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(54) Title: NOVEL COMPOUNDS FOR INHIBITION OF JANUS KINASE 1

(57) Abstract: An object of the invention is to provide compounds as selective JAK1 inhibitor, a process for preparation of the inhibitors, a composition containing the compounds and utility of the compounds.

NOVEL COMPOUNDS FOR INHIBITION OF JANUS KINASE 1

FIELD OF THE INVENTION

The invention relates to inhibitors of Janus Kinase 1 (JAK1), a process for synthesis of the compounds of the present invention, composition comprising the compounds and use of the compounds for inhibition of JAK1.

BACKGROUND OF THE INVENTION

Cytokines are key drivers of several biological pathways and anti-cytokine therapy is indicated if there is any dysregulation in the pathway. Signalling pathways for Type I and Type II cytokine receptors, a family of receptors employed by over 50 cytokines, interleukins, interferons, colony stimulating factors, and hormones. Like other receptor super families, Type I and Type II cytokine receptors are related by their mode of intracellular signaling: they all employ JAKs. Janus Kinases (JAK) are intracellular tyrosine kinases linked to intracellular domains of many cytokine receptors. There are four JAK isoforms: JAK1, JAK2, JAK3 and TYK2. JAK1, JAK2, JAK3 and Tyrosine Kinase 2 (TYK2) bind directly to the intracellular domains of Type I/II cytokine receptors and not to other classes of cytokine receptors. Different cytokine receptor families utilize specific JAK isoforms for signal transduction. Phosphorylation of JAK when cytokine binds to its cognate receptor leads to phosphorylation of other intracellular molecules that eventually leads to gene transcription. JAK-dependent cytokines are major contributors to immunopathology and that blocking such cytokines with biologics can be beneficial in immune-mediated diseases and in cancers and several other major disease and disorders.

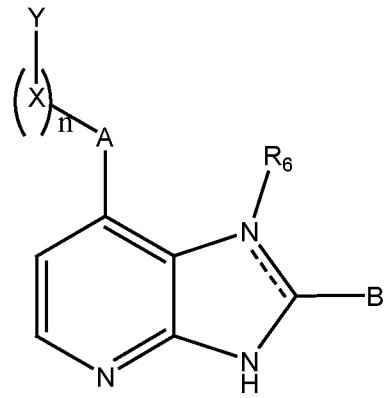
Several inhibitors of JAK kinase exist. They block multiple JAKs and therefore inhibit the actions of a large variety of cytokines and several pan-JAK inhibitors continue to be developed. The JAK isoforms vary in function, and therefore there exists a need in the art for isoform-specific inhibitors that can reduce undesired effects from the administration of generalized JAK inhibitors. JAK1 plays a key role in types I and II interferon signaling and elicits signals from the interleukin-2, interleukin-4, gp130 and class II receptor families. As such, small molecule inhibition of JAK1 may intervene in the signaling pathways involved in oncology, inflammation and autoimmune diseases. However, to minimize adverse effects, especially those arising from JAK2 inhibition, the generation of selective inhibitors could in principle maintain efficacy and improve safety.

OBJECT OF THE INVENTION

An object of the invention is to provide compounds as selective JAK1 inhibitor, a process for preparation of the inhibitors, a composition containing the compounds and utility of the compounds.

SUMMARY OF THE INVENTION

The present invention discloses 1H-imidazo[4,5-b]pyridin-2(3H)-one as selective inhibitor of JAK 1 their pharmaceutically acceptable salts and isomers of formula I:



Wherein;

A is a 5 membered or a 6 membered carbocycle or heterocycle comprising 1 to 3 heteroatom selected from the group comprising O, N, S optionally substituted with CH_3, F or Cl;

B is H or alkoxy or O, -CO-, optionally substituted 3 to 8 carbocyclic ring, 3 to 8 membered heterocyclic ring containing 1 to 3 heteroatoms selected from the group comprising O, N, S,

X is independently, H, $(CH_2)n$, -CO-, OCO, COO; $CO(CH_2)n$, $(NH_2)n$; $(CH_2)n(NH_2)n$; $(CH_2)n(NH_2)nCN$; CONH; $CONR_1R_2$, $CO(NH_2)n$; $(CH_2)nCO(NH_2)n$, $CO(NH_2)n(CH_2)CF_3$, $SO_2(CH_2)n$, $NH(CH_2)nCN$, unsubstituted or substituted 3-8 membered carbocylic ring or heterocyclic ring containing 1 to 3 heteroatoms selected from the group comprising O, N, S and SO_2, and substituents on the carboxylic or heterocyclic ring may be selected from Halogen, Alkoxy, CHMe, $-CH(CF_3)$, $-C(CF_3)(OH)$, $C(CF_3)(OMe)$, -CH(CN), CHOH, $CH(R_5)$,

Y may be absent or may be selected from H, R_1, R_2, halo, , C_1-C_6 Alkyl, C_1-C_6 Alkoxy CN, -CO-, COR_1, $(CH_2)n$, $-(CH_2)nCN$ -, CH_2CF_3, COOH, OR_1, NR_1R_2, $-COOR_1$, $-CON(R_1)_2$,$-SO_2(CH_2)n$,$-SO_2N(R_1)_2$, $-OCOR_1$, $CONHCH(CH_3)-CF_3$, CH_2CN,

$CH_2SO_2CH_3$ $-NR_1COR_1$, -CONH, $CONR_1R_2$, $-CO(NH_2)n(CH_2)nSO_2$; -$CONH(CH_2)nOH$, $CONH(CH_2)nSO_2R_1R_2$, $-CONH-(CH_2)nCF_3$, $-CONH(CH_2)nCF_3$,-$NHCONH(CH_2)nCF_3$, $NHCONHR_1$, $-NHCOR_1R_2$, $NR_1CONR_1R_2$, $(NH_2)n$, $-NH_2CH_2$, $NH_2CH_2CF_3$,$-CH(CF_3)-(CH)n-CO-N-R_1R_2$,$CH(CF3)-(CH)n-SO_2$, (CH)n;$CH(OH)(CF_3)$(Heretocycle)$R_1$, optionally substituted 3 to 8 membered carbocyclic ring, or 3 to 8 membered saturated, mono-, fused- or bridged heterocyclic ring containing 1 to 3 heteroatoms, selected from the group comprising O, N, S or SO_2, optionally substituted 3 to 8 membered heterocyclic ring containing 1 to 3 heteroatoms, selected from the group comprising O, N, S or SO_2, wherein the substitution may independently be R_1 and R_2 at any position of the ring;$C_{1\text{-}6}$alk-aryl, $ArC_{1\text{-}6}$alkyl;

R_1 and R_2 are independently selected from the group comprising H, halo, CN, CF3, hydroxyl, Amino, SO_2, SO_2, C_1-C_6 Alkyl, SO_2-C_3-C_8-cycloalkyl, CH_2CN, CH_2CF_3, unsubstituted or substituted C_1-C_6 straight or branched alkyl wherein the substituents are selected from halo, OH, CN, C_1-C_6 alkoxy, optionally substituted NH_2, C_1-C_6 alkylsulfonyl, optionally substituted $CONH_2$, unsubstituted or substituted C_3-C_8 carbocyclyl or 3-8 membered heterocyclic ring with 1-3 heteroatoms selected from O, N and S, SO_2, C_1-C_6 straight or branched alkenyl, C_1-C_6 straight or branched alkynyl, , C_1-C_6 alkyloxy; C_1-C_6 alkylamino, C_1-C_6 alkylcarbonyl, C(O)-C_3-C_8-cycloalkyl, heteroalkyl, optionally substituted $CONH_2$, C_3–C_8 cycloalkyl, C_3–C_8cycloalkenyl, C_3–C_8heterocycloalkyl, C_3–C_8heterocycloalkenyl, carbocycyl, aryl, and heteroaryl, -$CH(CF_3)-(CH)n-CO-N-R_3R_4$, $-CH(CF_3)-(CH)n-SO_2-NR_3R_4$, $CH(CF_3)-(CH)n-NR_3R_4$, $CH(CF_3)-NR_3R_4$, $CH(CF_3)-(CH)n-SO_2-CHR_3R_4$, wherein cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, carbocyclyl, aryl and heteroaryl groups are optionally substituted;

R_3 and R_4 are H, independently CH_3, C_3–C_8 cycloalkyl;

R_5 is unsubstituted or substituted 3-8 membered carbocylic ring or heterocyclic ring containing 1to 3 heteroatoms selected from the group comprising O, N, S, SO_2;

R_6, is independently H, C_1-C_6 straight or branched alkyl, halogen;

X can be connected to Y at any atom so as to arrive at chemically viable bond;

n is 0 to 3.

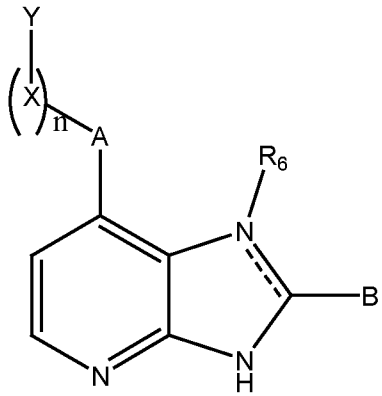
The present invention also discloses a process for preparing the compounds of the present invention, a composition comprising the compounds of the present invention and utility of the compounds of the present invention as selective JAK1 inhibitors.

BRIEF DESCRIPTION OF FIGURES

Figure 1 depicts cumulative Psoriasis Score and body weight of Example 1133 and 1215 in IMQ induced psoriasis mouse model. Figure 1a is based on the Psoriasis Score. Data is shown as Mean ± S.E.M.(n=8), * Significant difference as compared to Vehicle Control group. # Significant difference as compared to Naive Control group. Two-way ANOVA followed by Bonferroni Test. **P < 0.01 & ###/***P < 0.001. Figure 1(b) pertains to the body weight. Data is shown as Mean ± S.E.M.(n=8), # Significant difference as compared to Naive control. Two-way ANOVA followed by Bonferroni Test #P < 0.05.

DETAILED DESCRIPTION OF THE INVENTION

The present invention discloses 1H-imidazo[4,5-b]pyridin-2(3H)-one as selective inhibitor of JAK 1 their pharmaceutically acceptable salts and isomers of formula I:



Wherein;

A is a 5 membered or a 6 membered carbocycle or heterocycle comprising 1 to 3 heteroatom selected from the group comprising O, N, S optionally substituted with CH_3, F or Cl;

B is H or alkoxy or O, -CO-, optionally substituted 3 to 8 carbocyclic ring, 3 to 8 membered heterocyclic ring containing 1 to 3 heteroatoms selected from the group comprising O, N, S,

X is independently, H, $(CH_2)n$, -CO-, OCO, COO; $CO(CH_2)n$, $(NH_2)n$; $(CH_2)n(NH_2)n$; $(CH_2)n(NH_2)nCN$; CONH; $CONR_1R_2$, $CO(NH_2)n$; $(CH_2)nCO(NH_2)n$, $CO(NH_2)n(CH_2)CF_3$, $SO_2(CH_2)n$, $NH(CH_2)nCN$, unsubstituted or substituted 3-8 membered carbocylic ring or heterocyclic ring containing 1 to 3 heteroatoms selected from the group comprising O, N, S and

SO_2, and substituents on the carboxylic or heterocyclic ring may be selected from Halogen, Alkoxy, CHMe, -CH(CF_3), -C(CF_3)(OH), C(CF_3)(OMe), -CH(CN), CHOH, CH(R_5),

Y may be absent or may be selected from H, R_1, R_2, halo, , C_1-C_6 Alkyl, C_1-C_6 Alkoxy CN, -CO-, COR_1, (CH_2)n, -(CH_2)nCN -, CH_2CF_3, COOH, OR_1, NR_1R_2, -$COOR_1$, -$CON(R_1)_2$,-$SO_2(CH_2)$n,-$SO_2N(R_1)_2$, -$OCOR_1$, CONHCH(CH_3)-CF_3, CH_2CN, $CH_2SO_2CH_3$ -NR_1COR_1, -CONH, $CONR_1R_2$, -$CO(NH_2)n(CH_2)nSO_2$; -CONH(CH_2)nOH, CONH(CH_2)n$SO_2R_1R_2$, -CONH-(CH_2)nCF_3, -CONH(CH_2)nCF_3,-NHCONH(CH_2)nCF_3, $NHCONHR_1$, -$NHCOR_1R_2$, $NR_1CONR_1R_2$, (NH_2)n, -NH_2CH_2, $NH_2CH_2CF_3$,-CH(CF_3)-(CH)n-CO-N-R_1R_2,CH(CF_3)-(CH)n-SO_2, (CH)n;CH(OH)(CF_3)(Heretocycle)R_1, optionally substituted 3 to 8 membered carbocyclic ring, or 3 to 8 membered saturated, mono-, fused- or bridged heterocyclic ring containing 1 to 3 heteroatoms, selected from the group comprising O, N, S or SO_2, optionally substituted 3 to 8 membered heterocyclic ring containing 1 to 3 heteroatoms, selected from the group comprising O, N, S or SO_2, wherein the substitution may independently be R_1 and R_2 at any position of the ring;$C_{1\text{-}6}$alk-aryl, Ar$C_{1\text{-}6}$alkyl;

R_1 and R_2 are independently selected from the group comprising H, halo, CN, CF_3, hydroxyl, Amino, SO_2, SO_2, C_1-C_6 Alkyl, SO_2-C_3-C_8-cycloalkyl, CH_2CN, CH_2CF_3, unsubstituted or substituted C_1-C_6 straight or branched alkyl wherein the substituents are selected from halo, OH, CN, C_1-C_6 alkoxy, optionally substituted NH_2, C_1-C_6 alkylsulfonyl, optionally substituted $CONH_2$, unsubstituted or substituted C_3-C_8 carbocyclyl or 3-8 membered heterocyclic ring with 1-3 heteroatoms selected from O, N and S, SO_2, C_1-C_6 straight or branched alkenyl, C_1-C_6 straight or branched alkynyl, , C_1-C_6 alkyloxy; C_1-C_6 alkylamino, C_1-C_6 alkylcarbonyl, C(O)-C_3-C_8-cycloalkyl, heteroalkyl, optionally substituted $CONH_2$, C_3–C_8 cycloalkyl, C_3–C_8cycloalkenyl, C_3–C_8heterocycloalkyl, C_3–C_8heterocycloalkenyl, carbocycyl, aryl, and heteroaryl, -CH(CF_3)-(CH)n-CO-N-R_3R_4, -CH(CF3)-(CH)n-SO_2-NR_3R_4, CH(CF_3)-(CH)n-NR_3R_4, CH(CF_3)-NR_3R_4, CH(CF_3)-(CH)n-SO_2-CHR_3R_4, wherein cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, carbocyclyl, aryl and heteroaryl groups are optionally substituted;

R_3 and R_4 are H, independently CH_3, C_3–C_8 cycloalkyl;

R_5 is unsubstituted or substituted 3-8 membered carbocylic ring or heterocyclic ring containing 1 to 3 heteroatoms selected from the group comprising O, N, S, SO_2;

R_6, is independently H, C_1-C_6 straight or branched alkyl, halogen;

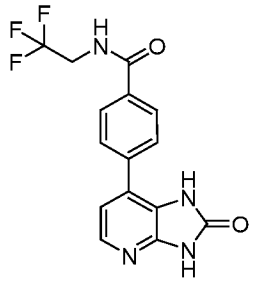
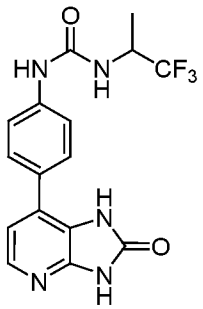
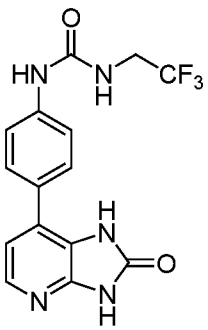
X can be connected to Y at any atom so as to arrive at chemically viable bond;

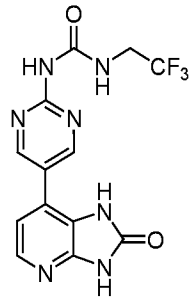
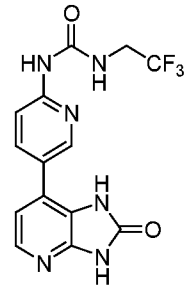
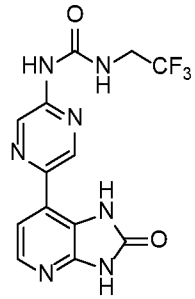
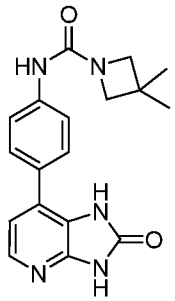
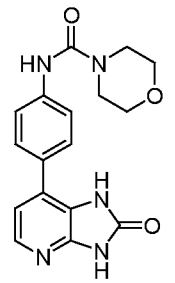
n is 0 to 3.

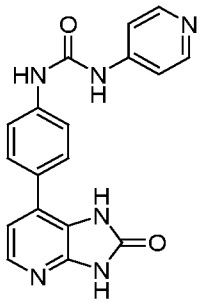
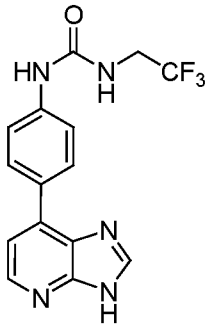
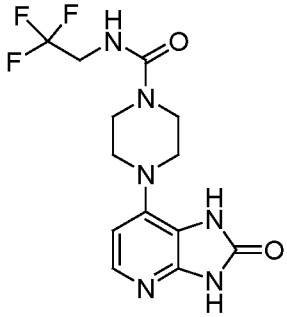
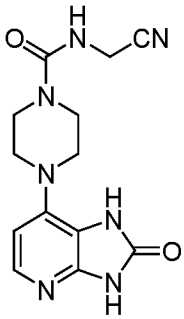
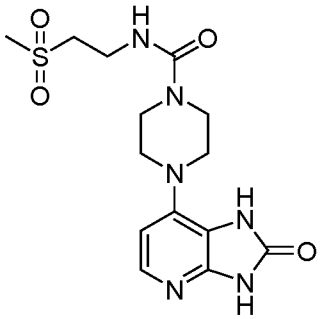
The compounds disclosed herein and their pharmaceutically acceptable salts can exist as single stereoisomers, racemates, and as mixtures of enantiomers and diastereomers. The compounds disclosed herein can also exist as geometric isomers. All such single stereoisomers, racemates and mixtures thereof, and geometric isomers are intended to be within the scope of the compounds disclosed herein.

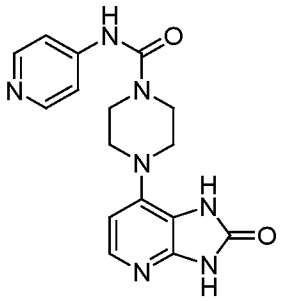
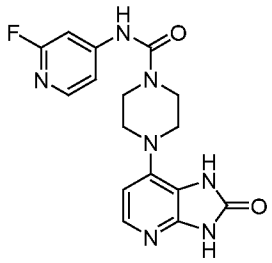
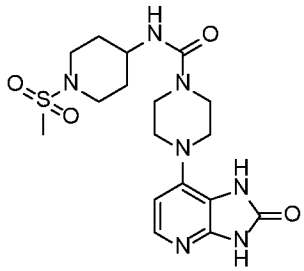
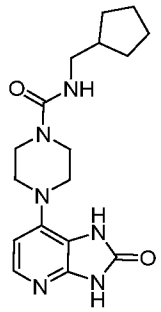
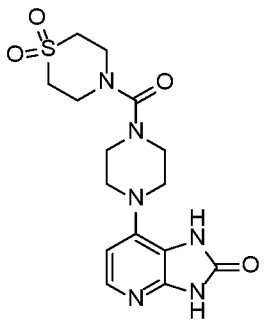
Exemplary compounds of the present invention of Formula I are illustrated herein below at Table 1.

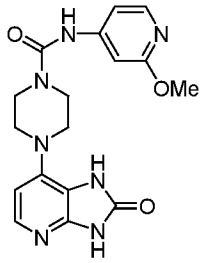
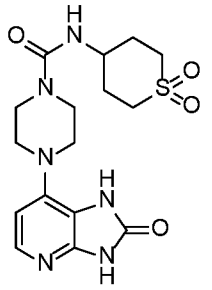
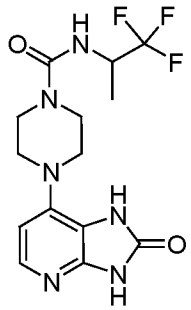
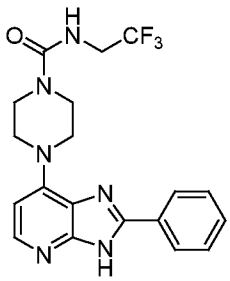
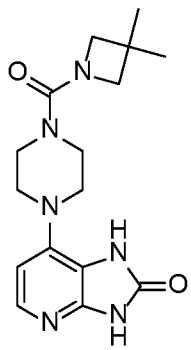
Table 1: Exemplary compounds of the present invention

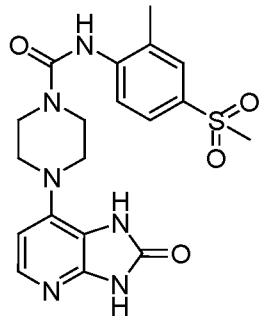
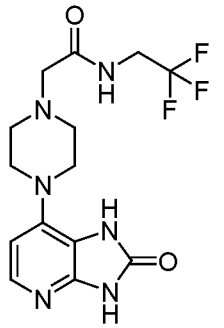
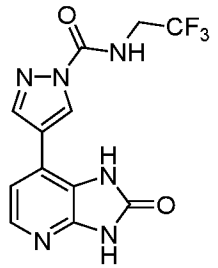
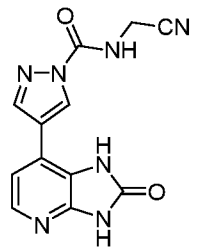
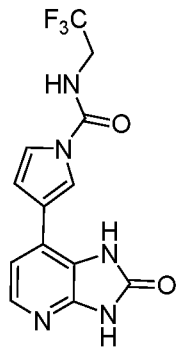
S. No	Structure	IUPAC Name
1001.		N-(2,2,2-trifluoroethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)benzamide
1002.		1-(1,1,1-trifluoropropan-2-yl)-3-(4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)phenyl)urea
1003.		1-(2,2,2-trifluoroethyl)-3-(4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)phenyl)urea

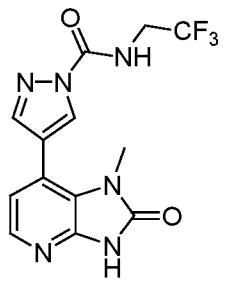
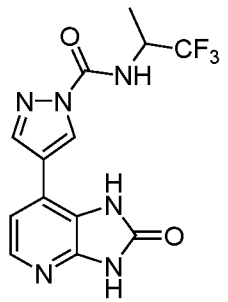
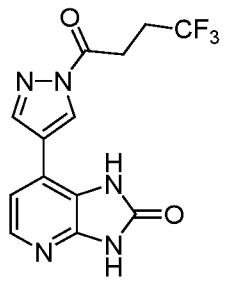
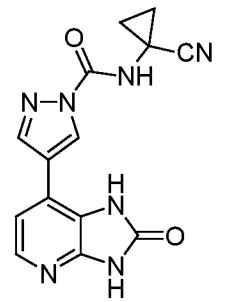
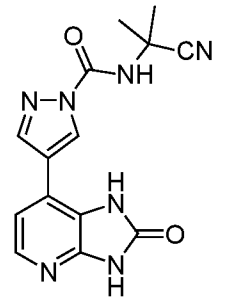
1004.		1-(2,2,2-trifluoroethyl)-3-(5-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)pyrimidin-2-yl)urea
1005.		1-(2,2,2-trifluoroethyl)-3-(5-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)pyridin-2-yl)urea
1006.		1-(5-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)pyrazin-2-yl)-3-(2,2,2-trifluoroethyl)urea
1007.		N-(4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)phenyl)-3,3-dimethylazetidine-1-carboxamide
1008.		N-(4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)phenyl)morpholine-4-carboxamide

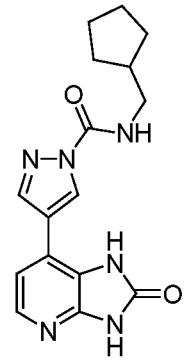
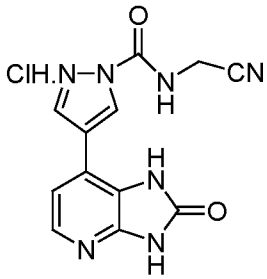
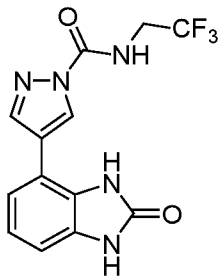
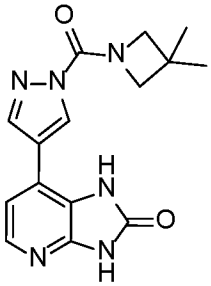
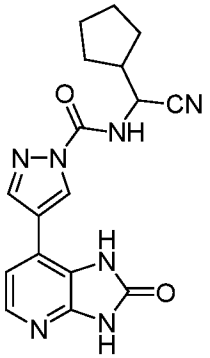
1009.		1-(4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)phenyl)-3-(pyridin-4-yl)urea
1010.		1-(4-(3H-imidazo[4,5-b]pyridin-7-yl)phenyl)-3-(2,2,2-trifluoroethyl)urea
1011.		N-(2,2,2-trifluoroethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)piperazine-1-carboxamide
1012.		N-(cyanomethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)piperazine-1-carboxamide
1013.		4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-N-(2-(methylsulfonyl)ethyl)piperazine-1-carboxamide

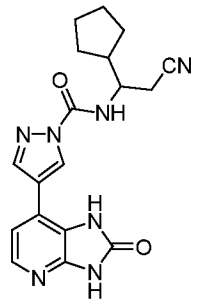
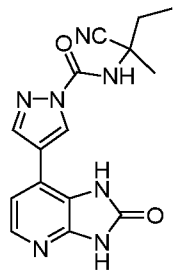
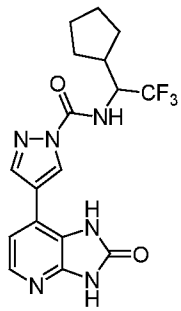
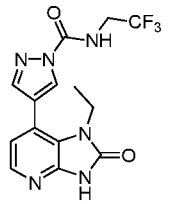
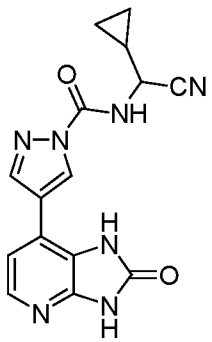
1014.		4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-N-(pyridin-4-yl)piperazine-1-carboxamide
1015.		N-(2-fluoropyridin-4-yl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)piperazine-1-carboxamide
1016.		N-(1-(methylsulfonyl)piperidin-4-yl)-4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)piperazine-1-carboxamide
1017.		N-(cyclopentylmethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)piperazine-1-carboxamide
1018.		7-(4-(1,1-dioxidothiomorpholine-4-carbonyl)piperazin-1-yl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one

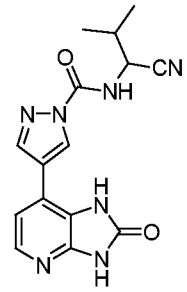
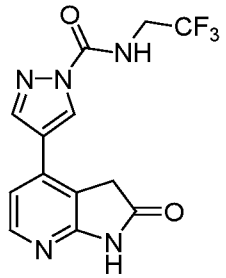
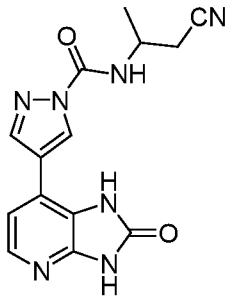
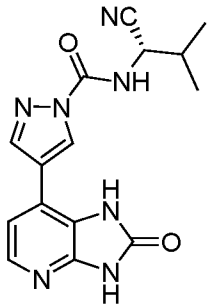
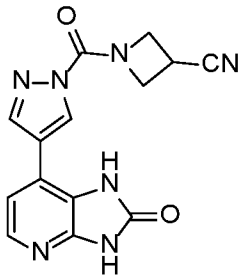
1019.		4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-N-(2-methoxypyridin-4-yl)piperazine-1-carboxamide
1020.		N-(1,1-dioxidotetrahydro-2H-thiopyran-4-yl)-4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)piperazine-1-carboxamide
1021.		N-(1,1,1-trifluoropropan-2-yl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)piperazine-1-carboxamide
1022.		N-(2,2,2-trifluoroethyl)-4-(2-phenyl-3H-imidazo[4,5-b]pyridin-7-yl)piperazine-1-carboxamide
1023.		7-(4-(3,3-dimethylazetidine-1-carbonyl)piperazin-1-yl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one

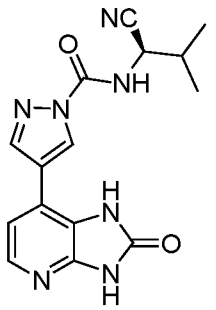
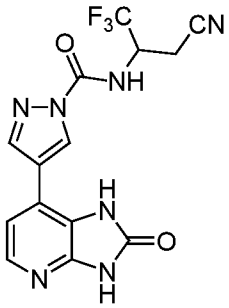
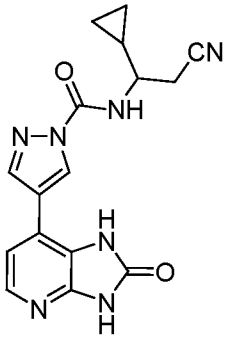
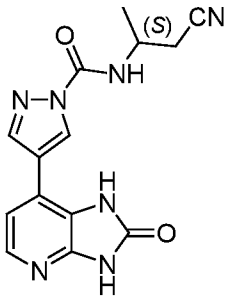
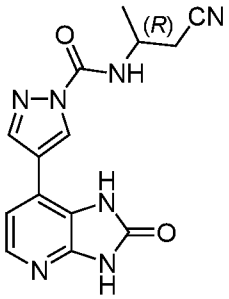
1024.		4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-N-(2-methyl-4-(methylsulfonyl)phenyl)piperazine-1-carboxamide
1025.		N-(2,2,2-trifluoroethyl)-2-(4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)piperazin-1-yl)acetamide
1026.		N-(2,2,2-trifluoroethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide
1027.		N-(cyanomethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide
1028.		N-(2,2,2-trifluoroethyl)-3-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrrole-1-carboxamide

