H), 1.45-1.30 (m, 2H).

MS: m/z = 466.2 (M+1), HPLC: 97.04% in method **A.**

Example 102A

(S)-1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperidin-1-yl)propan-2-ol



Step-i: tert-butyl 5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-5',6'-dihydro-[2,4'-bipyridine]-1'(21H)-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 5-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-5',6'-dihydro-[2,4'-bipyridine]-1'(21H)-carboxylate (intermediate 66I) (225mg, 0.342mmol) was coupled with 1-(3-fluorobenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 11) (155mg, 0.513mmol) using Pd(dppf)Cl_2(13mg, 0.017mol) and sodium carbonate (109mg, 0.017mmol) in toluene/ethanol/water(20/10/4 ml) to afford 127mg (47% yield) of the titled.

Step-ii: tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-82, tert-butyl 5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-5',6'-dihydro-[2,4'-bipyridine]-1'(21H)-carboxylate (100mg, 0.141mmol)was reduced with palladium hydroxide (25mg) in ethyl acetate/ethanol 12/12 mL to get 96mg (96.0% yield) of the titled compound.

MS: m/z = 706.3 (M+1)

Step-iii: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperidin-4-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-

1-carboxylate (96mg, 0.135mmol) was deprotected in HCl in dioxane/MeOH (5/5ml). This afforded 87mg (99% yield) of the titled compound.

MS: m/z = 607.2 (M+1)

Step-iv: (S)-1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperidin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-i of example-82A, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperidin-4-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride (85mg. 0.132mmol) was alkylated using (S)-2-methyloxirane (16mg, 0.264mmol), DIPEA (68mg, 0.528mmol) and ethanol (5mL) to get 86mg (97.8% yield) of the titled compound. MS: m/z = 665.2 (M+1)

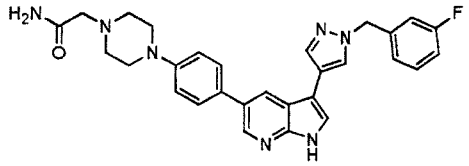
Step-v: (S)-1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperidin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-iii of example-1, (S)-1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperidin-1-yl)propan-2-ol (86mg, 0.129mmol) was hydrolyzed by lithium hydroxide (54mg, 1.293mmol) in THF/methanol/water (15/7/4 ml) to yield 17mg (25.7% yield) of the titled compound.

^{1}H NMR (CD_3OD, 300MHz): δ 9.01-9.00 (d, 1H), 8.56-8.55 (m, 2H), 8.45-8.42 (dd, 1H), 8.23 (s, 1H), 7.72 (s, 1H), 7.69-7.66 (d, 1H), 7.39-7.32 (m, 1H), 7.11-6.98 (m, 3H), 5.43 (s, 2H), 4.30-4.20 (m, 1H), 3.87-3.77 (t, 2H), 3.30-3.05 (m, 4H), 2.40-2.10 (m, 4H), 1.27-1.24 (d, 3H). MS: m/z = 511.3 (M+1), HPLC: 96.17% in method A.

Example 103

2-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)acetamide



Step-i: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (step 1, example 39) (370mg, 0.52mmol) was deprotected in ether(5ml) and

HCl in ether (3ml). This afforded 270mg (80.35% yield) of the titled compound. MS: m/z = 607.2 (M+1)

Step-ii 2-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)acetamide

Using similar reaction conditions as described in step-i of example-82A, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride (50mg. 0.077mmol) was alkylated using 2-chloroacetamide (10mg, 0.116mmol) and sodium bicarbonate (20mg, 0.231mmol) in acetone/ethanol (5/5mL) to get 25mg (49.01% yield) of the titled compound. MS: m/z = 663.7 (M+1).

Step-iii: 2-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)acetamide

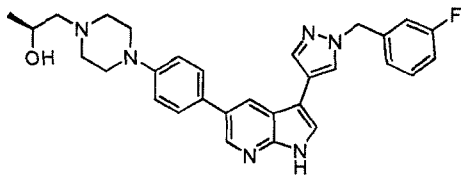
Using similar reaction conditions as described in step-iii of example-1, 2-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)acetamide (25mg, 0.037mmol) was hydrolyzed by lithium hydroxide (7mg, 0.188mmol) in THF/methanol/water(2/2/2 ml) to afford 10mg (52.6% yield) of the titled compound after purification by preparative TLC (Silicagel-1000micron) using 3%methanol in DCM as eluent. MS: m/z = 553.2 (M+1).

^{1}H NMR (CD_3OD, 400MHz): δ 8.45-8.44 (d, 1H), 8.32-8.31 (d, 1H), 8.20 (s, 1H), 7.93 (s, 1H), 7.62-7.60 (m, 3H), 7.42-7.34 (q, 1H), 7.13-7.11 (m, 3H), 7.05-7.02 (m, 2H), 5.45 (s, 2H), 3.12 (s, 2H), 2.76 (s, 4H).

MS: m/z = 510.3 (M+1), HPLC: 92.51% in method A

Example 104

(S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol



Step-i: (S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-i of example-82A, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride(step1 example 103) (50mg. 0.077mmol) was alkylated using (S)-2-

methyloxirane (9mg, 0.155mmol), DIPEA (29mg, 0.231mmol) and ethanol (2mL) to get 25mg (9.8% yield) of the titled compound. MS: m/z = 664.8 (M+1).

Step-ii: (S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol

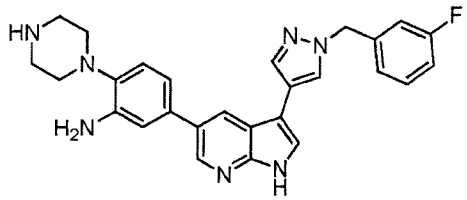
Using similar reaction conditions as described in step-iii of example-1, (S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol (25mg, 0.037mmol) was hydrolyzed by lithium hydroxide (7mg, 0.188mmol) in THF/methanol/water(2/2/1 ml) to afford 5mg (26.31% yield) of the titled compound after purification by preparative TLC (Silicagel-1000micron) using 3%methanol in DCM as eluent.

^{1}H NMR (CD_3OD, 400MHz): δ 8.45 (s, 1H), 8.30 (s, 1H), 8.20 (s, 1H), 7.95 (s, 1H), 7.65-7.55 (m, 3H), 7.45-7.35 (q, 1H), 7.15-7.00 (m, 4H), 5.45 (s, 2H), 4.05-3.95 (m, 1H), 3.70-3.45 (m, 2H), 2.85-2.35 (m, 6H), 1.22-1.98 (d, 3H).

MS: m/z = 511.6 (M+1), HPLC: 91.71% in method A.

Example 105

5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(piperazin-1-yl)aniline



Step-i: tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-nitrophenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 4-(4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-nitrophenyl)piperazine-1-carboxylate (intermediate 66J) (340mg, 0.48mmol) was coupled with 1-(3-fluorobenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 11) (189mg, 0.628mmol) using $Pd(dppf)Cl_2$(18mg, 0.024mol) and sodium carbonate (152mg, 1.44mmol) in toluene/ethanol/wate r(20/10/5 ml) to afford 120mg (33.05% yield) of the titled. MS: m/z = 752.2 (M+1).

Step-ii: tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-nitrophenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-nitrophenyl)piperazine-1-carboxylate (120mg, 0.15mmol) was hydrolyzed by lithium hydroxide (20mg, 0.47mmol) in THF/methanol/water (5/5/2 ml) to yield crude 100mg of the titled compound after purification by preparative TLC (Silicagel-1000micron) using ethyl acetate as eluent.

Step-iii: tert-butyl 4-(2-amino-4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in example-8, tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-nitrophenyl)piperazine-1-carboxylate (90mg, 0.15mmol) was reduced by 10%palladium on carbon(10mg, 10%W/W) in methanol(10 mL) to yield crude 90mg of the titled compound. MS: m/z = 567.8 (M+1).

Step-iv: 5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(piperazin-1-yl)aniline

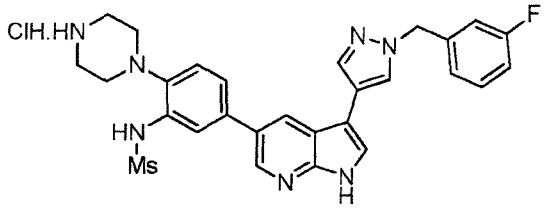
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(2-amino-4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (90mg, 0.15mmol) was deprotected in HCl in ether/MeOH (0.2/5ml). This afforded 5mg (6.3% yield) of the titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ 9.00 (s, 1H), 8.70 (s, 1H), 8.40 (s, 1H), 8.06 (s, 1H), 7.98 (s, 1H), 7.90-7.80 (m, 2H), 7.63-7.61 (d, 1H), 7.45-7.35 (q, 1H), 7.20-7.00 (m, 3H), 5.45 (s, 2H), 3.12 (s, 2H), 2.76 (s, 4H).

MS: m/z = 467.9 (M+1), HPLC: 95.53% in method A.

Example 106

N-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(piperazin-1-yl)phenyl)methanesulfonamide hydrochloride



Step-i: tert-butyl 5-(4-(4-(tert-butoxycarbonyl)piperazin-1-yl)-3-(methylsulfonamido)phenyl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 5-(4-(4-(tert-butoxycarbonyl)piperazin-1-yl)-3-(methylsulfonamido)phenyl)-3-iodo-1H-pyrrolo [2,3-b]pyridine-1-carboxylate (intermediate 50) (150mg, 0.215mmol) was coupled with 1-(3-fluorobenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 11) (78mg, 0.258mmol) using sodium carbonate(68mg, 0.645mmol) and $Pd(PPh_3)_2Cl_2$ (8mg, 0.0107mmol) in toluene/ethanol/water (5/2.5/1ml) to afford 30mg (18.7% yield) of titled compound after purification by preparative TLC (Silicagel-1000micron) using 1%methanol in DCM as eluent.

Step-ii: N-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(piperazin-1-yl)phenyl)methanesulfonamide hydrochloride

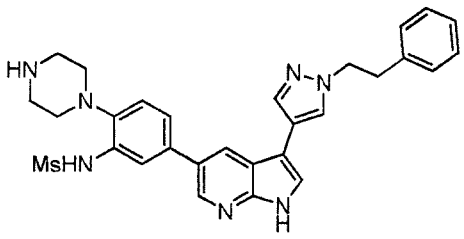
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 5-(4-(4-(tert-butoxycarbonyl)piperazin-1-yl)-3-(methylsulfonamido)phenyl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (27mg, mmol) was deprotected in methanol/HCl in diethyl ether (3/1ml) to afford 12mg (57% yield) of the titled compound.

^{1}H NMR (CD_3OD, 300MHz): δ 9.01-9.00 (d, 1H), 8.71-8.70 (d, 1H), 8.41 (s, 1H), 8.09 (s, 1H), 7.98 (s, 1H), 7.87-7.86 (d, 1H), 7.66-7.63 (dd, 1H), 7.49-7.46 (d, 1H), 7.40-7.34 (m, 1H), 7.16-7.13 (m, 1H), 7.07-7.02 (m, 2H), 5.47 (s, 2H), 3.50-3.46 (m, 4H), 3.26-3.23 (m, 7H).

MS: m/z = 546.2 (M+1), HPLC: 98.49% in method B.

Example 107

N-(5-(3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(piperazin-1-yl)phenyl)methanesulfonamide hydrochloride



Step-i: tert-butyl 5-(4-(4-(tert-butoxycarbonyl)piperazin-1-yl)-3-(methylsulfonamido)phenyl)-3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 5-(4-(4-(tert-butoxycarbonyl)piperazin-1-yl)-3-(methylsulfonamido)phenyl)-3-iodo-1H-pyrrolo [2,3-b]pyridine-1-carboxylate (intermediate 50) (150mg, 0.215mmol) was coupled with 1-

phenethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 59) (76mg, 0.258mmol) using sodium carbonate(68mg, 0.645mmol) and $Pd(PPh_3)_2Cl_2$ (8mg, 0.0107mmol) in toluene/ethanol/water (5/5/2ml) to afford 25mg (15.7% yield) of titled compound after purification by preparative TLC (Silicagel-1000micron) using 1%methanol in DCM as eluent. MS: m/z = 742.4 (M+1).

Step-ii: N-(5-(3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(piperazin-1-yl)phenyl)methanesulfonamide hydrochloride

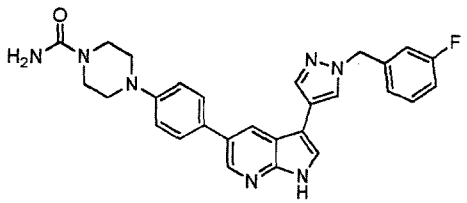
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 5-(4-(4-(tert-butoxycarbonyl)piperazin-1-yl)-3-(methylsulfonamido)phenyl)-3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (21mg, mmol) was deprotected in methanol/HCl in diethyl ether (2/1ml) to afford 11mg (68% yield) of the titled compound.

^{1}H NMR (CD_3OD, 300MHz): δ 8.859-8.853 (d, 1H), 8.736-8.73 (d, 1H), 8.37 (s, 1H), 8.33 (s, 1H), 8.00 (s, 1H), 7.867-7.861 (d, 1H), 7.66-7.63 (dd, 1H), 7.53-7.50 (d, 1H), 7.27-7.12 (m, 5H), 4.63-4.61 (t, 2H), 3.51-3.47 (t, 4H), 3.50-3.24 (m, 9H).

MS: m/z = 542.3 (M+1), HPLC: 98.49% in method B

Example 108

4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxamide



Step-i 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxamide

To a solution of 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride(step1 example 103) (150mg. 0.233mmol) in chloroform (10mL) triethyl amine (0.16mL, 1.165mmol) was added at 0°C drop wise. This solution was added to a solution of triphosgene (59mg, 0.233mmol) in chloroform (10mL) and stirred at RT for 30 minutes. Ammonia in THF was added to this solution drop wise and stirred at RT overnight. This was diluted with water and extracted in chloroform and distilled out the solvent to afford the 40mg (26.4% yield) of the titled compound after purification with preparative TLC (silicagel-1000micron) using 3% methanol in DCM as eluent. MS: m/z = 649.7 (M+1).

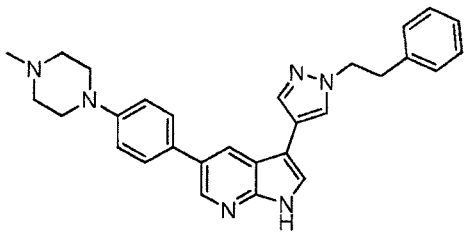
Step-ii: 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxamide

Using similar reaction conditions as described in step-iii of example-1, 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxamide (40mg, 0.075mmol) was hydrolyzed by lithium hydroxide (15mg, 0.377mmol) in THF/methanol/water(2/2/1 ml) to afford 10mg (33.33% yield) of the titled compound after purification by preparative TLC(Silicagel-1000micron) using 3%methanol in DCM as eluent. ^{1}H NMR (DMSO-d_6, 400MHz): δ 11.7 (s, 1H), 8.46-8.41 (m, 2H), 8.27-8.26 (d, 1H), 7.99 (s, 1H), 7.72 (s, 1H), 7.63-7.61 (d, 2H), 7.42-7.35 (q, 1H), 7.15-7.05 (m, 5H), 6.04 (s, 2H), 5.39 (s, 2H), 3.45-3.43 (m, 4H), 3.13-3.11 (m, 4H).

MS: m/z = 496.4 (M+1), HPLC: 92.43% in method B.

Example 109

5-(4-(4-methylpiperazin-1-yl)phenyl)-3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine



Step-i: 3 5-(4-(4-methylpiperazin-1-yl)phenyl)-3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-1, 3-iodo-5-(4-(4-methylpiperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (intermediate 48) (200mg, 0.349 mmol) was coupled with 1-phenethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 59) (104mg, 0.349mmol) using sodium carbonate(111mg, 1.048mmol) and Pd(dppf)Cl_2 (13mg, 0.017mmol) and toluene/ethanol/water (4/4/2ml) to afford 110mg of titled compound after purification by column (Silica gel 6/120) using 5% MeOH/DCM as eluent. MS: m/z = 617.4 (M+1).

Step-ii: 5-(4-(4-methylpiperazin-1-yl)phenyl)-3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-iii of example-1, 5-(4-(4-methylpiperazin-1-yl)phenyl)-3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-

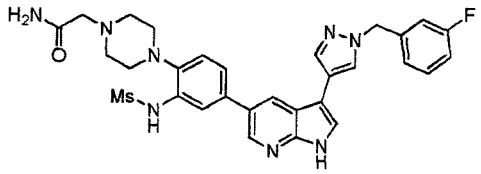
b]pyridine (60mg, 0.097mmol) was hydrolyzed by lithium hydroxide(12mg, 0.291mmol) in THF/methanol/water(1/1/1 ml) to afford 20mg (45.0% yield) of the titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ 8.24 (s, 1H), 7.88 (s, 1H), 7.78 (s, 1H), 7.67-7.65 (d, 2H), 7.61 (s, 1H), 7.28-7.15 (m, 6H), 4.49-4.45 (t, 2H), 4.00-3.97 (d, 2H), 3.69-3.66 (d, 2H), 3.23-3.12 (m, 6H), 3.02 (s, 3H).

MS: m/z = 462.9 (M+1), HPLC: 96.28% in method B.

Example 110

2-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(methylsulfonamido)phenyl)piperazin-1-yl)acetamide



Step-i: 2-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(methylsulfonamido)phenyl)piperazin-1-yl)acetamide

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (compound of Step-iof example 9) (100mg, 0.190mmol) was coupled with 2-(4-(2-(methylsulfonamido)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)piperazin-1-yl)acetamide (Intermediate 65A) 125mg, 0.285mmol) using sodium carbonate(60mg, 0.567mmol) and $Pd(PPh_3)_4$ (11mg, 0.0095mmol) in toluene/ethanol/water (2/2/1 mL). This afforded 82mg (56.9% yield) after preparative TLC (Silicagel-1000micron) using 5% ammoniated methanol in DCM as eluent.

MS: m/z = 757.2 (M+1).

Step-ii: 2-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(methylsulfonamido)phenyl)piperazin-1-yl)acetamide

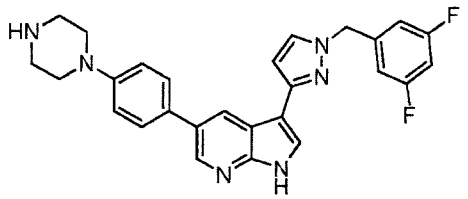
Using similar reaction conditions as described in step-iii of example-1, 2-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(methylsulfonamido)phenyl)piperazin-1-yl)acetamide (80mg, 0.1mmol) was hydrolyzed with lithium hydroxide(13mg, 0.3mmol) in THF/methanol/Water (2/2/1mL) to yield 15 mg (23.6% yield.

^{1}H NMR (DMSO-d_6, 400MHz): δ 8.45-8.40 (m, 3H), 8.3 (s, 1H), 7.94(s, 1H), 7.767-7.761 (d, 1H), 7.615-7.610 (d, 1H), 7.53-7.51 (d, 1H), 7.40-7.33 (m, 2H), 7.24-7.07 (m, 4H), 5.38 (s, 2H), 3.18 (s, 3H), 2.95-2.92 (m, 6H), 2.657 (s, 5H).

MS: m/z = 603.15 (M+1), HPLC: 93.36% in method A.

Example 111

3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine



Step-i: tert-butyl 4-(4-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (intermediate 63) (150mg, 0.276mmol) was coupled with 4-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)piperazine-1-carboxylate (intermediate 40) (139mg, 0.359mmol) using sodium carbonate (82mg, 0.78mmol) and $Pd(PPh_3)_4$ (10mg, 0.013mmol) in DME/water (10/1 ml). This afforded 58mg (28.7% yield) after purification by column (Silica gel 60/120) using 20%ethyl acetate in hexane as eluent. MS: m/z = 725.4 (M+1).

Step-ii: tert-butyl 4-(4-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (55mg, 0.0759mmol) was hydrolyzed by lithium hydroxide (10mg, 0.227mmol) in THF/methanol/water (2/2/1 ml) to yield 15mg (34.6% yield) of the titled compound.

Step-iii: 3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine hydrochloride

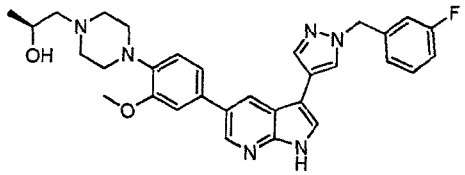
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (27mg, 0.047mmol) was deprotected in methanol/HCl in diethyl ether (2/1ml) to afford 15mg (62.5% yield) of the titled compound.

^{1}H NMR (DMSO-d_6, 300MHz): δ 11.9 (s, 1H), 9.10-9.00 (bs, 2H), 8.598-8.52 (m, 2H), 7.91-7.89 (m, 2H), 7.60-7.57 (d, 2H), 7.17-7.00 (m, 4H), 6.71-6.70 (d, 1H), 5.41 (s, 2H), 3.23 (s, 5H).

MS: m/z = 471.3 (M+1), HPLC: 97.74% in method B.

Example 112

(S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)piperazin-1-yl)propan-2-ol



Step-i: tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (compound of Step-iof example 9) (200mg, 0.380mmol) was coupled with tert-butyl 4-(2-methoxy-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)piperazine-1-carboxylate (175mg, 0.418mmol) using sodium carbonate(121mg, 1.1422mmol) and $Pd(dppf)Cl_2$(14mg, 0.019mmol) in toluene/ethanol/water (4/4/2 mL). This afforded 190mg (68.0% yield) after purification by column (Silica gel 60/120) using 40% ethyl acetate in hexane as eluent. MS: m/z = 737.1 (M+1).

Step-ii: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(3-methoxy-4-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)piperazine-1-carboxylate (190mg, 0.257mmol) was deprotected in methanol/HCl in diethyl ether (5/3ml) to afford 120mg (69.0% yield) of the titled compound. MS: m/z = 637.3 (M+1).

Step-iii (S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-i of example-82A, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(3-methoxy-4-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride (100mg. 0.148mmol) was alkylated using (S)-2-methyloxirane (26mg, 0.445mmol), DIPEA (115mg, 0.891mmol) and ethanol (5mL) to get crude 70mg of the titled compound. MS: m/z = 695.3 (M+1)

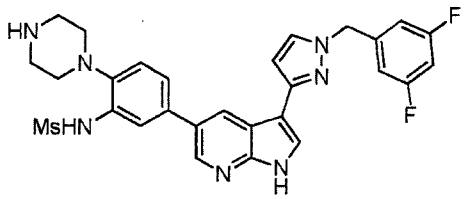
Step-iv: (S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-iii of example-1, (S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)piperazin-1-yl)propan-2-ol (70mg, 0.100mmol) was hydrolyzed with lithium hydroxide(13mg, 0.302mmol) in THF/methanol/water (2/2/1mL) to yield 35 mg (65% yield). ^{1}H NMR (CD_3OD, 400MHz): δ 8.48 (s, 1H), 8.34 (s, 1H), 8.20 (s, 1H), 7.95 (s, 1H), 7.39-7.36 (q, 1H), 7.30-7.28 (m, 2H), 7.13-7.11 (d, 2H), 7.07-7.02 (m, 2H), 5.45 (s, 2H), 4.20-4.30 (m, 1H), 3.99 (s, 3H), 3.60-3.80 (m, 4H), 3.1-3.3 (m, 3H), 1.29-1.28 (d, 3H).

MS: m/z = 541.6 (M+1), HPLC: 98.71% in method A.

Example 113

N-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(piperazin-1-yl)phenyl)methanesulfonamide



Step-i: tert-butyl 4-(4-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(methylsulfonamido)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (intermediate 63) (100mg, 0.184mmol) was coupled with tert-butyl 4-(2-(methylsulfonamido)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)piperazine-1-carboxylate (intermediate 69G) (106mg, 0.22mmol) using sodium carbonate (58mg, 0.552mmol) and $Pd(PPh_3)_4$ (10mg, 0.009mmol) in toluene/ethanol/water (2/2/1 ml). This afforded 60mg (39.9% yield) after preparative TLC (Silicagel-1000micron) using 40%ethyl acetate in hexane as eluent. MS: m/z = 818.6(M+1)

Step-ii: tert-butyl 4-(4-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(methylsulfonamido)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(methylsulfonamido)phenyl)piperazine-1-carboxylate (55mg, 0.067mmol) was hydrolyzed by lithium hydroxide (9mg, 0.201mmol) in THF/methanol/water (2/2/1 ml) to yield 35mg (79.0% yield) of the titled compound after preparative TLC (Silicagel-1000micron) using 60%ethyl acetate in hexane as eluent.

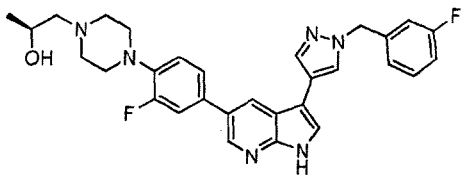
Step-iii: N-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(piperazin-1-yl)phenyl)methanesulfonamide

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(methylsulfonamido)phenyl)piperazine-1-carboxylate (12mg, 0.018mmol) was deprotected in methanol/HCl in diethyl ether (1/2ml) to afford 4mg (26.8% yield) of the titled compound. ^{1}H NMR (CD_3OD, 300MHz): δ 9.32-9.31 (m, 1H), 8.69 (s, 1H), 8.08 (s, 1H), 7.899-7.892 (d, 1H), 7.858-7.850 (d, 1H), 7.58-7.55 (dd, 1H), 7.46-7.44 (d, 1H), 6.93-6.77 (m, 4H), 5.46 (s, 2H), 3.49-3.46 (t, 4H), 3.24-3.20 (m, 4H).

MS: m/z = 564.1(M+1), HPLC: 96.35% in method B.

Example 114

(S)-1-(4-(2-fluoro-4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol



Step-i: tert-butyl 4-(2-fluoro-4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (compound of Step-iof example 9) (160g, 0.304mmol) was coupled with tert-butyl 4-(2-fluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)piperazine-1-carboxylate (intermediate 69) (216mg, 0.530mmol) using sodium carbonate(97mg, 0.912mmol) and $Pd(PPh_3)_2Cl_2$(11mg, 0.015mmol) in DME/water (5/2 mL). This afforded 150mg (68.10% yield) after purification by column (Silica gel 60/120) using 25% ethyl acetate in hexane as eluent. MS: m/z = 725.3 (M+1).