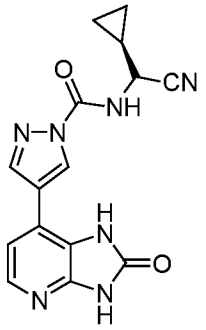
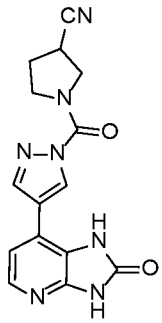
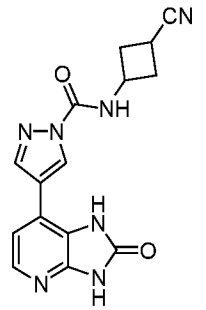
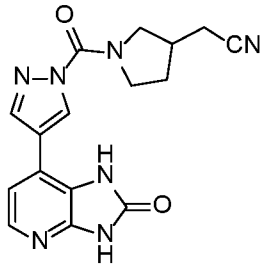
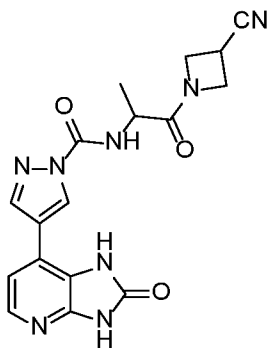
1029.		N-(2,2,2-trifluoroethyl)-4-(2,3-dihydro-1-methyl-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide
1030.		N-(1,1,1-trifluoropropan-2-yl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide
1031.		7-(1-(4,4,4-trifluorobutanoyl)-1H-pyrazol-4-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one
1032.		N-(1-cyanocyclopropyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide
1033.		N-(2-cyanopropan-2-yl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide

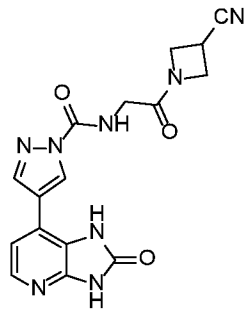
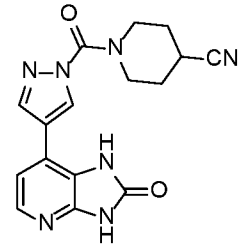
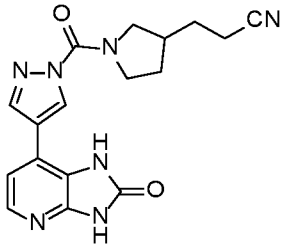
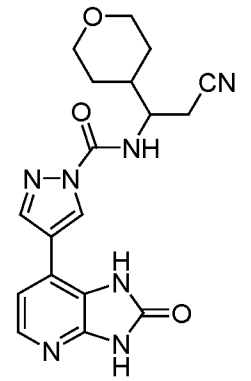
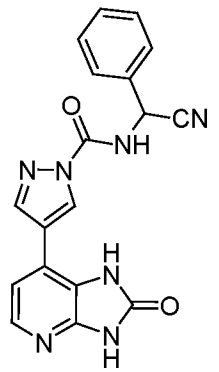
1034.		N-(cyclopentylmethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide
1035.		N-(cyanomethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide hydrochloride
1036.		N-(2,2,2-trifluoroethyl)-4-(2,3-dihydro-2-oxo-1H-benzo[d]imidazol-4-yl)-1H-pyrazole-1-carboxamide
1037.		7-(1-(3,3-dimethylazetidine-1-carbonyl)-1H-pyrazol-4-yl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one
1038.		N-(cyano(cyclopentyl)methyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide

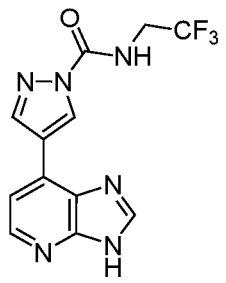
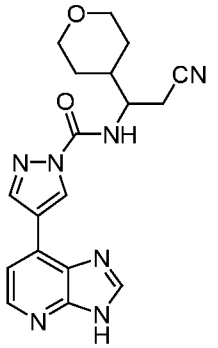
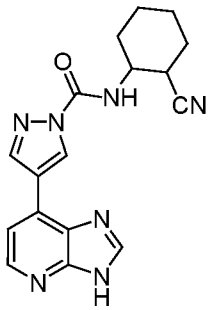
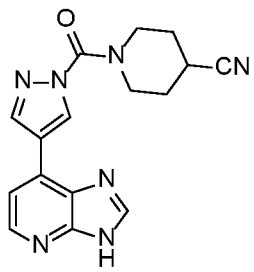
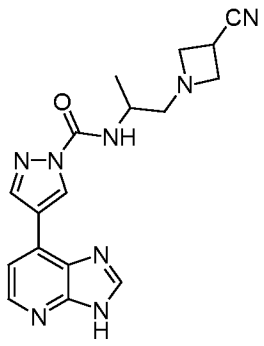
1039.		N-(2-cyano-1-cyclopentylethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide
1040.		N-(2-cyanobutan-2-yl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide
1041.		N-(1-cyclopentyl-2,2,2-trifluoroethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide
1042.		4-(1-ethyl-2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-N-(2,2,2-trifluoroethyl)-1H-pyrazole-1-carboxamide
1043.		N-(cyano(cyclopropyl)methyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide

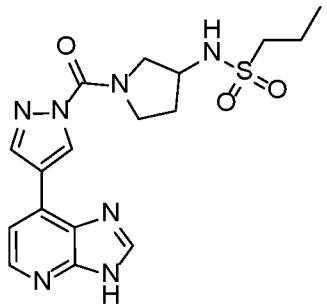
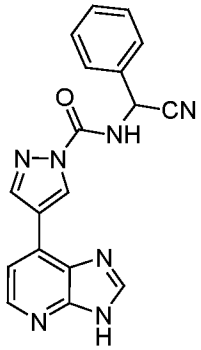
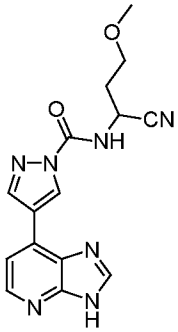
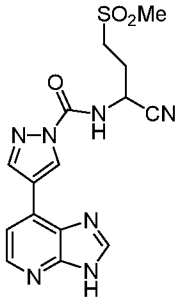
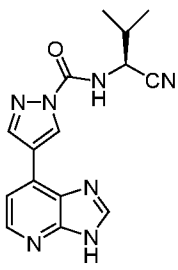
1044.		N-(1-cyano-2-methylpropyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide
1045.		N-(2,2,2-trifluoroethyl)-4-(2,3-dihydro-2-oxo-1H-pyrrolo[2,3-b]pyridin-4-yl)-1H-pyrazole-1-carboxamide
1046.		N-(1-cyanopropan-2-yl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide
1047.		N-((S)-1-cyano-2-methylpropyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide
1048.		1-(4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carbonyl)azetidine-3-carbonitrile

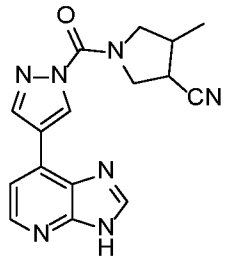
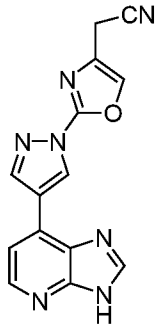
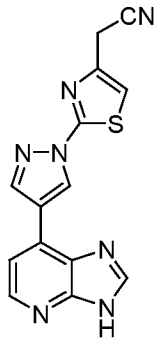
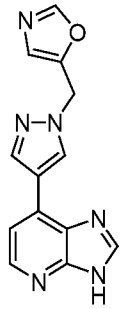
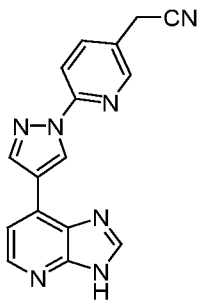
1049.		N-((R)-1-cyano-2-methylpropyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide
1050.		N-(3-cyano-1,1,1-trifluoropropan-2-yl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide
1051.		N-(2-cyano-1-cyclopropylethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide
1052.		N-(1-cyanopropan-2-yl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide
1053.		N-(1-cyanopropan-2-yl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide

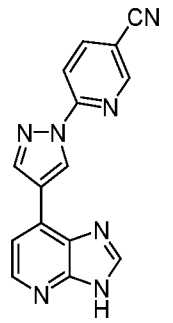
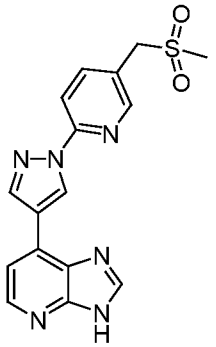
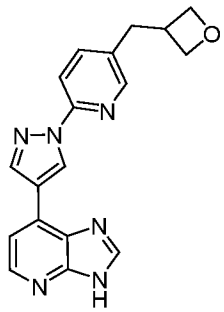
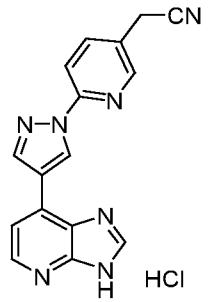
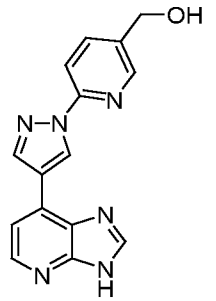
1054.		N-((R)-cyano(cyclopropyl)methyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide
1055.		1-(4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carbonyl)pyrrolidine-3-carbonitrile
1056.		N-(3-cyanocyclobutyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide
1057.		2-(1-(4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carbonyl)pyrrolidin-3-yl)acetonitrile
1058.		N-(1-(3-cyanoazetidin-1-yl)-1-oxopropan-2-yl)-4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide

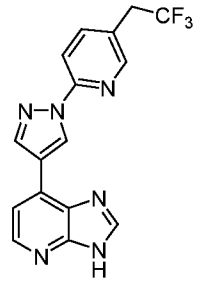
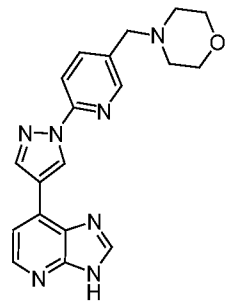
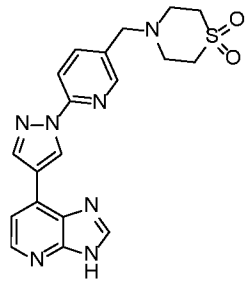
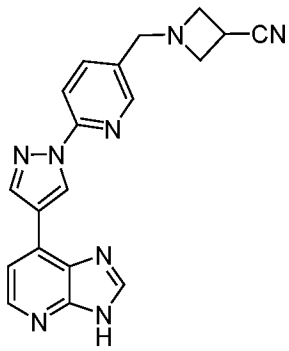
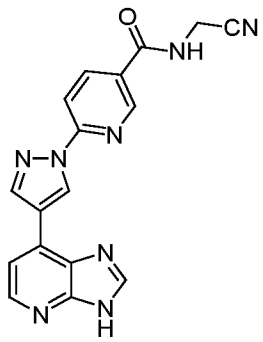
1059.		N-(2-(3-cyanoazetidin-1-yl)-2-oxoethyl)-4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide
1060.		N-(2-(3-cyanoazetidin-1-yl)-2-oxoethyl)-4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide
1061.		3-(1-(4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carbonyl)pyrrolidin-3-yl)propanenitrile
1062.		N-(2-cyano-1-(tetrahydro-2H-pyran-4-yl)ethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide
1063.		N-(cyano(phenyl)methyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide

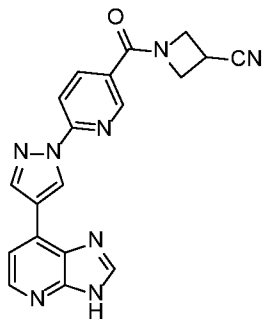
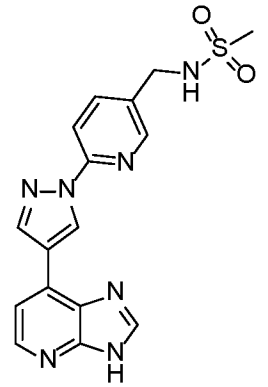
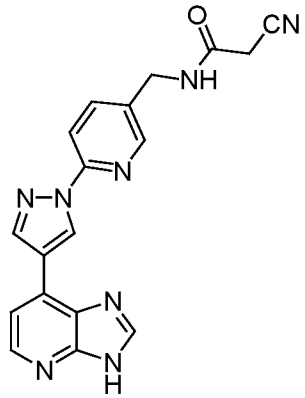
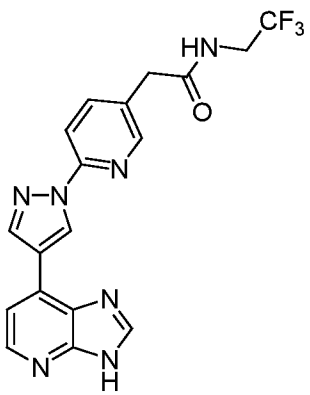
1064.		N-(2,2,2-trifluoroethyl)-4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide
1065.		N-(2-cyano-1-(tetrahydro-2H-pyran-4-yl)ethyl)-4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide
1066.		N-(2-cyanocyclohexyl)-4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide
1067.		1-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carbonyl)piperidine-4-carbonitrile
1068.		N-(1-(3-cyanoazetidin-1-yl)propan-2-yl)-4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide

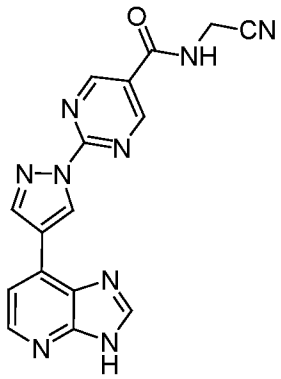
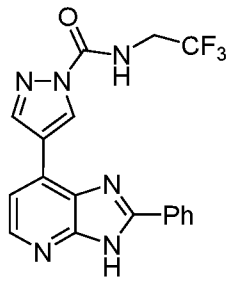
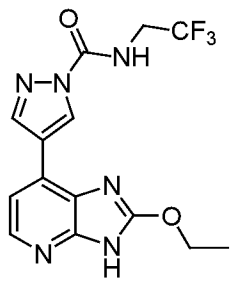
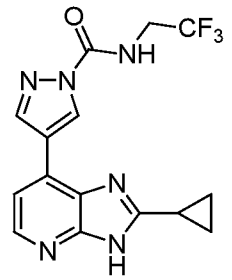
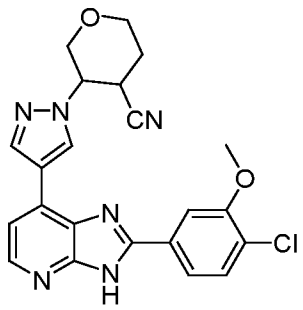
1069.		N-(1-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carbonyl)pyrrolidin-3-yl)propane-1-sulfonamide
1070.		N-(cyano(phenyl)methyl)-4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide
1071.		N-(1-cyano-3-methoxypropyl)-4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide
1072.		N-(1-cyano-3-(methylsulfonyl)propyl)-4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide
1073.		N-((S)-1-cyano-2-methylpropyl)-4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide

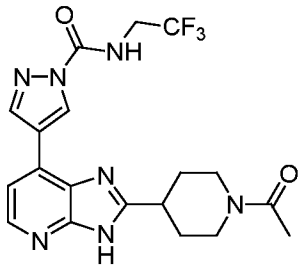
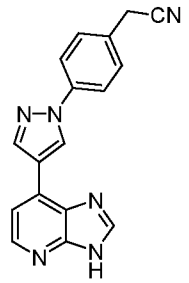
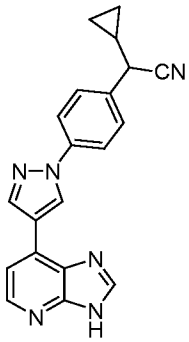
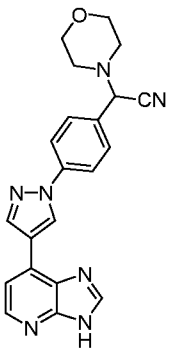
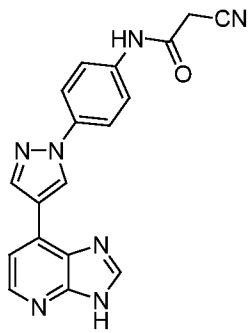
1074.		1-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carbonyl)-4-methylpyrrolidine-3-carbonitrile
1075.		2-(2-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)oxazol-4-yl)acetonitrile
1076.		2-(2-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)thiazol-4-yl)acetonitrile
1077.		7-(1-((oxazol-5-yl)methyl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1078.		2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)acetonitrile

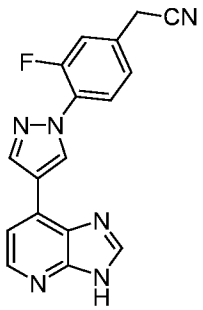
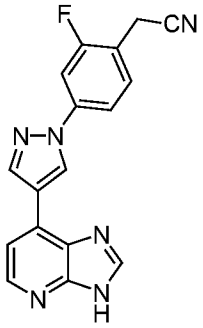
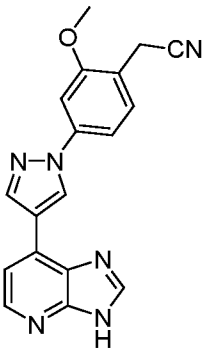
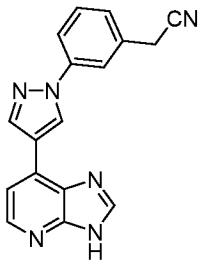
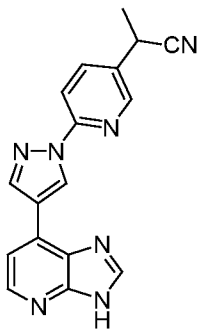
1079.		6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridine-3-carbonitrile
1080.		7-(1-(5-((methylsulfonyl)methyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1081.		7-(1-(5-((oxetan-3-yl)methyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1082.		2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)acetonitrile hydrochloride
1083.		(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)methanol

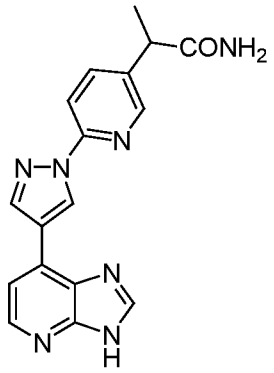
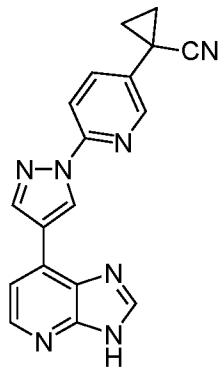
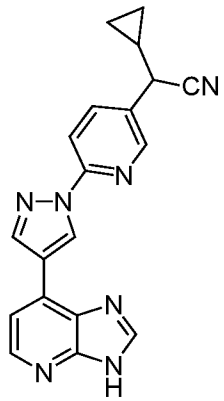
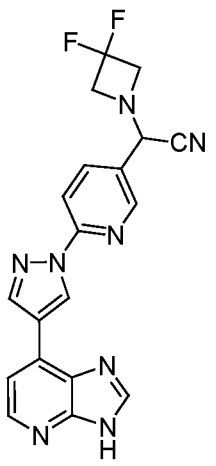
1084.		7-(1-(5-(2,2,2-trifluoroethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1085.		7-(1-(5-(morpholinomethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1086.		4-((6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)methyl)thiomorpholine 1,1-dioxide
1087.		1-((6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)methyl)azetidine-3-carbonitrile
1088.		6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)-N-(cyanomethyl)pyridine-3-carboxamide

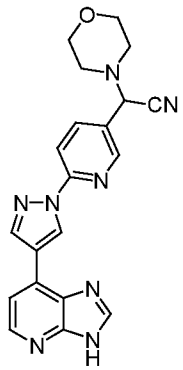
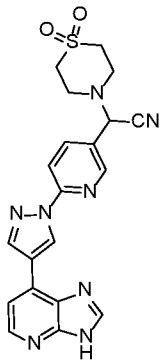
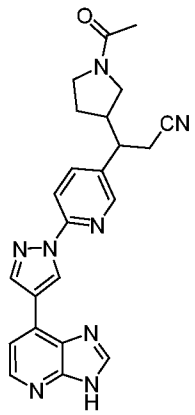
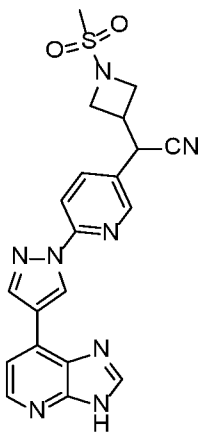
1089.		N-((6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)methyl)methanesulfonamide
1090.		N-((6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)methyl)methanesulfonamide
1091.		N-((6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)methyl)-2-cyanoacetamide
1092.		2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-N-(2,2,2-trifluoroethyl)acetamide

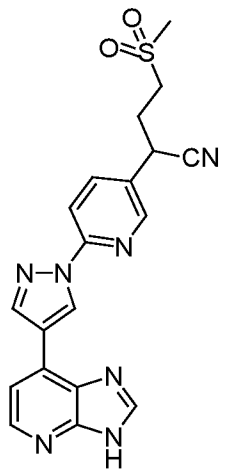
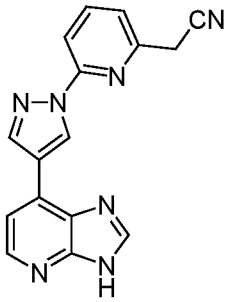
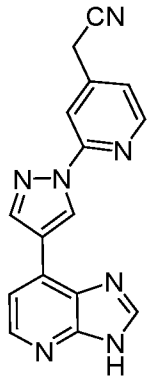
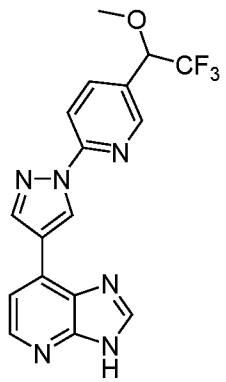
1093.		2-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)-N-(cyanomethyl)pyrimidine-5-carboxamide
1094.		N-(2,2,2-trifluoroethyl)-4-(2-phenyl-3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide
1095.		4-(2-ethoxy-3H-imidazo[4,5-b]pyridin-7-yl)-N-(2,2,2-trifluoroethyl)-1H-pyrazole-1-carboxamide
1096.		4-(2-cyclopropyl-3H-imidazo[4,5-b]pyridin-7-yl)-N-(2,2,2-trifluoroethyl)-1H-pyrazole-1-carboxamide
1097.		3-(4-(2-(4-chloro-3-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)-tetrahydro-2H-pyran-4-carbonitrile

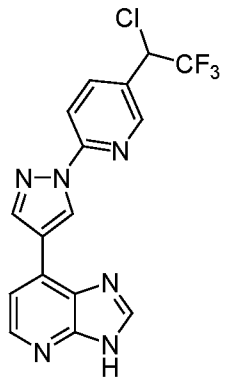
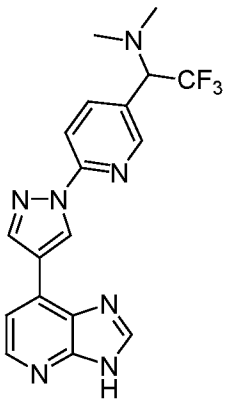
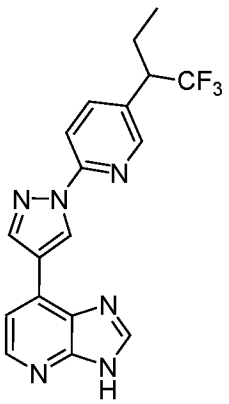
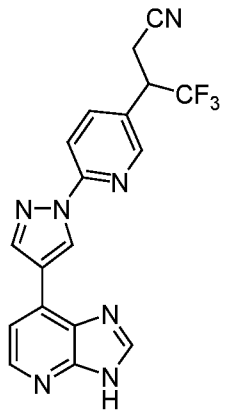
1098.		4-(2-(1-acetylpiperidin-4-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-N-(2,2,2-trifluoroethyl)-1H-pyrazole-1-carboxamide
1099.		2-(4-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)phenyl)acetonitrile
1100.		2-(4-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)phenyl)-2-cyclopropylacetonitrile
1101.		2-(4-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)phenyl)-2-morpholinoacetonitrile
1102.		N-(4-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)phenyl)-2-cyanoacetamide

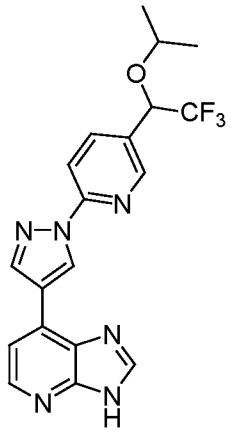
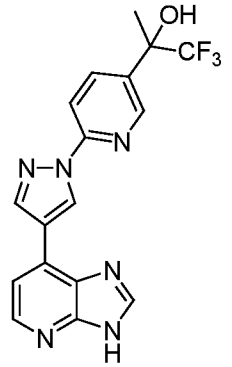
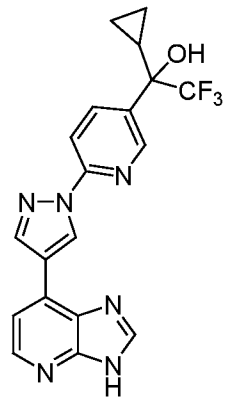
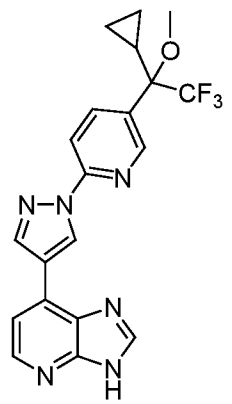
1103.		2-(4-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)-3-fluorophenyl)acetonitrile
1104.		2-(4-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)-2-fluorophenyl)acetonitrile
1105.		2-(4-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)-2-methoxyphenyl)acetonitrile
1106.		2-(3-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)phenyl)acetonitrile
1107.		2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)propanenitrile

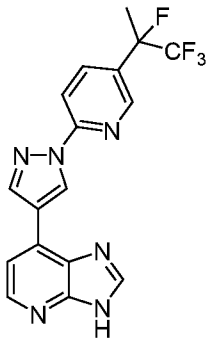
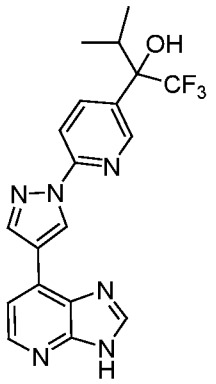
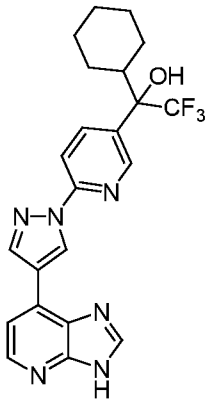
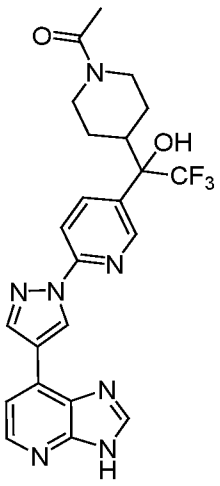
1108.		2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)propanamide
1109.		1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)cyclopropanecarbonitrile
1110.		2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-cyclopropylacetonitrile
1111.		2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-(3,3-difluoroazetidin-1-yl)acetonitrile

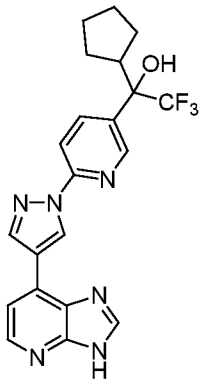
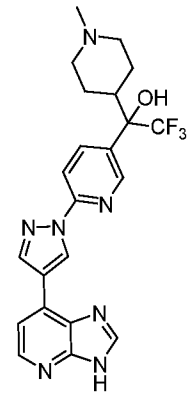
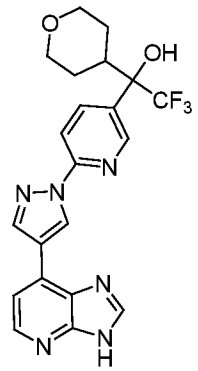
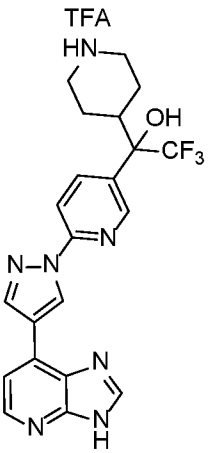
1112.		2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-morpholinoacetonitrile
1113.		2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-(1,1-dioxidothiomorpholino)acetonitrile
1114.		2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-(1-(methylsulfonyl)azetidin-3-yl)acetonitrile
1115.		2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-(1-(methylsulfonyl)azetidin-3-yl)acetonitrile