Step-ii: 5-(3-fluoro-4-(piperazin-1-yl)phenyl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(2-fluoro-4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (150mg, 0.206mmol) was deprotected in TFA/DCM (1/1ml) to afford 120mg (93% yield) of the titled compound. MS: m/z = 625.1 (M+1)

Step-iii: (S)-1-(4-(2-fluoro-4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-i of example-82A, 5-(3-fluoro-4-(piperazin-1-yl)phenyl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (120mg. 0.192mmol) was alkylated using (S)-2-methyloxirane (14mg, 0.23mmol), DIPEA (50mg, 0.384mmol) and ethanol (5mL) to get 100mg (76.9% yield) of the titled compound. MS: m/z = 683.2 (M+1)

Step-iv: (S)-1-(4-(2-fluoro-4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol

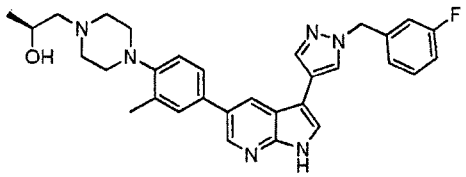
Using similar reaction conditions as described in step-iii of example-1, (S)-1-(4-(2-fluoro-4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol (100mg, 0.146mmol) was hydrolyzed with lithium hydroxide(30mg, 0.73mmol) in THF/methanol/water (2/2/1mL) to yield 45 mg (58.4% yield) of desired product.

^{1}H NMR (CD_3OD, 400MHz): δ 8.54 (s, 2H), 8.27 (s, 1H), 7.98 (s, 1H), 7.74 (s, 1H), 7.60-7.53 (m, 2H), 7.45-7.35 (q, 1H), 7.25-7.21 (t, 1H), 7.14-7.12 (d, 1H), 7.09-7.00 (m, 2H), 5.45 (s, 2H), 4.30-4.20 (m, 1H), 3.76-3.55 (m, 4H), 3.50-3.30 (m, 2H), 3.29-3.15 (m, 4H), 1.29-1.27 (d, 3H).

MS: m/z = 529.6 (M+1), HPLC: 98.28% in method A

Example 115

(S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methylphenyl)piperazin-1-yl)propan-2-ol



Step-i: tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methylphenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (compound of Step-iof example 9) (200g, 0.380mmol) was coupled with tert-butyl 4-(2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)piperazine-1-carboxylate (intermediate 69A) (280mg, 0.694mmol) using sodium carbonate(121mg, 1.142mmol) and $Pd(PPh_3)_2Cl_2$(14mg, 0.019mmol) in DME/water (15/4 mL). This afforded 212mg (77.3% yield) of the titled

compound after purification by column (Silica gel 60/120) using 15% ethyl acetate in hexane as eluent. MS: m/z = 721.3 (M+1).

Step-ii: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(3-methyl-4-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methylphenyl)piperazine-1-carboxylate (210mg, 0.291mmol) was deprotected in methanol/ HCl in dioxane (5/10ml) to afford 172mg (95.5% yield) of the titled compound. MS: m/z = 621.3 (M+1).

Step-iii: (S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methylphenyl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-i of example-82A, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(3-methyl-4-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride (172mg. 0.277mmol) was alkylated using (S)-2-methyloxirane (24mg, 0.416mmol), DIPEA (54mg, 0.416mmol) and ethanol (4mL) to get 183mg (97.3% yield) of the titled compound. MS: m/z = 679.3 (M+1)

Step-iv: (S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methylphenyl)piperazin-1-yl)propan-2-ol

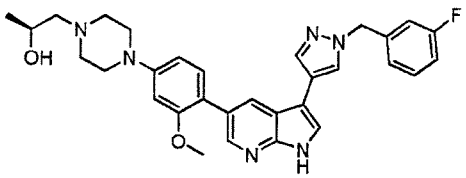
Using similar reaction conditions as described in step-iii of example-1, (S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methylphenyl)piperazin-1-yl)propan-2-ol (183mg, 0.269mmol) was hydrolyzed with lithium hydroxide(57mg, 1.347mmol) in THF/methanol/water (20/10/5mL) to yield 96 mg (55.8% yield) of desired product.

^{1}H NMR (CD_3OD, 300MHz): δ 8.63-8.62 (d, 1H), 8.54 (s, 1H), 8.26 (s, 1H), 7.97 (s, 1H), 7.77 (s, 1H), 7.65-7.63 (d, 1H), 7.60-7.56 (dd, 1H), 7.42-7.32 (q, 1H), 7.26-7.24 (d, 1H), 7.12-7.10 (d, 1H), 7.06-7.00 (m, 2H), 5.44 (s, 2H), 4.30-4.20 (m, 1H), 3.77-3.68 (t, 2H), 2.44 (s, 3H), 1.32-1.23 (m, 3H).

MS: m/z = 525.4 (M+1), HPLC: 90.77% in method B.

Example 116

(S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxyphenyl)piperazin-1-yl)propan-2-ol



Step-i: tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxyphenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 4-(4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxyphenyl)piperazine-1-carboxylate (intermediate 52) (300mg, 0.0435mmol) was coupled with 1-(3-fluorobenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 11) (145mg, 0.479mmol) using sodium carbonate (138mg, 1.307mmol) and $Pd(dppf)Cl_2$ (16mg, 0.0217mmol) in toluene/ethanol/water (6/6/3ml) to afford 220mg (62.0% yield) of titled compound after purification by column (Silica gel 60/120) using 10% ethyl acetate in DCM as eluent. MS: m/z = 737.2 (M+1).

Step-ii: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(2-methoxy-4-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxyphenyl)piperazine-1-carboxylate (220mg, 0.298mmol) was deprotected in methanol/HCl in ether (3/2ml) to afford 180mg (90.0% yield) of the titled compound. MS: m/z = 637.1 (M+1).

Step-iii: (S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxyphenyl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-i of example-82A, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(2-methoxy-4-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride (180mg. 0.267mmol) was alkylated using (S)-2-methyloxirane (47mg, 0.802mmol), DIPEA (207mg, 1.604mmol) and ethanol (5mL) to get 120mg (crude) of the titled compound. MS: m/z = 695.2 (M+1).

Step-iv: (S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxyphenyl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-iii of example-1, (S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxyphenyl)piperazin-1-yl)propan-2-ol (120mg, 0.172mmol) was hydrolyzed with

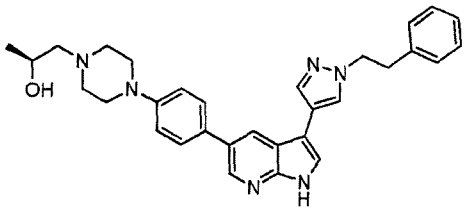
lithium hydroxide(22mg, 0.518mmol) in THF/methanol/water (2/2/1mL) to yield 27 mg (29.0% yield).

^{1}H NMR (CD_3OD, 400MHz): δ 8.55-8.54 (d, 1H), 8.438-8.434 (d, 1H), 8.19 (s, 1H), 7.94 (s, 1H), 7.76 (s, 1H), 7.42-7.38 (m, 2H), 7.14-7.12 (d, 1H), 7.05-7.03 (qd, 2H), 6.80-6.76 (m, 2H), 5.44 (s, 2H), 4.29-4.24 (m, 1H), 3.99-3.96 (m, 2H), 3.86 (s, 3H), 3.75-3.38 (m, 2H), 3.29-3.12 (m, 6H), 1.29-1.28 (d, 3H).

MS: m/z = 541.4 (M+1), HPLC: 92.28% in method A.

Example 117

(S)-1-(4-(4-(3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol



Step-i: tert-butyl 4-(4-(3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 4-(4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (intermediate 41) (200mg, 0.303 mmol) was coupled with 1-phenethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 59) (136mg, 0.455mmol) using sodium carbonate(81mg, 0.759mmol) and $Pd(PPh_3)_2Cl_2$ (11mg, 0.015mmol) in Toluene/ethanol/water (10/2/1ml) to afford 200mg of titled compound after purification by column (Silica gel 6/120) using 50% EtOAc / hexane as eluent. MS: m/z = 703.3(M+1).

Step-ii: 3-(1-phenethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (200mg, 0.284mmol) was deprotected in TFA/DCM (2/5ml) to afford 175mg (86.2% yield) of the titled compound. MS: m/z = 603.2 (M+1)

Step-iii: (S)-1-(4-(4-(3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-i of example-82A, 3-(1-phenethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (175mg.

0.244mmol) was alkylated using (S)-2-methyloxirane (26mg, 0.488mmol), DIPEA (171µL, 0.977mmol) and ethanol (5mL) to get 100mg (62.1% yield) of the titled compound. MS: m/z = 661.7 (M+1)

Step-iv: (S)-1-(4-(4-(3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol

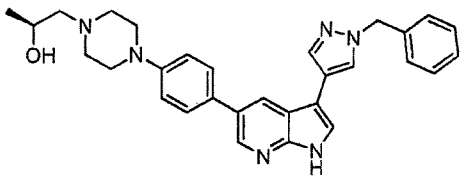
Using similar reaction conditions as described in step-iii of example-1, (S)-1-(4-(4-(3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol (100mg, 0.151mmol) was hydrolyzed with lithium hydroxide(13mg, 0.302mmol) in THF/methanol/water (5./1/1mL) to yield 30 mg (31.9% yield) desired product.

^{1}H NMR (CD_3OD, 400MHz): δ 8.56-8.55 (d, 1H), 8.49-8.48 (d, 1H), 7.90 (s, 1H), 7.84 (s, 1H), 7.73 (s, 1H), 7.68-7.66 (d, 2H), 7.26-7.19 (m, 4H), 7.14-7.10 (m, 3H), 4.47-4.44 (t, 2H), 4.30-4.25 (m, 1H), 3.99-3.94 (m, 2H), 3.78-3.74 (m, 2H), 3.31-3.21 (m, 2H), 3.19-3.12 (m, 4H), 1.29-1.28 (d, 3H).

MS: m/z = 507.60 (M+1), HPLC: 91.80% in method A.

Example 118

(S)-1-(4-(4-(3-(1-benzyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol



Step-i: tert-butyl 4-(4-(3-(1-benzyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 4-(4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (intermediate 41) (200mg, 0.303 mmol) was coupled with 1-benzyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 15) (130mg, 0.455mmol) using sodium carbonate(81mg, 0.759mmol) and $Pd(PPh_3)_2Cl_2$ (11mg, 0.015mmol) in toluene/ethanol/water (10/2/1ml) to afford 200mg (95.6% yield) of titled compound after purification by column (Silica gel 6/120) using 50% EtOAc/hexane as eluent. MS: m/z = 689.3 (M+1).

Step-ii: 3-(1-benzyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (200mg, 0.290mmol) was deprotected in TFA/DCM (2/5ml) to afford 175mg (85.7% yield) of the titled compound. MS: m/z = 589.2 (M+1).

Step-iii: (S)-1-(4-(4-(3-(1-benzyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-i of example-82A, 3-(1-benzyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (175mg. 0.249mmol) was alkylated using (S)-2-methyloxirane (27mg, 0.498mmol), DIPEA (129mg, 0.996mmol) and ethanol (5mL) to get 100mg (62.1% yield) of the titled compound. MS: m/z = 647.2 (M+1).

Step-iv: (S)-1-(4-(4-(3-(1-benzyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol

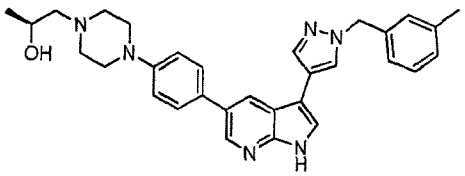
Using similar reaction conditions as described in step-iii of example-1, (S)-1-(4-(4-(3-(1-benzyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol (100mg, 0.154mmol) was hydrolyzed with lithium hydroxide(13mg, 0.309mmol) in THF/methanol/water (5./1/1mL) to yield 31 mg (32.9% yield) of desired product.

^{1}H NMR (CD_3OD, 400MHz): δ 8.605-8.601 (d, 1H), 8.537-8.533 (d, 1H), 8.22 (s, 1H), 7.95 (s, 1H), 7.75 (s, 1H), 7.69-7.67 (d, 2H), 7.38-7.29 (m, 5H), 7.17-7.15 (d, 2H), 5.42 (s, 2H), 4.29-4.25 (m, 1H), 4.00-3.80 (m, 2H), 3.35-3.20 (m, 2H), 3.35 (s, 2H), 3.25-3.20 (m, 2H), 3.19-3.10 (m, 2H), 1.30-1.27 (m, 3H).

MS: m/z = 493.2 (M+1), HPLC: 90.54% in method A.

Example 119

(S)-1-(4-(4-(3-(1-(3-methylbenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol



Step-i: tert-butyl 4-(4-(3-(1-(3-methylbenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 4-(4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (intermediate 41)

(200mg, 0.303 mmol) was coupled with 1-(3-methylbenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 64D) (136mg, 0.455mmol) using sodium carbonate(81mg, 0.759mmol) and $Pd(PPh_3)_2Cl_2$ (11mg, 0.015mmol) in toluene/ethanol/water (10/2/1ml) to afford 200mg (93.8% yield) of titled compound after purification by column (Silica gel 6/120) using 50% EtOAc/hexane as eluent. MS: m/z = 703.2 (M+1).

Step-ii: 3-(1-(3-methylbenzyl)-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(3-methylbenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (200mg, 0.284mmol) was deprotected in TFA/DCM (2/5ml) to afford 175mg (86.2% yield) of the titled compound. MS: m/z = 603.2 (M+1).

Step-iii: (S)-1-(4-(4-(3-(1-(3-methylbenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-i of example-82A, 3-(1-(3-methylbenzyl)-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (175mg. 0.244mmol) was alkylated using (S)-2-methyloxirane (26mg, 0.488mmol), DIPEA (171µL, 0.977mmol) and ethanol (5mL) to get 100mg (62.1% yield) of the titled compound. MS: m/z = 661.2(M+1).

Step-iv: (S)-1-(4-(4-(3-(1-(3-methylbenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol

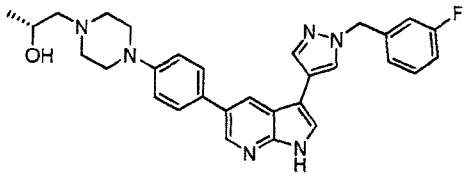
Using similar reaction conditions as described in step-iii of example-1, (S)-1-(4-(4-(3-(1-(3-methylbenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol (100mg, 0.151mmol) was hydrolyzed with lithium hydroxide(13mg, 0.302mmol) in THF/methanol/water (5./1/1mL) to yield 33 mg (35.1% yield) desired product.

^{1}H NMR (CD_3OD, 400MHz): δ 8.667-8.663 (d, 1H), 8.55-8.54 (d, 1H), 8.22 (s, 1H), 7.95 (s, 1H), 7.77 (s, 1H), 7.69-7.66 (d, 2H), 7.25-7.21 (t, 1H), 7.17-7.08 (m, 5H), 5.37 (s, 2H), 4.30-4.20 (m, 1H), 4.00-3.80 (m, 2H), 3.75-3.60 (m, 2H), 3.30-3.10 (m, 6H), 2.31 (s, 3H), 1.29-1.27 (d, 3H).

MS: m/z = 507.65 (M+1), HPLC: 91.66% in method A

Example 120

(R)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol



Step-i: (R)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-i of example-82A, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride (step1 example 103) (150mg. 0.606mmol) was alkylated using (R)-2-methyloxirane (22mg, 0.371mmol), DIPEA (96mg, 0.74mmol) and ethanol (3mL) to get 160mg (97.5% yield) of the titled compound. MS: m/z = 665.3 (M+1).

Step-ii: (R)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol

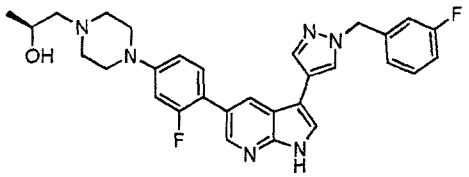
Using similar reaction conditions as described in step-iii of example-1, (R)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol (160mg, 0.24mmol) was hydrolyzed by lithium hydroxide (50mg, 1.2mmol) in THF/methanol/water(3/2/1 ml) to afford 35mg (28.6% yield) of the titled compound.

^{1}H NMR (CD_3OD, 300MHz): δ 8.58-8.57 (d, 1H), 8.53 (s, 1H), 8.24 (s, 1H), 7.969-7.967 (d, 1H), 7.74 (s, 1H), 7.71-7.68 (d, 2H), 7.41-7.35 (m, 1H), 7.19-7.16 (d, 2H), 7.13-7.00 (m, 3H), 5.44 (s, 2H), 4.28-4.21 (m, 1H), 3.90-3.60 (m, 4H), 3.28-3.09 (m, 4H), 1.28-1.26 (d, 3H).

MS: m/z = 511.3 (M+1), HPLC: 95.39% in method B.

Example 121

(S)-1-(4-(3-fluoro-4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol



Step-i: tert-butyl 4-(3-fluoro-4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (compound of Step-iof example 9) (130g, 0.248mmol) was coupled with tert-butyl 4-(3-fluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)piperazine-1-carboxylate (intermediate 69B)

(151mg, 0.372mmol) using sodium carbonate (79mg, 0.714mmol) and $Pd(PPh_3)_2Cl_2$ (9mg, 0.124mmol) in DME/water (5/2 mL). This afforded 150mg (83.3% yield) after purification by column (Silica gel 60/120) using 50%ethyl acetate in hexane as eluent. MS: m/z = 725.3 (M+1).

Step-ii: 5-(2-fluoro-4-(piperazin-1-yl)phenyl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(3-fluoro-4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (150mg, 0.206mmol) was deprotected in TFA/DCM (2/1ml) to afford 120mg (93% yield) of the titled compound. MS: m/z = 625.1 (M+1).

Step-iii: (S)-1-(4-(3-fluoro-4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-i of example-82A, 5-(2-fluoro-4-(piperazin-1-yl)phenyl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (120mg. 0.192mmol) was alkylated using (S)-2-methyloxirane (17mg, 0.288mmol), DIPEA (75mg, 0.576mmol) and ethanol (3mL) to get 100mg (76.3%) of the titled compound. MS: m/z = 683.2 (M+1).

Step-iv: (S)-1-(4-(3-fluoro-4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol

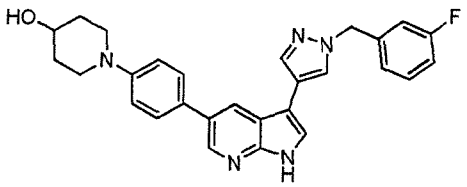
Using similar reaction conditions as described in step-iii of example-1, (S)-1-(4-(3-fluoro-4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol (100mg, 0.146mmol) was hydrolyzed with lithium hydroxide (30mg, 0.73mmol) in THF/methanol/water (3/2/1mL) to yield 45 mg (58.4% yield) of desired product.

^1H NMR (CD_3OD, 300MHz): δ 8.39-8.36 (m, 2H), 8.15 (s, 1H), 7.914-7.912 (d, 1H), 7.67 (s, 1H), 7.59-7.50 (t, 1H), 7.42-4.30 (m, 1H), 7.11-6.92 (m, 5H), 5.42 (s, 2H), 4.30-4.20 (m, 1H), 4.00-3.60 (m, 4H), 3.27-3.13 (m, 4H), 1.27-1.25 (d, 3H).

MS: m/z = 529.3 (M+1), HPLC: 95.98% in method A.

Example 122

1-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidin-4-ol



Step-i: 1-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidin-4-ol

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (compound of Step-iof example 9) (150mg, 0.28mmol) was coupled with 1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)piperidin-4-ol (130mg, 0.428mmol) using sodium carbonate(89mg, 0.84mmol) and Pd(dppf)Cl_2(10mg, 0.14mmol) in DME/water (10/1 mL). This afforded 130mg (crude). MS: m/z = 622.5 (M+1).

Step-ii: 1-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidin-4-ol

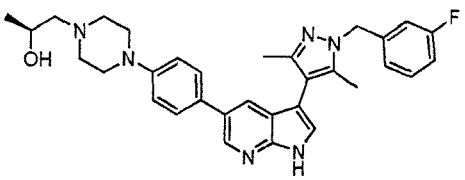
Using similar reaction conditions as described in step-iii of example-1, 1-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidin-4-ol (130mg, 0.209mmol) was hydrolyzed with lithium hydroxide(28mg, 0.62mmol) in THF/methanol/water (3/3/1mL) to yield 35 mg (28.7% yield) of desired product.

^{1}H NMR (CD_3OD, 300MHz): δ 8.56 (s, 2H), 8.24 (s, 1H), 7.97-7.94 (m, 3H), 7.74-7.70 (m, 3H), 7.38-7.35 (m, 1H), 7.12-6.99 (m, 3H), 4.10-4.08 (m, 1H), 3.90-3.84 (m, 2H), 3.64-3.57 (m, 2H), 2.27-2.20 (m, 2H), 2.04-1.97 (m, 2H).

MS: m/z = 468.4(M+1), HPLC: 91.74% in method B

Example 123

(2S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol



Step-i: 3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (example 40 step 1) (232mg, 0.315mmol) was

deprotected in methanol (5ml), HCl in dioxane (5ml). This afforded 198mg (93.8% yield) of the titled compound. MS: m/z = 651.1 (M+1)

Step-ii (2S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-i of example-82A, 3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride (197mg, 0.294mmol), DIPEA (76mg, 0.588mmol) and ethanol (4mL) to get 167mg (82.0%) of the titled compound. MS: m/z = 693.7 (M+1)

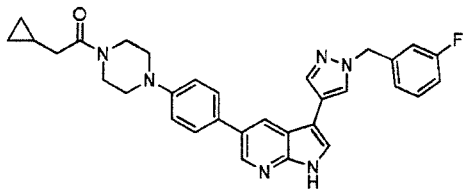
Step-iii: (2S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-iii of example-1, (2S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol (165mg, 0.238mmol) was hydrolyzed with lithium hydroxide(100mg, 2.38mmol) in THF/methanol/water (20/10/5mL) to yield 31 mg (13% yield) of desired product.

^{1}H NMR (CD_3OD, 300MHz): δ 8.43-8.42 (d, 1H), 7.838-7.831 (d, 1H), 7.50-7.57 (d, 2H), 7.40-7.30 (m, 2H), 7.05-6.95 (m, 4H), 6.95-6.84 (m, 1H), 5.35(s, 2H), 4.05-3.95(m, 1H), 3.25-3.22 (t, 4H), 2.80-2.62 (m, 4H), 2.50-2.30 (m, 2H), 2.20 (s, 3H), 2.16 (s, 3H), 1.17-1.15 (d, 3H). MS: m/z = 538.9 (M+1), HPLC: 95.51% in method A

Example 124

2-cyclopropyl-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)ethanone



Step-i: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (example 39 step 1) (1.75g, 2.475mmol) was deprotected in TFA/DCM (2/20 mL). This afforded 950mg (63.3% yield) of the titled compound after purification by column (Silica gel 60/120) using 4% methanol in DCM as eluent. MS: m/z = 608.0 (M+1)

Step-ii: 2-cyclopropyl-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)ethanone

To a solution of 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (75mg, 0.123mmol) and 2-cyclopropylacetic acid hydrochloride (26mg, 0.185mmol) in DMF (2mL) was added HATU (71mg, 0.185mmol), HOBt (25mg, 0.185mmol) and DIPEA (86µL, 0.494mmol) and stirred at RT overnight. Added ice water and extracted with 10% methanol in DCM. Organic layer was washed with brine solution, dried over sodium sulphate and distilled out the solvent to get 60mg (70.58%) yield of the title compound. MS: m/z = 689.2 (M+1).

Step-iii: 2-cyclopropyl-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)ethanone

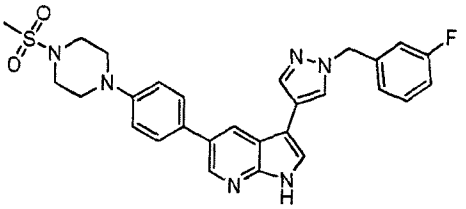
Using similar reaction conditions as described in step-iii of example-1, 2-cyclopropyl-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)ethanone (60mg, 0.087mmol) was hydrolyzed with lithium hydroxide(19mg, 0.435mmol) in THF/methanol/water (/5/1/1mL) to yield 9mg (16.0% yield) of the titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ 8.58-8.57 (d, 1H), 8.51 (s, 1H), 8.26 (s, 1H), 7.97 (s, 1H), 7.75 (s, 1H), 7.65-7.63 (s, 2H), 7.40-7.35 (m, 1H), 7.13-7.11 (d, 3H), 7.07-7.02 (m, 2H), 6.93-6.86 (m, 1H), 6.51-6.46 (dt, 1H), 5.44 (s, 2H), 3.84-3.81 (t, 4H), 3.27 (s, 4H), 2.33-2.17 (m, 2H), 1.13-1.10 (t, 3H).

MS: m/z = 534.9 (M+1), HPLC: 95.19% in method B

Example 125

3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(4-(methylsulfonyl)piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine



Step-i: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(4-(methylsulfonyl)piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step i of intermediate 17, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (product of step 1 of example 124) (75mg, 0.123mmol) was mesylated with

methane sulfonyl chloride (17mg, 0.148mol) using triethylamine(35µL, 0.247mmol) in DCM(5mL) to afford 60mg (71.42% yield) of the titled compound. MS: m/z = 685.1 (M+1)

Step-ii: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(4-(methylsulfonyl)piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine

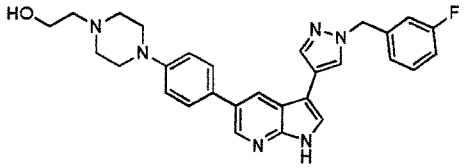
Using similar reaction conditions as described in step-iii of example-1, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(4-(methylsulfonyl)piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (60mg, 0.087mmol) was hydrolyzed with lithium hydroxide(19mg, 0.438mmol) in THF/methanol/water (5/1/1mL) to yield 40mg (70.17% yield) of the titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ 8.63-8.62 (d, 1H), 8.54 (s, 1H), 8.29(s, 1H), 7.99 (s, 1H), 7.77 (s, 1H), 7.69-7.67 (d, 2H), 7.40-7.38 (q, 1H), 7.18-7.02 (m, 5H), 5.46 (s, 2H), 3.40-3.37 (m, 8H), 2.91 (s, 3H).