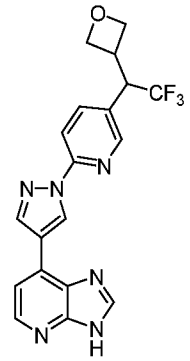
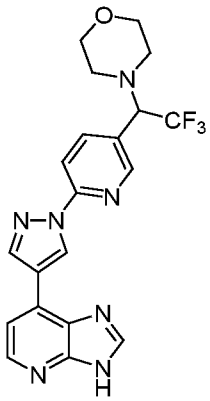
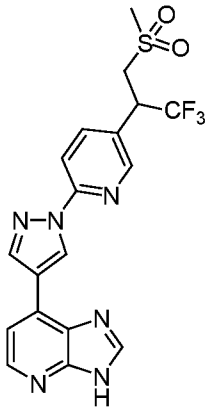
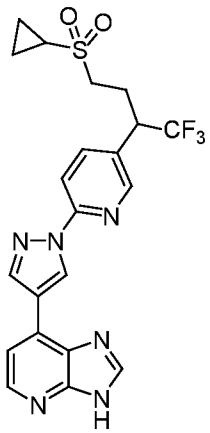
1116.		2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4-(methylsulfonyl)butanenitrile
1117.		2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-2-yl)acetonitrile
1118.		2-(2-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-4-yl)acetonitrile
1119.		7-(1-(5-(2,2,2-trifluoro-1-methoxyethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

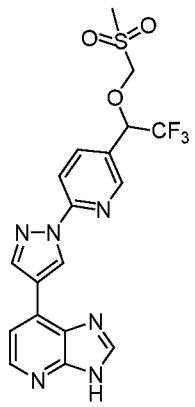
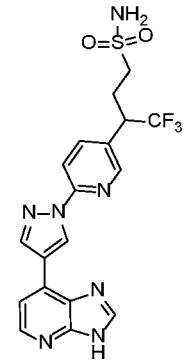
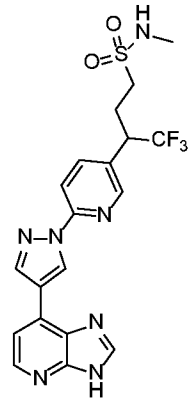
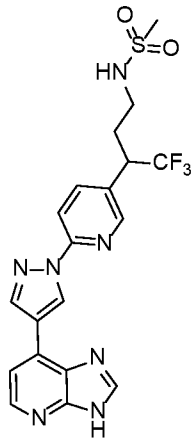
1120.		7-(1-(5-(1-chloro-2,2,2-trifluoroethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1121.		1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-N,N-dimethylethanamine
1122.		7-(1-(5-(1,1,1-trifluorobutan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1123.		3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutanenitrile

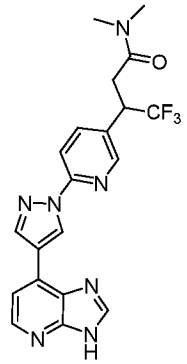
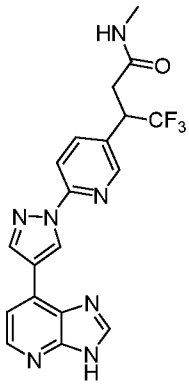
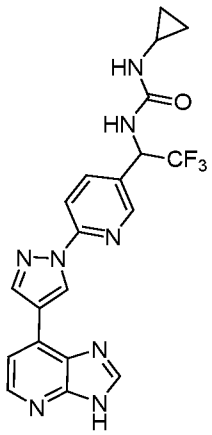
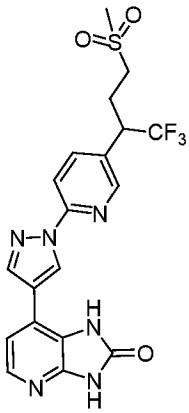
1124.		7-(1-(5-(2,2,2-trifluoro-1-isopropoxyethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1125.		2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1,1,1-trifluoropropan-2-ol
1126.		1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-cyclopropyl-2,2,2-trifluoroethanol
1127.		7-(1-(5-(1-cyclopropyl-2,2,2-trifluoro-1-methoxyethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

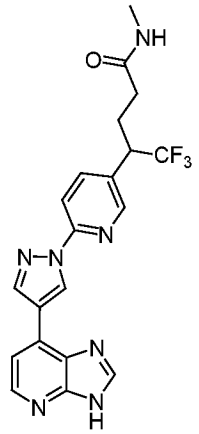
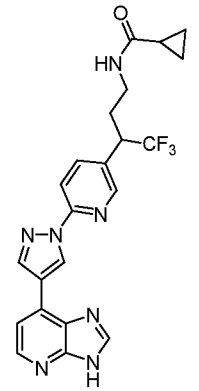
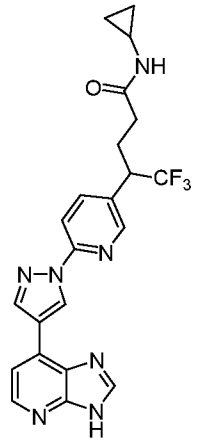
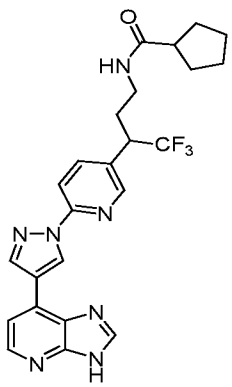
1128.		7-(1-(5-(1,1,1,2-tetrafluoropropan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1129.		2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1,1,1-trifluoro-3-methylbutan-2-ol
1130.		1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-cyclohexyl-2,2,2-trifluoroethanol
1131.		1-(4-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-hydroxyethyl)piperidin-1-yl)ethanone

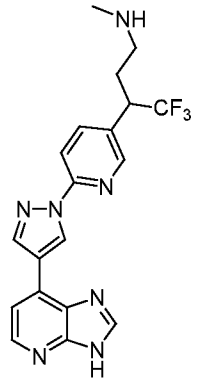
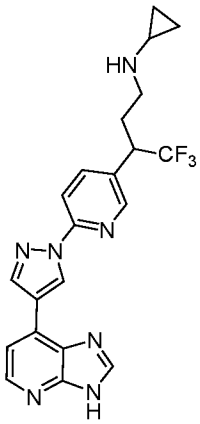
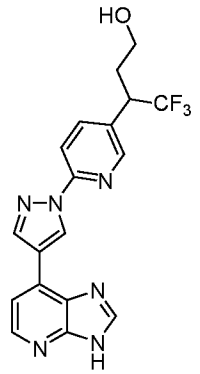
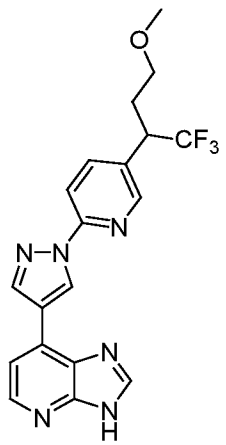
1132.		1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-cyclopentyl-2,2,2-trifluoroethanol
1133.		1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-methylpiperidin-4-yl)ethanol
1134.		1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(tetrahydro-2H-pyran-4-yl)ethanol
1135.		1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(piperidin-4-yl)ethan-1-ol

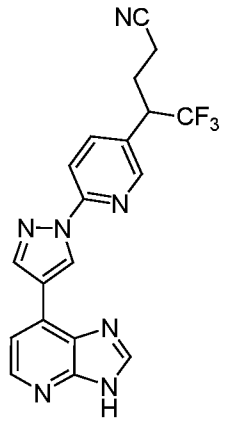
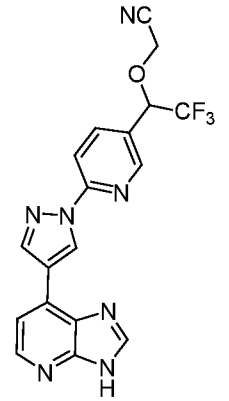
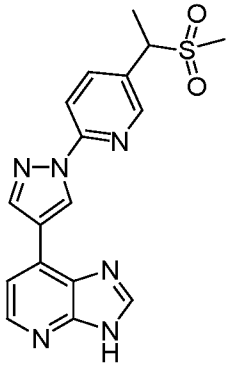
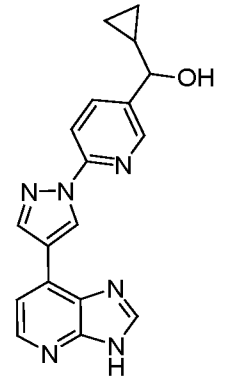
1136.		7-(1-(5-(2,2,2-trifluoro-1-(oxetan-3-yl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1137.		7-(1-(5-(2,2,2-trifluoro-1-morpholinoethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1138.		7-(1-(5-(1,1,1-trifluoro-3-(methylsulfonyl)propan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1139.		7-(1-(5-(4-(cyclopropylsulfonyl)-1,1,1-trifluorobutan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

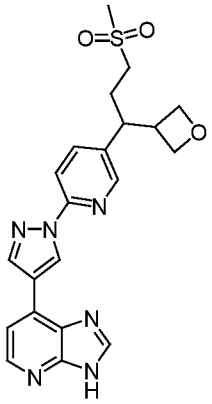
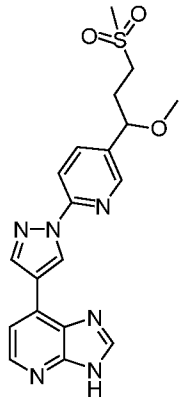
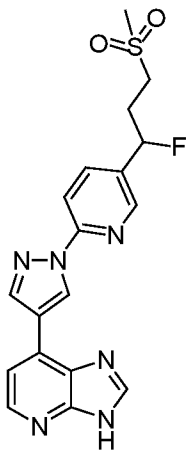
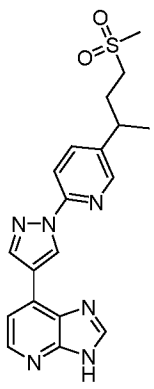
1140.		7-(1-(5-(1-((methylsulfonyl)methoxy)-2,2,2-trifluoroethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1141.		3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutane-1-sulfonamide
1142.		3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutane-1-sulfonamide
1143.		N-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)methanesulfonamide

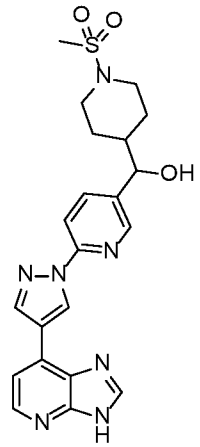
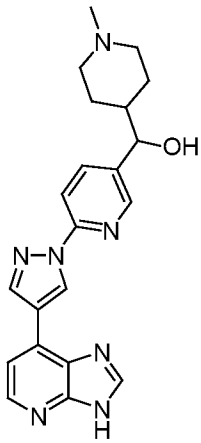
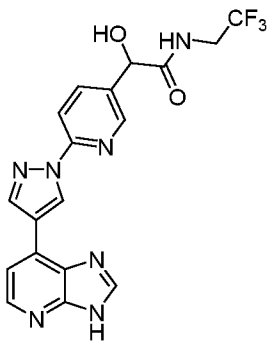
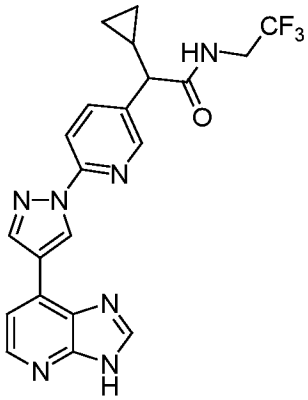
1144.		3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N,N-dimethylbutanamide
1145.		3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutanamide
1146.		1-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethyl)-3-cyclopropylurea
1147.		7-(1-(5-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

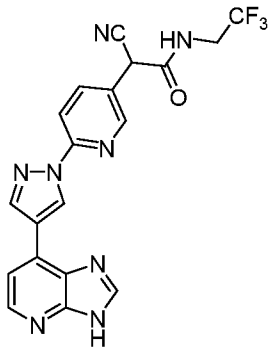
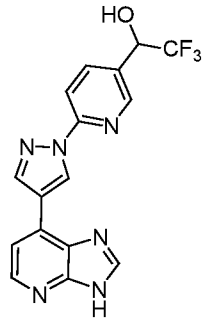
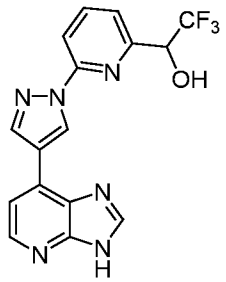
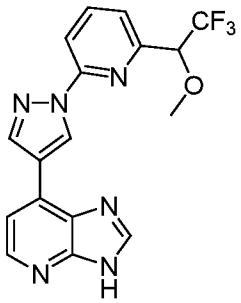
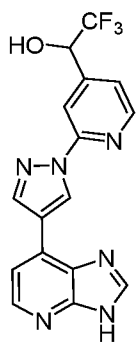
1148.		4-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-5,5,5-trifluoro-N-methylpentanamide
1149.		N-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)cyclopropanecarboxamide
1150.		4-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-N-cyclopropyl-5,5,5-trifluoropentanamide
1151.		N-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)cyclopentanecarboxamide

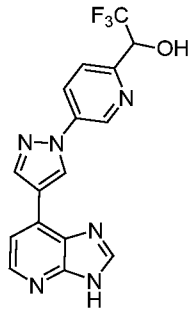
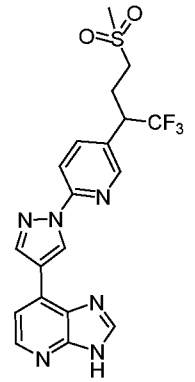
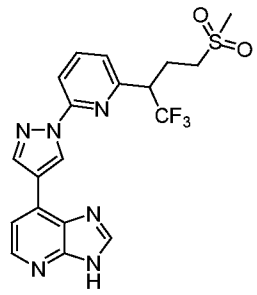
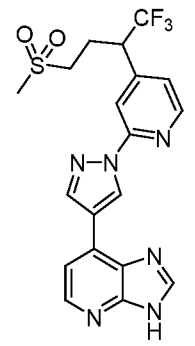
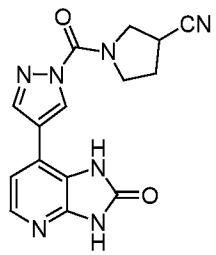
1152.		3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutan-1-amine
1153.		N-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)cyclopropanamine
1154.		3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutan-1-ol
1155.		7-(1-(5-(1,1,1-trifluoro-4-methoxybutan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

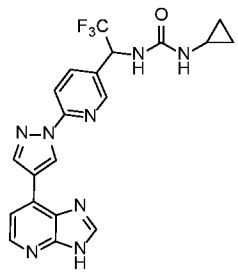
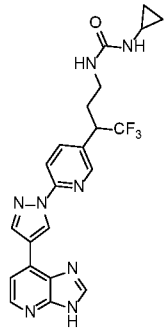
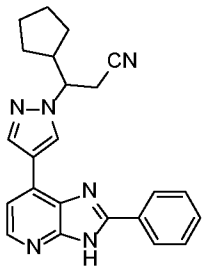
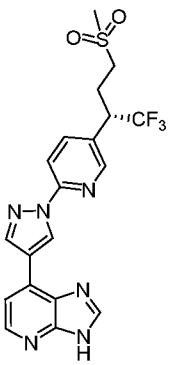
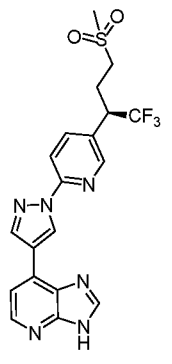
1156.		4-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-5,5,5-trifluoropentanenitrile
1157.		2-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethoxy)acetonitrile
1158.		7-(1-(5-(1-(methylsulfonyl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1159.		(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)(cyclopropyl)methanol

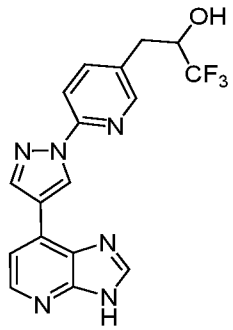
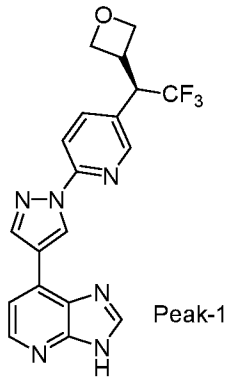
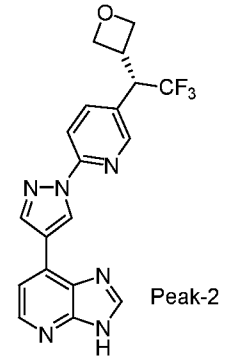
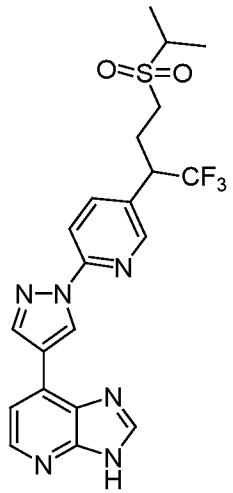
1160.		7-(1-(5-(3-(methylsulfonyl)-1-(oxetan-3-yl)propyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1161.		7-(1-(5-(1-methoxy-3-(methylsulfonyl)propyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1162.		7-(1-(5-(1-fluoro-3-(methylsulfonyl)propyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1163.		7-(1-(5-(4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

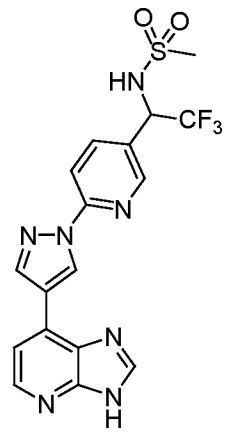
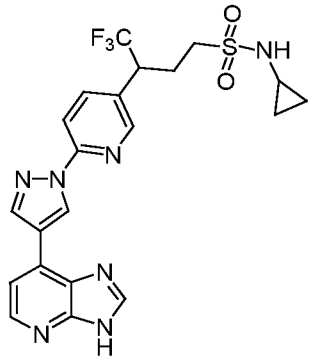
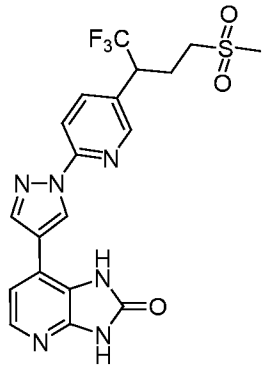
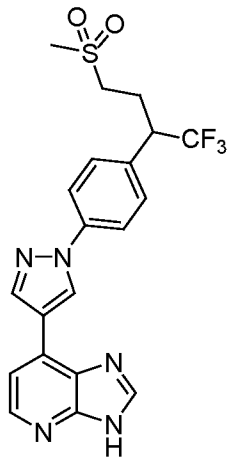
1164.		(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)(1-(methylsulfonyl)piperidin-4-yl)methanol
1165.		(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)(1-methylpiperidin-4-yl)methanol
1166.		2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-N-(2,2,2-trifluoroethyl)-2-hydroxyacetamide
1167.		2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-cyclopropyl-N-(2,2,2-trifluoroethyl)acetamide

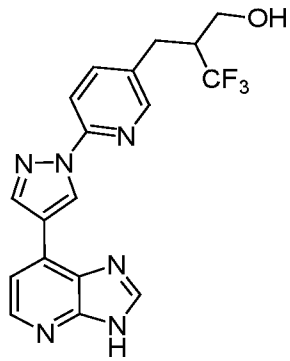
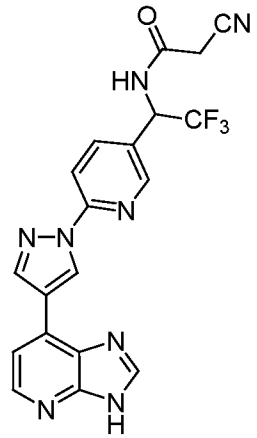
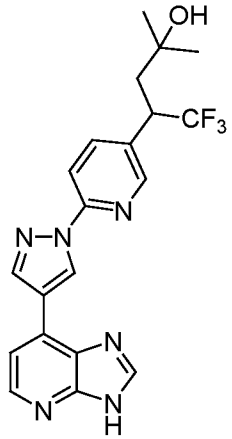
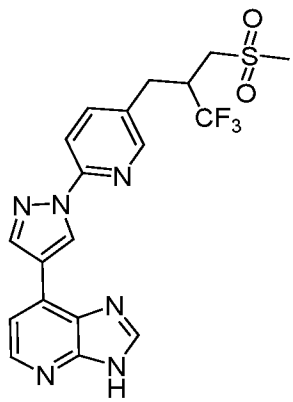
1168.		2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-cyano-N-(2,2,2-trifluoroethyl)acetamide
1169.		1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethanol
1170.		1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-2-yl)-2,2,2-trifluoroethanol
1171.		7-(1-(6-(2,2,2-trifluoro-1-methoxyethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1172.		1-(2-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-4-yl)-2,2,2-trifluoroethanol

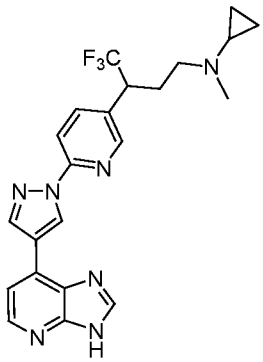
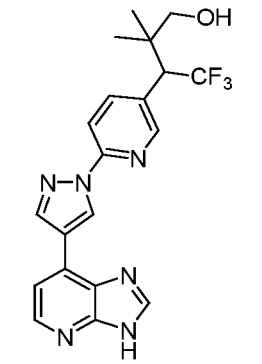
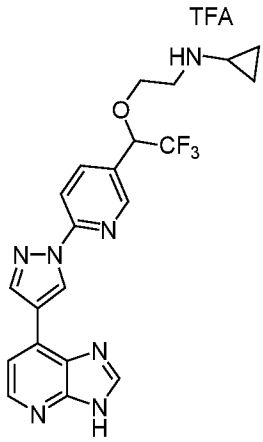
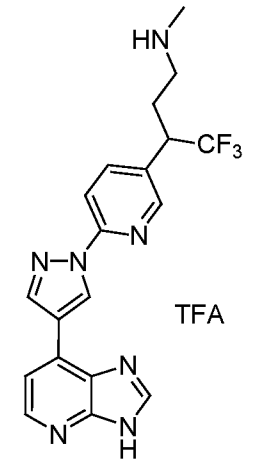
1173.		1-(5-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-2-yl)-2,2,2-trifluoroethanol
1174.		7-(1-(5-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1175.		7-(1-(6-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1176.		7-(1-(4-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1177.		1-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carbonyl)pyrrolidine-3-carbonitrile

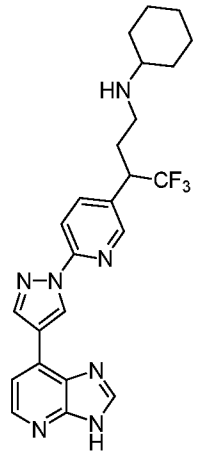
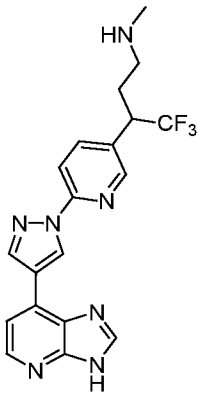
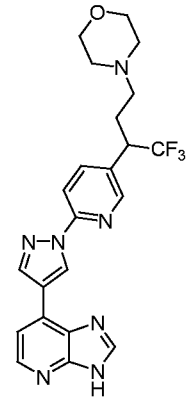
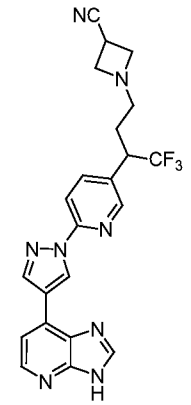
1178.		1-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethyl)-3-cyclopropylurea
1179.		1-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)-3-cyclopropylurea
1180.		3-cyclopentyl-3-(4-(2-phenyl-3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)propanenitrile
1181.		7-(1-(5-((S)-1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1182.		7-(1-(5-((R)-1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

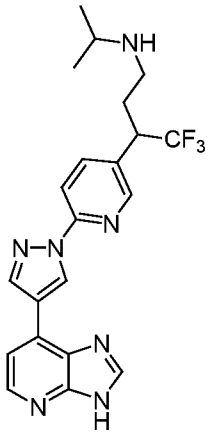
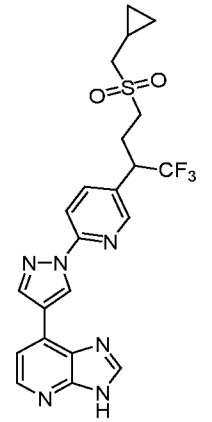
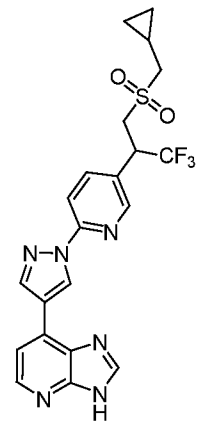
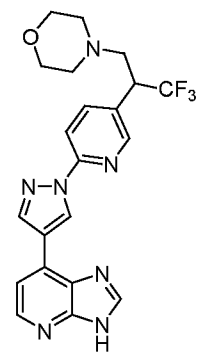
1183.		3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1,1,1-trifluoropropan-2-ol
1184.	 Peak-1	7-(1-(5-((R)-2,2,2-trifluoro-1-(oxetan-3-yl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1185.	 Peak-2	7-(1-(5-((S)-2,2,2-trifluoro-1-(oxetan-3-yl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1186.		7-(1-(5-(1,1,1-trifluoro-4-(isopropylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

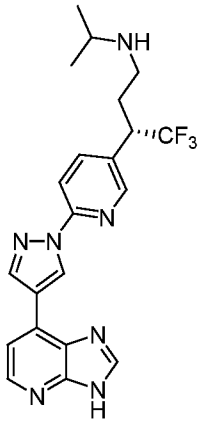
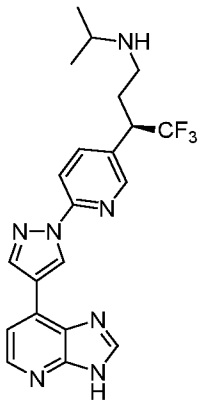
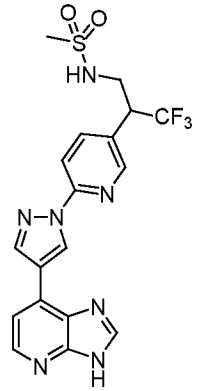
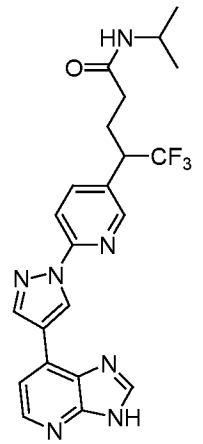
1187.		1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-(methyl sulfonyl) 1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethanamine
1188.		7-(1-(5-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-(cyclopropyl amino sulfonyl) 1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1189.		7-(1-(5-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one
1190.		7-(1-(4-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)phenyl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

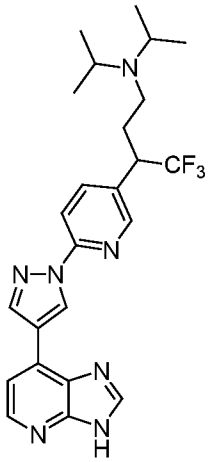
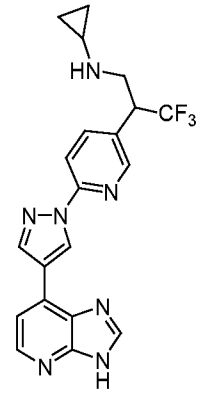
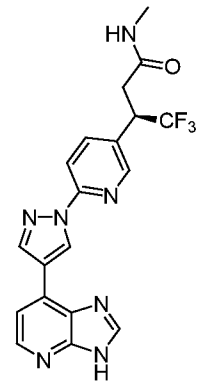
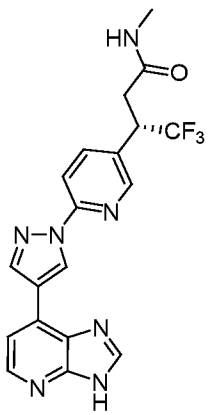
1191.		3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-(trifluoromethyl)propan-1-ol
1192.		N-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethyl)-2-cyanoacetamide
1193.		4-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-5,5,5-trifluoro-2-methylpentan-2-ol
1194.		7-(1-(5-(3,3,3-trifluoro-2-((methylsulfonyl)methyl)propyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

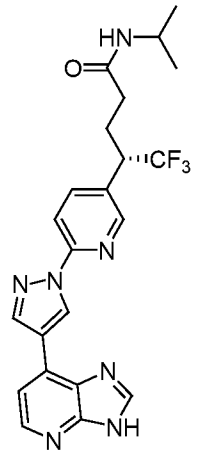
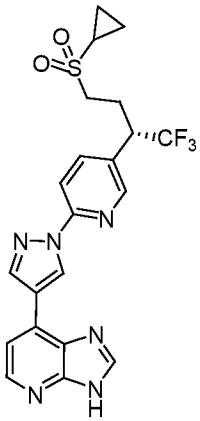
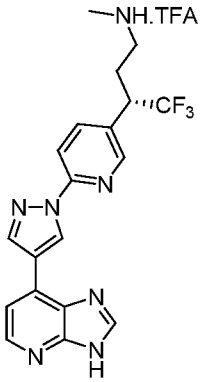
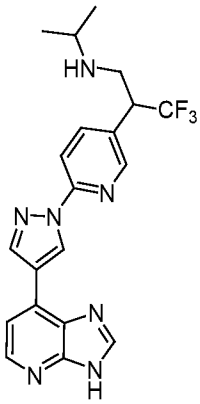
1195.		N-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)-N-methylcyclopropanamine
1196.		3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-2,2-dimethylbutan-1-ol
1197.		N-(2-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethoxy)ethyl)cyclopropanamine
1198.		3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutan-1-amine