MS: m/z = 531.0 (M+1), HPLC: 99.35% in method B.

Example 126

2-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)ethanol



Step-i: 2-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)ethanol

To a stirred solution of 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (product of step 1 of example 124) (75mg, 0.123mmol), potassium carbonate (24mg, 0.185mmol) and DMF(5ml) was added 2-bromoethanol (24mg, 0.185mmol) and the mixture stirred at RT for overnight. Then water was added, this was then extracted into 10% methanol in DCM, organic portion was dried over sodium sulfate and concentrated to give 60mg (75% yield) of the titled compound. MS: m/z = 651.2 (M+1).

Step-ii: 2-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)ethanol

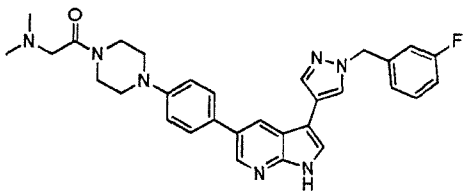
Using similar reaction conditions as described in step-iii of example-1, 2-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)ethanol (60mg, 0.092mmol) was hydrolyzed by lithium hydroxide (20mg, 0.461mmol) in THF/methanol/water(5/1/1 ml) to yield 40mg (13.3% yield) of the titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ 8.747-8.742 (d, 2H), 8.586-8.583 (d, 1H), 8.30 (s, 1H), 7.99 (s, 1H), 7.82 (s, 1H), 7.72-7.69 (d, 2H), 7.38-7.35 (q, 1H), 7.19-7.17 (d, 2H), 7.13-7.11 (d, 1H), 7.08-7.01(m, 2H), 5.44 (s, 2H), 3.99-3.90 (m, 5H), 3.85-3.75 (m, 2H), 3.39-3.33 (m, 3H), 3.30-3.20 (m, 2H).

MS: m/z = 496.9 (M+1), HPLC: 96.51% in method A.

Example 127

2-(dimethylamino)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)ethanone



Step-i: 2-(dimethylamino)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)ethanone

Using similar reaction conditions as described in step-ii of example-124, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (product of step 1 of example 124) (75mg, 0.123mmol) was coupled with 2-(dimethylamino)acetic acid hydrochloride (26mg, 0.185mmol) using HATU (71mg, 0.185mmol), HOBt (25mg, 0.185mmol) and DIPEA (86µL, 0.494mmol) in DMF (2mL) to get 80mg (85.52%) yield of the title compound. MS: m/z = 692.5 (M+1).

Step-ii: 2-(dimethylamino)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)ethanone

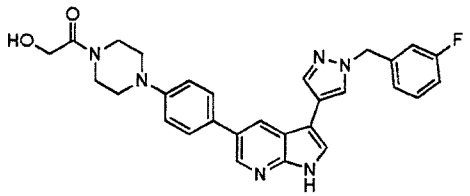
Using similar reaction conditions as described in step-iii of example-1, 2-(dimethylamino)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)ethanone (80mg, 0.115mmol) was hydrolyzed with lithium hydroxide(25mg, 0.578mmol) in THF/methanol/water (5/1/1mL) to yield 60mg (80.0% yield) of the titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ 8.826-8.822(d, 1H), 8.605-8.601 (d, 1H), 8.32 (s, 1H), 8.00 (s, 1H), 7.86 (s, 1H), 7.70-7.68 (d, 2H), 7.40-7.35 (q, 1H), 7.17-7.12 (m, 3H), 7.07-7.02 (m, 2H), 5.45 (s, 2H), 4.35 (s, 2H), 3.84-3.81 (t, 2H), 3.63-3.60 (t, 2H), 3.36-3.33 (t, 4H), 2.99 (s, 6H).

MS: m/z = 537.9 (M+1), HPLC: 91.53% in method A.

Example 128

1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)-2-hydroxyethanone



Step-i: 1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)-2-hydroxyethanone

Using similar reaction conditions as described in step-ii of example-124, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (product of step 1 of example 124) (75mg, 0.123mmol) was coupled with 2-hydroxyacetic acid (14mg, 0.185mmol) using HATU (71mg, 0.185mmol), HOBt (25mg, 0.185mmol) and DIPEA (86µL, 0.494mmol) in DMF (2mL) to get 60mg (73.1%) yield of the title compound. MS: m/z = 665.3 (M+1).

Step-ii: 1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)-2-hydroxyethanone

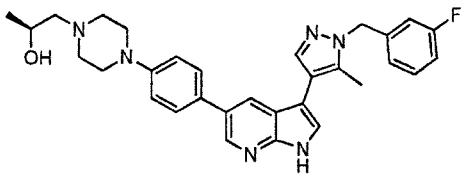
Using similar reaction conditions as described in step-iii of example-1, 1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)-2-hydroxyethanone (60mg, 0.090mmol) was hydrolyzed with lithium hydroxide(19mg, 0.451mmol) in THF/methanol/water (5/1/1mL) to yield 20mg (35.7 % yield) of the titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ 8.822-8.820 (d, 1H), 8.59 (s, 1H), 8.33 (s, 1H), 8.01 (s, 1H), 7.86 (s, 1H), 7.70-7.68 (d, 2H), 7.41-7.35 (q, 1H), 7.17-7.02 (m, 5H), 5.45 (s, 2H), 4.33 (s, 2H), 3.82-3.79 (t, 2H), 3.62 (s, 2H).

MS: m/ z= 510.8 (M+1), HPLC: 90.93% in method A.

Example 129

(S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-5-methyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol



Step-i: 3-(1-(3-fluorobenzyl)-5-methyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-5-methyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (example 44, step1) (290mg, 0.40mmol) was deprotected with HCl in ether (5ml). This afforded 240mg (96.1% yield) of the titled compound. MS: m/z = 621.2 (M+1).

Step-ii: (S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-5-methyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-i of example-82A, 3-(1-(3-fluorobenzyl)-5-methyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride (230mg, 0.349mmol) was alkylated using (S)-2-methyloxirane (41mg, 0.69mmol),, DIPEA (136mg, 1.0mmol) and ethanol (5mL) to get 200mg (crude) of the titled compound.

Step-iii: (S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-5-methyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol

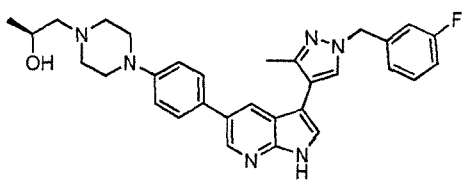
Using similar reaction conditions as described in step-iii of example-1, (S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-5-methyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol (200mg, 0.29mmol) was hydrolyzed with lithium hydroxide(37mg, 0.88mmol) in THF/methanol/water (6/4/2mL) to yield 10 mg (6.4% yield) after purification by preparative HPLC along with one more isomer example 130.

^{1}H NMR ($CDCl_3$, 300MHz): δ 9.12 (s, 1H), 8.548-8.542 (d, 1H), 8.02-8.01 (d, 1H), 7.59 (s, 1H), 7.54-7.51 (d, 2H), 7.36-7.29 (m, 2H), 7.26-6.91 (m, 5H), 5.32 (s, 2H), 3.95-3.90 (m, 1H), 3.30-3.23 (m, 4H), 2.90-2.86 (m, 2H), 2.62-2.60 (m, 2H), 2.43-2.31 (m, 5H), 1.19-1.17 (d, 3H).

MS: m/z = 524.9 (M+1), HPLC: 95.68% in method A.

Example 130

(S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-3-methyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol



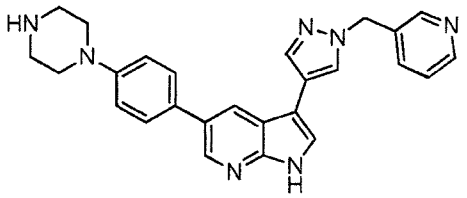
Yield 4mg (2.5%)

^{1}H NMR ($CDCl_3$, 300MHz): δ 9.25 (s, 1H), 8.56-8.55 (d, 1H), 8.09-8.08 (d, 1H), 7.77 (s, 1H), 7.60-7.51 (m, 2H), 7.35-7.28 (m, 2H), 7.04-6.84 (m, 5H), 5.38 (s, 2H), 4.00-3.85 (m, 1H), 3.29-3.27 (m, 4H), 2.90-2.86 (m, 2H), 2.62-2.58(m, 2H), 2.41-2.35 (m, 2H), 2.30 (s, 3H), 1.19-1.17 (d, 3H).

MS: m/z = 525.3 (M+1), HPLC: 95.37% in method A.

Example 131

5-(4-(piperazin-1-yl)phenyl)-3-(1-(pyridin-3-ylmethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine



Step-i: tert-butyl 4-(4-(3-(1-(pyridin-3-ylmethyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 4-(4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (intermediate 41) (150mg, 0.22mmol) was coupled with 3-((4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-yl)methyl)pyridine (intermediate 64) (130mg, 0.45mmol) using sodium carbonate(70mg, 0.66mmol) and $Pd(PPh_3)_2Cl_2$ (7.7mg, 0.011mmol) in toluene/ethanol/water (10/10/2 ml) to give 110mg (70% yield) of the titled compound after purification by column (Silica gel 60/120) using 35% ethyl acetate in hexane as eluent.

Step-ii: tert-butyl 4-(4-(3-(1-(pyridin-3-ylmethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(3-(1-(pyridin-3-ylmethyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (130mg, 0.188mmol) was hydrolyzed with lithium hydroxide(24mg, 0.565mmol) in THF/methanol/water (2/2/2mL) to yield 100 mg (crude) of the titled compound. MS: m/z = 536.7(M+1).

Step-iii: 5-(4-(piperazin-1-yl)phenyl)-3-(1-(pyridin-3-ylmethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(pyridin-3-ylmethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-

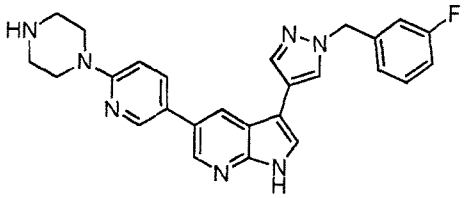
carboxylate (100mg, 0.186mmol) was deprotected with HCl in ether/methanol (2/3ml). This afforded 9mg (11.0% yield) of the titled compound.

^{1}H NMR (CD_3OD, 300MHz): δ 8.54 (s, 1H), 8.34-8.28(d, 1H), 8.50-8.49 (d, 1H), 8.43-8.42 (d, 1H), 8.307-8.300 (d, 1H), 8.23 (s, 1H), 7.93 (s, 1H), 7.79-7.77 (d, 1H), 7.64-7.61 (m, 3H), 7.45-7.41 (m, 1H), 7.14-7.11 (m, 2H), 5.49 (s, 2H), 3.38-3.31 (m, 4H), 3.30-3.23 (m, 4H).

MS: m/z = 436.2 (M+1), HPLC: 97.13% in method A.

Example 132

3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine



Step-i: tert-butyl 4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (compound of Step-iof example 9) (150mg, 0.286mmol) was coupled with tert-butyl 4-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-2-yl)piperazine-1-carboxylate (intermediate 69C) (167mg, 0.429mmol) in sodium carbonate(76mg, 0.715mmol), $Pd(PPh_3)_2Cl_2$ (10mg, 0.014mmol), DME/water (5/1 mL). This afforded 140mg (69.0% yield) after purification by column chromatography (60-120 silica gel) using 2% methanol in DCM as eluent. MS: m/z = 708.3 (M+1).

Step-ii: tert-butyl 4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate (140mg, 0.197mmol) was hydrolyzed with lithium hydroxide(17mg, 0.395mmol) in THF/methanol/water (5/2/1mL) to yield 70 mg (63.9% yield) after purification by column chromatography (60-120 silica gel) using 2% methanol in DCM as eluent. MS: m/z = 554.4(M+1).

Step-iii: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine

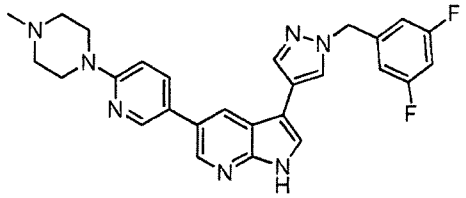
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate (70mg, 0.126mmol) was deprotected with TFA/DCM (1/5ml). This afforded 17.5mg (24.3% yield) of the titled compound.

^{1}H NMR (CD_3OD, 300MHz): δ 8.53 (s, 3H), 8.23 (s, 1H), 8.16-8.12 (dd, 1H), 7.97 (s, 1H), 7.73 (s, 1H), 7.40-7.30 (m, 1H), 7.20-7.10 (m, 2H), 7.09-6.95 (m, 1H), 5.43 (s, 2H), 3.92-2.89 (m, 4H), 3.40-3.36 (m, 4H).

MS: m/z = 464.2 (M+1), HPLC: 97.79% in method A.

Example 133

3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine



Step-i: tert-butyl 4-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (STEP 1 example 71) (1g, 1.515mmol) was coupled with tert-butyl 4-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-2-yl)piperazine-1-carboxylate (intermediate 69C) (581mg, 1.818 mmol) using sodium carbonate (481mg, 4.545mmol) and $Pd(PPh_3)_2Cl_2$ (53mg, 0.075mmol) in toluene/ethanol/water (10/15/2 ml). This afforded 1.12g (100% yield) of the titled compound after purification by column (Silica gel 60/120) using 40% ethyl acetate in hexane as eluent.

MS: m/z = 726.3 (M+1)

Step-ii: 3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate (1.12g, 1.544mmol) was deprotected in TFA/DCM (10/5ml). This afforded 600mg (64.8% yield) of the titled compound. MS: m/z= 625.8(M+1)

Step-iii: 3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

To the solution of 3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (100mg, 0.16mmol) and paraformaldehyde (10mg, 0.32mmol) in dichloroethane was added $Na(OAc)_3BH$ (68mg, 0.32mmol) and stirred at RT overnight. Distilled off the solvent to get 95mg (95.0% yield) of the titled compound after purification by column (Silica gel 60/120) using 5% methanol in dichloromethane as eluent.

MS: m/z = 640.2 (M+1)

Step-iv: 3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine

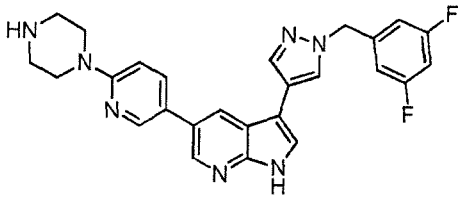
Using similar reaction conditions as described in step-iii of example-1, 3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (95mg, 0.148mmol) was hydrolyzed with lithium hydroxide(17mg, 0.399mmol) in THF/methanol/water (2/2/1mL) to yield 30 mg (81.0% yield) of the titled compound.

^1H NMR ($CDCl_3$, 300MHz): δ 9.14 (s, 1H), 8.49-8.46 (dd, 2H), 8.11 (s, 1H), 7.87 (s, 1H), 7.77-7.71 (m, 2H), 7.449-7.443 (d, 1H), 6.80-6.76 (m, 3H), 5.36 (s, 2H), 3.65-3.62 (m, 4H), 2.58-2.55 (m, 4H), 2.37 (s, 3H).

MS: m/z = 486.1 (M+1), HPLC: 93.44% in method B.

Example 134

3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine



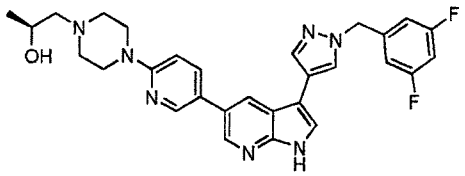
Using similar reaction conditions as described in step-iii of example-1, 3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (step 2 compound of example 133) (50mg, 0.079mmol) was hydrolyzed with lithium hydroxide(32mg, 0.743mmol) in THF/methanol/water (2/2/1mL) to yield 46 mg (63.8% yield) of the titled compound.

^1H NMR (CD_3OD, 300MHz): δ 8.58 (s, 1H), 8.537-8.530 (d, 2H), 8.28 (s, 1H), 8.19-8.16 (dd, 1H), 8.00 (s, 1H), 7.77 (s, 1H), 7.22-7.19 (d, 1H), 6.88-6.85 (m, 3H), 5.43 (s, 2H), 3.94-3.90 (t, 4H), 3.41-3.37 (t, 4H).

MS: m/z = 472.3 (M+1), HPLC: 95.01% in method A.

Example 135

(S)-1-(4-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol



Step-i: (S)-1-(4-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-i of example-82A, 3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (step 2 compound of example 133) (100mg, 0.16mmol) was alkylated using (S)-2-methyloxirane (14mg, 0.24mmol), DIPEA (31mg, 0.24mmol) and ethanol (2mL) to get 90mg (82.5%) of the titled compound after purification by column (Silica gel 60/120) using 5% methanol in dichloromethane as eluent. MS: m/z = 684.2 (M+1).

Step-ii: (S)-1-(4-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol

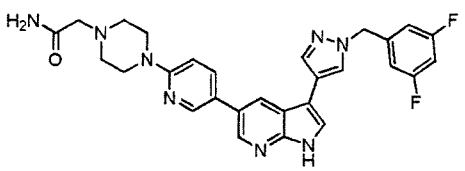
Using similar reaction conditions as described in step-iii of example-1, (S)-1-(4-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol (90mg, 0.131mmol) was hydrolyzed with lithium hydroxide(28mg, 0.658mmol) in THF/methanol/water (2/2/1mL) to yield 70 mg (100% yield) of desired product.

^{1}H NMR (CD_3OD, 300MHz): δ 8.74-8.73 (d, 1H), 8.61-8.56 (m, 2H), 8.31-8.25 (m, 2H), 8.02 (s, 1H), 7.83 (s, 1H), 7.30-7.27 (d, 1H), 7.10-6.85 (m, 2H), 5.44 (s, 2H), 4.30-4.20 (m, 1H), 3.60-3.50 (bs, 4H), 3.23-3.15 (m, 2H), 1.27-1.25 (d, 3H).

MS: m/z = 530.2 (M+1), HPLC: 97.51% in method A.

Example 136

2-(4-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)acetamide



Step-i: 2-(4-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)acetamide

Using similar reaction conditions as described in step-i of example-82A, 3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (step 2 compound of example 133) (100mg, 0.16mmol) was alkylated using 2-chloroacetamide (30mg, 0.32mmol), sodium bicarbonate (40mg, 0.48mmol) and ethanol/acetone (3/3mL) to get 100mg (91.7%) of the titled compound after purification by column (Silica gel 60/120) using 5% methanol in dichloromethane as eluent. MS: m/z= 683.3 (M+1).

Step-ii: 2-(4-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)acetamide

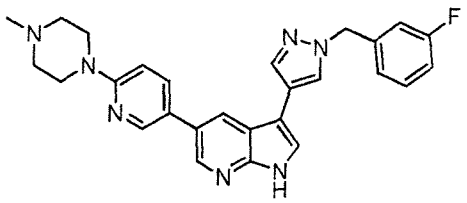
Using similar reaction conditions as described in step-iii of example-1, 2-(4-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)acetamide (100mg, 0.146mmol) was hydrolyzed with lithium hydroxide(31mg, 0.733mmol) in THF/methanol/water (2/2/1mL) to yield 28 mg (36.3% yield) of desired product.

^{1}H NMR (CD_3OD, 300MHz): δ 8.53-8.48 (m, 3H), 8.259-8.257 (d, 1H), 8.15-8.05 (dd, 1H), 7.988-7.986 (d, 1H), 7.72 (s, 1H), 7.19-7.10 (d, 1H), 6.90-6.82 (m, 3H), 5.43 (s, 2H), 4.05-3.90 (m, 6H), 3.51-3.49 (t, 4H).

MS: m/z= 529.2(M+1), HPLC: 98.61% in method A.

Example 137

3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine



Step-i: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate(step 1 of example 132) (700mg, 0.9889mmol) was deprotected

with TFA/DCM (5/20ml). This afforded 400mg (66.6% yield) of the titled compound. MS: m/z = 608.1 (M+1)

Step-ii: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-iii of example-133, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (100mg, 0.164mmol) was methylated using paraformaldehyde (15mg, 0.494mmol) and $Na(OAc)_3BH$ (105mg, 0.494mmol) in dichloroethane (5mL) to afford 90mg (88.2%yield) of the titled compound after purification by column (Silica gel 60/120) using 5% methanol in dichloromethane as eluent. MS: m/z = 622.1 (M+1).

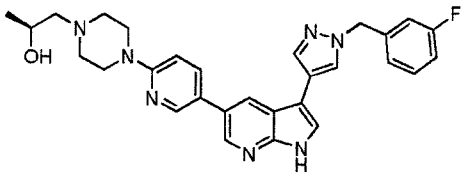
Step-iii: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-iii of example-1, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (90mg, 0.144mmol) was hydrolyzed with lithium hydroxide(12mg, 0.289mmol) in THF/methanol/water (5/2/1mL) to yield 40 mg (47.6% yield) of the titled compound.

^1H NMR (CD_3OD, 400MHz): δ 8.566-8.560 (d, 1H), 8.49-8.45 (m, 2H), 8.24 (s, 1H), 8.09-8.06 (dd,1 H), 7.97 (s, 1H), 7.71 (s, 1H), 7.40-7.38 (q, 1H), 7.14-7.12 (d, 2H), 7.10-7.00 (m, 2H), 5.45 (s, 2H), 3.00 (s, 3H). MS: m/z = 468.2 (M+1), HPLC: 99.02% in method B

Example 138

(S)-1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol



Step-i: (S)-1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-i of example-82A, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (step 1 compound of example 137) (100mg, 0.164mmol) was alkylated using (S)-2-methyloxirane (18mg, 0.329mmol),, DIPEA (86mg, 0.494mmol) and ethanol (5mL) to get 90mg (81.8%) of the titled compound after purification by column (Silica gel 60/120) using 5% methanol in dichloromethane as eluent. MS: m/z = 666.2 (M+1).

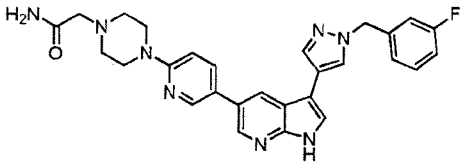
Step-ii: (S)-1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-iii of example-1, (S)-1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol (90mg, 0.135mmol) was hydrolyzed with lithium hydroxide(14mg, 0.270mmol) in THF/methanol/water (5/2/1mL) to yield 52 mg (63.0% yield) of desired product.

^{1}H NMR (CD_3OD, 400MHz): δ 8.56-8.55 (d, 1H), 8.485-8.481 (d, 1H), 8.44-8.43 (d, 1H), 8.24 (s, 1H), 8.09-8.06 (dd, 1H), 7.98 (s, 1H), 7.71 (s, 1H), 7.40-7.38 (q, 1H), 7.13-7.11 (m, 2H), 7.10-7.00 (m, 2H), 5.45 (s, 2H), 4.70-4.40 (bs, 2H), 4.30-4.20 (m, 1H), 3.90-3.50 (bs, 4H), 3.17-3.11 (m, 2H), 1.30-1.27 (m, 3H). MS: m/z = 512.3 (M+1), HPLC: 98.72% in method A.

Example 139

2-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)acetamide



Step-i: 2-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)acetamide

Using similar reaction conditions as described in step-i of example-82A, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (step 1 compound of example 137) (100mg, 0.164mmol) was alkylated using 2-chloroacetamide (23mg, 0.247mmol), sodium bicarbonate (42mg, 0.494mmol) and ethanol/acetone (3/3mL) to get 80mg (73.0%) of the titled compound after purification by column (Silica gel 60/120) chromatography using 5% methanol in dichloromethane as eluent.

^{1}H NMR ($CDCl_3$, 300MHz): δ 8.60-8.06 (d, 1H), 8.40-8.39 (d, 1H), 8.11-8.08 (d, 2H), 8.00-7.99 (d, 2H), 7.85 (s, 1H), 7.80 (s, 1H), 7.71-7.67 (m, 2H), 7.37-7.33 (m, 2H), 7.06-6.90 (m, 3H), 7.76-7.73 (d, 1H), 5.45 (s, 1H), 5.37 (s, 2H), 3.65-3.62 (t, 4H), 3.09 (s, 1H), 2.71-2.68 (t, 4H), 2.37 (s, 3H).

Step-ii: 2-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)acetamide

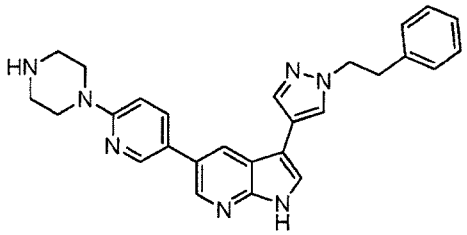
Using similar reaction conditions as described in step-iii of example-1, 2-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)acetamide (80mg, 0.120mmol) was hydrolyzed with lithium hydroxide(11mg, 0.240mmol) in THF/methanol/water (5/2/1mL) to yield 17 mg (27.8% yield) of desired product.

^{1}H NMR (DMSO-d_6, 400MHz): δ 8.57-8.56 (d, 1H), 8.49-8.47 (m, 2H), 8.348-8.343 (d, 1H), 8.00-7.97 (m, 2H), 7.77-7.76 (d, 1H), 7.43-7.38 (m, 1H), 7.28 (s, 1H), 7.19-7.08 (m, 3H), 6.97-6.95 (d, 1H), 5.41 (s, 2H), 3.60-3.59 (t, 4H), 2.93 (s, 2H), 2.56-2.50 (t, 4H).

MS: m/z = 511.3(M+1), HPLC: 90.86% in method A.

Example 140

3-(1-phenethyl-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine



Step-i: tert-butyl 4-(5-(3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 4-(5-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate (Intermediate 66K) (150mg, 0.227 mmol) was coupled with 1-phenethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (Intermediate 59) (101 mg, 0.34 mmol) using sodium carbonate (73 mg, 0.68 mmol) and $Pd(PPh_3)_2Cl_2$(10 mg, 0.011 mmol) in toluene/ethanol/water (3/5/1 ml) to afford 140 mg (88.0% yield) of the pure product after column purification using 5% methanol in dichloromethane as eluent. MS: m/z = 704.3 (M+1).