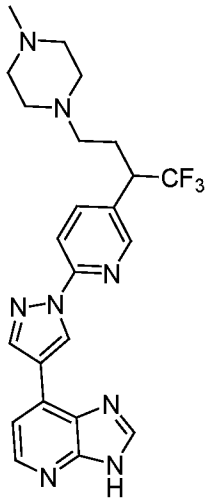
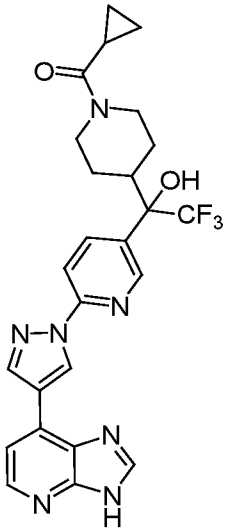
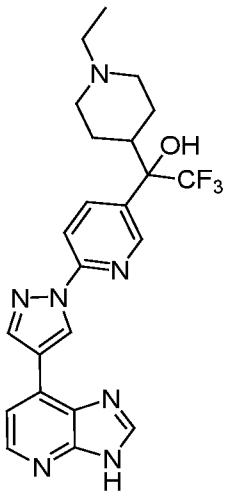
1199.		N-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)cyclohexanamine
1200.		3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutan-1-amine
1201.		7-(1-(5-(1,1,1-trifluoro-4-morpholinobutan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1202.		1-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)azetidine-3-carbonitrile

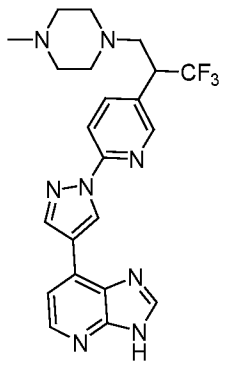
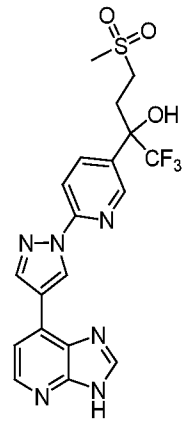
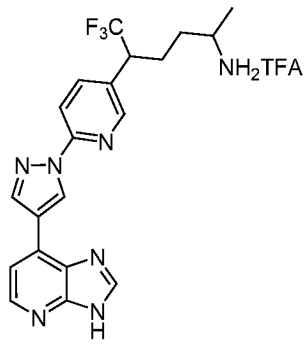
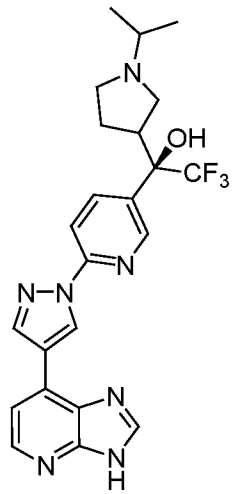
1203.		3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-isopropylbutan-1-amine
1204.		7-(1-(5-(4-(cyclopropylmethylsulfonyl)-1,1,1-trifluorobutan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1205.		7-(1-(5-(3-(cyclopropylmethylsulfonyl)-1,1,1-trifluoropropan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1206.		7-(1-(5-(1,1,1-trifluoro-3-morpholinopropan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

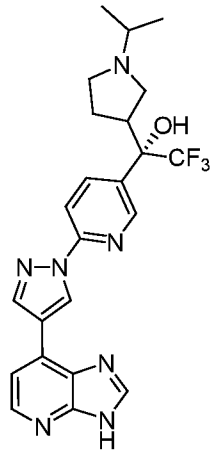
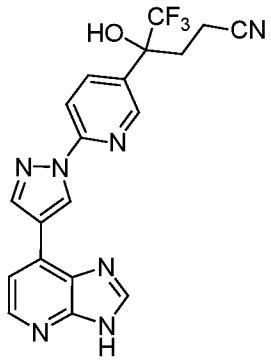
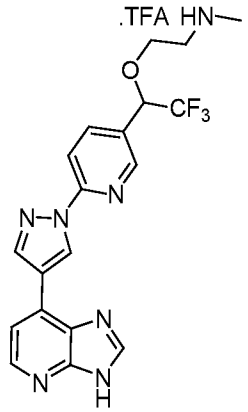
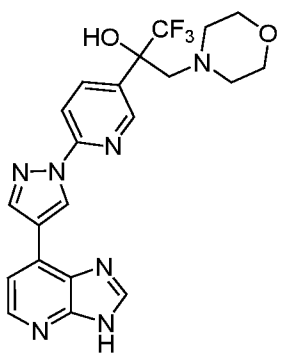
1207.		(S)-3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-isopropylbutan-1-amine
1208.		(R)-3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-isopropylbutan-1-amine
1209.		2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-(Methyl sulfonyl)1H-pyrazol-1-yl)pyridin-3-yl)-3,3,3-trifluoropropan-1-amine
1210.		4-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-5,5,5-trifluoro-N-isopropylpentanamide

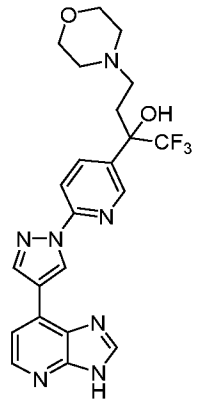
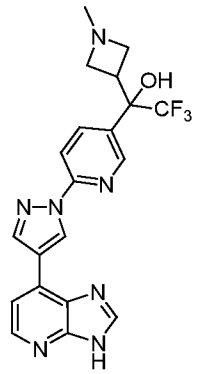
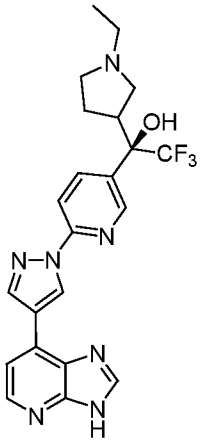
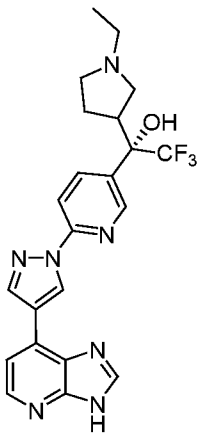
1211.		3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N,N-diisopropylbutan-1-amine
1212.		N-(2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-3,3,3-trifluoropropyl)cyclopropanamine
1213.		(R)-3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutanamide
1214.		(S)-3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutanamide

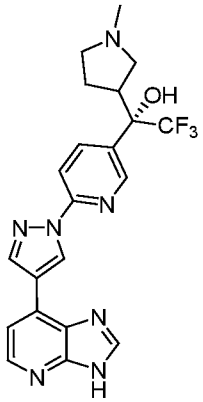
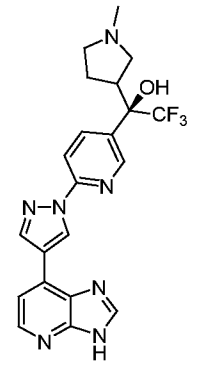
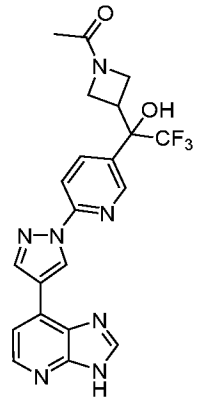
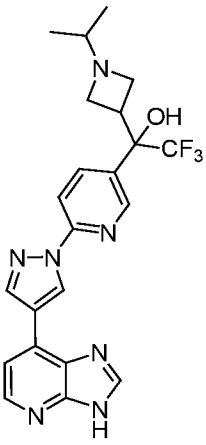
1215.		(S)-4-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-5,5,5-trifluoro-N-isopropylpentanamide
1216.		7-(1-(5-((S)-4-(cyclopropylsulfonyl)-1,1,1-trifluorobutan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1217.		(S)-3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutan-1-amine,TFA salt
1218.		2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-3,3,3-trifluoro-N-isopropylpropan-1-amine

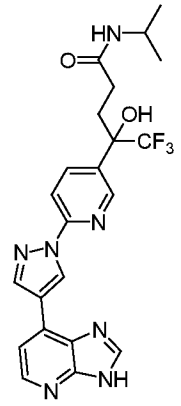
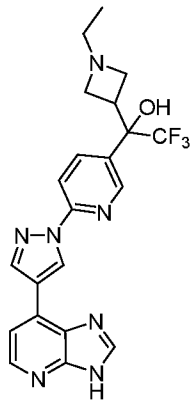
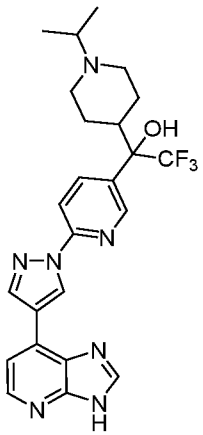
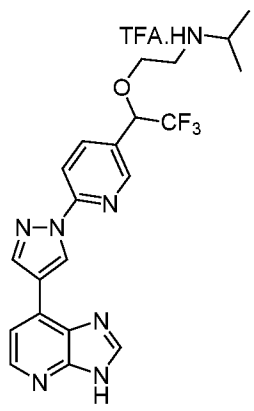
1219.		7-(1-(5-(1,1,1-trifluoro-4-(4-methylpiperazin-1-yl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1220.		(4-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-hydroxyethyl)piperidin-1-yl)(cyclopropyl)methanone
1221.		1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-(1-ethylpiperidin-4-yl)-2,2,2-trifluoroethanol

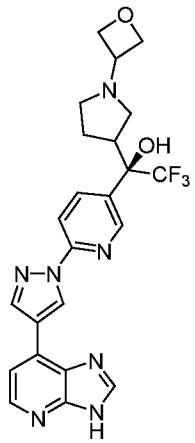
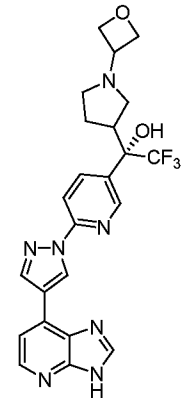
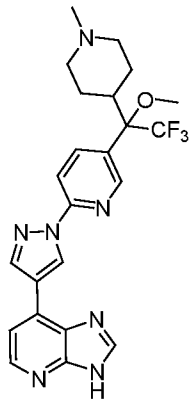
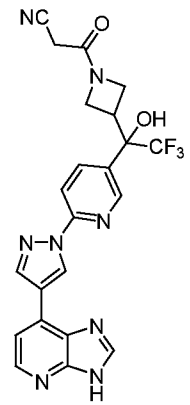
1222.		7-(1-(5-(1,1,1-trifluoro-3-(4-methylpiperazin-1-yl)propan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1223.		2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1,1,1-trifluoro-4-(methylsulfonyl)butan-2-ol
1224.		5-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-6,6,6-trifluorohexan-2-amine,TFA salt
1225.		(R)-1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-isopropylpyrrolidin-3-yl)ethanol

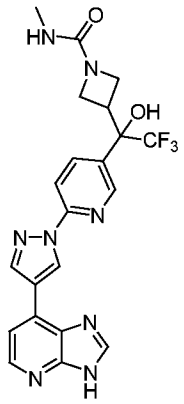
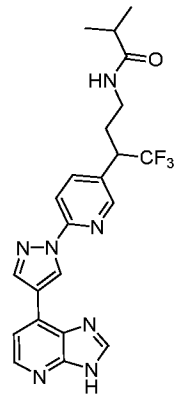
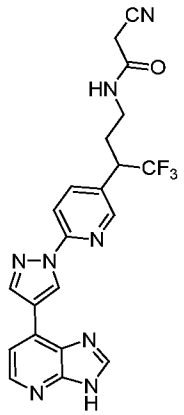
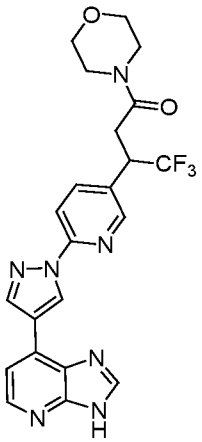
1226.		(S)-1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-isopropylpyrrolidin-3-yl)ethanol
1227.		4-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-5,5,5-trifluoro-4-hydroxypentanenitrile
1228.		2-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethoxy)-N-methylethanamine
1229.		2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1,1,1-trifluoro-3-morpholinopropan-2-ol

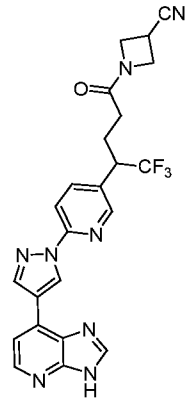
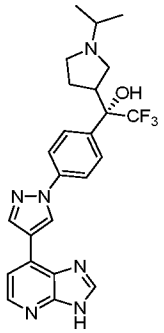
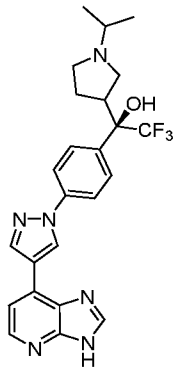
1230.		2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1,1,1-trifluoro-4-morpholinobutan-2-ol
1231.		1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-methylazetidin-3-yl)ethanol
1232.		(R)-1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-(1-ethylpyrrolidin-3-yl)-2,2,2-trifluoroethanol
1233.		(S)-1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-(1-ethylpyrrolidin-3-yl)-2,2,2-trifluoroethanol

1234.		(S)-1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-methylpyrrolidin-3-yl)ethanol
1235.		(R)-1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-methylpyrrolidin-3-yl)ethanol
1236.		1-(3-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-hydroxyethyl)azetidin-1-yl)ethanone
1237.		1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-isopropylazetidin-3-yl)ethanol

1238.		4-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-5,5,5-trifluoro-4-hydroxy-N-isopropylpentanamide
1239.		1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-(1-ethylazetidin-3-yl)-2,2,2-trifluoroethanol
1240.		1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-isopropylpiperidin-4-yl)ethanol
1241.		N-(2-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethoxy)ethyl)propan-2-amine,TFA salt

1242.		(R)-1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-(oxetan-3-yl)pyrrolidin-3-yl)ethanol
1243.		(S)-1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-(oxetan-3-yl)pyrrolidin-3-yl)ethanol
1244.		7-(1-(5-(2,2,2-trifluoro-1-methoxy-1-(1-methylpiperidin-4-yl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine
1245.		3-(3-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-hydroxyethyl)azetidin-1-yl)-3-oxopropanenitrile

1246.		3-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-hydroxyethyl)-N-methylazetidine-1-carboxamide
1247.		N-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)isobutyramide
1248.		N-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)-2-cyanoacetamide
1249.		3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-1-morpholinobutan-1-one

1250.		1-(4-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-5,5,5-trifluoropentanoyl)azetidine-3-carbonitrile
1251.		(S)-1-(4-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)phenyl)-2,2,2-trifluoro-1-(1-isopropylpyrrolidin-3-yl)ethanol
1252.		(R)-1-(4-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)phenyl)-2,2,2-trifluoro-1-(1-isopropylpyrrolidin-3-yl)ethanol

The compounds of the present invention include:

1001. N-(2,2,2-trifluoroethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)benzamide;

1002. 1-(1,1,1-trifluoropropan-2-yl)-3-(4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)phenyl)urea;

1003. 1-(2,2,2-trifluoroethyl)-3-(4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)phenyl)urea;

1004. 1-(2,2,2-trifluoroethyl)-3-(5-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)pyrimidin-2-yl)urea;

1005. 1-(2,2,2-trifluoroethyl)-3-(5-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)pyridin-2-yl)urea;

1006. 1-(5-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)pyrazin-2-yl)-3-(2,2,2-trifluoroethyl)urea;

1007. N-(4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)phenyl)-3,3-dimethylazetidine-1-carboxamide;

1008. N-(4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)phenyl)morpholine-4-carboxamide;

1009. 1-(4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)phenyl)-3-(pyridin-4-yl)urea;

1010. 1-(4-(3H-imidazo[4,5-b]pyridin-7-yl)phenyl)-3-(2,2,2-trifluoroethyl)urea;

1011. N-(2,2,2-trifluoroethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)piperazine-1-carboxamide;

1012. N-(cyanomethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)piperazine-1-carboxamide;

1013. 4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-N-(2-(methylsulfonyl)ethyl)piperazine-1-carboxamide;

1014. 4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-N-(pyridin-4-yl)piperazine-1-carboxamide;

1015. N-(2-fluoropyridin-4-yl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)piperazine-1-carboxamide;

1016. N-(1-(methylsulfonyl)piperidin-4-yl)-4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)piperazine-1-carboxamide;

1017. N-(cyclopentylmethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)piperazine-1-carboxamide;

1018. 7-(4-(1,1-dioxidothiomorpholine-4-carbonyl)piperazin-1-yl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one;

1019. 4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-N-(2-methoxypyridin-4-yl)piperazine-1-carboxamide;

1020. N-(1,1-dioxidotetrahydro-2H-thiopyran-4-yl)-4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)piperazine-1-carboxamide;

1021. N-(1,1,1-trifluoropropan-2-yl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)piperazine-1-carboxamide;

1022. N-(2,2,2-trifluoroethyl)-4-(2-phenyl-3H-imidazo[4,5-b]pyridin-7-yl)piperazine-1-carboxamide;

1023. 7-(4-(3,3-dimethylazetidine-1-carbonyl)piperazin-1-yl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one;

1024. 4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-N-(2-methyl-4-(methylsulfonyl)phenyl)piperazine-1-carboxamide;

1025. N-(2,2,2-trifluoroethyl)-2-(4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)piperazin-1-yl)acetamide;

1026. N-(2,2,2-trifluoroethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1027. N-(cyanomethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1028. N-(2,2,2-trifluoroethyl)-3-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrrole-1-carboxamide;

1029. N-(2,2,2-trifluoroethyl)-4-(2,3-dihydro-1-methyl-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1030. N-(1,1,1-trifluoropropan-2-yl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1031. 7-(1-(4,4,4-trifluorobutanoyl)-1H-pyrazol-4-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one;

1032. N-(1-cyanocyclopropyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1033. N-(2-cyanopropan-2-yl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1034. N-(cyclopentylmethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1035. N-(cyanomethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide hydrochloride;

1036. N-(2,2,2-trifluoroethyl)-4-(2,3-dihydro-2-oxo-1H-benzo[d]imidazol-4-yl)-1H-pyrazole-1-carboxamide;

1037. 7-(1-(3,3-dimethylazetidine-1-carbonyl)-1H-pyrazol-4-yl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one;

1038. N-(cyano(cyclopentyl)methyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1039. N-(2-cyano-1-cyclopentylethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1040. N-(2-cyanobutan-2-yl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1041. N-(1-cyclopentyl-2,2,2-trifluoroethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1042. 4-(1-ethyl-2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-N-(2,2,2-trifluoroethyl)-1H-pyrazole-1-carboxamide;

1043. N-(cyano(cyclopropyl)methyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1044. N-(1-cyano-2-methylpropyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1045. N-(2,2,2-trifluoroethyl)-4-(2,3-dihydro-2-oxo-1H-pyrrolo[2,3-b]pyridin-4-yl)-1H-pyrazole-1-carboxamide;

1046. N-(1-cyanopropan-2-yl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1047. N-((S)-1-cyano-2-methylpropyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1048. 1-(4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carbonyl)azetidine-3-carbonitrile;

1049. N-((R)-1-cyano-2-methylpropyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1050. N-(3-cyano-1,1,1-trifluoropropan-2-yl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1051. N-(2-cyano-1-cyclopropylethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1052. N-(1-cyanopropan-2-yl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1053. N-(1-cyanopropan-2-yl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1054. N-((R)-cyano(cyclopropyl)methyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1055. 1-(4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carbonyl)pyrrolidine-3-carbonitrile;

1056. N-(3-cyanocyclobutyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1057. 2-(1-(4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carbonyl)pyrrolidin-3-yl)acetonitrile;

1058. N-(1-(3-cyanoazetidin-1-yl)-1-oxopropan-2-yl)-4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1059. N-(2-(3-cyanoazetidin-1-yl)-2-oxoethyl)-4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1060. N-(2-(3-cyanoazetidin-1-yl)-2-oxoethyl)-4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1061. 3-(1-(4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carbonyl)pyrrolidin-3-yl)propanenitrile;

1062. N-(2-cyano-1-(tetrahydro-2H-pyran-4-yl)ethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1063. N-(cyano(phenyl)methyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1064. N-(2,2,2-trifluoroethyl)-4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1065. N-(2-cyano-1-(tetrahydro-2H-pyran-4-yl)ethyl)-4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1066. N-(2-cyanocyclohexyl)-4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1067. 1-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carbonyl)piperidine-4-carbonitrile;

1068. N-(1-(3-cyanoazetidin-1-yl)propan-2-yl)-4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1069. N-(1-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carbonyl)pyrrolidin-3-yl)propane-1-sulfonamide;

1070. N-(cyano(phenyl)methyl)-4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1071. N-(1-cyano-3-methoxypropyl)-4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1072. N-(1-cyano-3-(methylsulfonyl)propyl)-4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1073. N-((S)-1-cyano-2-methylpropyl)-4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1074. 1-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carbonyl)-4-methylpyrrolidine-3-carbonitrile;

1075. 2-(2-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)oxazol-4-yl)acetonitrile;

1076. 2-(2-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)thiazol-4-yl)acetonitrile;

1077. 7-(1-((oxazol-5-yl)methyl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1078. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)acetonitrile;

1079. 6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridine-3-carbonitrile;

1080. 7-(1-(5-((methylsulfonyl)methyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1081. 7-(1-(5-((oxetan-3-yl)methyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1082. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)acetonitrile hydrochloride;

1083. (6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)methanol;

1084. 7-(1-(5-(2,2,2-trifluoroethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1085. 7-(1-(5-(morpholinomethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1086. 4-((6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)methyl)thiomorpholine 1,1-dioxide;

1087. 1-((6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)methyl)azetidine-3-carbonitrile;

1088. 6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)-N-(cyanomethyl)pyridine-3-carboxamide;

1089. N-((6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)methyl)methanesulfonamide;

1090. N-((6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)methyl)methanesulfonamide;

1091. N-((6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)methyl)-2-cyanoacetamide;

1092. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-N-(2,2,2-trifluoroethyl)acetamide;

1093. 2-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)-N-(cyanomethyl)pyrimidine-5-carboxamide;

1094. N-(2,2,2-trifluoroethyl)-4-(2-phenyl-3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1095. 4-(2-ethoxy-3H-imidazo[4,5-b]pyridin-7-yl)-N-(2,2,2-trifluoroethyl)-1H-pyrazole-1-carboxamide;

1096. 4-(2-cyclopropyl-3H-imidazo[4,5-b]pyridin-7-yl)-N-(2,2,2-trifluoroethyl)-1H-pyrazole-1-carboxamide;

1097. 3-(4-(2-(4-chloro-3-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)-tetrahydro-2H-pyran-4-carbonitrile;

1098. 4-(2-(1-acetylpiperidin-4-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-N-(2,2,2-trifluoroethyl)-1H-pyrazole-1-carboxamide;

1099. 2-(4-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)phenyl)acetonitrile;

1100. 2-(4-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)phenyl)-2-cyclopropylacetonitrile;

1101. 2-(4-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)phenyl)-2-morpholinoacetonitrile;

1102. N-(4-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)phenyl)-2-cyanoacetamide;

1103. 2-(4-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)-3-fluorophenyl)acetonitrile;

1104. 2-(4-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)-2-fluorophenyl)acetonitrile;

1105. 2-(4-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)-2-methoxyphenyl)acetonitrile;

1106. 2-(3-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)phenyl)acetonitrile;

1107. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)propanenitrile;

1108. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)propanamide;

1109. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)cyclopropanecarbonitrile;

1110. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-cyclopropylacetonitrile;

1111. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-(3,3-difluoroazetidin-1-yl)acetonitrile;

1112. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-morpholinoacetonitrile;

1113. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-(1,1-dioxidothiomorpholino)acetonitrile;

1114. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-(1-(methylsulfonyl)azetidin-3-yl)acetonitrile;

1115. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-(1-(methylsulfonyl)azetidin-3-yl)acetonitrile;

1116. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4-(methylsulfonyl)butanenitrile;

1117. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-2-yl)acetonitrile;

1118. 2-(2-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-4-yl)acetonitrile;

1119. 7-(1-(5-(2,2,2-trifluoro-1-methoxyethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1120. 7-(1-(5-(1-chloro-2,2,2-trifluoroethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1121. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-N,N-dimethylethanamine;

1122. 7-(1-(5-(1,1,1-trifluorobutan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1123. 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutanenitrile;

1124. 7-(1-(5-(2,2,2-trifluoro-1-isopropoxyethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1125. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1,1,1-trifluoropropan-2-ol;

1126. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-cyclopropyl-2,2,2-trifluoroethanol;

1127. 7-(1-(5-(1-cyclopropyl-2,2,2-trifluoro-1-methoxyethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1128. 7-(1-(5-(1,1,1,2-tetrafluoropropan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1129. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1,1,1-trifluoro-3-methylbutan-2-ol;

1130. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-cyclohexyl-2,2,2-trifluoroethanol;

1131. 1-(4-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-hydroxyethyl)piperidin-1-yl)ethanone;

1132. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-cyclopentyl-2,2,2-trifluoroethanol;

1133. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-methylpiperidin-4-yl)ethanol;

1134. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(tetrahydro-2H-pyran-4-yl)ethanol;

1135. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(piperidin-4-yl)ethan-1-ol

1135. 7-(1-(5-(2,2,2-trifluoro-1-(oxetan-3-yl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1136. 7-(1-(5-(2,2,2-trifluoro-1-morpholinoethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1137. 7-(1-(5-(1,1,1-trifluoro-3-(methylsulfonyl)propan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1138. 7-(1-(5-(4-(cyclopropylsulfonyl)-1,1,1-trifluorobutan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1139. 7-(1-(5-(1-((methylsulfonyl)methoxy)-2,2,2-trifluoroethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1140. 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutane-1-sulfonamide;

1141. 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutane-1-sulfonamide;

1142. N-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)methanesulfonamide;

1143. 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N,N-dimethylbutanamide;

1144. 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutanamide;

1145. 1-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethyl)-3-cyclopropylurea;

1146. 7-(1-(5-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one;

1147. 4-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-5,5,5-trifluoro-N-methylpentanamide;

1148. N-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)cyclopropanecarboxamide;

1149. 4-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-N-cyclopropyl-5,5,5-trifluoropentanamide;

1150. N-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)cyclopentanecarboxamide;

1151. 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutan-1-amine;

1152. N-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)cyclopropanamine;

1153. 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutan-1-ol;

1154. 7-(1-(5-(1,1,1-trifluoro-4-methoxybutan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1155. 4-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-5,5,5-trifluoropentanenitrile;

1156. 2-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethoxy)acetonitrile;

1157. 7-(1-(5-(1-(methylsulfonyl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1158. (6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)(cyclopropyl)methanol;

1159. 7-(1-(5-(3-(methylsulfonyl)-1-(oxetan-3-yl)propyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1160. 7-(1-(5-(1-methoxy-3-(methylsulfonyl)propyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1161. 7-(1-(5-(1-fluoro-3-(methylsulfonyl)propyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1162. 7-(1-(5-(4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1163. (6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)(1-(methylsulfonyl)piperidin-4-yl)methanol;

1164. (6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)(1-methylpiperidin-4-yl)methanol;

1165. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-N-(2,2,2-trifluoroethyl)-2-hydroxyacetamide;

1166. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-cyclopropyl-N-(2,2,2-trifluoroethyl)acetamide;

1167. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-cyano-N-(2,2,2-trifluoroethyl)acetamide;

1168. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethanol;

1169. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-2-yl)-2,2,2-trifluoroethanol;

1170. 7-(1-(6-(2,2,2-trifluoro-1-methoxyethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1171. 1-(2-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-4-yl)-2,2,2-trifluoroethanol;

1172. 1-(5-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-2-yl)-2,2,2-trifluoroethanol;

1173. 7-(1-(5-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1174. 7-(1-(6-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1175. 7-(1-(4-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1176. 1-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carbonyl)pyrrolidine-3-carbonitrile

1177. 1-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethyl)-3-cyclopropylurea

1178. 1-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)-3-cyclopropylurea

1179. 3-cyclopentyl-3-(4-(2-phenyl-3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)propanenitrile

1180. 3-cyclopentyl-3-(4-(2-phenyl-3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)propanenitrile

1181. 7-(1-(5-((S)-1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

1182. 7-(1-(5-((R)-1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

1183. 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1,1,1-trifluoropropan-2-ol

1184. 7-(1-(5-((R)-2,2,2-trifluoro-1-(oxetan-3-yl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

1185. 7-(1-(5-((S)-2,2,2-trifluoro-1-(oxetan-3-yl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

1186. 7-(1-(5-(1,1,1-trifluoro-4-(isopropylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

1187. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-(methyl sulfonyl) 1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethanamine

1188. 7-(1-(5-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-(cyclopropyl amino sulfonyl) 1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

1189. 7-(1-(5-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one

1190. 7-(1-(4-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)phenyl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

1191. 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-(trifluoromethyl)propan-1-ol

1192. N-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethyl)-2-cyanoacetamide

1193. 4-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-5,5,5-trifluoro-2-methylpentan-2-ol

1194. 7-(1-(5-(3,3,3-trifluoro-2-((methylsulfonyl)methyl)propyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

1195. N-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)-N-methylcyclopropanamine

1196. 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-2,2-dimethylbutan-1-ol

1197. N-(2-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethoxy)ethyl)cyclopropanamine

1198. 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutan-1-amine

1199. N-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)cyclohexanamine

1200. 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutan-1-amine

1201. 7-(1-(5-(1,1,1-trifluoro-4-morpholinobutan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