Step-ii: 3-(1-phenethyl-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(5-(3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate (140mg, 0.199mmol) was deprotected with TFA/DCM (2/1ml). This afforded 110mg (91.6% yield) of the titled compound. MS: m/z = 604.1 (M+1)

Step-iii: 3-(1-phenethyl-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine

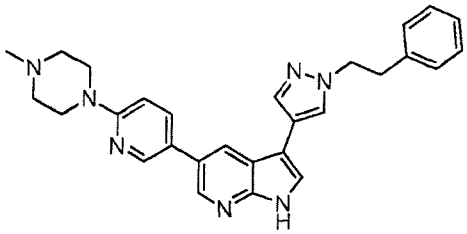
Using similar reaction conditions as described in step-iii of example-1, 3-(1-phenethyl-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (55mg, 0.09mmol) was hydrolyzed with lithium hydroxide(20mg, 0.45mmol) in THF/methanol/water (2/1/1mL) to yield 40 mg (100% yield) of desired product.

^{1}H NMR (CD_3OD, 300MHz): δ 8.51-8.50 (d, 1H), 8.43(s, 1H), 8.25-8.15 (dd, 1H), 7.91-7.86 (d, 2H), 7.68 (s, 1H), 7.27-7.21 (m, 3H), 7.14-7.12 (m, 3H), 4.50-4.40 (t, 2H), 3.97-3.94 (t, 4H), 3.43-3.34 (t, 4H), 3.20-3.18 (t, 2H).

MS: m/z = 450.4(M+1), HPLC: 92.83% in method A.

Example 141

5-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)-3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine



Step-i: 5-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)-3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-iii of example-133, 3-(1-phenethyl-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (product of step 2 of example 140) (50mg, 0.082mmol) was methylated using paraformaldehyde (8mg, 0.24mmol) and $Na(OAc)_3BH$ (35mg, 0.164mmol) in dichloroethane (10mL) to afford 50mg (99%yield) of the titled compound. MS: m/z = 618.2 (M+1).

Step-ii: 5-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)-3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine

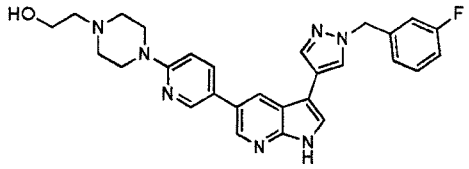
Using similar reaction conditions as described in step-iii of example-1, 5-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)-3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (50mg, 0.088mmol) was hydrolyzed with lithium hydroxide(18mg, 0.44mmol) in THF/methanol/water (2/2/1mL) to yield 40 mg (98.5% yield) of the titled compound.

^{1}H NMR (CD_3OD, 300MHz): δ 8.55-8.50 (d, 2H), 8.40 (s, 1H), 8.19-8.10 (dd, 1H), 7.89-7.84 (d, 2H), 7.68 (s, 1H), 7.24-7.21 (m, 3H), 7.15-7.11 (m, 3H), 4.50-4.50 (t, 2H), 3.20-3.10 (t, 2H), 2.98 (s, 3H).

MS: m/z = 464.2 (M+1), HPLC: 93.96% in method A.

Example 142

2-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)ethanol



Step-i: 2-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)ethanol

Using similar reaction conditions as described in step-i of example-126, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (step 1 compound of example 137) (150mg, 0.297mmol) was alkylated using 2-bromoethanol (62mg, 0.494mmol) and potassium carbonate (69mg, 0.494mmol) in DMF(1ml) to afford 85mg (52.7% yield) of the titled compound after purification by column (Silica gel 60/120) chromatography using 5% methanol in dichloromethane as eluent. MS: m/z = 652.2 (M+1)

Step-ii: 2-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)ethanol

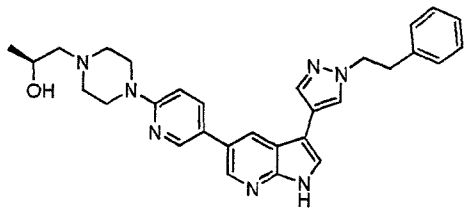
Using similar reaction conditions as described in step-iii of example-1, 2-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)ethanol (85mg, 0.130mmol) was hydrolyzed by lithium hydroxide(11mg, 0.261mmol) in THF/methanol/water (5/2/1 ml) to yield 15mg (23.0% yield) of the titled compound.

^{1}H NMR ($CDCl_3$, 400MHz): δ 9.75 (s, 1H), 8.52-8.49 (dd, 2H), 8.149-8.144 (d, 1H), 7.88 (s, 1H), 7.80-7.77 (dd, 1H), 7.72 (s, 1H), 7.478-7.473 (d, 1H), 7.36-7.34 (q, 1H), 7.09-6.97 (m, 3H), 6.81-6.78 (d, 1H), 5.40 (s, 2H), 3.73-3.70 (t, 2H), 3.66-3.64 (t, 4H), 2.95-2.85 (bs, 1H), 2.70-2.64 (m, 6H).

MS: m/z = 498.3 (M+1), HPLC: 96.68% in method A.

Example 143

(S)-1-(4-(5-(3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol



Step-i: (S)-1-(4-(5-(3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-i of example-82A, 3-(1-phenethyl-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (product of step 2 of example 140) (85mg, 0.14mmol) was alkylated using (S)-2-methyloxirane (10mg, 0.169mmol), DIPEA (22mg, 0.169mmol) and ethanol (3mL) to get 80mg (86%) of the titled compound. MS: m/z = 662.3 (M+1).

Step-ii: (S)-1-(4-(5-(3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol

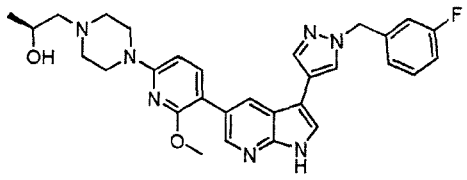
Using similar reaction conditions as described in step-iii of example-1, (S)-1-(4-(5-(3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol (80mg, 0.12mmol) was hydrolyzed with lithium hydroxide(25mg, 0.6mmol) in THF/methanol/water (2/2/1mL) to yield 50 mg (83.3% yield) of desired product.

^{1}H NMR (CD_3OD, 300MHz): δ 8.53-8.52 (d, 2H), 8.36-8.35 (d, 1H), 8.12-8.08 (dd, 1H), 7.896-7.893 (d, 1H), 7.818-7.816 (d, 1H), 7.67 (s, 1H), 7.26-7.20 (m, 3H), 7.17-7.12 (m, 3H), 4.47-4.43 (d, 2H), 4.30-4.20 (t, 1H), 3.60-3.40 (bs, 4H), 3.25-3.10 (m, 4H), 1.27-1.25 (d, 3H).

MS: m/z = 408.6 (M+1), HPLC: 93.50% in method A

Example 144

(S)-1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-6-methoxypyridin-2-yl)piperazin-1-yl)propan-2-ol



Step-i: tert-butyl 4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-6-methoxypyridin-2-yl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 4-(5-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-6-methoxypyridin-2-yl)piperazine-1-carboxylate (Intermediate 66L) (75mg, 0.108mmol) was coupled with 1-(3-fluorobenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 11) (65mg, 0.217mmol) using sodium carbonate(35mg, 0.326mmol) and $Pd(dppf)Cl_2$ (4mg, 0.005mmol) in toluene/ethanol/water (20/10/5 mL). This afforded 68mg (85% yield) of the titled compound.

Step-ii: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(2-methoxy-6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-6-methoxypyridin-2-yl)piperazine-1-carboxylate (67mg, 0.090mmol) was deprotected in methanol/HCl in dioxane (2/5ml) to afford 52mg (89% yield) of the titled compound. MS: m/z = 638.2 (M+1).

Step-iii: (S)-1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-6-methoxypyridin-2-yl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-i of example-82A, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(2-methoxy-6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (52mg. 0.081mmol) was alkylated using (S)-2-methyloxirane (8mg, 0.137mmol), DIPEA (18mg, 0.137mmol) and ethanol (5mL) to get 61mg (95.3%) of the titled compound.

Step-iv: (S)-1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-6-methoxypyridin-2-yl)piperazin-1-yl)propan-2-ol

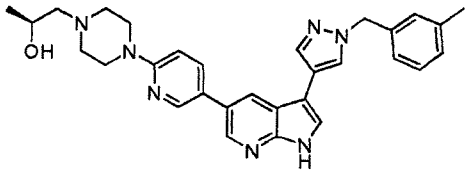
Using similar reaction conditions as described in step-iii of example-1, (S)-1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-6-methoxypyridin-2-yl)piperazin-1-yl)propan-2-ol (60mg, 0.086mmol) was hydrolyzed with lithium hydroxide (36mg, 0.862mmol) in THF/methanol/water (10/5/2mL) to yield 14 mg (25% yield) of desired product.

^1H NMR (CD_3OD, 400MHz): δ 8.615-8.612 (d, 1H), 8.51 (s, 1H), 8.20 (s, 1H), 7.95 (s, 1H), 7.82-7.80 (d, 1H), 7.76 (s, 1H), 7.41-7.36 (m, 1H), 7.14-7.12 (d, 1H), 7.08-7.01 (m, 2H), 6.61-6.59 (d, 1H), 5.44 (s, 2H), 4.52 (s, 2H), 4.29-4.24 (m, 1H), 3.96 (s, 3H), 3.74 (s, 2H), 3.36 (s, 2H), 3.26-3.11 (m, 4H), 1.28-1.27 (d, 2H).

MS: m/z = 542.2 (M+1), HPLC: 96.86% in method B.

Example 145

(S)-1-(4-(5-(3-(1-(3-methylbenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol



Step-i: tert-butyl 4-(5-(3-(1-(3-methylbenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 4-(5-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate (Intermediate 66K) (200mg, 0.303 mmol) was coupled with 1-(3-methylbenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 64D) (99mg, 0.333mmol) using sodium carbonate(96mg, 0.909mmol) and $Pd(PPh_3)_2Cl_2$ (11mg, 0.015mmol) in toluene/ethanol/water (2/2/0.5ml) to afford 200mg (94% yield) of titled compound after purification by column (Silica gel 60/120) using 0.5% methanol in DCM as eluent. MS: m/z = 704.3 (M+1).

Step-ii: 3-(1-(3-methylbenzyl)-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(5-(3-(1-(3-methylbenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate (200mg, 0.284mmol) was deprotected in HCl in ether/methanol (2/3ml) to afford 120mg (66% yield) of the titled compound. MS: m/z = 605.2(M+1).

Step-iii: (S)-1-(4-(5-(3-(1-(3-methylbenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol

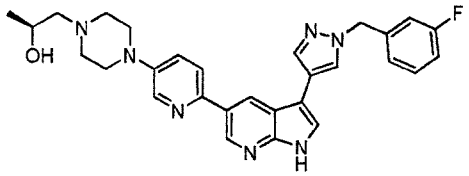
Using similar reaction conditions as described in step-i of example-82A, 3-(1-(3-methylbenzyl)-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride (120mg. 0.187mmol) was alkylated using (S)-2-methyloxirane (33mg, 0.562mmol), DIPEA (145mg, 1.124mmol) and ethanol (5mL) to get 100mg (crude) of the titled compound. MS: m/z= 662.3(M+1).

Step-iv: (S)-1-(4-(5-(3-(1-(3-methylbenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-iii of example-1, (S)-1-(4-(5-(3-(1-(3-methylbenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol (100mg, 0.151mmol) was hydrolyzed with lithium hydroxide (19mg, 0.453mmol) in THF/methanol/water (2/2/0.5mL) to yield 25 mg (21% yield) of desired product.

^{1}H NMR (CD_3OD, 400MHz): δ 8.559-8.553 (d, 1H), 8.479-8.474 (d, 1H), 8.425-8.420 (d, 1H), 8.17 (s, 1H), 8.08-8.06 (dd, 1H), 7.94(s, 1H), 7.69 (s, 1H), 7.28-7.22 (t, 1H), 7.15-7.10 (m, 4H), 5.39 (s, 2H), 4.25-4.32 (m, 1H), 3.10-3.30 (m, 2H), 2.34 (s, 3H), 1.28-1.27 (d, 3H). MS: m/z = 508.2 (M+1), HPLC: 98.90% in method A.

Example 146



Step-i: tert-butyl 4-(6-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-3-yl)piperazine-1-carboxylate

Using the same reaction conditions as described in step-ii of example-1, tert-butyl 4-(6-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-3-yl)piperazine-1-carboxylate (Intermediate 66M) (1.0g, 1.515mmol) was coupled with 1-(3-fluorobenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 11) (596mg, 1.969mmol) using sodium carbonate(402mg, 3.787mmol) and $Pd(PPh_3)_2Cl_2$ (54mg, 0.075mmol) in toluene/ ethanol/water (10/3/3 mL) to afford 800mg (74.6% yield) of the titled compound after purification by column (Silica gel 60/120) using 1.5% methanol in DCM as eluent. MS: m/z = 708.3 (M+1).

Step-ii: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(5-(piperazin-1-yl)pyridin-2-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(6-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-3-yl)piperazine-1-carboxylate (800mg, 1.130mmol) was deprotected in TFA/DCM (3/10ml) to afford 600mg (87.4% yield) of the titled compound. MS: m/z = 608.2(M+1).

Step-iii: (S)-1-(4-(6-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-3-yl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-i of example-82A, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(5-(piperazin-1-yl)pyridin-2-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (100mg. 0.164mmol) was alkylated using (S)-2-methyloxirane (18mg, 0.329mmol), DIPEA (58μL, 0.329mmol) and ethanol (10mL) to get 100mg (91.7%) of the titled compound.

Step-iv: (S)-1-(4-(6-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-3-yl)piperazin-1-yl)propan-2-ol

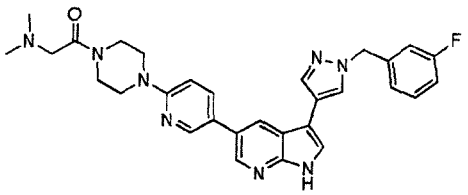
Using similar reaction conditions as described in step-iii of example-1, (S)-1-(4-(6-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-3-yl)piperazin-1-yl)propan-2-ol (100mg, 0.150mmol) was hydrolyzed with lithium hydroxide (13mg, 0.300mmol) in THF/methanol/water (5/2/1mL) to yield 17 mg (22.0% yield) of desired product.

^{1}H NMR ($CDCl_3$, 400MHz): δ 9.01 (s, 1H), 8.879-8.874 (d, 1H), 8.60-8.59 (d, 1H), 8.42-8.41 (d, 1H), 7.88 (s, 1H), 7.78 (s, 1H), 7.69-7.67 (d, 1H), 7.742-7.41 (d, 1H), 7.34-7.29 (m, 2H), 7.07-6.96 (m, 3H), 5.39 (s, 2H), 4.00 (3.90,m 1H), 3.60-3.50 (bs, 1H), 3.36-3.32 (m, 4H), 2.95-2.90 (m, 2H), 2.70-2.60 (m, 2H), 2.50-2.30 (m, 2H), 1.19-1.18 (d, 3H).

MS: m/z = 512.35 (M+1), HPLC: 91.12% in method A.

Example 147

2-(dimethylamino)-1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)ethanone



Step-i: 2-(dimethylamino)-1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)ethanone

Using similar reaction conditions as described in step-ii of example-124, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (step 1 compound of example 137) (75mg, 0.124mmol) was coupled with 2-(dimethylamino)acetic acid hydrochloride (26mg, 0.186mmol) using HATU (71mg, 0.186mmol), HOBt (26mg, 0.186mmol) and DIPEA (87µL, 0.498mmol) in DMF (2mL) to get 80mg (93.0%) yield of the title compound. MS: m/z = 693.3 (M+1).

Step-ii: 2-(dimethylamino)-1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)ethanone

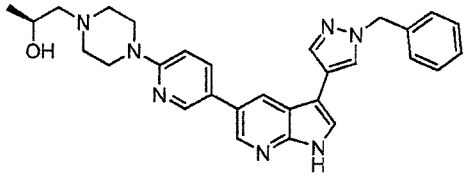
Using similar reaction conditions as described in step-iii of example-1, 22-(dimethylamino)-1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)ethanone (80mg, 0.115mmol) was hydrolyzed with lithium hydroxide (10mg, 0.230mmol) in THF/methanol/water (5/2/1mL) to yield 32mg (42.6% yield) of the titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ 8.51-8.48 (m, 2H), 8.42-8.41 (d, 1H), 8.37-8.34 (dd, 1H), 8.25 (s, 1H), 7.98 (s, 1H), 7.73 (s, 1H), 7.40-7.35 (m, 2H), 7.13-7.11 (d, 1H), 7.06-7.00 (m, 2H), 5.44 (s, 2H), 4.36 (s, 1H), 3.88-3.82 (m, 6H), 3.72-3.679 (m, 2H), 3.00 (s, 6H).

MS: m/z = 539.4 (M+1), HPLC: 96.57% in method A.

Example 148

(S)-1-(4-(5-(3-(1-benzyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol



Step-i: tert-butyl 4-(5-(3-(1-benzyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 4-(5-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate (Intermediate 66K) (200mg, 0.3mmol) was coupled with 1-benzyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 15) (103mg, 0.36mmol) using sodium carbonate(95mg, 0.9mmol) and $Pd(dppf)Cl_2$ (11mg, 0.015mmol) in toluene/ethanol/water (4/4/2 mL) to afford 100mg (47.8% yield) of the titled compound after purification by column (Silica gel 60/120) using 30% ethyl acetate in hexane as eluent. MS: m/z = 690.3(M+1).

Step-ii: 3-(1-benzyl-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(5-(3-(1-benzyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate (100mg, 0.144mmol) was deprotected in HCl in ether (8ml) to afford 60mg (66.1% yield) of the titled compound.

Step-iii: (S)-1-(4-(5-(3-(1-benzyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-i of example-82A, 33-(1-benzyl-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (60mg. 0.095mmol) was alkylated using (S)-2-methyloxirane (17mg, 0.28mmol), DIPEA (36mg, 0.28mmol) and ethanol (5mL) to get 50mg (crude) of the titled compound.

Step-iv: (S)-1-(4-(5-(3-(1-benzyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol

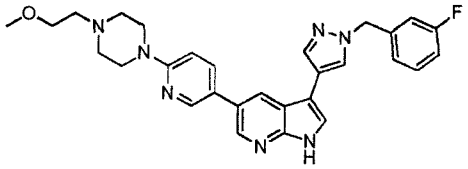
Using similar reaction conditions as described in step-iii of example-1, (S)-1-(4-(5-(3-(1-benzyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol (155mg, 0.239mmol) was hydrolyzed with lithium hydroxide(50mg, 1.19mmol) in THF/methanol/water (4/4/2mL) to yield 40mg (24.9% yield) of desired product.

^{1}H NMR (DMSO-d_6, 300MHz): δ 11.8 (s, 1H), 9.6 (s, 1H), 8.63-8.62 (d, 1H), 8.52-8.51 (d, 1H), 8.42 (s, 1H), 8.36-8.35 (d, 1H), 8.11-8.07 (dd, 1H), 7.97 (s, 1H), 7.769-7.761 (d, 1H), 7.38-7.27 (m, 4H), 7.10-7.07 (d, 1H), 5.38 (s, 2H), 4.47-4.35 (m, 2H), 4.20-4.10 (m, 1H), 3.50-3.00 (m, 6H), 1.15-1.13 (d, 3H).

MS: m/z = 494.6 (M+1), HPLC: 96.64% in method B.

Example 149

3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(4-(2-methoxyethyl)piperazin-1-yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine



Step-i: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(4-(2-methoxyethyl)piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-i of example-126, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (step 1 compound of example 137) (75mg, 0.123mmol) was alkylated using 2-1-bromo-2-methoxyethane (26mg, 0.185mmol) and potassium carbonate (43mg, 0.308mmol) in DMF(1ml) to afford 70mg (85.3% yield) of the titled compound. MS: m/z = 666.1(M+1).

Step-ii: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(4-(2-methoxyethyl)piperazin-1-yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine

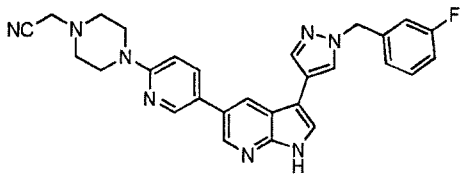
Using similar reaction conditions as described in step-iii of example-1, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(4-(2-methoxyethyl)piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (70mg, 0.105mmol) was hydrolyzed by lithium hydroxide(25mg, 0.63mmol), THF/methanol/water (3/2/1 ml) to yield 20mg (37.7% yield) of the titled compound.

^{1}H NMR (CD_3OD, 300MHz): δ 8.55-8.51 (m, 3H), 8.23 (s, 1H), 8.12-8.09 (dd,1 H), 7.97 (s, 1H), 7.73 (s, 1H), 7.40-7.30 (m, 1H), 7.15-7.10 (m, 2H), 7.06-7.00 (m, 2H), 5.45 (s, 2H), 3.79-3.76 (t, 2H), 3.60-2.90 (m, 8H).

MS: m/z = 512.15 (M+1), HPLC: 95.27% in method A.

Example 150

2-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)acetonitrile



Step-i: 2-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)acetonitrile

Using similar reaction conditions as described in step-i of example-126, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (step 1 compound of example 137) (75mg, 0.123mmol) was alkylated using 2-bromoacetonitrile (23mg, 0.185mmol) and potassium carbonate (43mg, 0.308mmol) in DMF(1ml) to afford 60mg (75.0% yield) of the titled compound. MS: m/z= 647.1(M+1)

Step-ii: 2-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)Acetonitrile

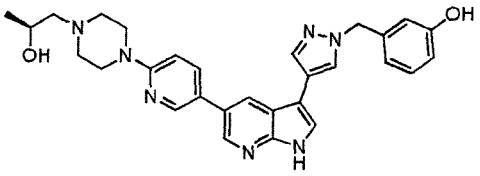
Using similar reaction conditions as described in step-iii of example-1, 2-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)acetonitrile (60mg, 0.092mmol) was hydrolyzed by lithium hydroxide(8mg, 0.185mmol) in THF/methanol/water (5/1/1 ml) to yield 15mg (33.3% yield) of the titled compound.

^{1}H NMR ($CDCl_3$, 400MHz): δ 9.19 (s, 1H), 8.50-8.47 (dd,2 H), 8.128-8.123 (d, 1H), 7.86 (s, 1H), 7.79-7.76 (dd, 1H), 7.70 (s, 1H), 7.447-7.441 (d, 1H), 7.35-7.30 (m, 1H), 7.10-6.90 (m, 3H), 6.80-6.78 (d, 1H), 5.39 (s, 2H), 3.70-3.67 (t, 4H), 3.61 (s, 2H), 2.76-2.74 (t, 4H).

MS: m/z = 493.4 (M+1), HPLC: 97.07% in method A.

Example 151

(S)-3-((4-(5-(6-(4-(2-hydroxypropyl)piperazin-1-yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-3-yl)-1H-pyrazol-1-yl)methyl)phenol



Step-i: tert-butyl 4-(5-(3-(1-(3-(benzyloxy)benzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 4-(5-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate (Intermediate 66K) (300mg, 0.454mmol) was coupled with 1-(3-(benzyloxy)benzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 64E) (195mg, 0.500mmol) using sodium carbonate(145mg, 1.364mmol) and $Pd(dppf)Cl_2$ (17mg, 0.022mmol) in toluene/ ethanol/water (3/3/2 mL) to afford 250mg (69% yield) of the titled compound after purification by column (Silica gel 60/120) using 0.5% methanol in DCM as eluent. MS: m/z = 796.3 (M+1).

Step-ii: 3-(1-(3-(benzyloxy)benzyl)-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(5-(3-(1-(3-(benzyloxy)benzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate (250mg, 0.314mmol) was deprotected in HCl in ether/ methanol (2/3ml) to afford 200mg (87% yield) of the titled compound. MS: m/z = 696.2 (M+1)

Step-iii: (S)-1-(4-(5-(3-(1-(3-(benzyloxy)benzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-i of example-82A, 3-(1-(3-(benzyloxy)benzyl)-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride (200mg. 0.273mmol) was alkylated using (S)-2-methyloxirane (48mg, 0.819mmol), DIPEA (211mg, 1.638mmol) and ethanol (20mL) to get 200mg (crude) of the titled compound. MS: m/z = 754.3 (M+1).

Step-iv: (S)-3-((4-(5-(6-(4-(2-hydroxypropyl)piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-3-yl)-1H-pyrazol-1-yl)methyl)phenol

To the solution of (S)-1-(4-(5-(3-(1-(3-(benzyloxy)benzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol (200mg, 0265mmol) in toluene/TFA (10/5mL) was heated at 100°C for 16 hours and distilled out the solvent. This was basified with triethylamine and distilled out the solvent to get 180mg (crude) of the titled compound. MS: m/z = 664.2 (M+1).

Step-v: (S)-3-((4-(5-(6-(4-(2-hydroxypropyl)piperazin-1-yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-3-yl)-1H-pyrazol-1-yl)methyl)phenol

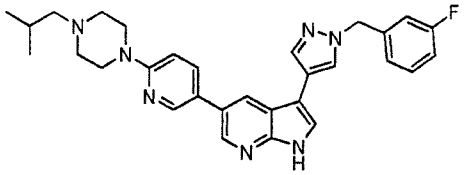
Using similar reaction conditions as described in step-iii of example-1, (S)-3-((4-(5-(6-(4-(2-hydroxypropyl)piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-3-yl)-1H-pyrazol-1-yl)methyl)phenol (180mg, 0.271mmol) was hydrolyzed with lithium hydroxide(34mg, 0.813mmol) in THF/methanol/water (2/2/0.5mL) to yield 12mg (9% yield) of desired product.

^{1}H NMR (CD_3OD, 400MHz): δ 8.51-8.45 (m, 2H), 8.32-8.31 (m, 1H), 8.16 (s, 1H), 7.99-7.92 (m, 2H), 7.20-7.16 (t, 1H), 7.06-6.97 (m, 1H), 6.78-6.69 (m, 3H), 5.36 (s, 2H), 4.70-4.60 (m, 1H), 4.26-4.20 (t, 1H), 4.10-4.05 (q, 1H), 3.78-3.70 (m, 4H), 3.58-3.49 (m, 2H), 2.92-2.61 (m, 2H), 2.63-2.61 (m, 1H), 1.22-1.21 (m, 3H).

MS: m/z= 510.2 (M+1), HPLC: 98.41% in method A.