1202. 1-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)azetidine-3-carbonitrile

1203. 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-isopropylbutan-1-amine

1204. 7-(1-(5-(4-(cyclopropylmethylsulfonyl)-1,1,1-trifluorobutan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

1205. 7-(1-(5-(3-(cyclopropylmethylsulfonyl)-1,1,1-trifluoropropan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

1206. 7-(1-(5-(1,1,1-trifluoro-3-morpholinopropan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

1207. (S)-3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-isopropylbutan-1-amine

1208. (R)-3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-isopropylbutan-1-amine

1209. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-(Methyl sulfonyl)1H-pyrazol-1-yl)pyridin-3-yl)-3,3,3-trifluoropropan-1-amine

1210. 4-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-5,5,5-trifluoro-N-isopropylpentanamide

1211. 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N,N-diisopropylbutan-1-amine

1212. N-(2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-3,3,3-trifluoropropyl)cyclopropanamine

1213. (R)-3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutanamide

1214. (S)-3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutanamide

1215. (S)-4-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-5,5,5-trifluoro-N-isopropylpentanamide

1216. 7-(1-(5-((S)-4-(cyclopropylsulfonyl)-1,1,1-trifluorobutan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

1217. (S)-3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutan-1-amine,TFA salt

1218. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-3,3,3-trifluoro-N-isopropylpropan-1-amine

1219. 7-(1-(5-(1,1,1-trifluoro-4-(4-methylpiperazin-1-yl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

1220. (4-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-hydroxyethyl)piperidin-1-yl)(cyclopropyl)methanone

1221. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-(1-ethylpiperidin-4-yl)-2,2,2-trifluoroethanol

1222. 7-(1-(5-(1,1,1-trifluoro-3-(4-methylpiperazin-1-yl)propan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

1223. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1,1,1-trifluoro-4-(methylsulfonyl)butan-2-ol

1224. 5-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-6,6,6-trifluorohexan-2-amine,TFA salt

1225. (R)-1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-isopropylpyrrolidin-3-yl)ethanol

1226. (S)-1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-isopropylpyrrolidin-3-yl)ethanol

1227. 4-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-5,5,5-trifluoro-4-hydroxypentanenitrile

1228. 2-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethoxy)-N-methylethanamine

1229. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1,1,1-trifluoro-3-morpholinopropan-2-ol

1230. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1,1,1-trifluoro-4-morpholinobutan-2-ol

1231. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-methylazetidin-3-yl)ethanol

1232. (R)-1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-(1-ethylpyrrolidin-3-yl)-2,2,2-trifluoroethanol

1233. (S)-1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-(1-ethylpyrrolidin-3-yl)-2,2,2-trifluoroethanol

1234. (S)-1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-methylpyrrolidin-3-yl)ethanol

1235. (R)-1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-methylpyrrolidin-3-yl)ethanol

1236. 1-(3-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-hydroxyethyl)azetidin-1-yl)ethanone

1237. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-isopropylazetidin-3-yl)ethanol

1238. 4-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-5,5,5-trifluoro-4-hydroxy-N-isopropylpentanamide

1239. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-(1-ethylazetidin-3-yl)-2,2,2-trifluoroethanol

1240. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-isopropylpiperidin-4-yl)ethanol

1241. N-(2-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethoxy)ethyl)propan-2-amine,TFA salt

1242. (R)-1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-(oxetan-3-yl)pyrrolidin-3-yl)ethanol

1243. (S)-1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-(oxetan-3-yl)pyrrolidin-3-yl)ethanol

1244. 7-(1-(5-(2,2,2-trifluoro-1-methoxy-1-(1-methylpiperidin-4-yl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

1245. 3-(3-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-hydroxyethyl)azetidin-1-yl)-3-oxopropanenitrile

1246. 3-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-hydroxyethyl)-N-methylazetidine-1-carboxamide

1247. N-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)isobutyramide

1248. N-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)-2-cyanoacetamide

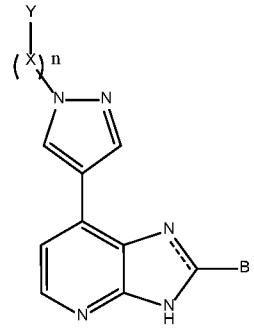
1249. 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-1-morpholinobutan-1-one

1250. 1-(4-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-5,5,5-trifluoropentanoyl)azetidine-3-carbonitrile

1251. (S)-1-(4-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)phenyl)-2,2,2-trifluoro-1-(1-isopropylpyrrolidin-3-yl)ethanol

1252. (R)-1-(4-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)phenyl)-2,2,2-trifluoro-1-(1-isopropylpyrrolidin-3-yl)ethanol

The present invention discloses novel compounds of 1H-imidazo[4,5-b]pyridin-2(3H)-one their pharmaceutically acceptable salts and isomers of formula II:



Wherein;

B is H;

X is independently, H, $(CH_2)n$, -CO-, OCO, COO; $CO(CH_2)n$, $(NH_2)n$; $(CH_2)n(NH_2)n$; $(CH_2)n(NH_2)nCN$; CONH; $CONR_1R_2$, $CO(NH_2)n$; $(CH_2)nCO(NH_2)n$, $CO(NH_2)n(CH_2)CF_3$, $SO_2(CH_2)n$, $NH(CH_2)nCN$, unsubstituted or substituted 3-8 membered carbocylic ring or heterocyclic ring containing 1 to 3 heteroatoms selected from the group comprising O, N, S and SO_2, and substituents on the carboxylic or heterocyclic ring may be selected from Halogen, Alkoxy, CHMe, $-CH(CF_3)$, $-C(CF_3)(OH)$, $C(CF_3)(OMe)$, -CH(CN), CHOH, $CH(R_5)$,

H, R_1, R_2, halo, , C_1-C_6 Alkyl, C_1-C_6 Alkoxy CN, -CO-, COR_1, $(CH_2)n$, $-(CH_2)nCN$ -, CH_2CF_3, COOH, OR_1, NR_1R_2, $-COOR_1$, $-CON(R_1)_2$,$-SO_2(CH_2)n$,$-SO_2N(R_1)_2$, $-OCOR_1$, $CONHCH(CH_3)$-CF_3, CH_2CN, $CH_2SO_2CH_3$ $-NR_1COR_1$, -CONH, $CONR_1R_2$, $-CO(NH_2)n(CH_2)nSO_2$; $-CONH(CH_2)nOH$, $CONH(CH_2)nSO_2R_1R_2$, $-CONH-(CH_2)nCF_3$, $-CONH(CH_2)nCF_3$,$-NHCONH(CH_2)nCF_3$, $NHCONHR_1$, $-NHCOR_1R_2$, $NR_1CONR_1R_2$, $(NH_2)n$, $-NH_2CH_2$, $NH_2CH_2CF_3$,$-CH(CF_3)$-(CH)n-CO-N-R_1R_2,CH(CF3)-(CH)n-SO_2, (CH)n;$CH(OH)(CF_3)$(Heretocycle)R_1, optionally substituted 3 to 8 membered carbocyclic ring, or 3 to 8 membered saturated, mono-, fused- or bridged heterocyclic ring containing 1 to 3 heteroatoms, selected from the group comprising O, N, S or SO_2, optionally substituted 3 to 8 membered heterocyclic ring containing 1 to 3 heteroatoms, selected from the group comprising O, N, S or SO_2, wherein the substitution may independently be R_1 and R_2 at any position of the ring;$C_{1\text{-}6}$alk-aryl, $ArC_{1\text{-}6}$alkyl;

R_1 and R_2 are independently selected from the group comprising H, halo, CN, CF_3, hydroxyl, Amino, SO_2, SO_2, C_1-C_6 Alkyl, SO_2-C_3-C_8-cycloalkyl, CH_2CN, CH_2CF_3, unsubstituted or substituted C_1-C_6 straight or branched alkyl wherein the substituents are selected from halo, OH, CN, C_1-C_6 alkoxy, optionally substituted NH_2, C_1-C_6 alkylsulfonyl, optionally substituted $CONH_2$, unsubstituted or substituted C_3-C_8 carbocyclyl or 3-8 membered heterocyclic ring with 1-3 heteroatoms selected from O, N and S, SO_2, C_1-C_6 straight or branched alkenyl, C_1-C_6 straight or branched alkynyl, , C_1-C_6 alkyloxy; C_1-C_6 alkylamino, C_1-C_6 alkylcarbonyl, C(O)-C_3-C_8-cycloalkyl, heteroalkyl, optionally substituted $CONH_2$, C_3–C_8 cycloalkyl, C_3–C_8cycloalkenyl, C_3–C_8heterocycloalkyl, C_3–C_8heterocycloalkenyl, carbocycyl, aryl, and heteroaryl, -$CH(CF_3)$-(CH)n-CO-N-R_3R_4, -CH(CF3)-(CH)n-SO_2-NR_3R_4, $CH(CF_3)$-(CH)n-NR_3R_4, $CH(CF_3)$-NR_3R_4, $CH(CF_3)$-(CH)n-SO_2-CHR_3R_4, wherein cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, carbocyclyl, aryl and heteroaryl groups are optionally substituted;

R_3 and R_4 are H, independently CH_3, C_3–C_8 cycloalkyl;

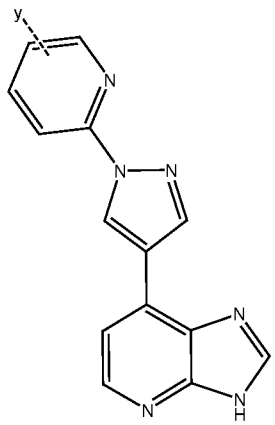
R_5 is unsubstituted or substituted 3-8 membered carbocylic ring or heterocyclic ring containing 1 to 3 heteroatoms selected from the group comprising O, N, S, SO_2;

R_6, is independently H, C_1-C_6 straight or branched alkyl, halogen;

X can be connected to Y at any atom so as to arrive at chemically viable bond;

n is 0 to 3.

The present invention discloses novel compounds of 1H-imidazo[4,5-b]pyridin-2(3H)-one their pharmaceutically acceptable salts and isomers of formula III:



Wherein;

Y may be present at any position of the pyridine ring, preferably, at 4th or 5th position of pyridine;

Y is H, R_1, R_2, halo, CN, -CO-, COR_1, $(CH_2)n$, $-(CH_2)nCN$ -, CH_2CF_3, COOH, $-COOR_1$, $-CON(R_1)_2$,$-SO_2(CH_2)n$,$-SO_2N(R_1)_2$, $-OCOR_1$, $-NR_1COR_1$, -CONH, $CONR_1R_2$, $-CO(NH_2)n(CH_2)nSO_2$; $-CONH(CH_2)nOH$, $CONH(CH_2)nSO_2R_1R_2$, $-CONH-(CH_2)nCF_3$, $-CONH(CH_2)nCF_3$,$-NHCONH(CH_2)nCF_3$, , $-CH(CF_3)-(CH)n-CO-N-R_1R_2$,$CH(CF_3)-(CH)n-SO_2-(CH)n$; $CH(OH)(CF_3)$(Heretocycle)R_1, $NHCONHR_1$, $-NHCOR_1R_2$, $NR_1CONR_1R_2$, $(NH_2)n$, $-NH_2CH_2-$, $NH_2CH_2CF_3$,

wherein the heterocycle is optionally substituted 3 to 8 membered saturated, mono-, fused- or bridged heterocyclic ring containing 1 to 3 heteroatoms, selected from the group comprising O, N, S.

wherein the substitution may independently be R_1 and R_2 at any position of the heterocyclic ring; C_{1-6}alk-aryl, Ar C_{1-6} alkyl;

R_1 and R_2 are absent or independently selected from the group comprising H, halo, CN, CF_3, hydroxyl, Amino, SO_2, SO_2C_1-C_6 Alkyl, CH_2CF_3, C_1-C_6 straight or branched alkyl, C_1-C_6 straight or branched alkenyl, C_1-C_6 straight or branched alkynyl, halo-C_1-C_6 alkyl, C_1-C_6 alkyloxy; C_1-C_6 alkylamino,

n is 0 to 3.

The present invention discloses exemplary compounds of formula III as below:

1133.1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-methylpiperidin-4-yl)ethanol;

1134.1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(tetrahydro-2H-pyran-4-yl)ethanol;

1176.1-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carbonyl)pyrrolidine-3-carbonitrile

1181.7-(1-(5-((S)-1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

1182.7-(1-(5-((R)-1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

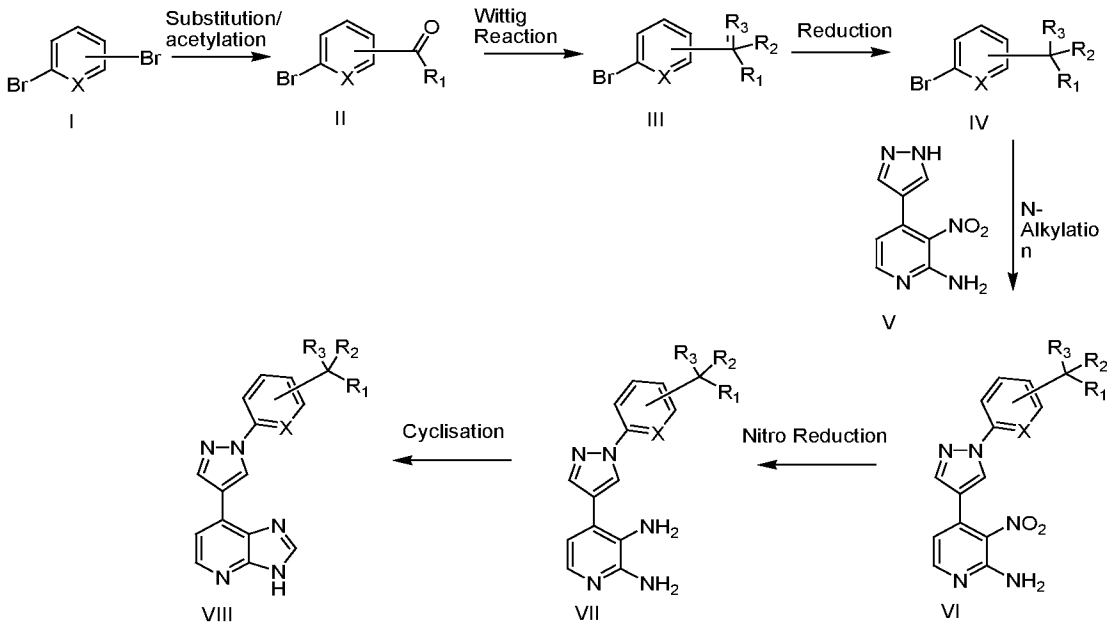
1225.(R)-1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-isopropylpyrrolidin-3-yl)ethanol

1226.(S)-1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-isopropylpyrrolidin-3-yl)ethanol

1231. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-methylazetidin-3-yl)ethanol

In an embodiment, the present invention also discloses a process of preparing the compounds of the present invention. The compounds of the present invention can be prepared by the general synthetic schemes 1 to 4, presented here below:

General Synthetic Scheme 1:

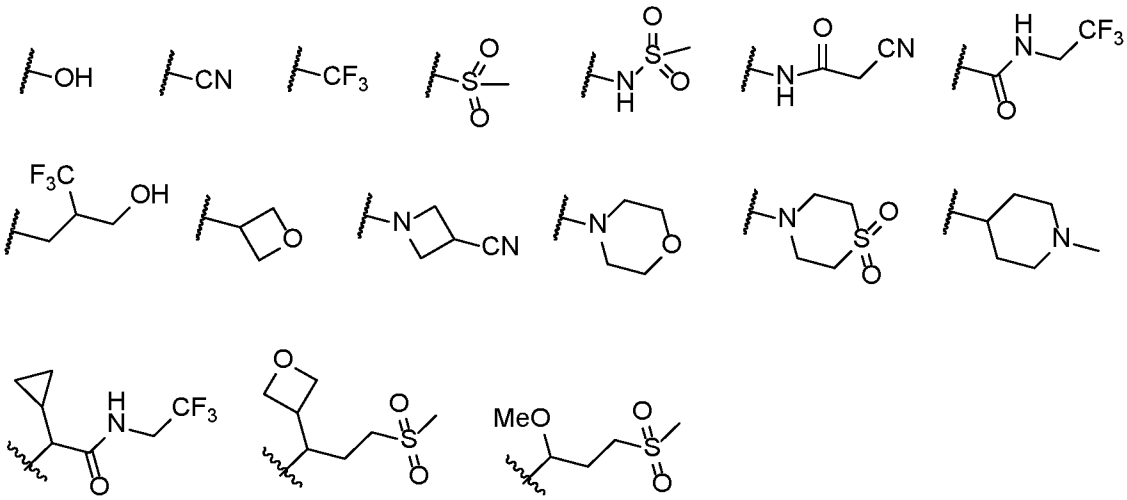


Wherein,

X is C, N,

R_2 and R_3 is H,

R1:

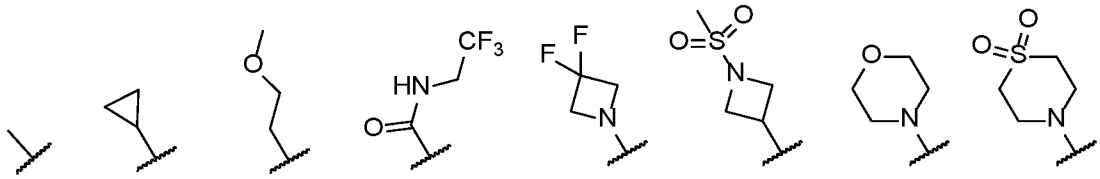


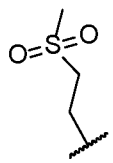
Wherein,

X is C, N,

R_1 is CN and R_2 is H

R3;



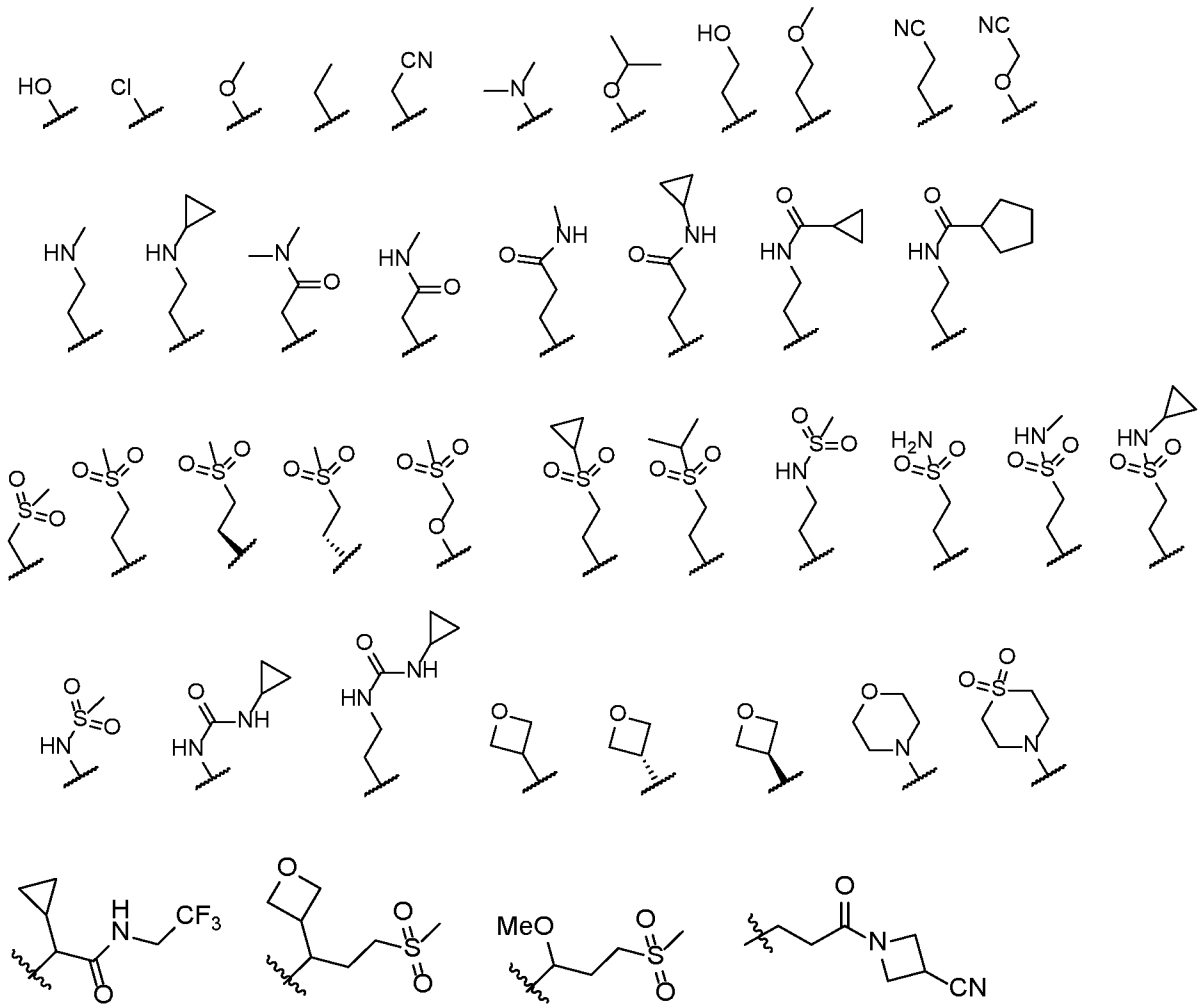


Wherein,

X is C, N,

R_1 CF_3 and R_2 is H,

R_3;

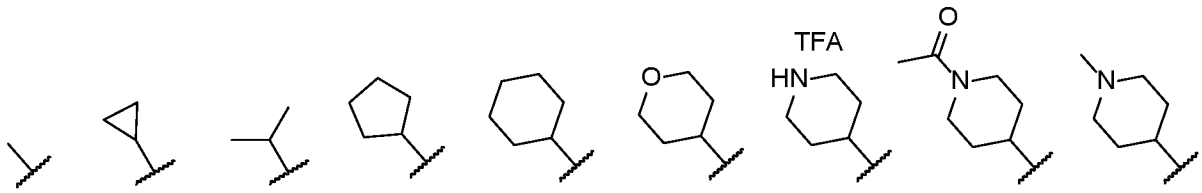


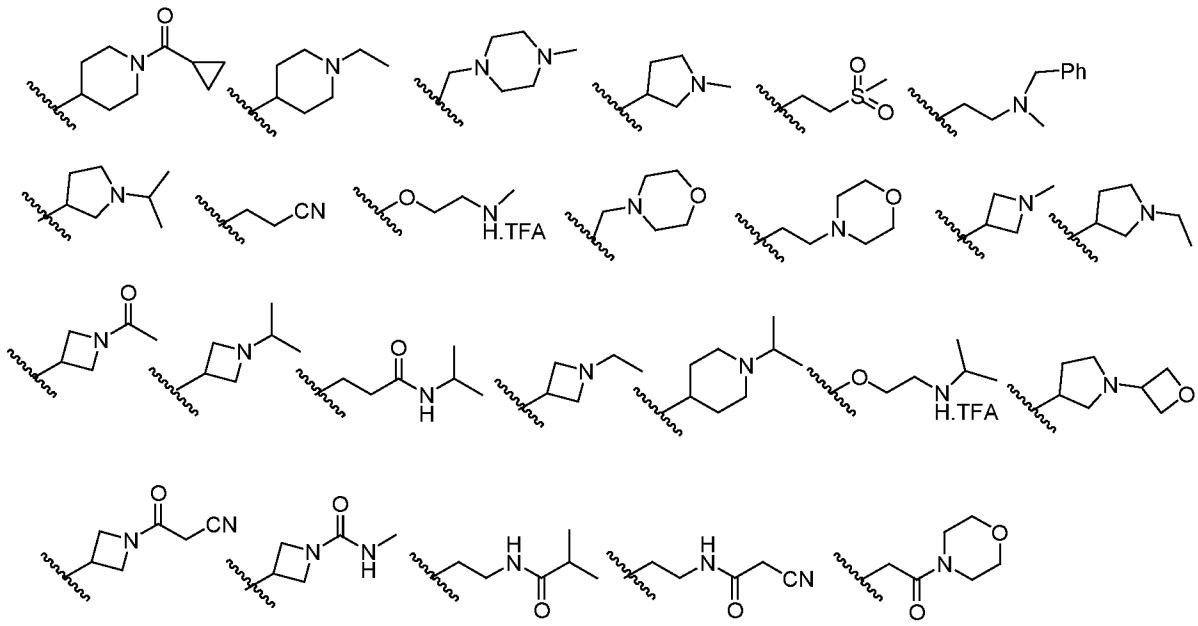
Wherein,

X is C, N,

R_1 is CF_3 and R_2 is OH

R3

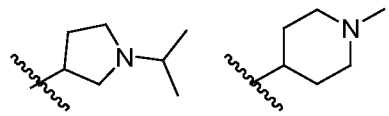




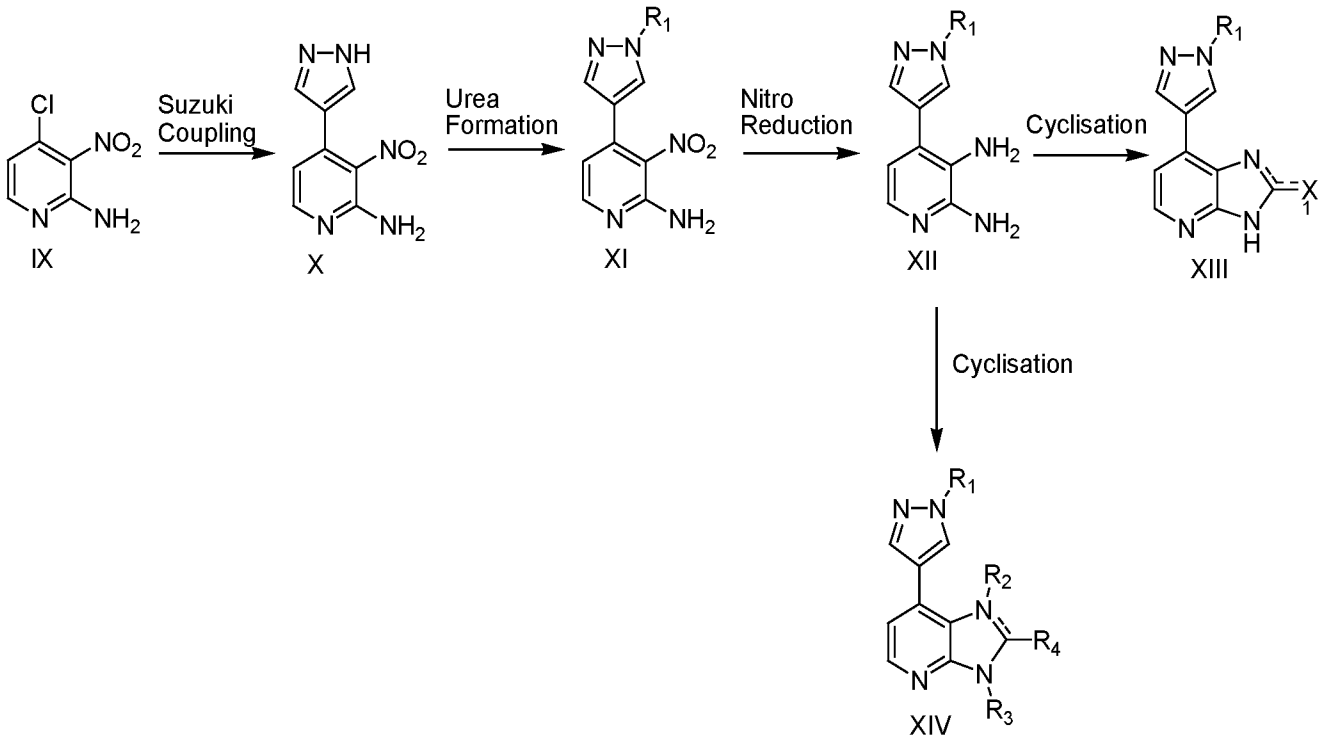
X is C, N,

R_1 is CF_3 and R_2 is OCH_3

R_3

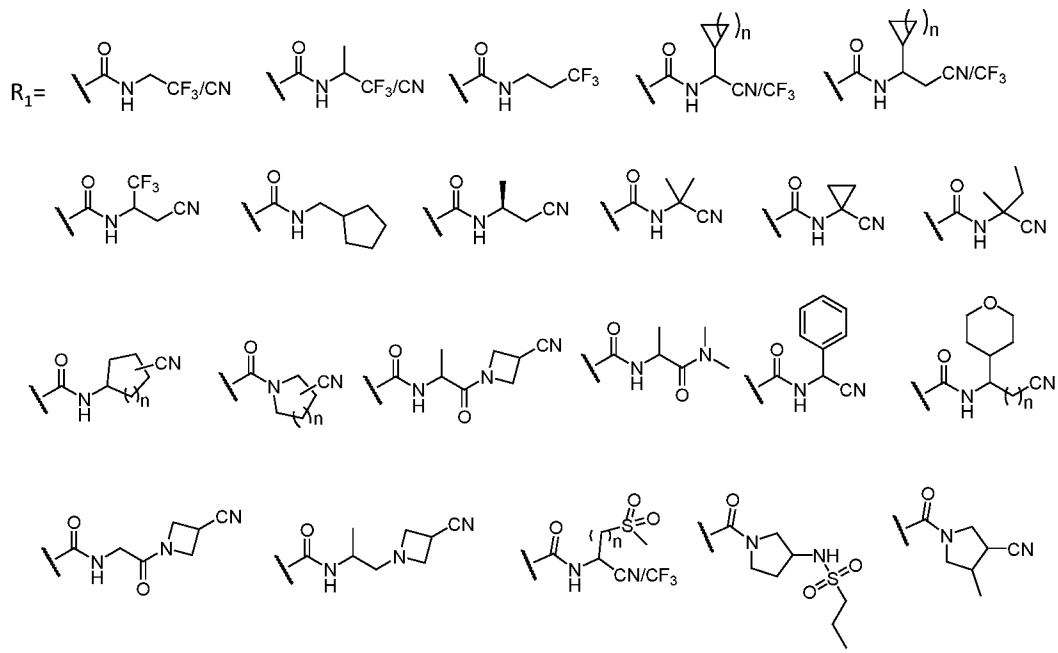


General Synthetic Scheme 2:

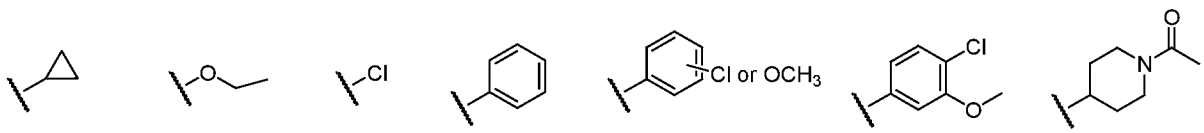


X_1= O or H R_2= H or –CH_3 R_3= H or –CH_3

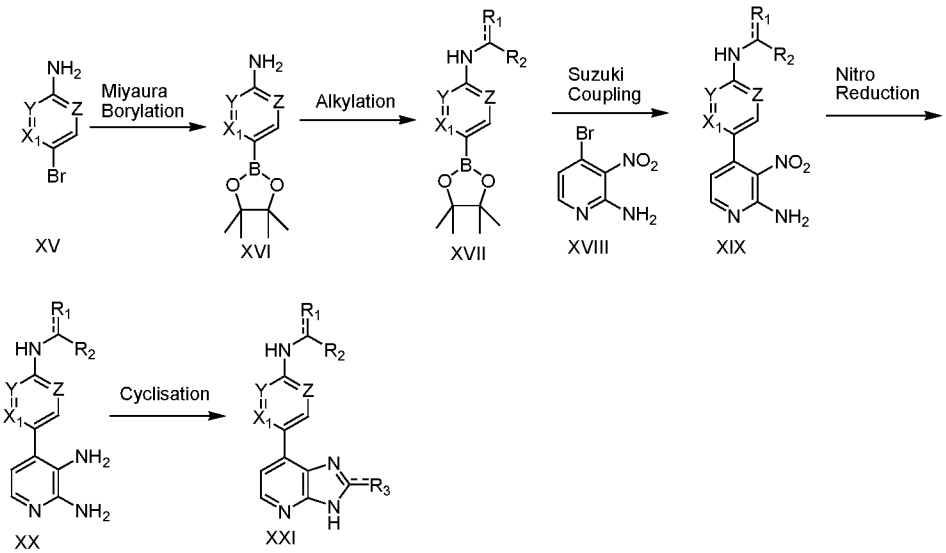
R_1;



R_4;

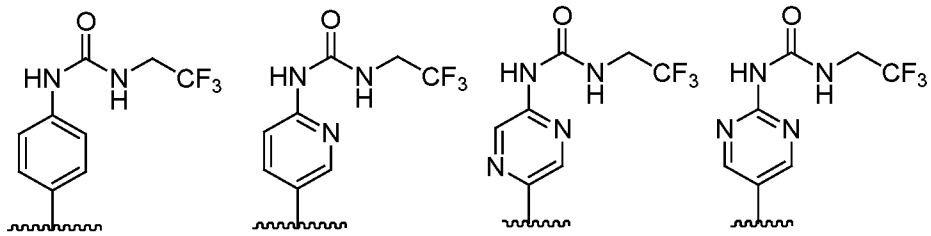


General Synthetic Scheme 3:

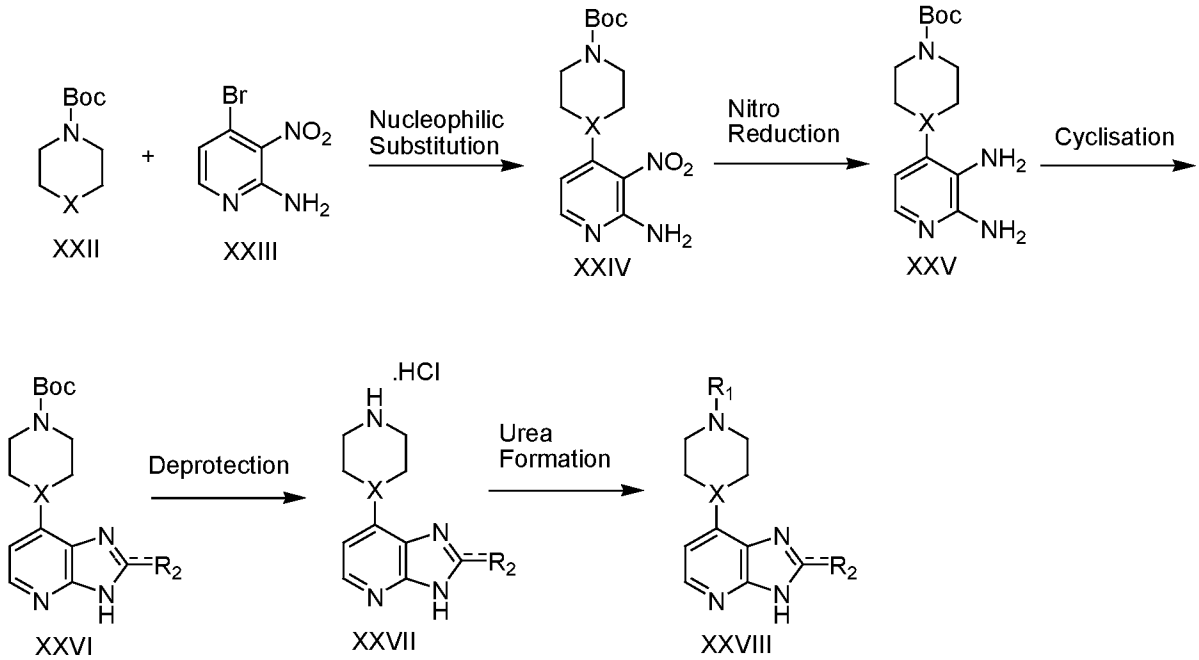


X1, Y, Z is C, N.

R_3 is H, O, carbocycle,



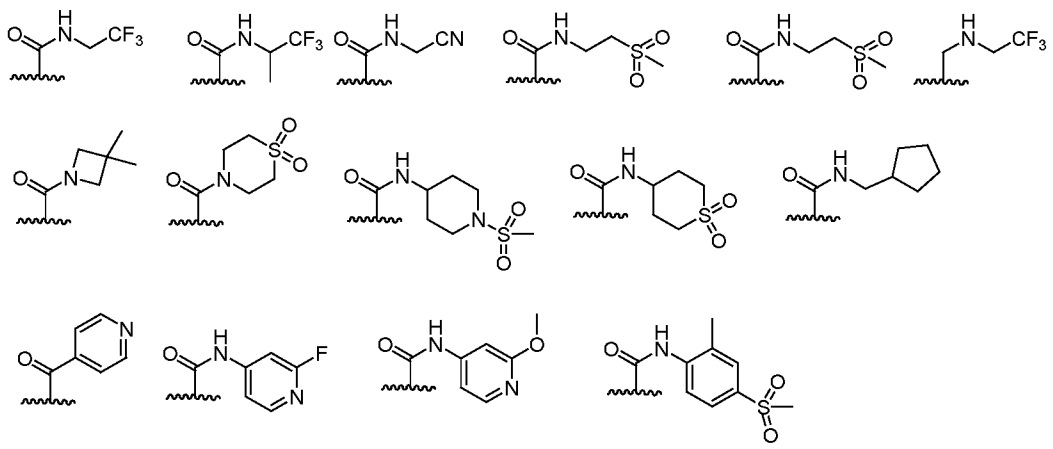
General Synthetic Scheme 4:



X is C, N.

R_2 is H, O, carbocycle,

R_1 =



The invention also comprises as another embodiment, a composition comprising a JAK1 inhibitor compound according to any one of the preceding embodiments together with a pharmaceutically acceptable diluent, excipient, and/or carrier. The compositions will include a conventional pharmaceutical carrier, excipient, and/or diluent and a compound of this disclosure as the/an active agent, and, in addition, can include carriers and adjuvants, etc. The pharmaceutically acceptable compositions will contain about 1% to about 99% by weight of a compound(s) of this disclosure, or a pharmaceutically acceptable salt thereof, and 99% to 1% by weight of a suitable pharmaceutical excipient.

Administration of the compounds of this disclosure, or their pharmaceutically acceptable salts, in pure form or in an appropriate pharmaceutical composition, can be carried out via any of the accepted modes of administration or agents for serving similar utilities. Thus, administration can be, for example, orally, nasally, parenterally (intravenous, intramuscular, or subcutaneous), topically, transdermally, intravaginally, intravesically, intracisternally, or rectally, in the form of solid, semi-solid, lyophilized powder, or liquid dosage forms, such as for example, tablets, suppositories, pills, soft elastic and hard gelatin capsules, powders, solutions, suspensions, or aerosols, or the like, preferably in unit dosage forms suitable for simple administration of precise dosages.

Solid dosage forms for oral administration include capsules, tablets, pills, powders, and granules. Solid dosage forms, as described above, can be prepared with coatings and shells, such as enteric coatings. Liquid dosage forms for oral administration include pharmaceutically acceptable emulsions, solutions, suspensions, syrups, and elixirs. Compositions for rectal administrations are, for example, suppositories that can be prepared by mixing the compounds of this disclosure with, for example, suitable non-irritating excipients or carriers. They are also be parenteral and administered as sterile powders for reconstitution into sterile injectable solutions or dispersions. Dosage forms for topical administration of a compound of this disclosure include ointments, powders, sprays. Ophthalmic formulations, eye ointments, powders, inhalation formulations and solutions are also contemplated for the compounds in this disclosure. Compressed gases can be used to disperse a compound of this disclosure in aerosol form.

The invention comprises as a further embodiment a method for treating a disease JAK1 mediates or is implicated in a subject in need thereof comprising administrating to the subject a therapeutically effective amount of a JAK1 inhibitor compound according to any one of the

preceding embodiments, or a composition comprising a JAK1 inhibitor according to any one of the preceding embodiments together with a pharmaceutically acceptable diluent, excipient, and/or carrier. The diseases JAK1 mediates or is implicated in that may be treated includes, without limitation, cancer, inflammatory disorders, and autoimmune diseases.

The selective JAK1 inhibitors of the present invention may be effective in treating cancer, including, but not limited to, carcinomas, sarcomas, lymphomas, leukemias, myelomas, germ cell tumors, blastomas, tumors of the central and peripheral nervous system and other tumors including melanomas, seminoma and Kaposi's sarcoma and the like.

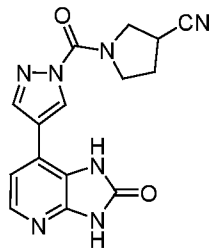
The compounds of the present invention may also be useful in disorder and diseases pertaining to acquired immunodeficiency syndrome (AIDS), Addison's disease, adult respiratory distress syndrome, allergies, ankylosing spondylitis, amyloidosis, asthma, autoimmune hemolytic anemia, autoimmune thyroiditis, Crohn's disease, episodic lymphopenia with lymphocytotoxins, erythroblastosis fetalis, Goodpasture's syndrome, Graves' disease, Hashimoto's thyroiditis, hypereosinophilia, irritable bowel syndrome and other interbowel diseases, Lupus, myasthenia gravis, myocardial or pericardial inflammation, pancreatitis, polymyositis, psoriasis, Reiter's syndrome, scleroderma, systemic analphylaxis, ulcerative colitis, nephritis (including glomerulonephritis), gout, arthritis (such as rheumatoid arthritis and osteoarthritis), erythema, dermatitis, dermatomyositis, bronchitis, cholecystitis, sepsis and gastritis.

Without being limited by theory, the compounds of the present invention exhibit selective inhibition of JAK1 with respect to JAK 2, JAK 3 and TYK 2. Therefore, it is submitted that the compounds of the present invention demonstrate selective inhibition and therefore are more specific and advantageous than other compounds in prior art, as they are expected to result in less adverse effects.

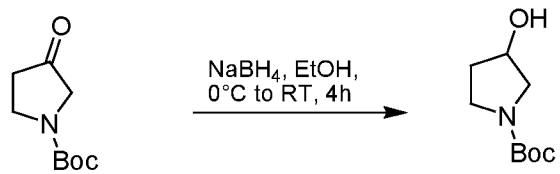
The examples and scheme below depict the general synthetic procedure for the compounds disclosed herein. Synthesis of the compounds of Formulae I disclosed herein, and embodiments thereof, are not limited by these examples and schemes. One skilled in the art will know that other procedures can be used to synthesize the compounds of Formulae I disclosed herein, and that the procedures described in the examples and schemes is only one such procedure. In the descriptions below, one of ordinary skill in the art would recognize that specific reaction conditions, added reagents, solvents, and reaction temperatures can be modified for the

synthesis of specific compounds that fall within the scope of this disclosure. All intermediate compounds described below, for which there is no description of how to synthesize such intermediates within these examples below, are commercially available compounds unless otherwise specified.

Synthesis of Compound no. 1177: 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)acetonitrile



Step-1: Synthesis of tert-butyl 3-hydroxypyrrolidine-1-carboxylate:



1 2

To a stirred solution solution of tert-butyl 3-oxopyrrolidine-1-carboxylate (0.50 g, 2.699 mmol) in ethanol (5 mL) was added sodium borohydride (0.20 g, 5.399 mmol) at 0ºC and the mixture was stirred at room temperature for 4h. Progress of reaction was monitored by TLC. After reaction completion water (10 mL) was added to the reaction mixture and the product extracted with ethyl acetate. The organic layer was dried over sodium sulphate, concentrated under reduced pressure to give tert-butyl 3-hydroxypyrrolidine-1-carboxylate (0.5 g, 99%) as yellow solid.

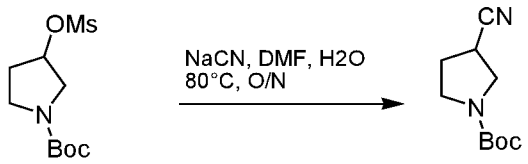
MS: 188.24 [M+1]

Step-2: Synthesis of 1-(tert-butoxycarbonyl)pyrrolidin-3-yl methanesulfonate

3 4

To a stirred solution of tert-butyl 3-hydroxypyrrolidine-1-carboxylate (1.0 g, 5.347 mmol) in DCM (10.0 mL) at 0ºC was added MsCl (0.673 g, 5.882 mmol) under nitrogen. To resultant reaction mixture DIPEA (0.898 g, 6.951 mmol) solution in DCM (1.0 mL) was added drop wise, stirred for 4h at RT and progress of reaction was monitored by TLC. On completion, quenched with water, extracted with ethyl acetate. Organic layer was dried over sodium sulphate, concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 10% ethyl acetate in hexane as eluent to 1-(tert-butoxycarbonyl)pyrrolidin-3-yl methanesulfonate (0.25 g, 25 %) as crude yellow oily mass. MS: 266.33 [M+1]

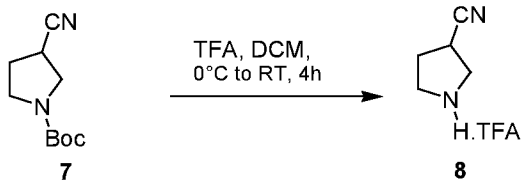
Step-3: synthesis of tert-butyl 3-cyanopyrrolidine-1-carboxylate



5 **6**

To a stirred solution of 1-(tert-butoxycarbonyl) pyrrolidin-3-yl methanesulfonate (0.25 g, 0.9432 mmol) in DMF (5 mL) and water (1 mL) was added KCN (0.138 g, 2.830 mmol) under nitrogen and the resulted solution heated overnight at 80ºC. Progress of reaction was monitored by TLC. After reaction completion reaction mass was cooled to 0ºC and quenched with water. Product was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 6% acetone/hexane as eluent to obtain tert-butyl 3-cyanopyrrolidine-1-carboxylate (0.15 g, 81 %) as yellow oil. MS: 197.25 [M+1]

Step-4: synthesis of pyrrolidine-3-carbonitrile trifluoroacetate



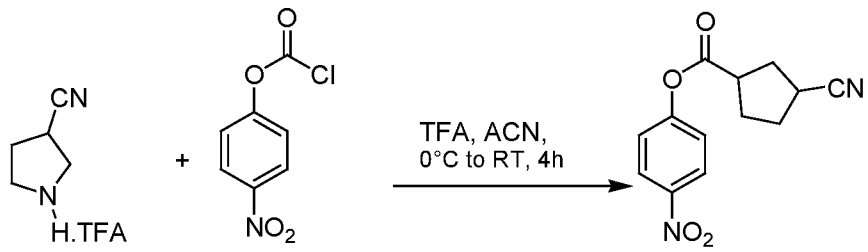
7 **8**

To a stirred solution of tert-butyl 3-cyanopyrrolidine-1-carboxylate (0.15 g, 0.765 mmol) in DCM (5 mL) was added TFA (0.8 mL) at 0ºC and reaction allowed to stir at room temperature for 4h. Reaction was monitored by TLC. On completion all volatiles were evaporated under reduced pressure, residue was triturated with diethtyl ether, filtered and dried to obtained

pyrrolidine-3-carbonitrile trifluoroacetate (0.1 g, 62.2 %) as off brown solid.

MS: 194.15 [M+1]

Step-5: synthesis of 4-nitrophenyl 3-cyanocyclopentanecarboxylate

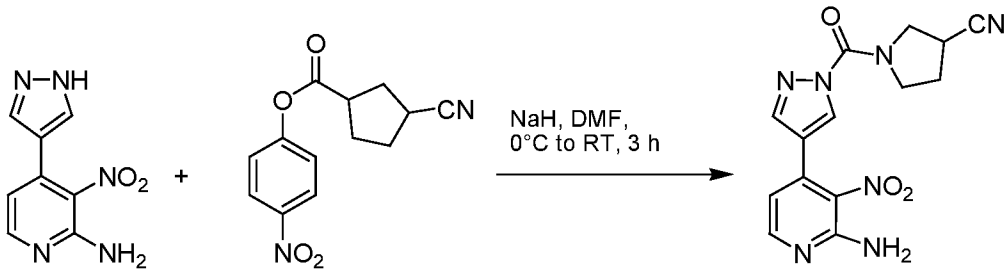


9 10 11

To a stirred solution of pyrrolidine-3-carbonitrile trifluoroacetate (0.05 g, 0.238 mmol) in ACN (5.0 mL), trimethylamine (0.072 g , 0.714 mmol) was added followed by 4-nitrophenyl chloroformate (0.047 g , 0.238 mmol) at 0^0C. The resultant reaction mixture was stirred for 4h at room temperature. Completion of reaction was monitored by TLC. On completion product was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure to give 4-nitrophenyl 3-cyanocyclopentanecarboxylate (0.05 g, 80.5%) as white solid

MS: 261.25 [M+1]

Step-6: synthesis of 1-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazole-1-carbonyl)pyrrolidine-3-carbonitrile



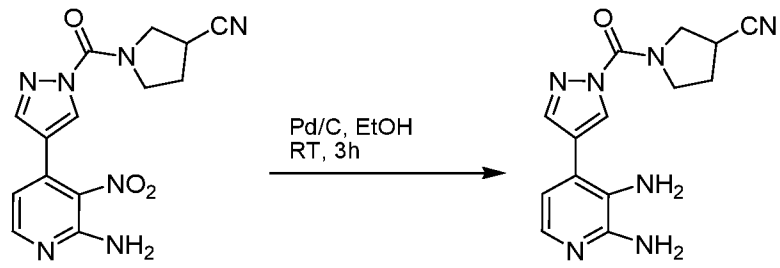
12 13 14

To a stirred solution of 3-nitro-4-(1H-pyrazol-4-yl)pyridin-2-amine (0.05 g, 0.2439 mmol) in DMF (2 mL) at 0^oC was added NaH (0.02 g, 0.4878 mmol) under nitrogen and stirred for 30 min. at same temperature. To resultant reaction mass solution of 4-nitrophenyl 3-cyanocyclopentanecarboxylate (0.094 g, 0.7894 mmol) in DMF was added at 0^oC and stirred

for 4h at RT. Progress of reaction was monitored by TLC. After reaction completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 0.5 % Methanol in DCM as eluent to obtain 1-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazole-1-carbonyl)pyrrolidine-3-carbonitrile (0.03 g, 37.6 %) as yellow solid.

MS: 328.3 [M+1]

Step-7: Synthesis of 1-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazole-1-carbonyl)pyrrolidine-3-carbonitrile

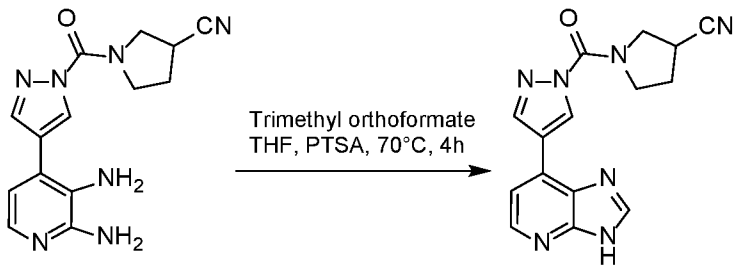


15 16

To a stirred solution of 1-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazole-1-carbonyl)pyrrolidine-3-carbonitrile (0.03 g, 0.0917 mmol) in methanol (5 mL) was hydrogenated by 10% Pd/C (0.003 g, 10 % wt/wt) using hydrogen balloon. Progress of the reaction was monitored by TLC. After reaction completion reaction mass filtered through celite and filtrate was evaporated under reduced pressure to give **2**-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)acetonitrile (0.02 g, 73.5 %) as brown solid.

MS: 298.3 [M+1]

Step-8: Synthesis of 1-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carbonyl)pyrrolidine-3-carbonitrile

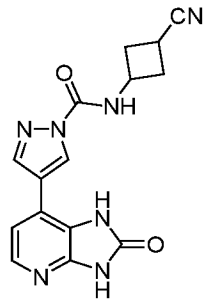


17 1177

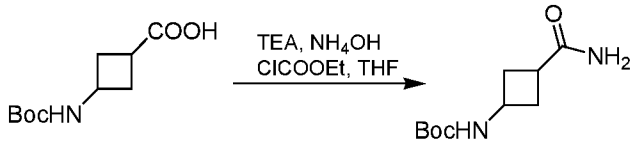
To a stirred solution of 2-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)acetonitrile (0.025 g, 0.0841 mmol) in trimethyl orthoformate (1.0 mL) was added. To resultant reaction mixture, PTSA (0.004 g) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, quenched with aq. sodium bicarbonate solution, extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 3% to 5% MeOH in DCM to obtain 1-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carbonyl)pyrrolidine-3-carbonitrile (0.01 g, 40 %) as off white solid.

MS: 308.3 [M+1]

Synthesis of Compound No: 1056: N-(3-cyanocyclobutyl)-4- (2,3-dihydro-2-oxo-1H-imidazo [4,5-b] pyridin-7-yl) -1H-pyrazole-1- carboxamide



Step-1: Synthesis of tert-butyl 3-carbamoylcyclobutylcarbamate:

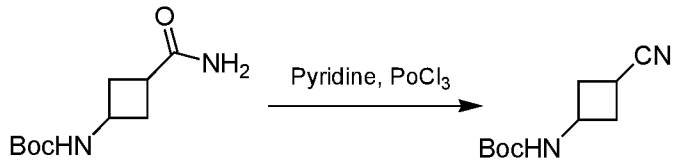


18 19

To a stirred solution of tert-butyl 3-cyanopyrrolidine-1-carboxylate (0.500 g, 2.325 mmol) in THF (15 mL) was added ethyl chloroformate (0.301 mg, 2.79mmol) at 0°C and reaction allowed to stir at room temperature for 1h. To resultant reaction mass solution of ammonium hydroxide (5.0 mL) was added at 0°C and stirred for 4h at RT. Reaction was monitored by TLC. On completion product was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure to give to obtained tert-butyl 3-carbamoylcyclobutylcarbamate (0.430 g, 85.65 %) as colourless liquid.

MS: 215.12 [M+1]

Step-2: Synthesis of tert-butyl 3-cyanocyclobutylcarbamate:

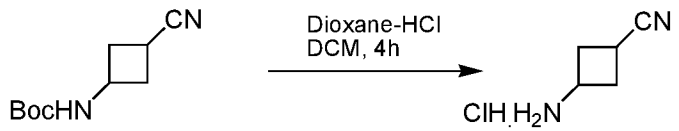


20 21

To a stirred solution of tert-butyl 3-carbamoylcyclobutylcarbamate (0.400 g, 1.869 mmol) in pyridine (5.0 mL) was added POCl3 (1.84g, 1.200 mmol) at 0°C and reaction allowed to stir at room temperature for 1h. Reaction was monitored by TLC. On completion product was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure to give to obtained tert-butyl 3-cyanocyclobutylcarbamate (0.340 g, 98.8 %) as colourless liquid.

MS: 197.15 [M+1]

Step-3: Synthesis of 3-aminocyclobutanecarbonitrile hydrochloride:

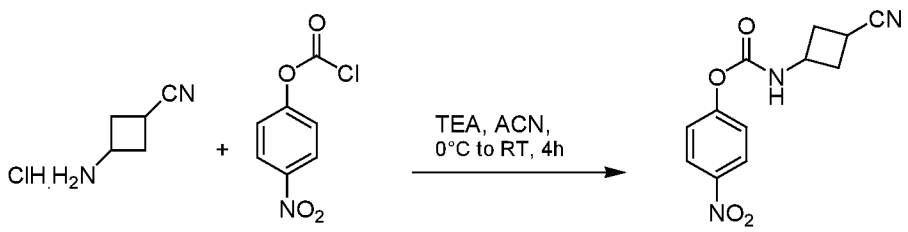


22 23

To a stirred solution of tert-butyl 3-cyanocyclobutylcarbamate (0.300 g, 1.522 mmol) in DCM (5 mL) was added Dioxane-HCl (2.5 mL) at 0°C and reaction allowed to stir at room temperature for 4h. Reaction was monitored by TLC. On completion all volatiles were evaporated under reduced pressure, residue was triturated with di-ethyl ether, filtered and dried to obtained 3-aminocyclobutanecarbonitrile hydrochloride (0.240 g, 94.63 %) as off white solid.

MS: 133.05 [M+1]

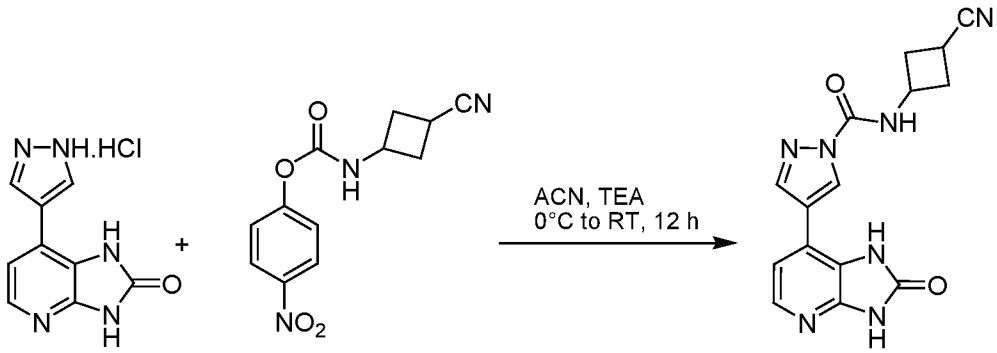
Step-4: synthesis of 4-nitrophenyl 3-cyanocyclobutylcarbamate



To a stirred solution of 3-aminocyclobutanecarbonitrile hydrochloride (0.300 g, 2.247 mmol) in ACN (5.0 mL), trimethylamine (0.493 g, 4.89 mmol) was added followed by 4-nitrophenyl chloroformate (0.544 g, 2.706 mmol) at 0^0C. The resultant reaction mixture was stirred for 4h at room temperature. Completion of reaction was monitored by TLC. On completion product was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure to give 4-nitrophenyl 3-cyanocyclobutylcarbamate (0.250 g, 42.23%) as yellowish solid.

MS: 262.05 [M+1]

Step-5: synthesis of N-(3-cyanocyclobutyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide

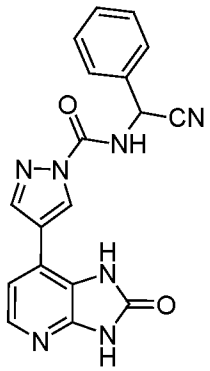


27 28 1056

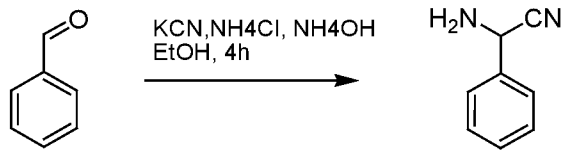
To a stirred solution of 7-(1H-pyrazol-4-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one hydrochloride (0.05 g, 0.210 mmol) in ACN (2.5 mL) at 0^0C was added TEA (0.053 g, 0.527 mmol) under nitrogen and stirred for 30 min. at same temperature. To resultant reaction mass solution of 4-nitrophenyl 3-cyanocyclobutylcarbamate (0.081 g, 0.315 mmol) in ACN was added at 0^0C followed by TEA (0.035 g, 0.315 mmol) under nitrogen and stirred for 4h at RT. Progress of reaction was monitored by TLC. After reaction completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 3-5 % Methanol in DCM as eluent to obtain N-(3-cyanocyclobutyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide (0.03 g, 37.6 %) as off white solid.