Example 152

3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(4-isobutylpiperazin-1-yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine



Step-i: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(4-isobutylpiperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-i of example-126, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (step 1 compound of example 137) (75mg, 0.123mmol) was alkylated using 1-bromo-2-methylpropane (26mg, 0.185mmol) and potassium carbonate (43mg, 0.308mmol) in DMF(1ml) to afford 70mg (85.3% yield) of the titled compound. MS: m/z = 664.6 (M+1)

Step-ii: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(4-isobutylpiperazin-1-yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-iii of example-1, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(4-isobutylpiperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (70mg, 0.105mmol) was hydrolyzed by lithium hydroxide(27mg, 0.632mmol) in THF/methanol/water (3/2/1 ml) to yield 8mg (15.0% yield) of the titled compound.

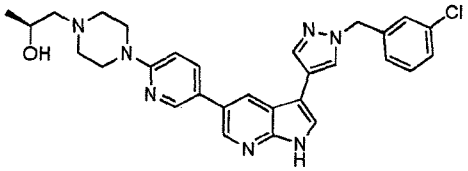
^{1}H NMR ($CDCl_3$, 300MHz): δ 8.83 (s, 1H), 8.49-8.45 (dd, 2H), 8.11-8.10 (d, 1H), 7.85 (s, 1H), 7.76-7.69 (m, 2H), 7.42-7.41 (d, 1H), 7.39-7.30 (m, 1H), 7.10-6.90 (m, 3H), 6.77-6.74

(d, 1H), 5.38 (s, 2H), 3.60-3.59 (t, 4H), 2.60-2.50 (t, 4H), 2.16-2.14 (d, 2H), 1.90-1.80 (m, 1H), 0.95-0.93 (d, 6H).

MS: m/z = 510.3 (M+1), HPLC: 93.26% in method A.

Example 153

(S)-1-(4-(5-(3-(1-(3-chlorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol



Step-i: tert-butyl 4-(5-(3-(1-(3-chlorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 4-(5-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate (Intermediate 66K) (200mg, 0.303mmol) was coupled with 1-(3-chlorobenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 64F) (116mg, 0.36mmol) using sodium carbonate (96mg, 0.909mmol) and Pd(dppf)Cl_2 (11mg, 0.015mmol) in toluene/ ethanol/water (5/5/2 mL) to afford 188mg (85.6% yield) of the titled compound after purification by column (Silica gel 60/120) using 50% ethyl acetate in hexane as eluent.

Step-ii: 3-(1-(3-chlorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(5-(3-(1-(3-chlorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate (185mg, 0.25mmol) was deprotected in HCl in ether (10ml) to afford 133mg (78.8% yield) of the titled compound.

Step-iii (S)-1-(4-(5-(3-(1-(3-chlorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-i of example-82A, 3-(1-(3-chlorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride (130mg. 0.197mmol) was alkylated using (S)-2-methyloxirane (34mg, 0.59mmol), DIPEA (73mg, 0.59mmol) and ethanol (5mL) to get 124mg (92.3% yield) of the titled compound.

Step-iv: (S)-1-(4-(5-(3-(1-(3-chlorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol

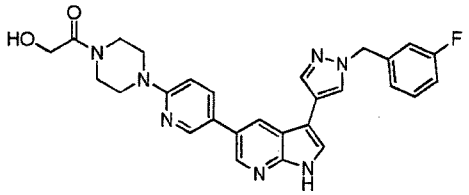
Using similar reaction conditions as described in step-iii of example-1, (S)-1-(4-(5-(3-(1-(3-chlorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol (124mg, 0.181mmol) was hydrolyzed with lithium hydroxide(38mg, 0.908mmol) in THF/methanol/water (2/2/1mL) to yield 30mg (26.0% yield).

^{1}H NMR (CD_3OD, 300MHz): δ 8.54-8.53 (d, 1H), 8.45-8.41 (d, 1H), 8.41-8.40 (d, 1H), 8.21 (s, 1H), 8.07-8.03 (dd, 1H), 7.957-7.955 (d, 1H), 7.68 (s, 1H), 7.34-7.30 (m, 3H), 7.24-7.21 (dt, 1H), 7.11-7.08 (d, 1H), 5.42 (s, 2H), 4.30-4.20 (m, 1H), 3.26-3.08 (m, 2H), 1.27-1.25 (d, 3H).

MS: m/z = 528.4 (M+1), HPLC: 97.22% in method A.

Example 154

1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)-2-hydroxyethanone



Step-i: 1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)-2-hydroxyethanone

Using similar reaction conditions as described in step-ii of example-124, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (step 1 compound of example 137) (75mg, 0.123mmol) was coupled with 2-hydroxyacetic acid (14mg, 0.185mmol) using HATU (71mg, 0.185mmol), HOBt (25mg, 0.185mmol) and DIPEA (86µL, 0.493mmol) in DMF (1mL) to get 70mg (85.3.0%) yield of the title compound after purification by column (Silica gel 60/120) chromatography using 5% methanol in dichloromethane as eluent. MS: m/z = 666.5 (M+1).

Step-ii: 1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)-2-hydroxyethanone

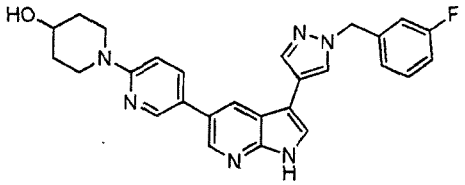
Using similar reaction conditions as described in step-iii of example-1, 1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)-2-hydroxyethanone (70mg, 0.105mmol) was hydrolyzed with lithium hydroxide(9mg, 0.210mmol) in THF/methanol/water (5/1/1mL) to yield 7mg (10.7% yield) of the titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ 8.497-8.493 (d, 1H), 8.44-8.43 (d, 1H), 8.39-8.38 (d, 1H), 8.32-8.29 (dd, 1H), 8.23 (s, 1H), 7.99 (s, 1H), 7.71 (s, 1H), 7.42-7.31 (m, 2H), 7.13-7.12 (d, 1H), 7.07-7.01 (m, 2H), 5.45 (s, 2H), 4.33 (s, 2H), 3.84-3.70 (m, 8H).

MS: m/z = 512.55 (M+1), HPLC: 96.01% in method A.

Example 155

1-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperidin-4-ol



Step-i: 1-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperidin-4-ol

Using similar reaction conditions as described in step-i of example-1, 5-bromo-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (compound of Step-iof example 9) (150mg, 0.28mmol) was coupled with 1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)piperidin-4-ol (intermediate 69E) (173mg, 0.56mmol) using sodium carbonate (89mg, 0.84mmol) and $Pd(dppf)Cl_2$ (11mg, 0.014mmol) in DME/water (10/1 mL) to afford 160mg (crude) of the titled compound. MS: m/z = 623.6 (M+1)

Step-ii: 1-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperidin-4-ol

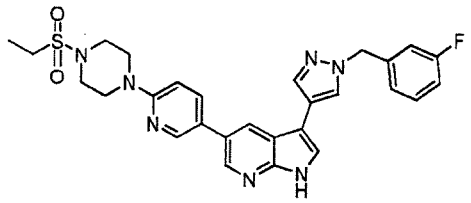
Using similar reaction conditions as described in step-iii of example-1, 1-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperidin-4-ol (160mg, 0.25mmol) was hydrolyzed with lithium hydroxide(33mg, 0.77mmol) in THF/methanol/water (3/3/1mL) to yield 38mg (25.4%) of desired product.

^{1}H NMR (CD_3OD, 300MHz): δ 8.49-8.41 (m, 3H), 8.21 (s, 2H), 7.98 (s, 1H), 7.70 (s, 1H), 7.55-7.51 (s, 1H), 7.42-7.33 (m, 1H), 7.11-6.97 (m, 3H), 5.43 (s, 2H), 4.06-3.98 (m, 3H), 3.65-3.57 (m, 2H), 2.09-2.03 (m, 2H), 1.80-1.65 (m, 2H).

MS: m/z = 469.2 (M+1), HPLC: 93.72% in method A.

Example 156

5-(6-(4-(ethylsulfonyl)piperazin-1-yl)pyridin-3-yl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine



Step-i: 5-(6-(4-(ethylsulfonyl)piperazin-1-yl)pyridin-3-yl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step i of intermediate 17, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (step 1 compound of example 137) (80mg, 0.13mmol) was alkylated with ethanesulfonyl chloride (25mg, 0.196mmol) using triethylamine (40mg, 0.39mmol) in DCM(3mL) to afford 100mg (100% yield) of the titled compound. MS: m/z = 700.2 (M+1)

Step-ii: 5-(6-(4-(ethylsulfonyl)piperazin-1-yl)pyridin-3-yl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine

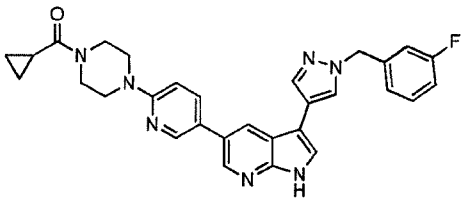
Using similar reaction conditions as described in step-iii of example-1, 5-(6-(4-(ethylsulfonyl)piperazin-1-yl)pyridin-3-yl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (100mg, 0.143mmol) was hydrolyzed with lithium hydroxide(30mg, 0.715mmol) in THF/methanol/water (3/2/1mL) to yield 45mg (58.4% yield) of the titled compound.

^{1}H NMR (CD_3OD, 300MHz): δ 8.51-8.49 (m, 2H), 8.44-8.43 (d, 2H), 8.41-8.40 (d, 1H), 8.36-8.35 (d, 1H), 8.22 (s, 1H), 7.98 (s, 1H), 7.72 (s, 1H), 7.48-7.45 (d, 1H), 7.38-7.36 (m, 1H), 7.12-7.09 (d, 1H), 7.08-6.96 (m, 2H),5.44 (s, 2H), 3.85-3.83 (t, 4H), 3.53-3.50 (t, 4H), 3.15-3.05 (q, 2H), 1.38-1.33 (t, 3H).

MS: m/z= 546.1 (M+1), HPLC: 94.35% in method A

Example 157

cyclopropyl(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)methanone



Step-i: cyclopropyl(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)methanone

Using similar reaction conditions as described in step i of intermediate 17, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (step 1 compound of example 137) (80mg, 0.13mmol) was acylated with cyclopropane carbonyl chloride (22mg, 0.196mmol) using triethylamine(40mg, 0.39mmol) in DCM(3mL) to afford 100mg (100% yield) of the titled compound. MS: m/z = 676.2 (M+1).

Step-ii: cyclopropyl(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)methanone

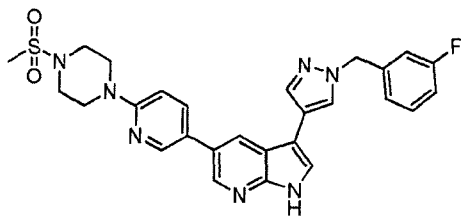
Using similar reaction conditions as described in step-iii of example-1, cyclopropyl(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)methanone (100mg, 0.148mmol) was hydrolyzed with lithium hydroxide(31mg, 0.74mmol) in THF/methanol/water (3/2/1mL) to yield 42mg (54.5% yield) of the titled compound.

^{1}H NMR (CD_3OD, 300MHz): δ 8.53 (s, 2H), 8.49-8.48 (d, 1H), 8.46-8.45(d, 1H), 8.24 (s, 1H), 7.998-7.995 (d, 1H), 7.74 (s, 1H), 7.50-7.47 (d, 1H), 7.37-7.35 (m, 1H), 7.12-6.98 (m, 3H), 5.44 (s, 2H), 4.08-3.83 (m, 8H), 2.05-1.95 (m, 1H), 0.95-0.87 (m, 2H).

MS: m/z = 522.4 (M+1), HPLC: 96.90% in method A.

Example 158

3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(4-(methylsulfonyl)piperazin-1-yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine



Step-i: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(4-(methylsulfonyl)piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step i of intermediate 17, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (step 1 compound of example 137) (80mg, 0.13mmol) was mesylated with methanesulfonyl chloride (23mg, 0.196mmol) using triethylamine (40mg, 0.39mmol) in DCM (3mL) to afford 100mg (100% yield) of the titled compound. MS: m/z = 686.2(M+1)

Step-ii: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(4-(methylsulfonyl)piperazin-1-yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine

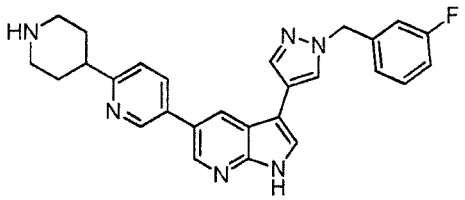
Using similar reaction conditions as described in step-iii of example-1, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(4-(methylsulfonyl)piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (100mg, 0.145mmol) was hydrolyzed with lithium hydroxide(30mg, 0.729mmol) in THF/methanol/water (3/2/1mL) to yield 27mg (35.0% yield) of the titled compound after purification by preparative HPLC.

^{1}H NMR (CD_3OD, 300MHz): δ 8.55 (s, 2H), 8.47-8.43 (dd, 1H), 8.386-8.380 (d, 1H), 8.247 (s, 1H), 7.997-7.995 (d, 1H), 7.75 (s, 1H), 7.50-7.47 (d, 1H), 7.37-7.35 (d, 1H), 7.42-7.32 (m, 1H), 7.12-6.97 (m, 3H), 5.43 (s, 2H), 3.88-3.85 (t, 4H), 3.47-3.44 (t, 4H), 2.92 (s, 3H).

MS: m/z = 532.05 (M+1), HPLC: 95.94% in method A

Example 159

3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperidin-4-yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine



Step-i: tert-butyl 4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperidine-1-carboxylate (step ii of example 102A) (126mg, 0.178mmol) was hydrolyzed by lithium hydroxide (75mg, 1.78mmol) in THF/methanol/water (20/10/5 ml) to yield 96mg (98% yield) of the titled compound. MS: m/z = 553.2 (M+1).

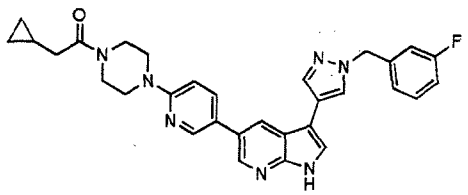
Step-ii 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperidin-4-yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperidine-1-carboxylate (96mg, 0.173mmol) was deprotected in methanol/HCl in dioxane (5/5ml) to afford 49mg (63% yield) of the titled compound.

^{1}H NMR (CD_3OD, 300MHz): δ 9.178-9.170 (d, 1H), 8.78-8.74 (dd, 1H), 8.71-8.66 (dd, 2H), 8.26 (s, 1H), 7.99 (s, 1H), 7.95-7.92 (d, 1H), 7.77 (s, 1H), 7.40-7.31 (q, 1H), 7.10-7.08 (d, 1H), 7.03-6.96 (m, 2H), 5.42 (s, 2H), 3.63-3.59 (d, 2H), 3.55-3.40 (m, 1H), 3.30-3.19 (m, 2H), 2.32-2.08 (m, 4H). MS: m/z = 453.5 (M+1), HPLC: 93.40% in method A

Example 160

2-cyclopropyl-1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)ethanone



Step-i: 2-cyclopropyl-1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)ethanone

Using similar reaction conditions as described in step-ii of example-124, 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (step 1 compound of example 137) (75mg, 0.123mmol) was coupled with 2-cyclopropylacetic acid (19mg, 0.185mmol) using HATU (70mg, 0.185mmol), HOBt (25mg, 0.185mmol) and DIPEA (48mg, 0.37mmol) in DMF (3mL) to get 80mg (95.2.0%) yield of the title compound. MS: m/z = 690.6 (M+1).

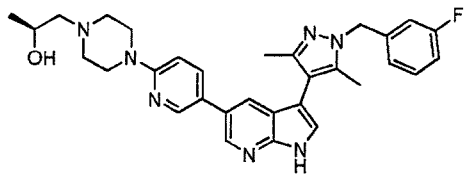
Step-ii: 2-cyclopropyl-1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)ethanone

Using similar reaction conditions as described in step-iii of example-1, 2-cyclopropyl-1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)ethanone (80mg, 0.116mmol) was hydrolyzed with lithium hydroxide(25mg, 0.58mmol) in THF/methanol/water (3/2/1mL) to yield 4mg (6.4% yield) of the titled compound.

^{1}H NMR (CD_3OD, 300MHz): δ 8.52-8.45 (m, 3H), 8.33-8.32 (d, 1H), 8.225-8.222 (d, 1H), 7.993-7.990 (d, 1H), 7.73 (s, 1H), 7.50-7.46 (d, 1H), 7.38-7.33 (m, 1H), 7.12-7.09 (d, 1H), 7.04-6.89 (m, 3H), 6.50-6.43 (dt, 1H), 5.44(s, 2H), 3.93-3.85 (m, 8H), 2.35-2.25 (m, 2H), 1.13-1.08 (t, 3H). MS: m/z = 536.4 (M+1), HPLC: 97.55% in method B.

Example 161

(2S)-1-(4-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol



Step-i: tert-butyl 4-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, 5-bromo-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b] pyridine (Step-i of example-14) (200mg, 0.361mmol) was coupled with tert-butyl 4-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-2-yl)piperazine-1-carboxylate (intermediate 69C) (140mg, 0.361mmol) using $Pd(dppf)Cl_2$ (14mg, 0.018mmol) and sodium carbonate (114, 0.018mmol) in DME/water (25/5ml). This afforded 221mg (83% yield) of the titled compound. MS: m/z = 736.2 (M+1).

Step-ii: 3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate (221mg, 0.299mmol) was deprotected in methanol/HCl in dioxane (5/5ml) to afford 186mg (93% yield) of the titled compound. MS: m/z = 636.1 (M+1).

Step-iii (2S)-1-(4-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-i of example-82A, 3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride (186mg. 0.277mmol) was alkylated using (S)-2-methyloxirane (32mg, 0.554mmol), DIPEA (72mg, 0.554mmol) and ethanol (4mL) to get 157mg (82% yield) of the titled compound. MS: m/z= 694.2 (M+1).

Step-iv: (2S)-1-(4-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol

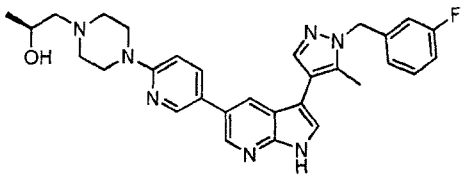
Using similar reaction conditions as described in step-iii of example-1, (2S)-1-(4-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol (165mg, 0.238mmol) was hydrolyzed with lithium hydroxide(100mg, 2.38mmol) in THF/methanol/water (20/10/5mL) to yield 31mg (13% yield) of desired product.

^{1}H NMR (CD_3OD, 300MHz): δ 8.64-8.63 (d, 1H), 8.48-8.47 (d, 1H), 8.327-8.321 (d, 1H), 8.23-8.19 (dd, 1H), 7.64 (s, 1H), 7.42-7.35 (m, 1H), 7.31-7.28 (d, 1H), 7.07-7.02 (m, 2H), 6.95-6.91 (dt, 1H), 5.41 (s, 2H), 4.45-4.30 (m, 1H), 3.56 (s, 4H), 3.30-3.10 (m, 2H), 2.24 (s, 3H), 2.23 (s, 3H), 1.26-1.24 (d, 3H).

MS: m/z= 539.9 (M+1), HPLC: 95.5% in method A.

Example 162

(S)-1-(4-(5-(3-(1-(3-fluorobenzyl)-5-methyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol



Step-i: tert-butyl 4-(5-(3-(1-(3-fluorobenzyl)-5-methyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 4-(5-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate (Intermediate 66K) (200mg, 0.303mmol) was coupled with 1-(3-fluorobenzyl)-3-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 12) (116mg, 0.363mmol) using sodium carbonate(96mg, 0.909mmol) and $Pd(dppf)Cl_2$ (11mg, 0.015mmol) in toluene/ethanol/water (10/10/1 mL) to afford 250mg (crude) of the titled compound after purification by column (Silica gel 60/120) using 50% ethyl acetate in hexane as eluent. MS: m/z = 722.5 (M+1)

Step-ii: 3-(1-(3-fluorobenzyl)-5-methyl-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(5-(3-(1-(3-fluorobenzyl)-5-methyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate (250mg, 0.34mmol) was deprotected in HCl in ether (5ml) to afford 270mg (crude) of the titled compound. MS: m/z = 622.5 (M+1)

Step-iii: (S)-1-(4-(5-(3-(1-(3-fluorobenzyl)-5-methyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-i of example-82A, 3-(1-(3-fluorobenzyl)-5-methyl-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride (270mg. 0.41mmol) was alkylated using (S)-2-

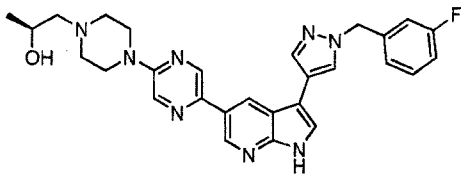
methyloxirane (48mg, 0.82mmol), DIPEA (159mg, 1.23mmol) and ethanol (10mL) to get 350mg (crude) of the titled compound. MS: m/z = 680.2 (M+1)

Step-iv: (S)-1-(4-(5-(3-(1-(3-fluorobenzyl)-5-methyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-iii of example-1, (S)-1-(4-(5-(3-(1-(3-fluorobenzyl)-5-methyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol (350mg, 0.51mmol) was hydrolyzed with lithium hydroxide(65mg, 1.54mmol) in THF/methanol/water (6/4/2mL) to yield 40mg (11% yield) after purification by preparative HPLC as a mixture of two isomers. MS: m/z = 526.5 (M+1) HPLC: 89.1% in method B.

Example 163

(S)-1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyrazin-2-yl)piperazin-1-yl)propan-2-ol



Step-i: tert-butyl 4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyrazin-2-yl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 4-(5-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyrazin-2-yl)piperazine-1-carboxylate (Intermediate 66N) (465mg, 0.7mmol) was coupled with 1-(3-fluorobenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 11) (234mg, 0.77mmol) using sodium carbonate(223mg, 2.1mmol) and Pd(dppf)Cl_2 (26mg, 0.035mmol) in toluene/ ethanol/water (6/6/2 mL) to afford 410mg (82.1% yield) of the titled compound after purification by column (Silica gel 60/120) using 30% ethyl acetate in hexane as eluent. MS: m/z = 709.3 (M+1)

Step-ii: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(5-(piperazin-1-yl)pyrazin-2-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyrazin-2-yl)piperazine-1-carboxylate (400mg, 0.56mmol) was deprotected in HCl in ether (10ml) to afford crude compound. Using similar reaction conditions as described in Step-i of example-82A, above crude was alkylated using (S)-2-methyloxirane (163mg, 2.8mmol), DIPEA

(217mg, 1.68mmol) and ethanol (10mL) to get 240mg (63.7% yield) of the titled compound. MS: m/z = 667.1 (M+1)

Step-iii: (S)-1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyrazin-2-yl)piperazin-1-yl)propan-2-ol

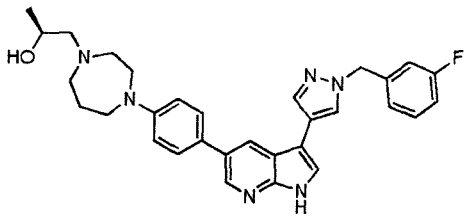
Using similar reaction conditions as described in step-iii of example-1, (S)-1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyrazin-2-yl)piperazin-1-yl)propan-2-ol (230mg, 0.34mmol) was hydrolyzed with lithium hydroxide(44mg, 1.03mmol) in THF/methanol/water (4/4/2mL) to yield 40mg (18.5% yield) of desired product.

^{1}H NMR (CD_3OD, 300MHz): δ 8.83-8.75 (m, 3H), 8.44-8.43 (d, 1H), 8.22 (s, 1H), 7.972-7.970 (d, 1H), 7.68 (s, 1H), 7.44-7.32 (m, 1H), 7.16-6.96 (m, 3H), 5.44 (s, 2H), 4.70-4.45 (m, 3H), 4.30-4.10 (m, 2H), 3.80-3.60 (m, 2H), 3.60-3.30 (m, 4H), 1.27-1.25 (d, 3H).

MS: m/z = 513.3 (M+1), HPLC: 97.55% in method B.

Example 164

(S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-1,4-diazepan-1-yl)propan-2-ol



Step-i: tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-1,4-diazepane-1-carboxylate

Using similar reaction conditions as described in step-i of example-1, -bromo-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (compound of Step-iof example 9) (100 mg, 0.190 mmol) was coupled with tert-butyl 4-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-1,4-diazepane-1-carboxylate (intermediate 69F) (92mg, 0.229mmol) using sodium carbonate(60mg, 0.57mmol) and $Pd(PPh_3)_2Cl_2$ (7mg, 0.095mmol) in DME/water (3/1 mL) to afford 120mg (86.9% yield) of the titled compound after purification by column (Silica gel 60/120) using 50% ethyl acetate in hexane as eluent. MS: m/z = 722.3 (M+1)

Step-ii: 5-(4-(1,4-diazepan-1-yl)phenyl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-1,4-diazepane-1-carboxylate (120mg, 0.166mmol) was deprotected in TFA/DCM (3/1ml) to afford 100mg (97.0% yield) of the titled compound. MS: m/z = 621.2 (M+1)

Step-iii: (S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-1,4-diazepan-1-yl)propan-2-ol

Using similar reaction conditions as described in step-i of example-82A, 5-(4-(1,4-diazepan-1-yl)phenyl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (100mg, 0.161mmol) was alkylated using (S)-2-methyloxirane (14mg, 0.241mmol), DIPEA (62mg, 0.48mmol) and ethanol (3mL) to get 100mg (91.7% yield) of the titled compound. MS: m/z = 679.6 (M+1)

Step-iv: (S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-1,4-diazepan-1-yl)propan-2-ol

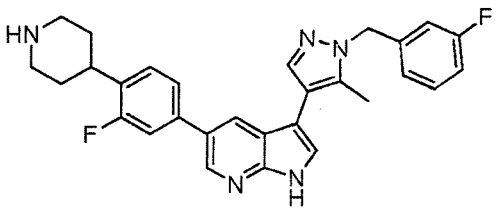
Using similar reaction conditions as described in step-iii of example-1, (S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-1,4-diazepan-1-yl)propan-2-ol (100mg, 0.147mmol) was hydrolyzed with lithium hydroxide(31mg, 0.736mmol) in THF/methanol/water (2/2/1mL) to yield 33mg (42.8% yield) of desired product.