MS: 324.11 [M+1]

Synthesis of compound No. 1063: N-(cyano(phenyl)methyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide



Step-1: 2-amino-2-phenylacetonitrile

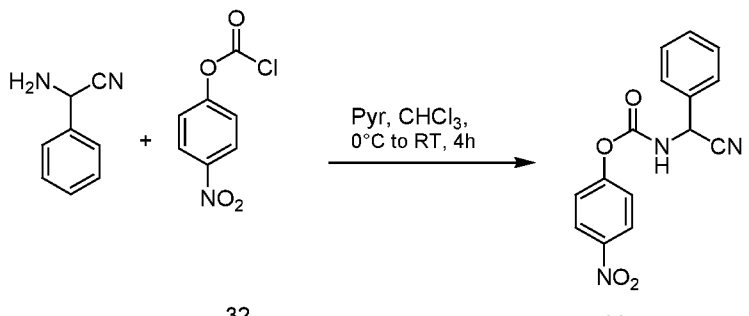


29 30

To a stirred solution of benzaldehyde (1.0 g, 0.934 mmol) in Ethanol (20 mL) was added ammonium chloride (0.99g, 1.86mmol), ammonium hydroxide (12.5 ml, 25%) and potassium cyanide (078g,1.21mmol) at room temperature. The resultant reaction mixture was stirred at same temperature for 4h. Completion of reaction was monitored by TLC. On completion, quenched with ice water, extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate, concentrated under reduced pressure to obtained 2-amino-2-phenylacetonitrile (0.600g, 48.3%) as orange solid.

MS: 133.04 [M+1]

Step-2 : 4-nitrophenyl cyano(phenyl)methylcarbamate

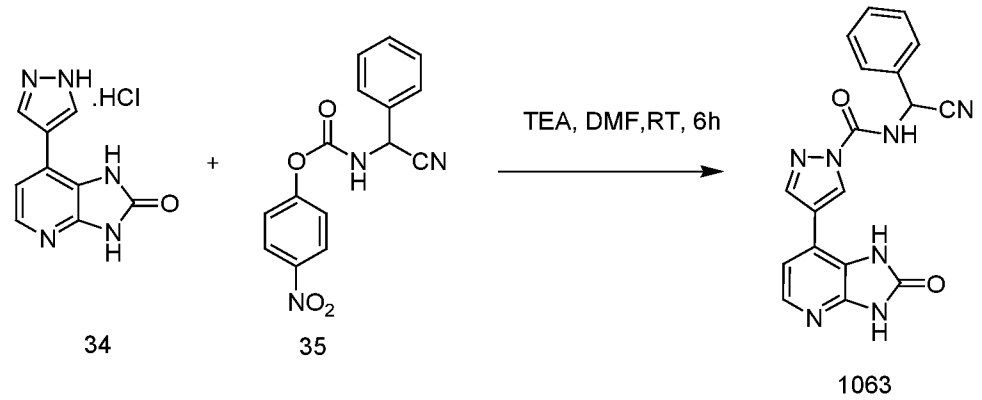


31 32 33

To a stirred solution of 2-amino-2-phenylacetonitrile (0.200 g, 1.515 mmol) in chloroform (5.0 mL), pyridine (0.3 g , 3.03 mmol) was added followed by 4-nitrophenyl chloroformate (0.3 g , 1.515 mmol) at 0^0C. The resultant reaction mixture was stirred for 4h at room temperature. Completion of reaction was monitored by TLC. On completion product was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure to give 4-nitrophenyl cyano(phenyl)methylcarbamate (0.200 g, 44.4%) as white solid

MS: 298.25 [M+1]

Step-3: 3 Synthesis of N-(cyano(phenyl)methyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide

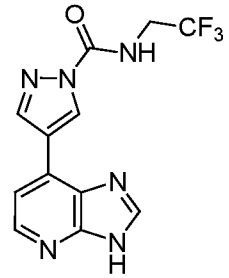


34 35 1063

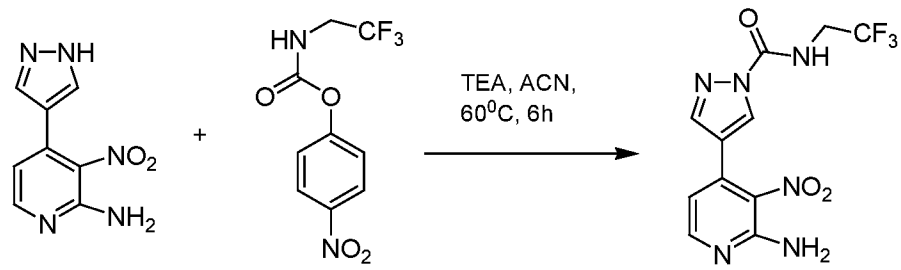
To a stirred solution of 7-(1H-pyrazol-4-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one hydrochloride (0.030g, 0.0127 mmol) in DMF (2.0 mL), trimethylamine (0.038g, 0.0381) and 4-nitrophenyl cyano(phenyl)methylcarbamate (0.037g, 0.0127 mmol) was added. The resultant reaction mixturewas stirred 6h at room temprature. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with 10% MeOH in DCM. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 8 to 9% MeOH in DCM to obtain N-(cyano(phenyl)methyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide (0.004 g, 8.7%) as off white solid.

MS: 360.1[M+1]

Synthesis of Compound No. 1064:- N-(2,2,2-trifluoroethyl)-4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide



Step-1: Synthesis of 4-(2-amino-3-nitropyridin-4-yl)-N-(2,2,2-trifluoroethyl)-1H-pyrazole-1-carboxamide

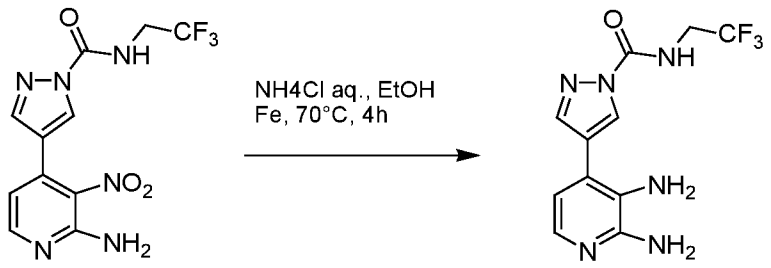


36 37 38

To a stirred solution of 3-nitro-4-(1H-pyrazol-4-yl)pyridin-2-amine (0.150 g, 0.073 mmol) in acetonitrile (10 mL) and trimethylamine(0.147g, 0.146mmol), was added 4-nitrophenyl 2,2,2-trifluoroethylcarbamate (0.231g, 0.087 mmol) at room temperature. The resultant reaction mixture was stirred at 60^0C temperature for 6h. Completion of reaction was monitored by TLC. On completion, quenched with ice water, extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate, concentrated under reduced pressure obtained crude reaction mass. Purification of the crude was done *via* silica gel (100-200 Mesh) column chromatography and desired compound eluted at 3 to 4% methanol in DCM to obtained 4-(2-amino-3-nitropyridin-4-yl)-N-(2,2,2-trifluoroethyl)-1H-pyrazole-1-carboxamide (0.160g, 67%) as yellow solid.

MS: 331.04 [M+1]

Step-2: Synthesis of 4-(2,3-diaminopyridin-4-yl)-N-(2,2,2-trifluoroethyl)-1H-pyrazole-1-carboxamide



39 40

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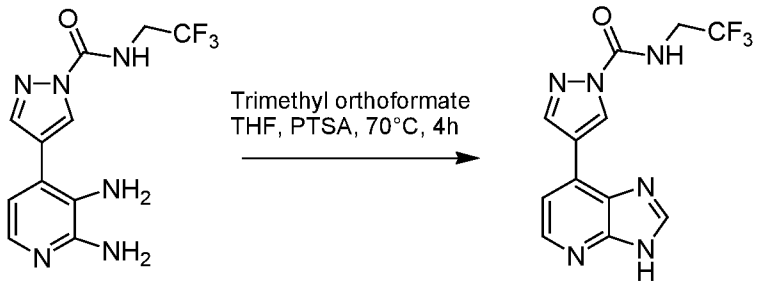
To a stirred solution of 4-(2-amino-3-nitropyridin-4-yl)-N-(2,2,2-trifluoroethyl)-1H-pyrazole-1-carboxamide (0.080g, 0.024 mmol) in EtOH (3.0 mL), NH_4Cl (2.0 mL) was added at room temperature. To resultant reaction mixture, Fe powder (0.064 g, 0.12 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, reaction mixture was diluted with H_2O: EtOAc (50 mL, 5:5) and pass over celite to remove inorganic impurities from the reaction mixture. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to obtained 4-(2,3-diaminopyridin-4-yl)-N-(2,2,2-trifluoroethyl)-1H-pyrazole-1-carboxamide (0.045 g, 62.5 %) as dark brown solid mass.

MS: 301.2 [M+1]

Step-: 3 Synthesis of N-(2,2,2-trifluoroethyl)-4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide



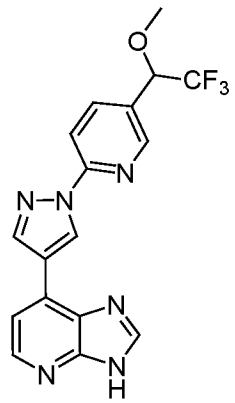
41 1064

To a stirred solution of 4-(2,3-diaminopyridin-4-yl)-N-(2,2,2-trifluoroethyl)-1H-pyrazole-1-carboxamide (0.045g, 0.015 mmol) in THF (1.0 mL), trimethyl orthoformate (2.0 mL) was added. To resultant reaction mixture, PTSA (0.0051 g, 0.0030 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, quenched with

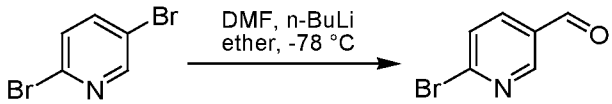
bicarbonate water, extracted with 10% MeOH in DCM. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 8 to 9% MeOH in DCM to obtained N-(2,2,2-trifluoroethyl)-4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide (0.023 g, 50%) as off white solid.

MS: 311.1[M+1]

Synthesis of Compound No. 1119: 7-(1-(5-(2,2,2-trifluoro-1-methoxy ethyl)pyridin-2-yl)-1H- pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine



Step-1: Synthesis of 6-bromopyridine-3-carbaldehyde:

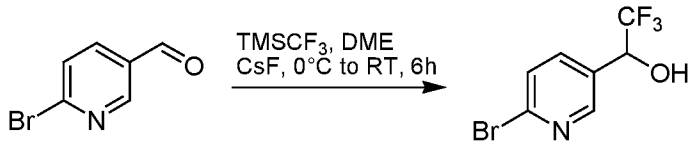


42 43

To a stirred solution of 2,5-dibromopyridine (26.0 g, 109.75 mmol) in diethyl ether (500 mL) at -78°C was added n-Butyl lithium (2.5M in hexane) (66 mL, 164.63 mmol) under nitrogen and stirred for 1h at same temperature. DMF (13 mL, 164.63 mmol) was then added drop wise to the reaction mixture, stirred for 1h at -78°C. Progress of reaction was monitored by TLC. After reaction completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with diethyl ether. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 4% ethyl acetate in hexane as eluent to obtain 6-bromopyridine-3-carbaldehyde (12.20 g, 59.8 %) as yellow oil.

MS: 187.0 [M+1]

Step-2: Synthesis of 1-(6-bromopyridin-3-yl)-2,2,2-trifluoroethanol

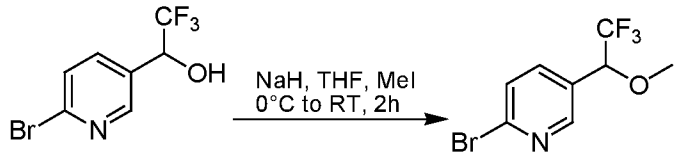


44 45

To a stirred solution of 6-bromopyridine-3-carbaldehyde (2.0 g, 10.75mmol) in DME (50 mL) at 0°C was added $TMSCF_3$ (1.61 g, 16.12 mmol) under nitrogen, followed by portion wise addition of CsF (2.44 g, 16.12 mmol) and stirred for 1h at same temperature. Allow to warm to RT and Stirred for 6h. Progress of reaction was monitored by TLC. After reaction completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) on flash column chromatography using 20% ethyl acetate in hexane as eluent to obtain 1-(6-bromopyridin-3-yl)-2,2,2-trifluoroethanol (1.24 g, 47.69 %) as yellow oil.

MS: 257.8 [M+1]

Step-3: synthesis of 2-bromo-5-(2,2,2-trifluoro-1-methoxyethyl)pyridine

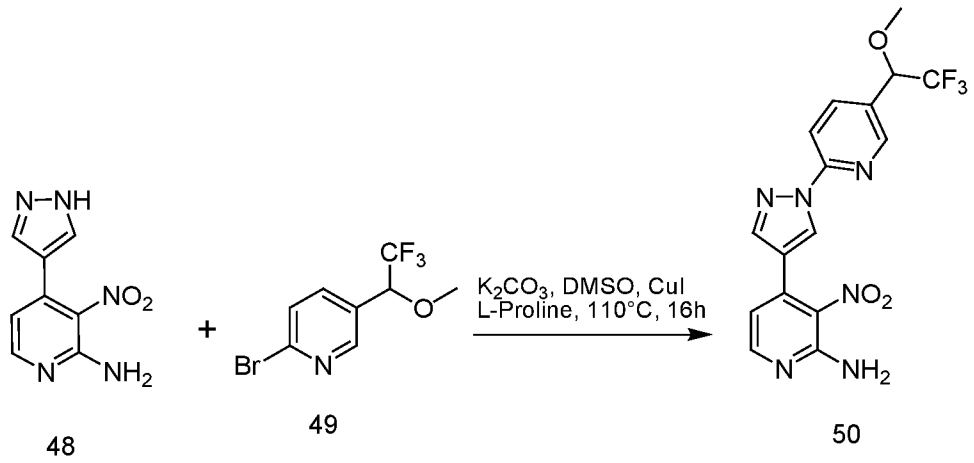


46 47

To a stirred solution of 1-(6-bromopyridin-3-yl)-2,2,2-trifluoroethanol (0.40 g, 15.56 mmol) in THF (5.0 mL) at 0°C was added NaH (0.081 g, 20.23 mmol) under nitrogen and stirred for 1h at same temperature. To resultant reaction mass MeI (0.232 g, 20.23mmol) solution in THF (3.0 mL) was added Allow to warm to RT and Stirred for 1h. Progress of reaction was monitored by TLC. After reaction completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 10% acetone in hexane as eluent to obtain 2-bromo-5-(2,2,2-trifluoro-1-methoxyethyl)pyridine (0.39 g, 92.19 %) as colourless oil.

MS: 271.0 [M+1]

Step-4: Synthesis of 4-(1-(5-(2,2,2-trifluoro-1-methoxyethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine

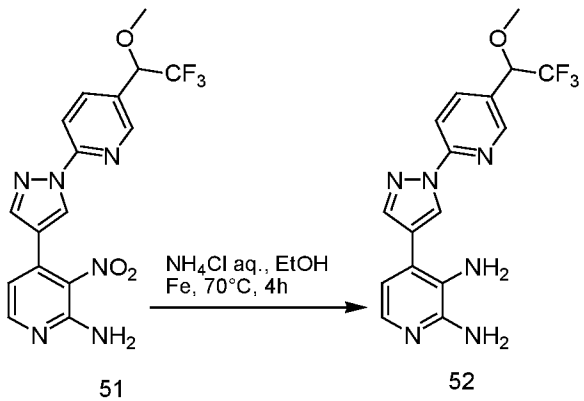


48 49 50

To a stirred solution of 3-nitro-4-(1H-pyrazol-4-yl) pyridin-2-amine (0.15g, 0.73 mmol) and compound 2-bromo-5-(2,2,2-trifluoro-1-methoxyethyl)pyridine (0.278g, 1.02 mmol) in DMSO (5 ml) was added K_2CO_3 (0.251g, 1.825 mmol) followed by CuI (0.013g, 0.073 mmol) and L-Proline (0.056g, 0.365 mmol). Reaction was heated at 110°C for 16h. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 40-60% acetone in n-hexane to obtained 4-(1-(5-(2,2,2-trifluoro-1-methoxyethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine (0.075 g, 37.87 %) as yellow solid.

MS: 394.4[M+1]

Step-5: Synthesis of 4-(1-(5-(2,2,2-trifluoro-1-methoxyethyl)pyridin-2-yl)-1H-pyrazol-4-yl)pyridine-2,3-diamine

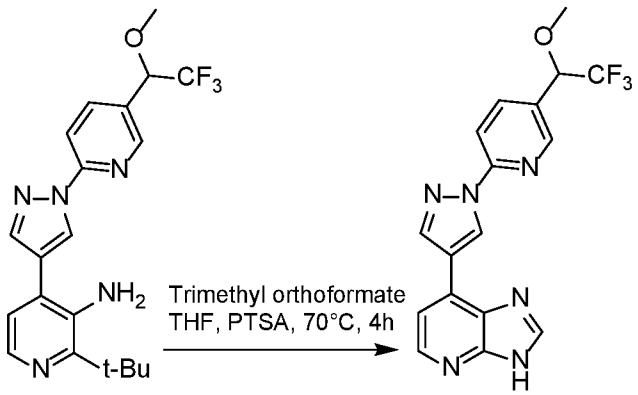


51 52

To a stirred solution of 4-(1-(5-(2,2,2-trifluoro-1-methoxyethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine (0.070g, 1.77 mmol) in EtOH (3.0 mL), NH_4Cl (2.5 mL) was added at room temperature. To resultant reaction mixture, Fe powder (0.025 g, 0.45 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, reaction mixture was diluted with H_2O: EtOAc (50 mL, 5:5) and pass over celite to remove inorganic impurities from the reaction mixture. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to obtained pure 4-(1-(5-(2,2,2- trifluoro-1- methoxy ethyl) pyridin-2-yl)-1H-pyrazol-4-yl) pyridine -2,3-diamine (0.035g, 53.03%) as dark brown solid mass.

MS: 364.2 [M+1]

Step-6: Synthesis of 7-(1-(5-(2,2,2-trifluoro-1-methoxyethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

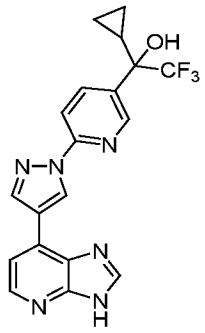


53 1119

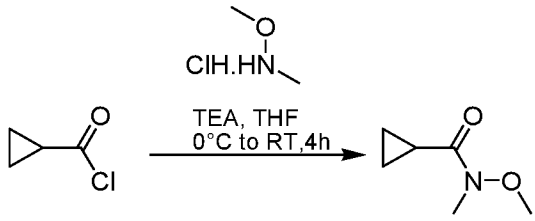
To a stirred solution of 4-(1-(5-(2,2,2-trifluoro-1- methoxy ethyl) pyridin-2-yl)-1H-pyrazol-4-yl) pyridine -2,3-diamine (0.035g, 0.093 mmol) in THF (1.0 mL), Trimethyl orthoformate (1.5 mL) was added. To resultant reaction mixture, PTSA (0.002 g, 0.018 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with 10% MeOH in DCM. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 3% to 5% MeOH in DCM to obtained 7-(1-(5-(2,2,2- trifluoro-1-methoxy ethyl)pyridin-2-yl)-1H-pyrazol-4-yl) -3H-imidazo [4,5-b] pyridine (0.07 g, 19.44%) as off white solid.

MS: 375.9[M+1]

Synthesis of Compound No. 1126: 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-cyclopropyl-2,2,2-trifluoroethanol



Step-1: Synthesis of N-methoxy-N-methyl cyclopropane carboxamide:

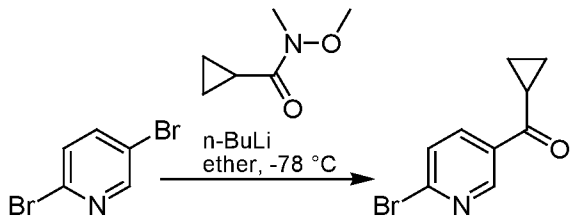


54 55

To a stirred solution of cyclopropane carbonyl chloride (10.0 g, 961.5 mmol) and N-methoxy methanamine hydrochloride (11.20 g, 1153.8 mmol) in THF (150 mL), TEA (24.20g, 2403.8 mmol) was added drop-wise at 0°C and allow to stirred for 30 min. Resultant reaction mass was then placed at RT and stirred for 4h. Completion of reaction was monitored by TLC. On completion, concentrated under reduced pressure to obtained crude mass. Purification of the crude was done *via* silica gel (100-200 Mesh) column chromatography and desired compound eluted at 5% ether/n-Hexane to obtained N-methoxy-N-methyl cyclopropane carboxamide (7.45g, 60%) as colourless oily mass.

MS: 130.07 [M+1]

Step-2: Synthesis of (6-bromopyridin-3-yl)(cyclopropyl)methanone:



56 57

To a stirred solution of 2,5-dibromopyridine (12.0 g, 50.63mmol) in diethyl ether (250 mL) at -78°C was added n-Butyl lithium (2.5M in hexane) (24.30 mL, 65.81mmol) under nitrogen and stirred for 1h at same temperature. N-methoxy-N-methyl cyclopropane carboxamide (7.1 g, 55.69 mmol) was then added drop wise to the reaction mixture, stirred for 1h at -78°C. Progress of reaction was monitored by TLC. After reaction completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with diethyl ether. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 4% ethyl acetate in hexane as eluent to obtain (6-bromopyridin-3-yl) (cyclopropyl)methanone (6.46 g, 68.07 %) as yellow oil.

MS: 227.1 [M+1]

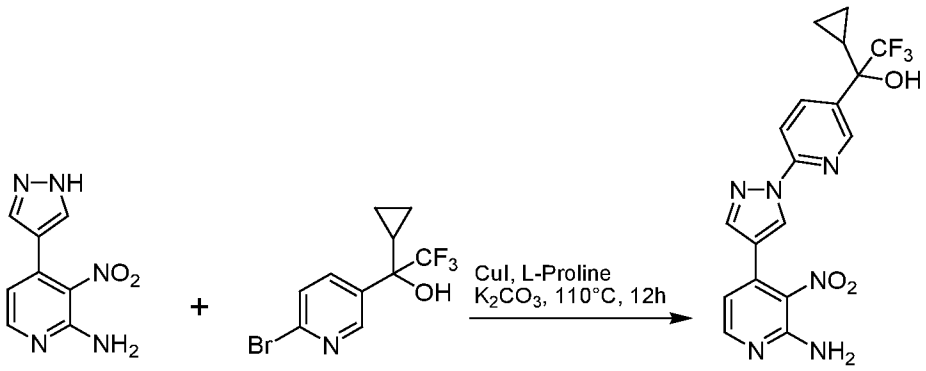
Step-3: Synthesis of 1-(6-bromopyridin-3-yl)-1-cyclopropyl-2,2,2-trifluoroethanol

58 59

To a stirred solution of (6-bromopyridin-3-yl) (cyclopropyl) methanone (2.0 g, 88.49mmol) in DME (25 mL) at 0°C was added $TMSCF_3$ (1.86 g, 132.74 mmol) under nitrogen, followed by portion wise addition of CsF (2.01 g, 132.74 mmol) and stirred for 1h at same temperature. Allow to warm to RT and Stirred for 6h. Progress of reaction was monitored by TLC. After reaction completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) on flash column chromatography using 15-20% ethyl acetate in hexane as eluent to obtain 1-(6-bromopyridin-3-yl)-1-cyclopropyl-2,2,2-trifluoroethanol (1.45 g, 55.76 %) as yellow oil.

MS: 297.4 [M+1]

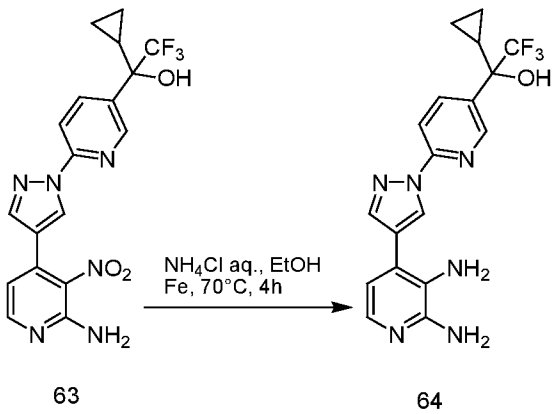
Step-4: Synthesis of 1-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-cyclopropyl-2,2,2-trifluoroethanol



To a stirred solution of 3-nitro-4-(1H-pyrazol-4-yl) pyridin-2-amine (0.15g, 0.73 mmol) and compound 1-(6-bromopyridin-3-yl)-1-cyclopropyl-2,2,2-trifluoroethanol (0.320g, 1.02 mmol) in DMSO (5 ml) was added K_2CO_3 (0.251g, 1.825 mmol) followed by CuI (0.013g, 0.073 mmol) and L-Proline (0.056g, 0.365 mmol). Reaction was heated at 110°C for 12h. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 40-60% acetone in n-hexane to obtained 1-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-cyclopropyl-2,2,2-trifluoroethanol (0.065 g, 21.10 %) as yellow solid.

MS: 421.37 [M+1]

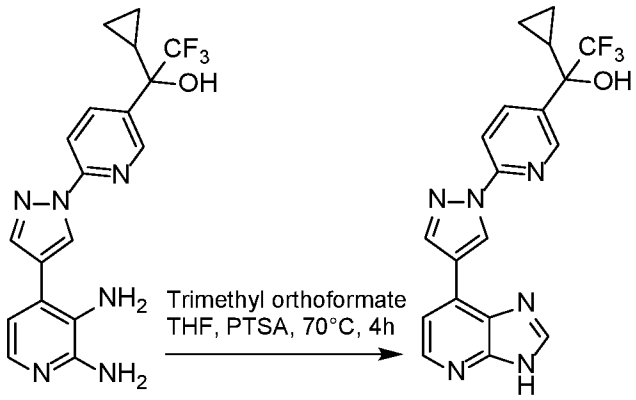
Step-5: Synthesis of 1-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-cyclopropyl-2,2,2-trifluoroethanol



To a stirred solution of 1-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl) pyridin-3-yl)-1-cyclopropyl-2,2,2-trifluoroethanol (0.065g, 1.54 mmol) in EtOH (3.0 mL), NH_4Cl (2.5 mL) was added at room temperature. To resultant reaction mixture, Fe powder (0.043 g, 7.8 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, reaction mixture was diluted with H_2O: EtOAc (50 mL, 5:5) and pass over celite to remove inorganic impurities from the reaction mixture. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to obtained 1-(6-(4-(2,3-diamino pyridin -4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-cyclopropyl-2,2,2-trifluoroethanol (0.035 g, 57.37 %) as dark brown solid mass.

MS: 391.2 [M+1]

Step-6: Synthesis of 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-cyclopropyl-2,2,2-trifluoroethanol

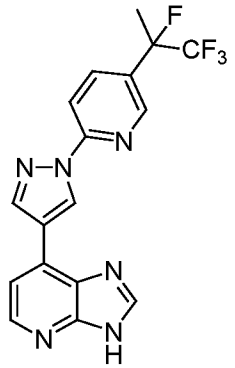


65 1126

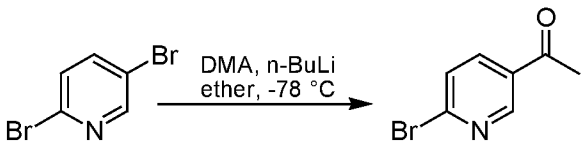
To a stirred solution of 1-(6-(4-(2,3-diamino pyridin -4-yl)-1H- pyrazol-1-yl) pyridin-3-yl)-1-cyclopropyl-2,2,2-trifluoroethanol (0.035g, 0.089 mmol) in THF (1.0 mL), Trimethyl orthoformate (1.5 mL) was added. To resultant reaction mixture, PTSA (0.003 g, 0.0017 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water and extracted with 10% MeOH in DCM. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 3% to 5% MeOH in DCM to obtained 7-(1-(5-(2,2,2-trifluoro-1-methoxy ethyl)pyridin-2-yl)-1H-pyrazol-4-yl) -3H-imidazo [4,5-b] pyridine (0.06 g, 17.19%) as off white solid.

MS: 400.9[M+1]

Synthesis of Compound No. 1128: 7-(1-(5-(1,1,1,2-tetrafluoropropan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine



Step-1: Synthesis of 1-(6-bromopyridin-3-yl)ethanone:

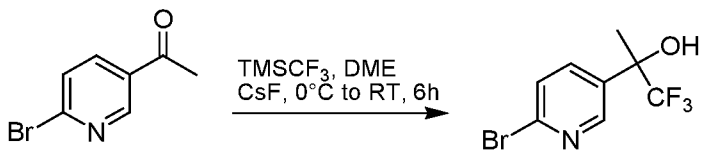


66 67

To a stirred solution of 2,5-dibromopyridine (12.0 g, 50.63mmol) in diethyl ether (250 mL) at -78°C was added n-Butyl lithium (2.5M in hexane) (24.30 mL, 65.81mmol) under nitrogen and stirred for 1h at same temperature. DMA (7.89 g, 60.75 mmol) was then added drop wise to the reaction mixture, stirred for 1h at -78°C. Progress of reaction was monitored by TLC. After reaction completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with diethyl ether. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 4% ethyl acetate in hexane as eluent to obtain 1-(6-bromopyridin-3-yl)ethanone (4.5 g, 44.03 %) as yellow oil.