^{1}H NMR ($CDCl_3$, 300MHz): δ 8.83 (s, 1H), 8.538-8.531 (d, 1H), 8.13-8.12 (d, 1H), 7.86 (s, 1H), 7.70 (s, 1H), 7.52-7.49 (d, 2H), 7.39-7.30 (m, 2H), 7.07-6.91 (m, 3H), 6.82-6.79 (d, 2H), 5.38 (s, 2H), 3.85-3.75 (m, 1H), 3.70-3.55 (m, 4H), 3.15-3.00 (m, 1H), 2.90-2.80 (m, 2H), 2.70-2.55 (m, 2H), 2.35-2.25 (m, 1H), 2.15-1.95 (m, 2H), 1.14-1.12 (d, 3H).

MS: m/z = 525.3 (M+1), HPLC: 92.75% in method A.

Example 165

5-(3-fluoro-4-(piperidin-4-yl)phenyl)-3-(1-(3-fluorobenzyl)-5-methyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine



Step-i: 5-bromo-3-(1-(3-fluorobenzyl)-3-methyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-i of example-1, 5-bromo-3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridine (Intermediate 1) (300 mg, 0.709 mmol) was coupled with 1-(3-fluorobenzyl)-3-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 12) (270mg, 0.851 mmol) using sodium carbonate (220 mg, 2.12 mmol) and $Pd(PPh_3)_2Cl_2$ (25 mg, 0.035 mmol) in acetonitrile/water (10/2.5 ml) to afford 300 mg (78.5% yield) of the pure product after column purification using 40% ethyl acetate in hexane as eluent. MS: m/z = 539.2 (M+1)

Step-ii: tert-butyl 4-(2-fluoro-4-(3-(1-(3-fluorobenzyl)-3-methyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5,6-dihydropyridine-1(2H)-carboxylate

Using similar reaction conditions as described in step-i of example-1, 5-bromo-3-(1-(3-fluorobenzyl)-3-methyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (300 mg, 0.55 mmol) was coupled with tert-butyl 4-(2-fluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-5,6-dihydropyridine-1(2H)-carboxylate (intermediate 70) (270mg, 0.66 mmol) using sodium carbonate (175 mg, 1.65 mmol) and $Pd(PPh_3)_2Cl_2$ (20 mg, 0.027 mmol) in DME/water (10/2.5 ml) to afford 250mg (61.2% yield) of the pure product after column purification using 50% ethyl acetate in hexane as eluent. MS: m/z = 736.4 (M+1).

Step-iii: tert-butyl 4-(2-fluoro-4-(3-(1-(3-fluorobenzyl)-3-methyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-82, tert-butyl 4-(2-fluoro-4-(3-(1-(3-fluorobenzyl)-3-methyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5,6-dihydropyridine-1(2H)-carboxylate (250mg, 0.34mmol) was reduced with palladium hydroxide (250mg) in ethyl acetate/ ethanol 10/10 mL to afford 200mg (80.0% yield) of the titled compound. MS: m/z = 738.6 (M+1).

Step-iv: tert-butyl 4-(2-fluoro-4-(3-(1-(3-fluorobenzyl)-3-methyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(2-fluoro-4-(3-(1-(3-fluorobenzyl)-3-methyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (200mg, 0.271mmol) was hydrolyzed by lithium hydroxide (57mg, 1.356mmol) in THF/methanol/water (5/4/1 ml) to yield 140mg (88.6% yield) of the titled compound. MS: m/z = 584.5 (M+1)

Step-v: 5-(3-fluoro-4-(piperidin-4-yl)phenyl)-3-(1-(3-fluorobenzyl)-3-methyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(2-fluoro-4-(3-(1-(3-fluorobenzyl)-3-methyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-

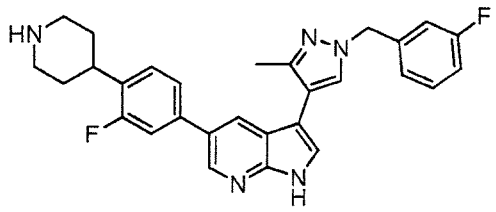
yl)phenyl)piperidine-1-carboxylate (140mg, 0.239mmol) was deprotected in TFA/DCM (5/1mL) to afford 25mg (17.48% yield) of the titled compound after purification by preparative HPLC along with one more isomer Example 166.

^{1}H NMR (CD_3OD, 300MHz): δ 8.70-8.60 (bs, 1H), 8.59 (s, 1H), 8.20 (s, 1H), 7.70 (s, 1H), 7.60-7.30 (m, 4H), 7.20-6.95 (m, 3H), 5.37 (s, 2H), 3.60-3.50 (m, 2H), 3.30-3.10 (m, 3H), 2.40 (s, 3H), 2.15-2.00 (m, 4H).

MS: m/z= 484.4(M+1), HPLC: 98.76% in method B.

Example 166

5-(3-fluoro-4-(piperidin-4-yl)phenyl)-3-(1-(3-fluorobenzyl)-3-methyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine

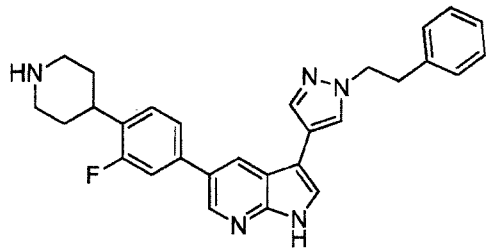


Yield 18mg (12.58%)

^{1}H NMR (CD_3OD, 300MHz): δ 8.70-8.60 (bs, 1H), 8.60 (s, 1H), 7.85 (s, 1H), 7.60-7.30 (m, 4H), 7.05-7.00 (m, 2H), 6.95-6.90 (dd, 1H), 5.46 (s, 2H), 3.60-3.50 (m, 2H), 3.30-3.10 (m, 3H), 2.35 (s, 3H), 2.15-2.00 (m, 4H). MS: m/z = 484.4 (M+1), HPLC: 94.72% in method B.

Example 167

5-(3-fluoro-4-(piperidin-4-yl)phenyl)-3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine



Step-i: tert-butyl 4-(2-fluoro-4-(3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5,6-dihydropyridine-1(2H)-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 4-(2-fluoro-4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5,6-dihydropyridine-1(2H)-carboxylate (intermediate 66Q) (170mg, 0.253mmol) was coupled with 1-phenethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 59) (151mg, 0.506mmol) using $Pd(dppf)Cl_2$ (10mg, 0.012mol) and sodium carbonate (161mg,

0.759mmol) in toluene/ ethanol/water (20/10/5 ml) to afford 171mg (94% yield) of the titled. MS: m/z = 718.3 (M+1).

Step-ii: tert-butyl 4-(2-fluoro-4-(3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-82, tert-butyl 4-(2-fluoro-4-(3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5,6-dihydropyridine-1(2H)-carboxylate (190mg, 0.264mmol) was reduced with palladium hydroxide (100mg) in ethyl acetate/ ethanol 10/20 mL to afford 141mg (74% yield) of the titled compound. MS: m/z = 720.7 (M+1).

Step-iii: tert-butyl 4-(2-fluoro-4-(3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(2-fluoro-4-(3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (140mg, 0.194mmol) was hydrolyzed by sodium hydroxide (78mg, 1.947mmol) in THF/methanol/water (12/4/3 mL) to yield 83mg (75% yield) of the titled compound. MS: m/z = 566.3 (M+1).

Step-iv: 5-(3-fluoro-4-(piperidin-4-yl)phenyl)-3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine

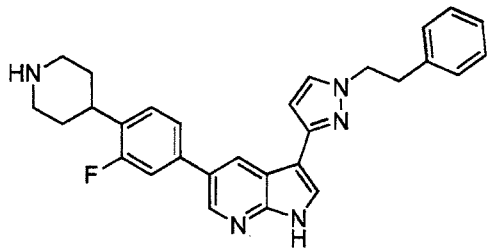
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(2-fluoro-4-(3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (82mg, 0.145mmol) was deprotected in methanol/HCl in dioxane (5/5mL) to afford 8.2mg (12.2% yield) of the titled compound after purification by preparative TLC using 8% methanol in chloroform as eluent.

^{1}H NMR (CD_3OD, 300MHz): δ 8.448-8.442 (d, 1H), 8.098-8.091 (d, 1H), 7.839-7.837 (d, 1H), 7.73 (s, 1H), 7.54 (s, 1H), 7.48-7.38 (m, 3H), 7.26-7.12 (m, 5H), 7.44-7.41 (t, 2H), 3.37-3.31 (m, 1H), 3.19-3.15 (t, 3H), 3.03-2.93 (td, 2H), 1.97-1.88 (m, 5H).

MS: m/z = 466.5 (M+1), HPLC: 98.63% in method A.

Example 168

5-(3-fluoro-4-(piperidin-4-yl)phenyl)-3-(1-phenethyl-1H-pyrazol-3-yl)-1H-pyrrolo[2,3-b]pyridine



Step-i: tert-butyl 4-(2-fluoro-4-(3-(1-phenethyl-1H-pyrazol-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5,6-dihydropyridine-1(2H)-carboxylate

Using similar reaction conditions as described in step-i of example-1, 5-bromo-3-(1-phenethyl-1H-pyrazol-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (intermediate 63A) (160 mg, 0.307 mmol) was coupled with tert-butyl 4-(2-fluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-5,6-dihydropyridine-1(2H)-carboxylate (intermediate 70) (307mg, 0.769 mmol) using potassium phosphate (195 mg, 0.918 mmol), tricyclohexyl phosphine (13 mg, 0.046 mmol) and $Pd_2(dba)_3$ (28mg, 0.030mmol) in dioxane/water (15/3 ml) to afford 126 mg (57.2% yield) of the pure product after column purification using 35% ethyl acetate in hexane as eluent. MS: m/z = 718.3 (M+1)

Step-ii: tert-butyl 4-(2-fluoro-4-(3-(1-phenethyl-1H-pyrazol-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-82, tert-butyl 4-(2-fluoro-4-(3-(1-phenethyl-1H-pyrazol-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5,6-dihydropyridine-1(2H)-carboxylate (125mg, 0.174mmol) was reduced with palladium hydroxide (90mg) in ethyl acetate/ethanol 10/20 mL to afford 103mg (81.6% yield) of the titled compound. MS: m/z = 720.7 (M+1)

Step-iii: tert-butyl 4-(2-fluoro-4-(3-(1-phenethyl-1H-pyrazol-3-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(2-fluoro-4-(3-(1-phenethyl-1H-pyrazol-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (102mg, 0.141mmol) was hydrolyzed by sodium hydroxide (57mg, 1.418mmol) in THF/methanol/water (12/4/4 ml) to yield 67mg (84% yield) of the titled compound. MS: m/z = 566.5 (M+1)

Step-iv: 5-(3-fluoro-4-(piperidin-4-yl)phenyl)-3-(1-phenethyl-1H-pyrazol-3-yl)-1H-pyrrolo[2,3-b]pyridine

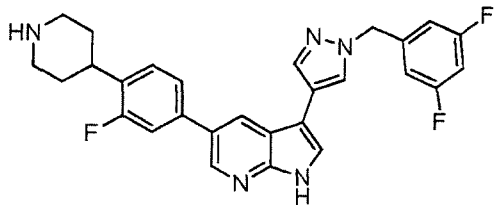
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(2-fluoro-4-(3-(1-phenethyl-1H-pyrazol-3-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-

carboxylate (66mg, 0.116mmol) was deprotected in TFA/toluene (5/5mL) to afford 23mg (34% yield) of the titled compound.

^{1}H NMR (CD_3OD, 300MHz): δ 8.82-8.81 (d, 1H), 8.58 (s, 1H), 7.87 (s, 1H), 7.58-7.45 (m, 4H), 7.23-7.11 (m, 5H), 6.577-6.570 (d, 1H), 4.48-4.44 (t, 2H), 3.56-3.52 (d, 2H), 3.24-3.15 (m, 5H), 2.15-2.03 (m, 4H). MS: m/z= 466.5(M+1), HPLC: 96.98% in method A.

Example 169

3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-5-(3-fluoro-4-(piperidin-4-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine



Step-i: tert-butyl 4-(4-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-fluorophenyl)-5,6-dihydropyridine-1(2H)-carboxylate

Using similar reaction conditions as described in step-i of example-1, 5-bromo-3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (step 1 product of example 71) (200 mg, 0.368 mmol) was coupled with tert-butyl 4-(2-fluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-5,6-dihydropyridine-1(2H)-carboxylate (intermediate 70) (296mg, 0.736 mmol) using potassium phosphate (234 mg, 1.104 mmol), tricyclohexyl phosphine (15 mg, 0.055 mmol) and $Pd_2(dba)_3$ (34mg, 0.036mmol) in dioxane/water (15/3 ml) to afford 104 mg (38.3% yield) of the pure product after column purification using 35% ethyl acetate in hexane as eluent. MS: m/z = 740.7 (M+1).

Step-ii: tert-butyl 4-(4-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-fluorophenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-82, tert-butyl 4-(4-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-fluorophenyl)-5,6-dihydropyridine-1(2H)-carboxylate (103mg, 0.139mmol) was reduced with palladium hydroxide (50mg) in ethyl acetate/ethanol 5/15 mL to afford 102mg (99% yield) of the titled compound. MS: m/z = 742.6 (M+1).

Step-iii: tert-butyl 4-(4-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-fluorophenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-

fluorophenyl)piperidine-1-carboxylate (101mg, 0.136mmol) was hydrolyzed by lithium hydroxide (57mg, 1.363mmol) in THF/methanol/water (12/4/4 ml) to yield 65mg (81% yield) of the titled compound. MS: m/z = 588.4 (M+1).

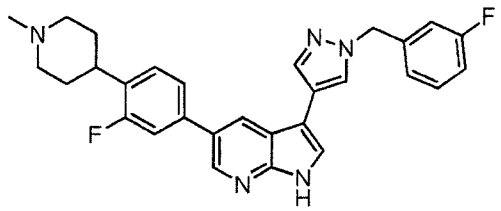
Step-iv: 3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-5-(3-fluoro-4-(piperidin-4-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-fluorophenyl)piperidine-1-carboxylate (64mg, 0.109mmol) was deprotected in TFA/toluene (5/5mL) to afford 14.9mg (28.3% yield) of the titled compound after purification by preparative TLC using 6% methanol in chloroform as eluent.

^{1}H NMR (CD_3OD, 300MHz): δ 8.48-8.47 (d, 1H), 8.38-8.37 (d, 1H), 8.25 (s, 1H), 7.96 (s, 1H), 7.66 (s, 1H), 7.53-7.39 (m, 3H), 6.92-6.86 (m, 3H), 5.44 (s, 2H), 3.24-3.20 (d, 2H), 3.09-3.07 (m, 1H), 2.87-2.80 (td, 2H), 1.89-1.77 (m, 4H). MS: m/z= 488.3 (M+1), HPLC: 95.30% in method A.

Example 170

5-(3-fluoro-4-(1-methylpiperidin-4-yl)phenyl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine



Step-i: 5-(3-fluoro-4-(piperidin-4-yl)phenyl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(2-fluoro-4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (product of step 1 of example 84) (130mg, 0.179mmol) was deprotected in methanol/HCl in dioxane (5/5mL) to afford 110mg (98.2% yield) of the titled compound. MS: m/z = 624.4 (M+1)

Step-ii: 5-(3-fluoro-4-(piperidin-4-yl)phenyl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-iii of example-133, tert-butyl 4-(2-fluoro-4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (109mg, 0.175mmol) was methylated using

paraformaldehyde (16mg, 0.524mmol), $Na(OAc)_3BH$ (111mg, 0.524mmol) and 3 drops of acetic acid in dichloroethane (10mL) to afford 89mg (80%yield) of the titled compound. MS: m/z = 638.4 (M+1).

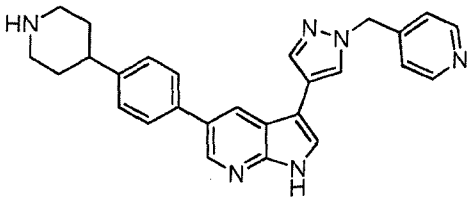
Step-iii: 5-(3-fluoro-4-(1-methylpiperidin-4-yl)phenyl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-iii of example-1, 5-(3-fluoro-4-(piperidin-4-yl)phenyl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (88mg, 0.138mmol) was hydrolyzed with lithium hydroxide(58mg, 1.381mmol) in THF/methanol/water (12/4/4mL) to yield 17 mg (20.7% yield) of the titled compound.

^1H NMR (CD_3OD, 300MHz): δ 8.68-8.67 (d, 1H), 8.60 (s, 1H), 8.29 (s, 1H), 7.98 (s, 1H), 7.79 (s, 1H), 7.60-7.30 (m, 4H), 7.13-7.00 (m, 3H), 5.44 (s, 2H), 3.70-3.50 (m, 2H), 3.30-3.10 (m, 3H), 2.93 (s, 3H), 2.16-2.02 (m, 4H). MS: m/z = 484.4 (M+1), HPLC: 97.49% in method A.

Example 171

5-(4-(piperidin-4-yl)phenyl)-3-(1-(pyridin-4-ylmethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine



Step-i: tert-butyl 4-(4-(3-(1-(pyridin-4-ylmethyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 4-(4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (Intermediate 67B) (150mg, 0.52mmol) was coupled with 4-((4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-yl)methyl)pyridine (intermediate 64G) (180mg, 0.63mmol) using sodium carbonate (165mg, 1.56mmol) and $Pd(dppf)Cl_2$ (18mg, 0.026mmol) in toluene/ ethanol/water (10/10/2 mL) to afford 142mg (crude) of the titled compound. MS:m/z = 589.4 (M-Boc+1).

Step-ii: tert-butyl 4-(4-(3-(1-(pyridin-4-ylmethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(3-(1-(pyridin-4-ylmethyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (142mg, 0.206mmol) was hydrolyzed with lithium

hydroxide(43mg, 1.030mmol) in THF/methanol/water (4/4/2mL) to yield 120mg (99.6% yield). MS: m/z = 535.3 (M+1)

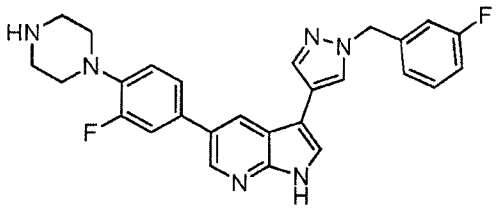
Step-iii: 5-(4-(piperidin-4-yl)phenyl)-3-(1-(pyridin-4-ylmethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(pyridin-4-ylmethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (120mg, 0.224mmol) was deprotected in TFA/DCM (5/5ml) to afford 14mg (14.3% yield) of the titled compound.

^{1}H NMR (CD_3OD, 300MHz): δ 8.78-8.76 (d, 2H), 8.53-8.51 (t, 2H), 8.35 (s, 1H), 8.07 (s, 1H), 7.75-7.70 (m, 5H), 7.43-7.41 (d, 2H), 5.78 (s, 2H), 3.55-3.51 (d, 2H), 3.21-3.13 (td, 2H), 3.03-2.95 (m, 1H), 2.03-1.90 (m, 2H). MS: m/z = 435.6(M+1), HPLC: 99.16% in method A.

Example 172

5-(3-fluoro-4-(piperazin-1-yl)phenyl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine



Step-i: tert-butyl 4-(2-fluoro-4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(2-fluoro-4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (product of step 1 of example 114) (120mg, 0.165mmol) was hydrolyzed with lithium hydroxide (35mg, 0.827mmol) in THF/methanol/water (5/5/2mL) to afford 80 mg (85% yield) of the titled compound. MS: m/z = 571.6 (M+1)

Step-ii: 5-(3-fluoro-4-(piperazin-1-yl)phenyl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine

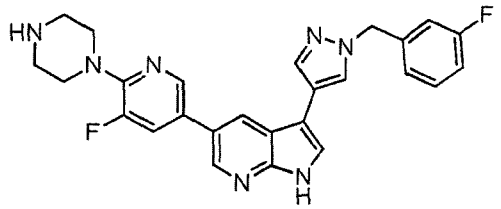
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(2-fluoro-4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (80mg, 0.140mmol) was deprotected in TFA/DCM (5/5ml) to afford 12mg (93% yield) of the titled compound.

^{1}H NMR (CD_3OD, 300MHz): δ 8.54 (s, 2H), 8.262-8.260 (d, 1H), 7.975-7.973 (d, 1H), 7.74 (s, 1H), 7.59-7.52 (m, 2H), 7.38-7.00 (m, 5H), 5.4 4 (s, 2H), 3.42-3.40 (m, 8H).

MS: m/z = 471.2 (M+1), HPLC: 97.06% in method B.

Example 173

5-(5-fluoro-6-(piperazin-1-yl)pyridin-3-yl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine



Step-i: tert-butyl 4-(3-fluoro-5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 4-(3-fluoro-5-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate (Intermediate 66R) (170mg, 0.251mmol) was coupled with 1-(3-fluorobenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 11) (113mg, 0.376mmol) using sodium carbonate(80mg, 0.753mmol) and Pd(dppf)Cl_2 (9.7mg, 0.012mmol) in toluene/ethanol/water (20/10/4 mL) to afford 160mg (88% yield) of the titled compound after purification by column (Silica gel 60/120) using 37% ethyl acetate in hexane as eluent. MS: m/z = 726.3 (M+1).

Step-ii: tert-butyl 4-(3-fluoro-5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(3-fluoro-5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate (100mg, 0.220mmol) was hydrolyzed with lithium hydroxide(93mg, 2.20mmol) in THF/methanol/water (16/4/6mL) to yield 125mg (99% yield). MS: m/z = 572.2 (M+1).

Step-iii: 5-(5-fluoro-6-(piperazin-1-yl)pyridin-3-yl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine

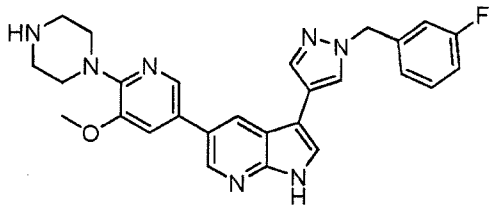
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(3-fluoro-5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate (125mg, 0.218mmol) was deprotected in methanol/ HCl in ether

(5/2.5ml) to afford 72mg (56.2% yield) of the titled compound after purification by prep HPLC.

^{1}H NMR (CD_3OD, 300MHz): δ 8.646-8.640 (d, 1H), 8.56 (s, 1H), 8.419-8.415 (d, 1H), 8.28 (s, 1H), 7.97 (s, 1H), 7.94-7.93 (d, 1H), 7.77 (s, 1H), 7.36-7.33 (m, 1H), 7.11-6.98 (m, 3H), 5.42 (s, 2H), 3.80-3.77 (m, 4H), 3.40-3.31 (m, 4H). MS: m/z = 472.3(M+1), HPLC: 98.87% in method A.

Example 174

3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(5-methoxy-6-(piperazin-1-yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine



Step-i: tert-butyl 4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxypyridin-2-yl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 4-(5-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxypyridin-2-yl)piperazine-1-carboxylate (Intermediate 66S) (175mg, 0.254mmol) was coupled with 1-(3-fluorobenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 11) (115mg, 0.380mmol) using sodium carbonate(81mg, 0.764mmol) and Pd(dppf)Cl_2 (9.4mg, 0.012mmol) in toluene/ethanol/water (20/10/4 mL) to afford 131mg (70% yield) of the titled compound after purification by column (Silica gel 60/120) using 37% ethyl acetate in hexane as eluent.

Step-ii: tert-butyl 4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxypyridin-2-yl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxypyridin-2-yl)piperazine-1-carboxylate (130mg, 0.176mmol) was hydrolyzed with lithium hydroxide(75g, 1.763mmol) in THF/methanol/water (16/4/6mL) to yield 92mg (90% yield). MS: m/z = 584.00 (M+1)

Step-iii: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(5-methoxy-6-(piperazin-1-yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxypyridin-2-

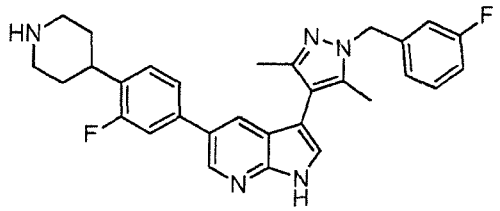
yl)piperazine-1-carboxylate (91mg, 0.156mmol) was deprotected in methanol/ HCl in dioxane (5/5ml) to afford 52mg (56% yield) of the titled compound.

^{1}H NMR (CD_3OD, 300MHz): δ 8.727-8.722 (d, 1H), 8.626-8.622 (d, 1H), 8.29 (s, 1H), 8.19-8.18 (d, 1H), 8.00 (s, 1H), 7.81 (s, 1H), 7.75-7.74 (d, 1H), 7.37-7.35 (q, 1H), 7.12-7.10 (d, 1H), 7.02-6.99 (m, 2H), 5.44 (s, 2H), 4.03 (s, 3H), 3.78-3.74 (t, 4H), 3.39-3.32 (m, 4H).

MS: m/z = 484.3 (M+1), HPLC: 97.58% in method A.

Example 175

5-(3-fluoro-4-(piperidin-4-yl)phenyl)-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine



Step-i: tert-butyl 4-(2-fluoro-4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5,6-dihydropyridine-1(2H)-carboxylate

Using similar reaction conditions as described in step-i of example-1, tert-butyl 4-(2-fluoro-4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5,6-dihydropyridine-1(2H)-carboxylate (intermediate 66Q) (300mg, 0.445mmol) was coupled with 1-(3-fluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 16) (177mg, 0.534mmol) using $Pd(dppf)Cl_2$(16mg, 0.022mol) and sodium carbonate (141mg, 1.335mmol) in toluene/ethanol/water(5/8/1 mL) to afford 250mg (74.8% yield) of the titled compound. MS: m/z= 750.4 (M+1).

Step-ii: tert-butyl 4-(2-fluoro-4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-82, tert-butyl 4-(2-fluoro-4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-5,6-dihydropyridine-1(2H)-carboxylate (250mg, 0.333mmol) was reduced with palladium hydroxide (250mg) in ethyl acetate/ethanol 10/10 mL to afford 200mg (80% yield) of the titled compound. MS: m/z = 752.9 (M+1).

Step-iii: tert-butyl 4-(2-fluoro-4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(2-fluoro-4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-

yl)phenyl)piperidine-1-carboxylate (200mg, 0.265mmol) was hydrolyzed by lithium hydroxide (56mg, 1.329mmol) in THF/methanol/water (5/3/1 mL) to yield 110mg (69.6% yield) of the titled compound. MS: m/z = 598.5 (M+1)

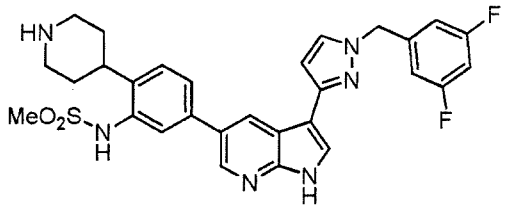
Step-iv: 5-(3-fluoro-4-(piperidin-4-yl)phenyl)-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(2-fluoro-4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidine-1-carboxylate (110mg, 0.184mmol) was deprotected in TFA/DCM (3/0.5mL) to afford 9mg (8.1% yield) of the titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ 8.6 (s, 1H), 8.14-8.13 (d, 1H), 7.55 (s, 1H), 7.50-7.30 (m, 4H), 7.05-6.95 (td, 2H), 6.90-6.85 (d, 1H), 5.37 (s, 2H), 3.52-3.49 (d, 2H), 3.24-3.14 (m, 3H), 2.20 (s, 3H), 2.18 (s, 3H), 2.10-1.95 (m, 4H). MS: m/z = 497.8 (M+1), HPLC: 96.3% in method A.

Example 176

N-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(piperidin-4-yl)phenyl)methanesulfonamide



Step-i: tert-butyl 4-(4-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(methylsulfonamido)phenyl)-5,6-dihydropyridine-1(2H)-carboxylate

Using similar reaction conditions as described in step-i of example-1, 5-bromo-3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (intermediate 63B) (200mg, 0.368mmol) was coupled with tert-butyl 4-(2-(methylsulfonamido)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-5,6-dihydropyridine-1(2H)-carboxylate (intermediate 65E) (210mg, 0.44mmol) using $Pd(PPh_3)_2Cl_2$(13mg, 0.018mol) and sodium carbonate (117mg, 1.1mmol) in DME/water(10/1 mL) to afford 250mg (83.3% yield) of the titled compound. MS: m/z = 814.7(M+1).

Step-ii: tert-butyl 4-(4-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(methylsulfonamido)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-82, tert-butyl 4-(4-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-

(methylsulfonamido)phenyl)-5,6-dihydropyridine-1(2H)-carboxylate (250mg, 0.307mmol) was reduced with palladium hydroxide (250mg) in ethyl acetate/ethanol 10/10 mL to afford 200mg (80% yield) of the titled compound. MS: m/z = 817.7(M+1).

Step-iii: tert-butyl 4-(4-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(methylsulfonamido)phenyl)piperidine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(methylsulfonamido)phenyl)piperidine-1-carboxylate (200mg, 0.245mmol) was hydrolyzed by lithium hydroxide (52mg, 1.225mmol) in THF/methanol/water (3/5/2 mL) to yield 110mg (66.6% yield) of the titled compound. MS: m/z = 662.8 (M+1)

Step-iv: N-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(piperidin-4-yl)phenyl)methanesulfonamide

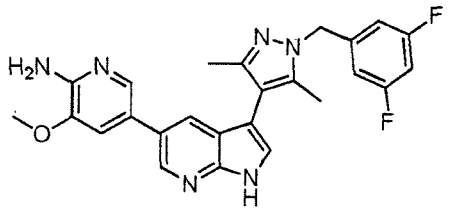
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(methylsulfonamido)phenyl)piperidine-1-carboxylate (110mg, 0.165mmol) was deprotected in TFA/DCM (5/1mL) to afford 3mg (2.6% yield) of the titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ 8.70-8.69 (d, 1H), 8.49-8.48 (d, 1H), 7.81 (s, 1H), 7.78-7.77 (d, 1H), 7.70-7.60 (m, 2H), 750-7.49 (d, 1H), 6.88-6.84 (m, 3H), 6.69-6.68 (d, 1H), 5.42 (s, 2H), 3.59-3.49 (m, 3H), 3.20-3.10 (t, 2H), 3.00 (s, 3H), 2.09-2.06 (d, 2H), 1.93-1.90 (m, 2H).

MS: m/z = 563.2 (M+1), HPLC: 95.6% in method A.

Example 177

5-(3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxypyridin-2-amine



Step-i: tert-butyl (5-(3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxypyridin-2-yl)carbamate

Using similar reaction conditions as described in step-i of example-1, tert-butyl (5-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxypyridin-2-yl)carbamate (intermediate 66B) (200mg, 0.322mmol) was coupled with 1-(3,5-difluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 24) (169mg, 0.483mmol)

using $Pd(dppf)Cl_2$ (12mg, 0.016mol) and sodium carbonate (103mg, 0.967mmol) in toluene/ethanol/water (5/2/1 ml) to afford 200mg (86.9% yield) of the titled compound after column purification using 2% methanol in DCM as eluent. MS: m/z = 615.2 (M-Boc+1).

Step-ii: tert-butyl (5-(3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxypyridin-2-yl)carbamate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl (5-(3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxypyridin-2-yl)carbamate (200mg, 0.279mmol) was hydrolyzed by lithium hydroxide (118mg, 2.798mmol) in THF/methanol/water (5/5/2 ml) to yield 100mg (63.6% yield) of the titled compound. MS: m/z = 560.9 (M+1)

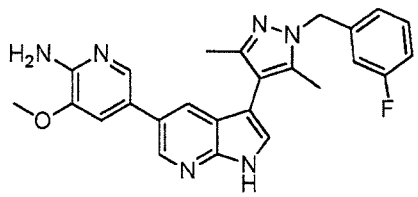
Step-iii: 5-(3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxypyridin-2-amine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl (5-(3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxypyridin-2-yl)carbamate (100mg, 0.178mmol)was was deprotected in TFA/DCM (2/5ml) to afford 10mg (9.8% yield) of the titled compound.

^1H NMR (CD_3OD, 400MHz): δ 8.56 (s, 1H), 8.14-8.13 (d, 1H), 7.70-7.69 (d, 2H), 7.53 (s, 1H), 6.91-6.86 (td, 1H), 6.79-6.76 (d, 2H), 5.36 (s, 2H), 4.07 (s, 3H), 2.20 (s, 3H), 2.18 (s, 3H). MS: m/z = 461.3 (M+1), HPLC: 95.61% in method B.

Example 178

5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxypyridin-2-amine



Step-i: tert-butyl (5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxypyridin-2-yl)carbamate

Using similar reaction conditions as described in step-i of example-1, tert-butyl (5-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxypyridin-2-yl)carbamate (intermediate 66B) (200mg, 0.322mmol) was coupled with 1-(3-fluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 16) (160mg, 0.483mmol) using $Pd(dppf)Cl_2$ (12mg, 0.016mol) and sodium carbonate (103mg, 0.967mmol) in

toluene/ethanol/water (5/2/1 ml) to afford 200mg (89.2% yield) of the titled compound after column purification using 2% methanol in DCM as eluent. MS: m/z = 597.5 (M-Boc+1).

Step-ii: tert-butyl (5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxypyridin-2-yl)carbamate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl (5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxypyridin-2-yl)carbamate (200mg, 0.287mmol) was hydrolyzed by lithium hydroxide (121mg, 2.870mmol) in THF/methanol/water (5/5/2 ml) to yield 100mg (64.5% yield) of the titled compound.

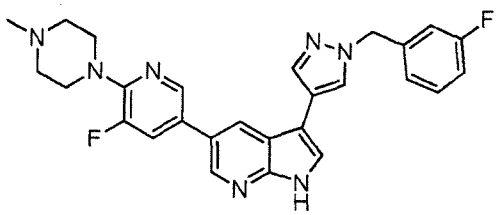
Step-iii: 5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxypyridin-2-amine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl (5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxypyridin-2-yl)carbamate (100mg, 0.184mmol)was was deprotected in TFA/DCM (2/5ml). This afforded 5.2mg (5.0% yield) of the titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ 8.54 (s, 1H), 8.10-8.09 (d, 1H), 7.689-7.687 (d, 2H), 7.50 (s, 1H), 7.40-7.30 (m, 1H), 7.05-6.95 (m, 2H), 6.90-6.87 (t, 1H), 5.36 (s, 2H), 4.10 (s, 3H), 2.20 (s, 3H), 2.18 (s, 3H). MS: m/z = 443.4 (M+1), HPLC: 93.64% in method A.

Example 179

5-(5-fluoro-6-(4-methylpiperazin-1-yl)pyridin-3-yl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine



Step-i: 5-(5-fluoro-6-(piperazin-1-yl)pyridin-3-yl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(3-fluoro-5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazine-1-carboxylate (step 1 product of example 173) (550mg, 0.758mmol) was deprotected in methanol/ HCl in dioxane (5/5ml) to afford 342mg (72% yield) of the titled compound. MS: m/z = 626.5 (M+1).

Step-ii: 5-(5-fluoro-6-(4-methylpiperazin-1-yl)pyridin-3-yl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-iii of example-133, 5-(5-fluoro-6-(piperazin-1-yl)pyridin-3-yl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (170mg, 0.272mmol) was methylated using paraformaldehyde (24mg, 0.816mmol), $Na(OAc)_3BH$ (172mg, 0.816mmol) and 3 drops of acetic acid in dichloroethane (10mL) to afford 154mg (89%yield) of the titled compound. MS: m/z = 640.6 (M+1).

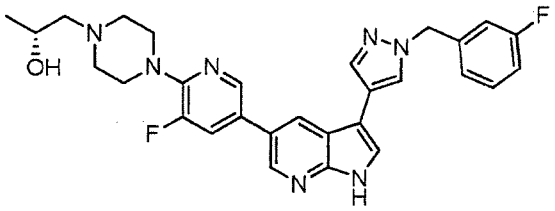
Step-iii: 5-(5-fluoro-6-(4-methylpiperazin-1-yl)pyridin-3-yl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-iii of example-1, 5-(5-fluoro-6-(4-methylpiperazin-1-yl)pyridin-3-yl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (150mg, 0.234mmol) was hydrolyzed with lithium hydroxide(98mg, 2.34mmol) in THF/methanol/water (12/4/4mL) to yield 34mg (30% yield) after purification by prep TLC using 8% methanol in chloroform as eluent.

^1H NMR (CD_3OD, 300MHz): δ 8.459-8.452 (d, 1H), 8.36-8.34 (m, 2H), 8.24 (s, 1H), 7.94 (s, 1H), 7.85-7.79 (dd, 1H), 7.65 (s, 1H), 7.41-7.33 (q, 1H), 7.12-7.00 (m, 3H), 5.43 (s, 2H), 3.57-3.54 (t, 4H), 2.65-2.62 (m, 4H), 2.37 (s, 3H). MS: m/z = 486.2 (M+1), HPLC: 98.03% in method A.

Example 180

(R)-1-(4-(3-fluoro-5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol



Step-i: (R)-1-(4-(3-fluoro-5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-i of example-82A, 5-(5-fluoro-6-(piperazin-1-yl)pyridin-3-yl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine(product of step 1 of example 179) (170mg, 0.272mmol) was alkylated using (S)-2-methyloxirane (32mg, 0.544mmol), DIPEA (105mg, 0.812mmol) and ethanol (5mL) to get 147mg (79% yield) of the titled compound. MS: m/z = 684.2 (M+1).

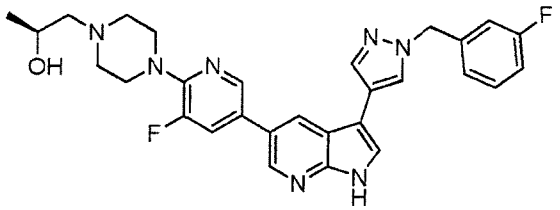
Step-ii: (R)-1-(4-(3-fluoro-5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-iii of example-1, (R)-1-(4-(3-fluoro-5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol (146mg, 0.213mmol) was hydrolyzed with lithium hydroxide (89mg, 2.137mmol) in THF/methanol/water (12/4/4mL) to yield 64mg (57% yield) after purification by prep TLC using 8% methanol in chloroform as eluent.

^{1}H NMR (CD_3OD, 300MHz): δ 8.45-8.44 (d, 1H), 8.35-8.32 (m, 2H), 8.32 (s, 1H), 7.94 (s, 1H), 7.83-7.78 (dd, 1H), 7.65 (s, 1H), 7.40-7.33 (m, 1H), 7.12-7.00 (m, 3H), 5.43 (s, 2H), 4.02-3.95 (m, 1H), 3.56-3.53 (t, 4H), 2.77-2.63 (m, 4H), 2.47-2.33 (m, 2H), 1.18-1.16 (d, 3H). MS: m/z = 530.2 (M+1), HPLC: 98.70% in method A.

Example 181

(S)-1-(4-(3-fluoro-5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol



Step-i: (S)-1-(4-(3-fluoro-5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-i of example-82A, 5-(5-fluoro-6-(piperazin-1-yl)pyridin-3-yl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine(product of step 1 of example 179) (127mg, 0.203mmol) was alkylated using (S)-2-methyloxirane (23mg, 0.406mmol), DIPEA (105mg, 0.812mmol) and ethanol (5mL) to get 135mg (97.8% yield) of the titled compound. MS: m/z = 684.7 (M+1).

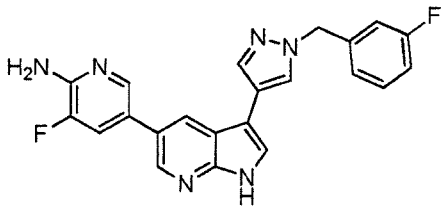
Step-ii: (S)-1-(4-(3-fluoro-5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol

Using similar reaction conditions as described in step-iii of example-1, (S)-1-(4-(3-fluoro-5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol (134mg, 0.196mmol) was hydrolyzed with lithium hydroxide(82mg, 1.964mmol) in THF/methanol/water (12/4/4mL) to yield 56mg (54.6% yield) after purification by prep TLC using 8% methanol in chloroform as eluent.

^{1}H NMR (CD_3OD, 300MHz): δ 8.449-8.442 (d, 1H), 8.35-8.32 (m, 2H), 8.23 (s, 1H), 7.94 (s, 1H), 7.82-7.77 (dd, 1H), 7.64 (s, 1H), 7.40-7.33 (q, 1H), 7.12-7.00 (m, 3H), 5.43 (s, 2H), 4.05-3.95 (m, 1H), 3.56-3.32 (t, 4H), 2.77-2.62 (m, 4H), 2.47-2.33 (m, 2H), 1.18-1.16 (d, 3H). MS: m/z = 530.3 (M+1), HPLC: 95.33% in method A.

Example 182

3-fluoro-5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-amine



Step-i: tert-butyl (3-fluoro-5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)carbamate

Using similar reaction conditions as described in step-i of example-1, tert-butyl (3-fluoro-5-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)carbamate (intermediate 66T) (150mg, 0.24mmol) was coupled with 1-(3-fluorobenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 11) (82mg, 0.27mmol) using $Pd(PPh_3)_2Cl_2$ (8mg, 0.012mol) and sodium carbonate (76mg, 0.72mmol) in toluene/ethanol/water (10/10/2 mL) to afford 122mg (crude) of the titled compound. MS: m/z = 657.2 (M+1)

Step-ii: tert-butyl (3-fluoro-5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)carbamate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl (3-fluoro-5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)carbamate (122mg, 0.185mmol) was hydrolyzed by lithium hydroxide (39mg, 0.928mmol) in THF/methanol/water (10/10/5 mL) to yield 90mg (96.4% yield) of the titled compound. MS: m/z = 447.1 (M+1) (de t-butyl).

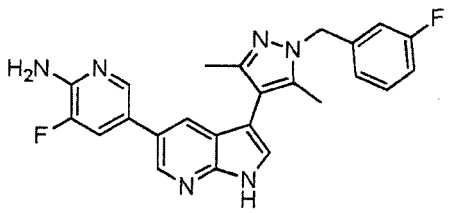
Step-iii: 3-fluoro-5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-amine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl (3-fluoro-5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)carbamate (90mg, 0.179mmol) was deprotected in TFA (10mL) to afford 15mg (16.3% yield) of the titled compound.

^{1}H NMR (CD_3OD, 300MHz): δ 8.47 (s, 1H), 8.42-8.41 (d, 1H), 8.26-8.21 (m, 2H), 8.11-.810 (d, 1H), 7.98 (s, 1H), 7.69 (s, 1H), 7.41-7.33 (m, 1H), 7.12-6.99 (m, 3H), 5.44 (s, 2H).
MS: m/z = 403.4 (M+1), HPLC: 97.56% in method A

Example 183

3-fluoro-5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-amine



Step-i: tert-butyl (3-fluoro-5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)carbamate

Using similar reaction conditions as described in step-i of example-1, tert-butyl (3-fluoro-5-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)carbamate (intermediate 66T) (150mg, 0.24mmol) was coupled with 1-(3-fluorobenzyl)-3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 16) (89mg, 0.27mmol) using $Pd(PPh_3)_2Cl_2$ (8.4mg, 0.012mol) and sodium carbonate (76mg, 0.72mmol) in toluene/ethanol/water(10/10/2 mL) to afford 110mg (crude yield) of the titled compound. MS: m/z = 685.2 (M+1).

Step-ii: tert-butyl (3-fluoro-5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)carbamate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl (3-fluoro-5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)carbamate (110mg, 0.16mmol) was hydrolyzed by lithium hydroxide (33mg, 0.8mmol) in THF/methanol/water (5/5/2 mL) to yield 78mg (91.5% yield) of the titled compound.

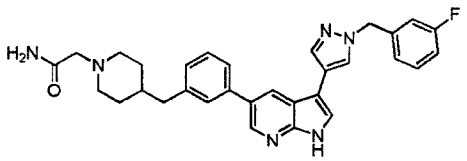
Step-iii: 3-fluoro-5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-amine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl (3-fluoro-5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)carbamate (78mg, 0.14mmol) was deprotected in TFA (10mL) to afford 10mg (12.5% yield) of the titled compound.

^{1}H NMR (DMSO-d_6, 300MHz): δ 11.95 (s, 1H), 8.51 (s, 1H), 8.14 (s, 1H), 8.05-7.95 (m, 1H), 7.89 (s, 1H), 7.49 (s, 1H), 7.43-7.38 (m, 1H), 7.16-6.91 (m, 3H), 5.32 (s, 2H), 2.17 (s, 3H), 2.13 (s, 3H). MS: m/z = 431.2 (M+1), HPLC: 98.88% in method B.

EXAMPLE 184

2-(4-(3-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)benzyl)piperidin-1-yl)acetamide



Step-i: 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(3-(piperidin-4-ylmethyl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(3-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)benzyl)piperidine-1-carboxylate (compound of step 1 of example 102) (32mg, 0.44mmol) was deprotected in methanol / ether HCl (5/0.3ml). This afforded 210mg (72.4% yield) of the titled compound.

Step-ii: 2-(4-(3-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)benzyl)piperidin-1-yl)acetamide

Using the same reaction conditions as described in step-i of example-82A 3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(3-(piperidin-4-ylmethyl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine hydrochloride (75mg, 0.114mmol) was alkylated using 2-chloroacetamide (16mg, 0.171mmol) and sodium bicarbonate (29mg, 0.342mmol) in acetone/ethanol (5/5mL) to get 30mg (38.96% yield) of the titled compound. MS: m/z = 676.8 (M+1).

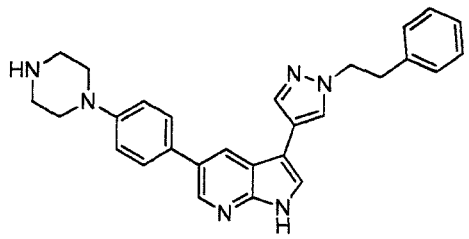
Step-iii: 2-(4-(3-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)benzyl)piperidin-1-yl)acetamide

Using similar reaction conditions as described in step-iii of example-1, 2-(4-(3-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)benzyl)piperidin-1-yl)acetamide (30mg, 0.044mmol) was hydrolyzed by lithium hydroxide (18mg, 0.44mmol) in THF/methanol/water (2/2/1 ml) to yield 10mg (43.4% yield) of the titled compound.

^{1}H NMR (DMSO-d_6, 400MHz): δ 8.516-8.512 (d, 1H), 8.43 (s, 1H), 8.347-8.343 (d, 1H), 7.98 (s, 1H), 7.77 (s, 1H), 7.59-7.54 (m, 2H), 7.42-7.38 (t, 2H), 7.17-7.09 (m, 5H), 5.41(s, 2H), 2.78 (s, 4H), 2.65-2.55 (m, 2H), 1.99-1.93 (t, 2H), 1.59-1.56 (m, 3H), 1.31-1.23 (m, 3H). MS: m/z = 523.4 (M+1), HPLC: 91.01% in method B.

Example 185

3-(1-phenethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine



Step-i: tert-butyl 4-(4-(3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-ii of example-1, tert-butyl 4-(4-(3-iodo-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (intermediate 41) (160mg, 0.2277mmol) was coupled with 1-phenethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (intermediate 59) (82mg, 0.2733mmol) in sodium carbonate (61mg, 0.5694mmol), $Pd(PPh_3)_2Cl_2$ (8mg, 0.0113mmol), toluene/ethanol/water (3/2/1 ml) to give 160mg (100% yield) of the titled compound. MS: m/z = 704.1 (M+1).

Step-ii: tert-butyl 4-(4-(3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate

Using similar reaction conditions as described in step-iii of example-1, tert-butyl 4-(4-(3-(1-phenethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (160mg, 0.227mmol) was hydrolyzed by lithium hydroxide(19mg, 0.455mmol), THF/Methanol/water (5/1/1 ml) to yield 130mg (crude) of the titled compound. MS: m/z = 549.4 (M+1).

Step-iii: 3-(1-phenethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine

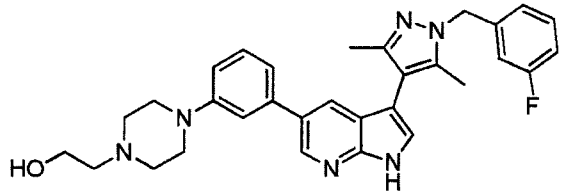
Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(4-(3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxylate (130mg, 0.238mmol) was deprotected in methanolic HCl (5ml). This afforded 78mg (58.6% yield) of the titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ 8.49 (s, 1H), 8.327-8.322 (d, 1H), 7.878-7.876 (d, 1H), 7.788-7.7.87 (d, 1H), 7.672-7.644 (m, 3H), 7.23-7.12 (m, 7H), 4.47-4.43 (t, 2H), 3.52-3.49

(m, 4H), 3.43-3.40 (m, 4H), 3.20-3.17 (t, 2H). MS: m/z = 449.4 (M+1), HPLC: 95.50% in method A.

Example 186

2-(4-(3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)ethanol



Step-i: 3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(3-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Using similar reaction conditions as described in step-ii of example-7, tert-butyl 4-(3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo [2,3-b] pyridin-5-yl)phenyl)piperazine-1-carboxylate (compound of Step-iii in example-38) (107mg, 0.145mmol) was deprotected in methanol (5ml), HCl in dioaxane (5ml).This afforded 94mg (95.9% yield)of the titled compound. MS: m/z = 635.2 (M+1).

Step-ii: 2-(4-(3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)ethanol

Using the same reaction conditions as described in step-ii of example-35, 3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(3-(piperazin-1-yl)phenyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (70mg, 0.104mmol) was alkylated with 2-bromoethanol (13mg, 0.104mmol) using potassium carbonate (73mg, 0.522mmol), DMF (2ml) to yield 60mg (84.5%) of the titled compound. MS: m/z = 679.3 (M+1).

Step-iii: 2-(4-(3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)ethanol

Using the same reaction conditions as described in step-iii of example-1, 2-(4-(3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1-tosyl-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)ethanol (58mg, 0.085mmol) was hydrolyzed by lithium hydroxide (36mg, 0.85mmol), THF/Methanol/water (12/6/3 ml) to yield 7mg (16%)of the titled compound.

^{1}H NMR (CD_3OD, 400MHz): δ 8.46-8.45 (d, 1H), 7.87-7.86 (d, 1H), 7.39-7.31 (m, 3H), 7.16 (s, 1H), 7.10-7.08 (m, 1H), 7.04-6.97 (m, 3H), 6.87-6.84 (m, 1H), 3.75-3.74 (t, 2H), 2.82 (b, 4H), 2.53 (m, 2H), 2.21 (s, 3H), 2.17 (s, 3H).

MS: m/z = 525.0 (M+1), HPLC: 91.007% in method A.

PHARMACOLOGICAL ACTIVITY

ALK Wild Type (WT)

The ALK WT cell free assay was set up to evaluate the effects of these compounds as inhibitors of ALK enzyme. The enzymatic assay was standardized using recombinant human ALK enzyme (Cat# 08-518) from Carna Biosciences using Ultra Light Poly GT (Cat# TRF 0100D) from Perkin Elmer as a substrate.TR-FRET (Time resolved fluorescence resonance energy transfer) detection technology was used for the read out. The final assay conditions were 50 mM HEPES pH 7.1, 10 mM $MgCl_2$, 2 mM $MnCl_2$, 0.01% BSA, 2.5 mM DTT, 0.1 mM $Na_3 VO_4$, 40 nM Ultra Light Poly GT, 2.5 ng ALK WT enzyme, 1µM ATP and 125 nM Lance Eu-W1024 labeled anti phospho tyrosine antibody (Cat# AD0203, Perkin Elmer) in 384 well format. The assay reaction time with the substrate was 30 minutes after which the antibody detection mix is added. The TR-FRET signal (Excitation at 340 nm, Emission at 615 nm and 665 nm) was read with 50 µs delay time on Victor^3 V fluorimeter. The data is calculated using the ratio of reading at 665 nM to 615 nM. The final concentration of DMSO was 1 % in the assay. Compounds were screened at 100 nM and 1 µM concentrations with pre-incubation of the enzymes with compound for 30 minutes. Each individual IC_{50} was determined using 10 point dose response curve generated by GraphPad Prism software Version 4 (San Diego, California, USA) using non linear regression curve fit for sigmoidal dose response (variable slope).

The compounds prepared were tested using the above assay procedure and the results obtained are given in Table-8. Percentage inhibition at concentrations of 100 nM and 1.0 µM are given in table along with the IC_{50} (nM) details for selected examples. The IC_{50} values of the compounds are set forth in Table-8 wherein "A" refers to an IC_{50} value of less than 50 nM, "B" refers to IC_{50} value in range of 50.01 to 250 nM and "C" refers to IC_{50} value of greater than 250 nM.

Table 8: In-vitro screening result of compounds of invention.

Example No	ALK-100 nM % inhibition	ALK-1µM % inhibition	IC_{50} (nM) ALK WT
1	-	92	B
2	-	33	C
3	-	65	C

Example No	ALK-100 nM % inhibition	ALK-1μM % inhibition	IC_{50} (nM) ALK WT
4	-	95	B
5	-	69	B
6	-	99	A
7	20	53	-
8	81	97	A
9	-	98	A
10	-	81	B
11	64	90	A
12	-	87	C
13	-	96	A
14	-	95	A
15	33	75	-
16	33	66	-
17	13	53	-
18	62	94	B
19	63	96	B
20	17	75	C
21	82	96	A
22	62	87	A
23	73	99	B
24	53	96	A
25	86	93	A
26	96	100	A
27	9	8	-
28	14	49	-
29	28	48	-
30	21	21	-
31	-	55	C
32	-	99	A
33	97	100	A

Example No	ALK-100 nM % inhibition	ALK-1μM % inhibition	IC_{50} (nM) ALK WT
34	91	99	A
35	98	99	A
36	96	99	A
37	93	98	A
38	87	99	A
39	92	99	A
40	94	100	A
41	90	100	A
42	92	100	A
43	92	99	A
44	95	100	A
45	51	80	B
46	80	98	A
47	90	100	A
48	52	83	B
49	70	91	A
50	60	89	A
51	84	100	A
52	12	80	C
53	-	-	-
54	0	25	-
55	2	43	-
56	91	100	A
57	93	100	A
58	92	100	A
59	49	77	B
60	9	10	-
61	73	96	A
62	87	100	A
63	15	48	-

Example No	ALK-100 nM % inhibition	ALK-1μM % inhibition	IC_{50} (nM) ALK WT
64	59	82	A
65	97	100	A
66	38	95	-
67	98	100	A
68	70	93	-
69	15	76	-
70	91	99	A
71	94	100	A
72	76	100	B
73	92	97	A
74	51	92	B
75	61	100	A
76	32	94	B
77	85	100	A
78	100	101	A
79	101	102	A
80	65	93	B
81	94	96	A
82	99	100	A
82A	96	98	A
83	96	100	A
84	98	100	A
85	95	100	A
86	96	98	A
87	84	99	A
88	89	99	A
89	84	98	A
90	97	100	A
91	99	100	A
92	98	100	A

Example No	ALK-100 nM % inhibition	ALK-1μM % inhibition	IC_{50} (nM) ALK WT
93	79	97	A
94	98	100	A
95	83	99	B
96	70	100	A
97	76	98	A
98	24	95	B
99	89	99	A
100	100	100	A
101	99	100	A
102	91	100	A
102A	91	94	A
103	95	100	A
104	98	100	A
105	98	100	A
106	97	100	A
107	99	100	A
108	97	100	A
109	76	100	-
110	94	98	A
111	82	100	A
112	90	100	-
113	90	97	A
114	92	99	-
115	94	100	-
116	68	97	B
117	91	95	A
118	94	98	A
119	86	93	A
120	95	99	A
121	91	95	A

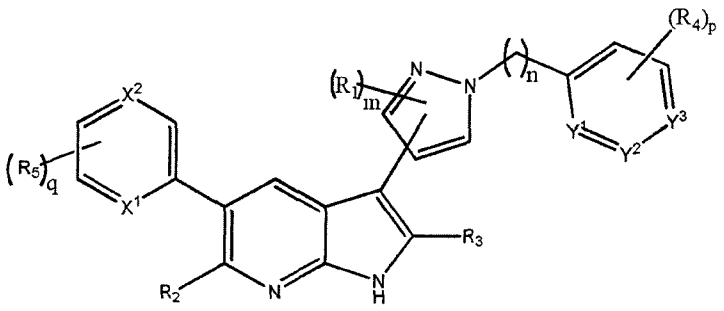
Example No	ALK-100 nM % inhibition	ALK-1μM % inhibition	IC_{50} (nM) ALK WT
122	90	96	A
123	92	96	A
124	17	86	C
125	86	97	A
126	95	97	A
127	96	97	A
128	92	94	A
129	96	99	A
130	88	99	A
131	83	99	A
132	100	100	A
133	97	100	A
134	97	100	A
135	95	100	A
136	97	99	A
137	99	100	A
138	100	100	A
139	99	100	A
140	80	95	A
141	58	96	A
142	94	100	-
143	60	98	-
144	76	94	A
145	83	99	A
146	60	97	B
147	99	100	A
148	94	100	A
149	95	100	A
150	92	100	A
151	92	97	A

Example No	ALK-100 nM % inhibition	ALK-1μM % inhibition	IC_{50} (nM) ALK WT
152	80	100	A
153	93	100	A
154	99	100	A
155	86	97	A
156	69	91	A
157	77	93	A
158	85	94	A
159	91	100	A
160	20	84	B
161	86	97	A
162	75	96	A
163	88	98	A
164	96	99	A
165	99	100	A
166	90	98	A
167	69	97	B
168	23	71	C
169	99	100	A
170	98	100	A
171	41	88	B
172	99	100	A
173	92	98	A
174	96	100	A
175	96	100	A
176	86	99	A
177	96	100	A
178	94	100	A
179	92	99	A
180	93	100	A
184	92	100	A

Example No	ALK-100 nM % inhibition	ALK-1μM % inhibition	IC_{50} (nM) ALK WT
185	80	86	-
186	83	96	A

We claim,

1. A compound of formula (I);



(I)

or pharmaceutically acceptable salts or stereoisomers thereof;

wherein,

X^1 and X^2 are independently selected from CH or N;

$-Y^1-Y^2-Y^3-$ is:

a) –N=CH-CH=

b) –CH=N-CH=

c) –CH=CH-N= or

d) –CH=CH-CH=

each R_1 represents alkyl;

R_2 and R_3 are independently selected from hydrogen, alkyl or cycloalkyl;

each R_4 is independently selected from alkyl, halo, haloalkyl, hydroxyl, alkoxy, haloalkoxy, $-N(R_a)R_b$, nitro, cyano or -NHC(O)alkyl;

each R_5 is independently selected from alkyl, $-OR_a$, $-O(CH_2)_qN(R_a)R_b$, $-O(CH_2)_qOR_a$, $-N(H)SO_2R_a$, $-SO_2NHR_a$, $-N(R_a)R_b$, halo, optionally substituted heterocyclylalkyl, optionally substituted heterocyclyl; wherein the optional substituent at each occurrence is independently selected from alkyl, cyanoalkyl, hydroxyl, hydroxyalkyl, $-C(O)OR_a$, $-C(O)R_a$, $-(CH_2)_nN(R_a)R_b$, $-(CH_2)_nC(O)N(R_a)R_b$, $-C(O)N(R_a)R_b$, $-C(O)(CH_2)_nR_a$, $-SO_2R_a$, $-C(O)(CH_2)_nN(R_a)R_b$, $-C(O)(CH_2)_nOR_a$, or $-(CH_2)_nOR_a$;

R_a and R_b are independently selected from hydrogen, alkyl, cycloalkyl or heterocyclyl;

'm' and 'p' are integers selected from 0 to 2, both inclusive;

'n' is an integer selected from 1 to 2, both inclusive;

'q' is an integer selected from 1 to 3 both inclusive.

2. The compound according to claim 1, wherein R_1 is methyl.

3. The compound according to claim 1, wherein X^1 and X^2 are CH.

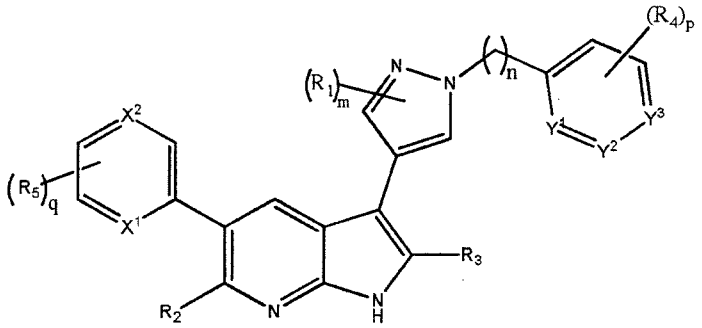
4. The compound according to claim 1, wherein X^1 is CH and X^2 is N.

5. The compound according to claim 1, wherein X^1 is N and X^2 is CH.

6. The compound according to claim 1, wherein $-Y^1-Y^2-Y^3-$ is $-CH=CH-CH=$.

7. The compound according to claim 1, wherein R_2 and R_3 are hydrogen.

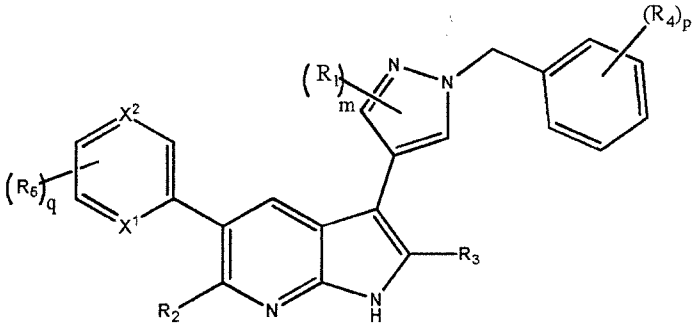
8. The compound of claim 1, wherein the compound of formula (I) is a compound of formula (IA):



(IA)

wherein, R_1, R_2, R_3, R_4, R_5, X^1, X^2, Y^1, Y^2, Y^3, m, n, p and q are same as defined in claim 1; or a pharmaceutically acceptable salts or a stereoisomers thereof.

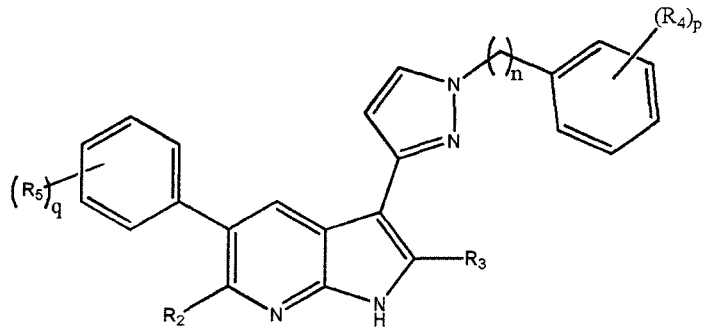
9. The compound of claim 1, wherein the compound of formula (I) is a compound of formula (IB):



(IB)

wherein, R_1, R_2, R_3, R_4, R_5, X^1, X^2, m, p and q are same as defined in claim 1; or a pharmaceutically acceptable salts or a stereoisomers thereof.

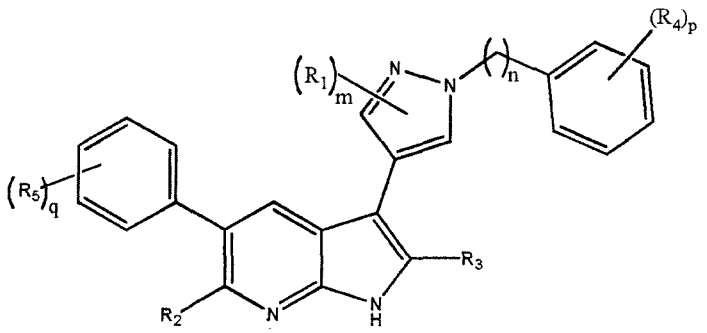
10. The compound of claim 1, wherein the compound of formula (I) is a compound of formula (IC):



(IC)

wherein, R_2, R_3, R_4, R_5, n, p and q are same as defined in claim 1; or a pharmaceutically acceptable salts or a stereoisomers thereof.

11. The compound of claim 1, wherein the compound of formula (I) is a compound of formula (ID):



(ID)

wherein, R_1, R_2, R_3, R_4, R_5, m, n, p and q are same as defined in claim 1; or a pharmaceutically acceptable salts or a stereoisomers thereof.

12. A compound selected from the group consisting of:

Ex. No	IUPAC NAME
1	N-(3-(3-(1-(2-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-

	yl)phenyl)methanesulfonamide;
2	N-(3-(3-(1-(3-(trifluoromethyl)benzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide;
3	N-(3-(3-(1-(4-methoxybenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide;
4	N-(3-(3-(1-(2,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide;
5	N-(3-(3-(1-(4-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide;
6	N-(3-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide;
7	N-(3-(3-(1-(3-nitrobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide;
8	N-(3-(3-(1-(3-aminobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide;
9	N-(3-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide;
10	N-(3-(3-(1-(3-chlorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide;
11	N-(3-(3-(1-(3-cyanobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide;
12	N-(3-(3-(1-benzyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide;
13	N-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide;

14	N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide;
15	N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)ethanesulfonamide;
16	N-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)cyclopropanesulfonamide;
17	N-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-morpholinophenyl)methanesulfonamide;
18	5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxy-N-methylbenzenesulfonamide;
19	N-(5-(3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide;
20	5-(3-(1-(2,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxy-N-methylbenzenesulfonamide;
21	5-(3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxy-N-methylbenzenesulfonamide;
22	N-(5-(3-(1-(2,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide;
23	N-(2-(2-(dimethylamino)ethoxy)-5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide;;
24	N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(2-hydroxyethoxy)phenyl)methanesulfonamide;
25	N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(3-hydroxypropoxy)phenyl)methanesulfonamide;
26	N-(2-(3-(dimethylamino)propoxy)-5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-

	pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide;
27	N-(5-(6-cyclopropyl-3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide;
28	N-(5-(6-cyclopropyl-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide;
29	N-(3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2,6-dimethoxyphenyl)methanesulfonamide;
30	N-(5-(2-cyclopropyl-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide;
31	N-(5-(2-cyclopropyl-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide;
32	3-(1-(2,5-difluorobenzyl)-1H-pyrazol-4-yl)-5-(3-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;
33	3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(3-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;
34	3-(4-(3-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propanenitrile;
35	3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(3-(4-isopropylpiperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;
36	3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(3-(4-methylpiperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;
37	3-(1-(3-fluorobenzyl)-3-methyl-1H-pyrazol-4-yl)-5-(3-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;
38	3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(3-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;

39	3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;
40	3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;
41	2-(4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)ethanol;
42	3-(1-(2,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine hydrochloride;
43	3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;
44	3-(1-(3-fluorobenzyl)-5-methyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;
45	4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)morpholine;
46	3-(1-(3-methoxybenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;
47	3-(1-(3-chlorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;
48	3-((3,5-dimethyl-4-(5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridin-3-yl)-1H-pyrazol-1-yl)methyl)benzonitrile;
49	1-(4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)ethanone;
50	N-(3-((3,5-dimethyl-4-(5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridin-3-yl)-1H-pyrazol-1-yl)methyl)phenyl)acetamide;
51	3-(3,5-dimethyl-1-(3-methylbenzyl)-1H-pyrazol-4-yl)-5-(4-(piperazin-1-

	yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;
52	3-(3,5-dimethyl-1-(3-(trifluoromethoxy)benzyl)-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;
53	3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(pyridin-4-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;
54	3-(1-(3-ethoxybenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;
55	6-cyclopropyl-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;
56	3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(4-methylpiperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;
57	2-(4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)-N,N-dimethylethanamine;
58	N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(piperazin-1-yl)phenyl)methanesulfonamide;
59	N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-morpholinophenyl)methanesulfonamide;
60	2-cyclopropyl-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;
61	3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(2-methoxy-4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;
62	3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(3-methoxy-4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;
63	2-cyclopropyl-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl) -1H-pyrrolo[2,3-b]pyridine;

64	N-(2-methoxy-5-(3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide;
65	5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxypyridin-3-amine;
66	N-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-hydroxypyridin-3-yl)methanesulfonamide;
67	N-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxypyridin-3-yl)methanesulfonamide;
68	N-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide;
69	N-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide;
70	N-(5-(3-(1-(2,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide;
71	N-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide;
72	N-(2-methoxy-5-(3-(1-(pyridin-3-ylmethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide;
73	N-(4-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide;
74	N-(5-(3-(1-(2-fluorophenethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide;
75	N-(5-(3-(1-(3-fluorophenethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)methanesulfonamide;
76	N-(5-(3-(1-(4-fluorophenethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-

	yl)-2-methoxyphenyl)methanesulfonamide;
77	N-(2-fluoro-5-(3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide;
78	N-(2-fluoro-5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)methanesulfonamide;
79	N-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-fluorophenyl)methanesulfonamide;
80	N-(5-(3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-fluorophenyl)methanesulfonamide;
81	5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxypyridin-2-amine;
82	3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(piperidin-4-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;
82A	(S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo [2,3-b]pyridin-5-yl)phenyl)piperidin-1-yl)propan-2-ol;
83	3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(1-methylpiperidin-4-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;
84	5-(3-fluoro-4-(piperidin-4-yl) phenyl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine;
85	3-(1-(3-methylbenzyl)-1H-pyrazol-4-yl)-5-(4-(piperidin-4-yl) phenyl)-1H-pyrrolo[2,3-b]pyridine;
86	Tert-butyl 4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo [2, 3-b] pyridin-5-yl)-2-methoxyphenyl) piperidine-1-carboxylate;
87	3-(1-(3-methoxybenzyl)-1H-pyrazol-4-yl)-5-(4-(piperidin-4-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;

88	3-(1-phenethyl-1H-pyrazol-4-yl)-5-(4-(piperidin-4-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;
89	5-(4-(piperidin-4-yl)phenyl)-3-(1-(pyridin-3-ylmethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine;
90	3-(1-(3-fluorobenzyl)-3-methyl-1H-pyrazol-4-yl)-5-(4-(piperidin-4-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;
91	3-(1-(3-fluorobenzyl)-5-methyl-1H-pyrazol-4-yl)-5-(4-(piperidin-4-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;
92	3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(4-(piperidin-4-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;
93	5-(4-(piperidin-4-yl)phenyl)-3-(1-(pyridin-2-ylmethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine;
94	N-(3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidin-4-amine;
95	N-(3-(3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidin-4-amine;
96	3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(3-(piperidin-4-yloxy)phenyl)-1H-pyrrolo[2,3-b]pyridine;
97	3-(1-phenethyl-1H-pyrazol-4-yl)-5-(3-(piperidin-4-yloxy)phenyl)-1H-pyrrolo[2,3-b]pyridine;
98	3-(1-phenethyl-1H-pyrazol-4-yl)-5-(3-(piperidin-4-ylmethyl) phenyl)-1H-pyrrolo[2, 3-b] pyridine;
99	3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-5-(3-(piperidin-4-ylmethyl)phenyl)-1H-pyrrolo[2,3-b]pyridine;
100	N-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-

	yl)phenyl)piperidin-4-amine;
101	N-(4-(3-(1-(3-fluorobenzyl)-3, 5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo [2, 3-b] pyridin-5-yl)phenyl) piperidin-4-amine;
102	3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(3-(piperidin-4-ylmethyl)phenyl)-1H-pyrrolo[2,3-b]pyridine;
102A	(S)-1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperidin-1-yl)propan-2-ol;
103	2-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)acetamide;
104	(S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol;
105	5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(piperazin-1-yl)aniline;
106	N-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(piperazin-1-yl)phenyl)methanesulfonamide hydrochloride;
107	N-(5-(3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(piperazin-1-yl)phenyl)methanesulfonamide hydrochloride;
108	4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazine-1-carboxamide;
109	5-(4-(4-methylpiperazin-1-yl)phenyl)-3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine;
110	2-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(methylsulfonamido)phenyl)piperazin-1-yl)acetamide;
111	3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;

112	(S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methoxyphenyl)piperazin-1-yl)propan-2-ol;
113	N-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(piperazin-1-yl)phenyl)methanesulfonamide;
114	(S)-1-(4-(2-fluoro-4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol;
115	(S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-methylphenyl)piperazin-1-yl)propan-2-ol;
116	(S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxyphenyl)piperazin-1-yl)propan-2-ol;
117	(S)-1-(4-(4-(3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol;
118	(S)-1-(4-(4-(3-(1-benzyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol;
119	(S)-1-(4-(4-(3-(1-(3-methylbenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol;
120	(R)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol;
121	(S)-1-(4-(3-fluoro-4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol;
122	1-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperidin-4-ol;
123	(2S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol;
124	2-cyclopropyl-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-

	pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)ethanone;
125	3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(4-(4-(methylsulfonyl)piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;
126	2-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)ethanol;
127	2-(dimethylamino)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)ethanone;
128	1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)-2-hydroxyethanone;
129	(S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-5-methyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol;
130	(S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-3-methyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)propan-2-ol;
131	5-(4-(piperazin-1-yl)phenyl)-3-(1-(pyridin-3-ylmethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine;
132	3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine;
133	3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine;
134	3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine;
135	(S)-1-(4-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol;
136	2-(4-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)acetamide;

137	3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine;
138	(S)-1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol;
139	2-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)acetamide;
140	3-(1-phenethyl-1H-pyrazol-4-yl)-5-(6-(piperazin-1-yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine;
141	5-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)-3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine;
142	2-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)ethanol;
143	(S)-1-(4-(5-(3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol;
144	(S)-1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-6-methoxypyridin-2-yl)piperazin-1-yl)propan-2-ol;
145	(S)-1-(4-(5-(3-(1-(3-methylbenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol;
146	(S)-1-(4-(6-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-3-yl)piperazin-1-yl)propan-2-ol;
147	2-(dimethylamino)-1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)ethanone;
148	(S)-1-(4-(5-(3-(1-benzyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol;
149	3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(4-(2-methoxyethyl)piperazin-1-

	yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine;
150	2-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)acetonitrile;
151	(S)-3-((4-(5-(6-(4-(2-hydroxypropyl)piperazin-1-yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-3-yl)-1H-pyrazol-1-yl)methyl)phenol;
152	3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(4-isobutylpiperazin-1-yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine;
153	(S)-1-(4-(5-(3-(1-(3-chlorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol;
154	1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)-2-hydroxyethanone;
155	1-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperidin-4-ol;
156	5-(6-(4-(ethylsulfonyl)piperazin-1-yl)pyridin-3-yl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine;
157	cyclopropyl(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)methanone;
158	3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(4-(methylsulfonyl)piperazin-1-yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine;
159	3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(6-(piperidin-4-yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine;
160	2-cyclopropyl-1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)ethanone;
161	(2S)-1-(4-(5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol;

162	(S)-1-(4-(5-(3-(1-(3-fluorobenzyl)-5-methyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol;
163	(S)-1-(4-(5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyrazin-2-yl)piperazin-1-yl)propan-2-ol;
164	(S)-1-(4-(4-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)-1,4-diazepan-1-yl)propan-2-ol;
165	5-(3-fluoro-4-(piperidin-4-yl)phenyl)-3-(1-(3-fluorobenzyl)-5-methyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine;
166	5-(3-fluoro-4-(piperidin-4-yl)phenyl)-3-(1-(3-fluorobenzyl)-3-methyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine ;
167	5-(3-fluoro-4-(piperidin-4-yl)phenyl)-3-(1-phenethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine;
168	5-(3-fluoro-4-(piperidin-4-yl)phenyl)-3-(1-phenethyl-1H-pyrazol-3-yl)-1H-pyrrolo[2,3-b]pyridine;
169	3-(1-(3,5-difluorobenzyl)-1H-pyrazol-4-yl)-5-(3-fluoro-4-(piperidin-4-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine;
170	5-(3-fluoro-4-(1-methylpiperidin-4-yl)phenyl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine;
171	5-(4-(piperidin-4-yl)phenyl)-3-(1-(pyridin-4-ylmethyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine;
172	5-(3-fluoro-4-(piperazin-1-yl)phenyl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine;
173	5-(5-fluoro-6-(piperazin-1-yl)pyridin-3-yl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine;
174	3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-5-(5-methoxy-6-(piperazin-1-

	yl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine;
175	5-(3-fluoro-4-(piperidin-4-yl)phenyl)-3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine;
176	N-(5-(3-(1-(3,5-difluorobenzyl)-1H-pyrazol-3-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-(piperidin-4-yl)phenyl)methanesulfonamide;
177	5-(3-(1-(3,5-difluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxypyridin-2-amine;
178	5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-methoxypyridin-2-amine;
179	5-(5-fluoro-6-(4-methylpiperazin-1-yl)pyridin-3-yl)-3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridine;
180	(R)-1-(4-(3-fluoro-5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol;
181	(S)-1-(4-(3-fluoro-5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-yl)piperazin-1-yl)propan-2-ol;
182	3-fluoro-5-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-amine;
183	3-fluoro-5-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-2-amine;
184	2-(4-(3-(3-(1-(3-fluorobenzyl)-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)benzyl)piperidin-1-yl)acetamide;
185	3-(1-phenethyl-1H-pyrazol-4-yl)-5-(4-(piperazin-1-yl)phenyl)-1H-pyrrolo[2,3-b]pyridine; and
186	2-(4-(3-(3-(1-(3-fluorobenzyl)-3,5-dimethyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)phenyl)piperazin-1-yl)ethanol;

or a pharmaceutically acceptable salt or a stereoisomer thereof.

13. A pharmaceutical composition, comprising at least one compound according to any one of claims 1 to 12 and/or pharmaceutically acceptable salts or stereoisomers thereof, and a pharmaceutically acceptable carrier or excipient.

14. A compound according to any one of claims 1 to 12, or pharmaceutically acceptable salts or stereoisomers thereof, for use as a medicament.

15. A compound according to any one of claims 1 to 12, or pharmaceutically acceptable salts or stereoisomers thereof, for use as a medicament, for the treatment of cancer or for inhibiting anaplastic lymphoma kinase (ALK).

16. The compound of any one of claims 1 to 12 or the pharmaceutical composition of claim 13 for use in treating cancer, wherein the cancer expresses an ALK oncogene.