MS: 201.1 [M+1]

Step-2: Synthesis of 2-(6-bromopyridin-3-yl)-1,1,1-trifluoropropan-2-ol

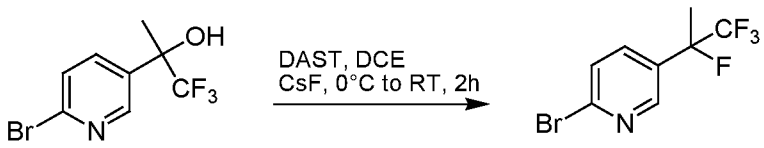


68 69

To a stirred solution of 1-(6-bromopyridin-3-yl)ethanone (2.0 g, 11.00mmol) in DME (50 mL) at 0°C was added $TMSCF_3$ (2.33 g, 14.30 mmol) under nitrogen, followed by portion wise addition of CsF (2.50 g, 16.50 mmol) and stirred for 1h at same temperature. Allow to warm to RT and Stirred for 6h. Progress of reaction was monitored by TLC. After reaction completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) on flash column chromatography using 15-20% ethyl acetate in hexane as eluent to obtain 2-(6-bromopyridin-3-yl)-1,1,1-trifluoropropan-2-ol (1.45 g, 53.50 %) as yellow oil.

MS: 271.0 [M+1]

Step-3: Synthesis of 2-bromo-5-(1,1,1,2-tetrafluoropropan-2-yl)pyridine

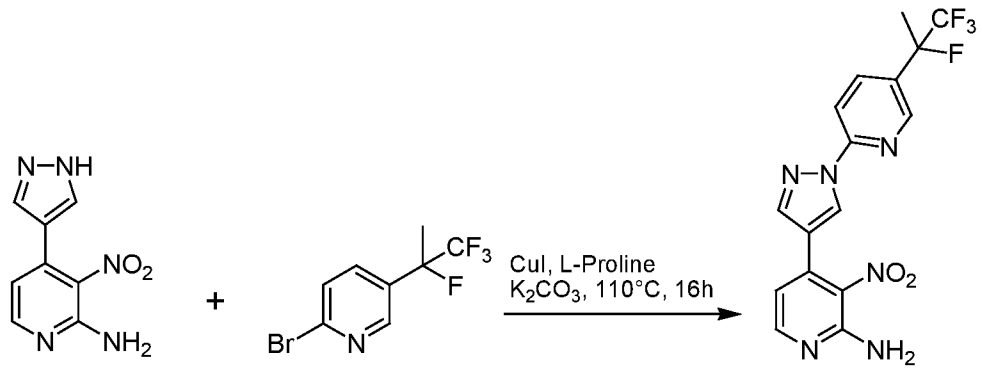


70 71

To a stirred solution of 2-(6-bromopyridin-3-yl)-1,1,1-trifluoropropan-2-ol (1.45 g, 53.70mmol) in DCE (35 mL) at 0°C was added DAST (1.12 g, 69.81 mmol) under nitrogen, followed by stirred for 15 min at same temperature. Allow to warm to RT and Stirred for 1h. Progress of reaction was monitored by TLC. After reaction completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) on flash column chromatography using 15-20% ethyl acetate in hexane as eluent to obtain 2-bromo-5-(1,1,1,2-tetrafluoropropan-2-yl)pyridine (1.1 g, 75.86 %) as yellow oil.

MS: 273.04 [M+1]

Step-4: Synthesis of 4-(1-(5-(1,1,1,2-tetrafluoropropan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine

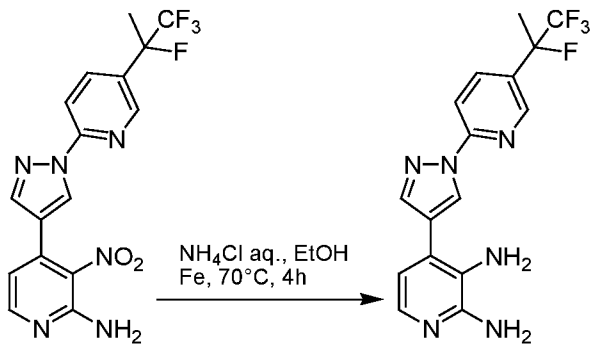


72 73 74

To a stirred solution of 3-nitro-4-(1H-pyrazol-4-yl) pyridin-2-amine (0.15g, 0.73 mmol) and compound 2-bromo-5-(1,1,1,2-tetrafluoropropan-2-yl)pyridine (0.298g, 1.09 mmol) in DMSO (5 ml) was added K_2CO_3 (0.251g, 1.825 mmol) followed by CuI (0.013g, 0.073 mmol) and L-Proline (0.056g, 0.365 mmol). Reaction was heated at 110°C for 16h. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography, eluent at 40-60% acetone in n-hexane to obtained 4-(1-(5-(1,1,1,2-tetrafluoropropan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine (0.065 g, 22.49 %) as yellow solid.

MS: 397.1 [M+1]

Step-5: Synthesis of 4-(1-(5-(1,1,1,2-tetrafluoropropan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)pyridine-2,3-diamine

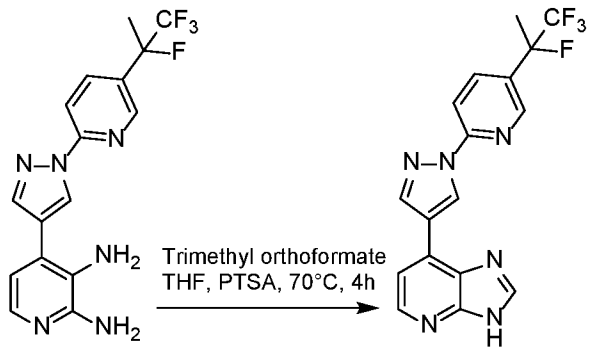


75 76

To a stirred solution of 4-(1-(5-(1,1,1,2-tetrafluoropropan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine (0.065g, 0.16 mmol) in EtOH (3.0 mL), NH_4Cl (2.5 mL) was added at room temperature. To resultant reaction mixture, Fe powder (0.041 g, 0.82 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, reaction mixture was diluted with H_2O: EtOAc (50 mL, 5:5) and pass over celite to remove inorganic impurities from the reaction mixture. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to obtained 4-(1-(5-(1,1,1,2-tetrafluoropropan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)pyridine-2,3-diamine (0.035 g, 58.32 %) as dark brown solid mass.

MS: 367.4 [M+1]

Step-6: Synthesis of 7-(1-(5-(1,1,1,2-tetrafluoropropan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

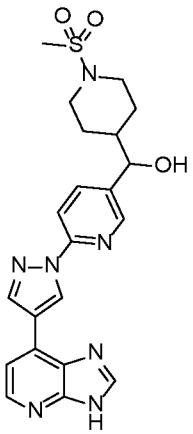


77 1128

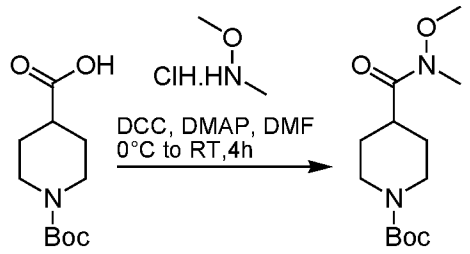
To a stirred solution of 4-(1-(5-(1,1,1,2-tetrafluoropropan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)pyridine-2,3-diamine (0.035g, 0.095 mmol) in THF (1.0 mL), Trimethyl orthoformate (1.5 mL) was added. To resultant reaction mixture, PTSA (0.003 g, 0.0017 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with 10% MeOH in DCM. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 3% to 5% MeOH in DCM to obtained 7-(1-(5-(1,1,1,2-tetrafluoropropan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine (0.06 g, 16.67%) as off white solid.

MS: 377.2 [M+1]

Synthesis of Compound No. 1164: (6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)(1-(methylsulfonyl)piperidin-4-yl)methanol



Step-1: Synthesis of N-methoxy-N-methyl cyclopropane carboxamide:

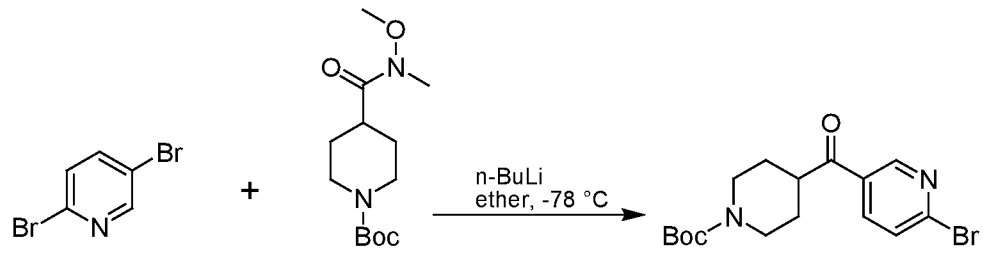


78 79

To a stirred solution of 1-(tert-butoxy carbonyl)piperidine-4-carboxylic acid (10.0 g, 43.66 mmol) and N-methoxy methanamine hydrochloride (5.56 g, 56.76 mmol) in DMF (35 mL), DCC (13.51g, 65.49 mmol) and DMAP (1.60g, 13.98 mmol) was added successively at 0°C and allow to stirred for 30 min. Resultant reaction mass was allow to warm to RT and stirred for 4h. Completion of reaction was monitored by TLC. On completion, quenched reaction mixture with 1N HCl water and extracted with EtOAc. The organic layer was washed with bicarbonate water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 20% acetone in n-hexane to obtained tert-butyl 4-(N-methoxy-N-methylcarbamoyl)piperidine-1-carboxylate (7.45g, 60%) as colourless oily mass.

MS: 273.1 [M+1]

Step-2: Synthesis of tert-butyl 4-(6-bromonicotinoyl)piperidine-1-carboxylate

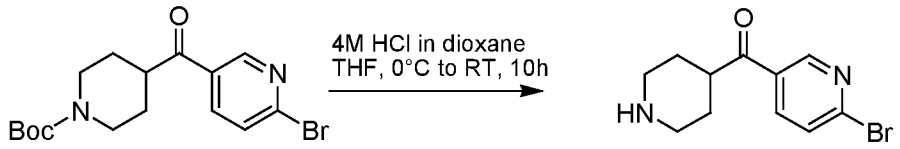


80 81 82

To a stirred solution of 2,5-dibromopyridine (5.0 g, 21.18 mmol) in diethyl ether (100 mL) at -78°C was added n-Butyl lithium (2.5M in hexane) (8.47 mL, 21.18 mmol) under nitrogen and stirred for 1h at same temperature. tert-butyl 4-(N-methoxy-N-methylcarbamoyl)piperidine-1-carboxylate (6.36 g, 23.29 mmol) was then added drop wise to the reaction mixture, stirred for 1h at -78°C. Progress of reaction was monitored by TLC. After reaction completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with 10% MeOH in DCM. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure to obtained tert-butyl 4-(6-bromonicotinoyl)piperidine-1-carboxylate (5.8 g, 67.12%) as colourless oily mass.

MS: 371.0 [M+1]

Step-3: Synthesis of (6-bromopyridin-3-yl)(piperidin-4-yl)methanone:



83 84

To a stirred solution of tert-butyl 4-(6-bromonicotinoyl)piperidine-1-carboxylate (5.0 g, 13.51 mmol) in THF (50 mL), 4M HCl in Dioxane (25 mL) was added at 0°C under nitrogen. Allow to warm reaction mixture to RT and stirred for 10h. On completion, reaction mixture quenched with bicarbonate solution and extracted with 10% MeOH in DCM. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 4-5% MeOH in DCM as eluent to obtain (6-bromopyridin-3-yl)(piperidin-4-yl)methanone (3.45g, 94.52%) as colourless crystalline solid.

MS: 271.0 [M+1]

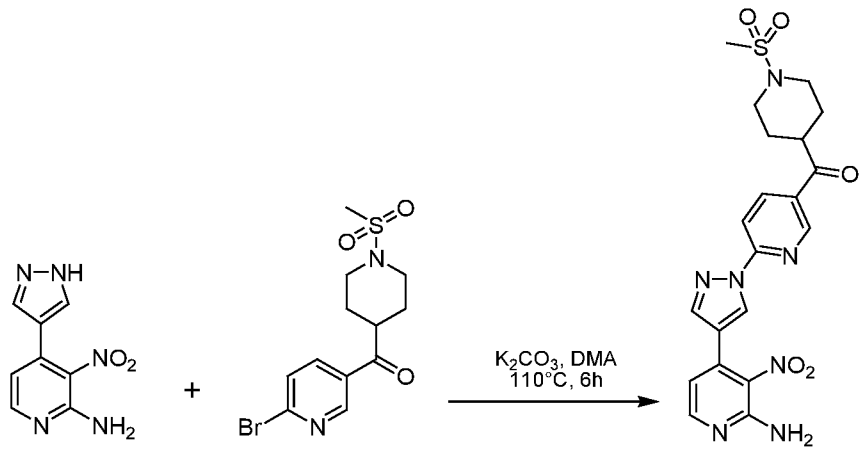
Step-4: Synthesis of (6-bromopyridin-3-yl)(1-(methylsulfonyl)piperidin-4-yl)methanone

85 86

To a stirred solution of (6-bromopyridin-3-yl)(piperidin-4-yl)methanone (2.0 g, 7.44mmol) in dry DCM (20 mL) at 0°C was added MsCl (1.11 g, 9.66 mmol) under nitrogen. To resultant reaction mixture TEA (1.12 g, 11.16 mmol) was added drop wise to the reaction mixture, stirred for 1h at 0°C. Allow to warm to RT and Stirred for 1h. Progress of reaction was monitored by TLC. After reaction completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) on flash column chromatography using 2-3% ethyl MeOH in DCM as eluent to obtain (6-bromopyridin-3-yl)(1-(methylsulfonyl)piperidin-4-yl)methanone (1.40 g, 56.00 %) as off white solid.

MS: 349.01 [M+1]

Step-5: Synthesis of (6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)(1-(methylsulfonyl)piperidin-4-yl)methanone



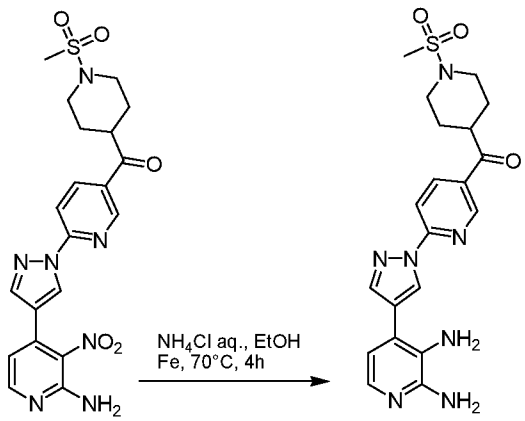
87 88 89

To a stirred solution of 3-nitro-4-(1H-pyrazol-4-yl) pyridin-2-amine (0.15g, 0.73 mmol) and compound (6-bromopyridin-3-yl)(1-(methylsulfonyl)piperidin-4-yl)methanone (0.254g,

mmol) in DMA (5 ml) was added K_2CO_3 (0.251g, 1.825 mmol). Reaction was heated at 110°C for 6h. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with EtOAc. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) on flash column chromatography using 4-5% MeOH in DCM as eluent to obtained (6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)(1-(methylsulfonyl)piperidin-4-yl)methanone (0.065 g, 18.84 %) as yellow solid.

MS: 472.02 [M+1]

Step-6: Synthesis of 1-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-cyclopropyl-2,2,2-trifluoroethanol

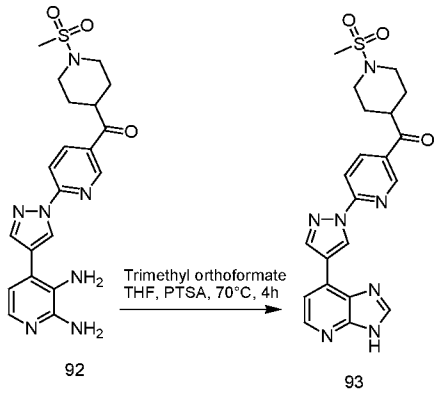


90 91

To a stirred solution of 1-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-cyclopropyl-2,2,2-trifluoroethanol (0.065g, 1.37 mmol) in EtOH (3.0 mL), NH_4Cl (2.5 mL) was added at room temperature. To resultant reaction mixture, Fe powder (0.037 g, 6.8 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, reaction mixture was diluted with H_2O: EtOAc (50 mL, 5:5) and pass over celite to remove inorganic impurities from the reaction mixture. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to obtained 1-(6-(4-(2,3-diamino pyridin -4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-cyclopropyl-2,2,2-trifluoroethanol (0.035 g, 57.37 %) as dark brown solid mass.

MS: 442.0 [M+1]

Step-7: Synthesis of (6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)(1-(methylsulfonyl)piperidin-4-yl)methanone

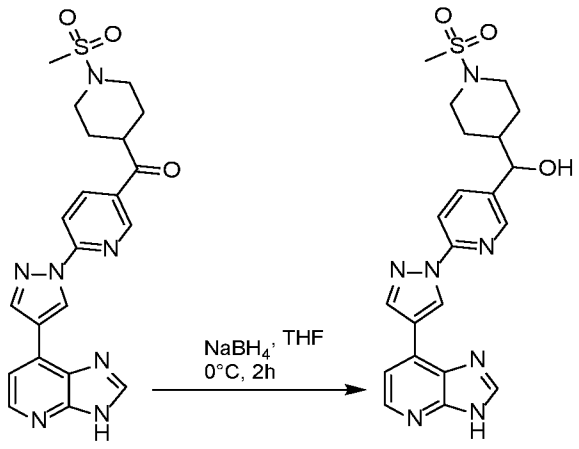


92 93

To a stirred solution of 1-(6-(4-(2,3-diamino pyridin -4-yl)-1H- pyrazol-1-yl)pyridin-3-yl)-1-cyclopropyl-2,2,2-trifluoroethanol (0.035g, 7.93 mmol) in THF (1.0 mL), trimethyl orthoformate (1.5 mL) was added. To resultant reaction mixture, PTSA (0.003 g, 0.0017 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with 10% MeOH in DCM. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) on flash column chromatography using 5-6% MeOH in DCM as eluent to obtained (6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)(1-(methylsulfonyl)piperidin-4-yl)methanone (0.006 g, 17.41%) as off white solid.

MS: 452.0 [M+1]

Step-8: Synthesis of 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-cyclopropyl-2,2,2-trifluoroethanol

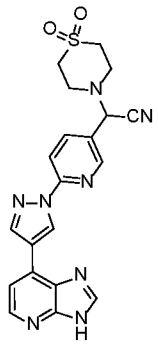


94 1164

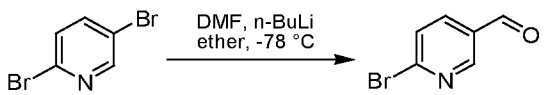
To a stirred solution of (6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)(1-(methylsulfonyl)piperidin-4-yl)methanone (0.006g, 0.013 mmol) in THF (1.0 mL), $NaBH_4$ (0.001 g, 0.026 mmol) was added and stirred for 2h at 0°C. Completion of reaction was monitored by TLC. On completion, quenched with water, extracted with 10% MeOH in DCM. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to obtained (6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)(1-(methylsulfonyl)piperidin-4-yl)methanol (0.03 g, 50.00%) as off white solid.

MS: 454.0 [M+1]

Synthesis of Compound No. 1166: 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-(1,1-dioxidothiomorpholino)acetonitrile



Step-1: Synthesis of 6-bromopyridine-3-carbaldehyde:

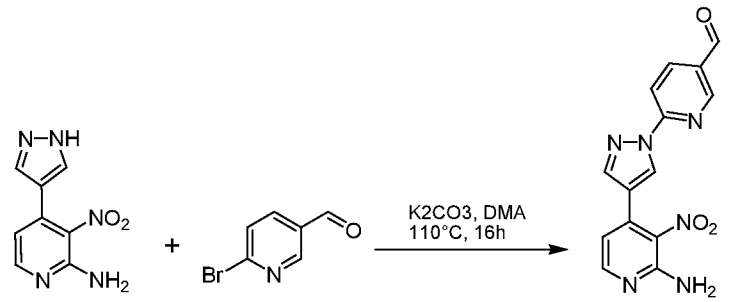


95 96

To a stirred solution of 2,5-dibromopyridine (26.0 g, 109.75 mmol) in diethyl ether (500 mL) at -78°C was added n-Butyl lithium (2.5M in hexane) (66 mL, 164.63 mmol) under nitrogen and stirred for 1h at same temperature. DMF (13 mL, 164.63 mmol) was then added drop wise to the reaction mixture, stirred for 1h at -78°C. Progress of reaction was monitored by TLC. After reaction completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with diethyl ether. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 4% ethyl acetate in hexane as eluent to obtain 6-bromopyridine-3-carbaldehyde (12.20 g, 59.8 %) as yellow oil.

MS: 187.0 [M+1]

Step-2: Synthesis of 6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl) pyridine-3-carbaldehyde

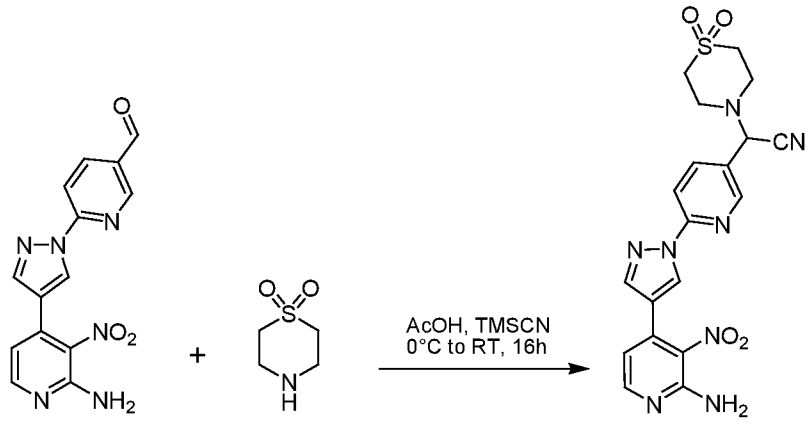


97 98 99

To a stirred solution of 3-nitro-4-(1H-pyrazol-4-yl) pyridin-2-amine (0.075g, 0.36 mmol) and compound 6-bromopyridine-3-carbaldehyde (0.075g, 0.40 mmol) in DMA (5 ml) was added K_2CO_3 (0.124g, 0.90 mmol) and reaction heated at 110°C for 16h. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 1% to 3% MeOH/DCM to obtained 6-(4-(2-amino-3- nitropyridin-4-yl) -1H-pyrazol-1-yl) pyridine-3-carbaldehyde (0.065 g, 51.58%) as yellow solid.

MS: 311[M+1]

Step-3: 2-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-(1,1-dioxidothiomorpholino)acetonitrile

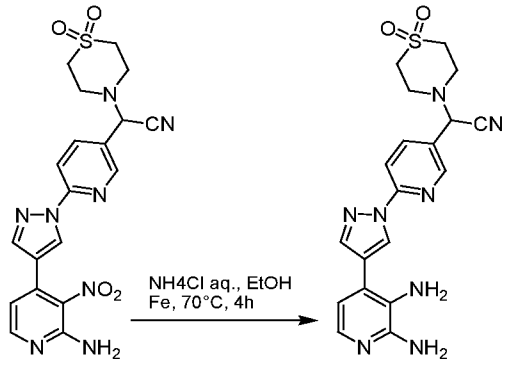


100 101 102

To a stirred solution of 6-(4-(2-amino-3- nitropyridin-4-yl) -1H-pyrazol-1-yl) pyridine-3-carbaldehyde (0.065g, 0.20 mmol) in AcOH (5mL) , Trimethyl silylcynide (TMSCN) (0.031g, 0.31 mmol) and TMSCN (0.051g, 0.38 mmol) in AcOH (1 mL) was added at 0°C and allow to warm to RT. Stirred for 16h. Reaction was monitored by TLC. On completion reaction mixture was quenched with bi-carbonate water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 2-3% MeOH in DCM as eluent to obtain obtained 2-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-(1,1-dioxidothiomorpholino)acetonitrile (0.045 g, 47.36%) as yellow solid.

MS: 454 [M+1]

Step-4: 2-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-(1,1-dioxidothiomorpholino)acetonitrile

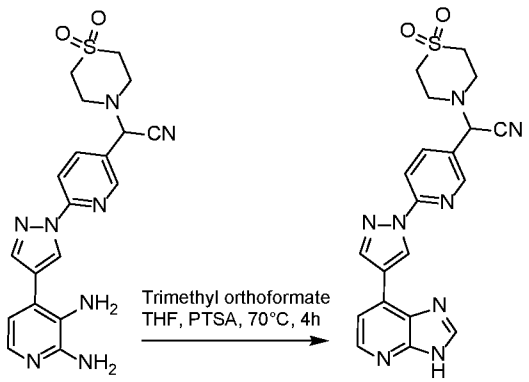


103 104

To a stirred solution of 2-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-(1,1-dioxidothiomorpholino)acetonitrile (0.045g, 0.09 mmol) in EtOH (10 mL), NH_4Cl (2.5 mL) was added at room temperature. To resultant reaction mixture, Fe powder (0.027 g, 0.49 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, reaction mixture was diluted with H_2O: EtOAc 5:5 (50 mL) and pass over celite to remove inorganic impurities from the reaction mixture. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to obtained pure 2-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-(1,1-dioxidothiomorpholino)acetonitrile (0.016g, 37.20%) as dark brown solid mass.

MS: 425.1 [M+1]

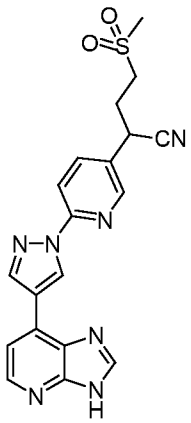
Step-5: 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-(1,1-dioxidothiomorpholino)acetonitrile



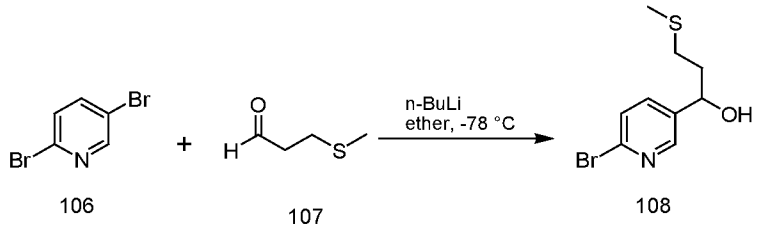
105 1166

To a stirred solution of 2-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-(1,1-dioxidothiomorpholino)acetonitrile (0.016g, 0.037 mmol) in THF (3.0 mL), Trimethyl orthoformate (1.5 mL) was added. To resultant reaction mixture, PTSA (0.003 g, 0.07 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with 10% MeOH in DCM. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 4-6% MeOH in DCM as eluent to obtained 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-(1,1-dioxidothiomorpholino)acetonitrile (0.03 g, 58.82%) as off white solid. MS: 435.2 [M+1]

Synthesis of Compound No. 1116: 2-(6-(4-(3H-imidazo [4,5-b]pyridin-7-yl) -1H-pyrazol-1-yl) pyridin-3-yl) -4-(methyl sulfonyl) butanenitrile



Step-1: Synthesis of 1-(6-bromopyridin-3-yl)-3-(methylthio)propan-1-ol:

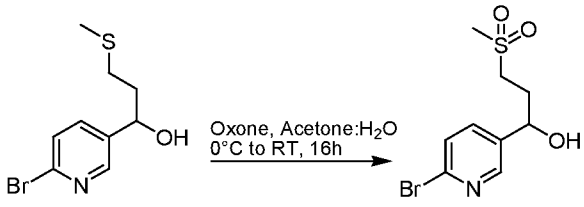


106 107 108

To a stirred solution of 2,5-dibromopyridine (1.5 g, 6.32 mmol) in diethyl ether (25 mL) at -78°C was added n-Butyl lithium (2.5M in hexane) (2.5 mL, 6.32 mmol) under nitrogen and stirred for 1h at same temperature. 3-(methylthio)propanal (0.73 g, 6.965 mmol) was then added drop wise to the reaction mixture, stirred for 1h at -78°C. Progress of reaction was monitored by TLC. After reaction completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with diethyl ether. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 4% ethyl acetate in hexane as eluent to obtain 1-(6-bromopyridin-3-yl)-3-(methylthio)propan-1-ol (0.580 g, 35.15 %) as colourless oil.

MS: 264.0 [M+1]

Step-2: Synthesis of 1-(6-bromopyridin-3-yl)-3-(methylsulfonyl)propan-1-ol:

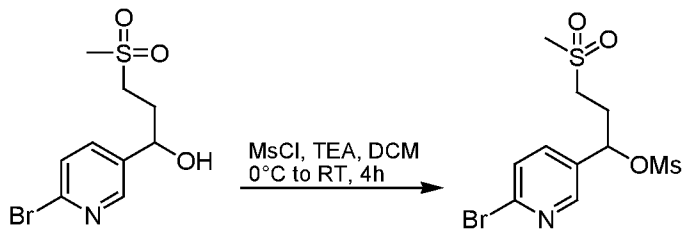


109 110

To a stirred solution of 1-(6-bromopyridin-3-yl)-3-(methylthio)propan-1-ol (0.58 g, 2.19 mmol) in Acetone:H_2O (50 mL, 7:3) at 0°C was added oxone (1.68 g, 5.49 mmol) under nitrogen and stirred for 16h at same temperature. Progress of reaction was monitored by TLC. After reaction completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 3% MeOH in DCM as eluent to obtain 1-(6-bromopyridin-3-yl)-3-(methylsulfonyl)propan-1-ol (0.60 g, 93.02 %) as colourless oil.

MS: 296.0 [M+1]

Step-3: Synthesis of 1-(6-bromopyridin-3-yl)-3-(methylsulfonyl)propyl methanesulfonate:

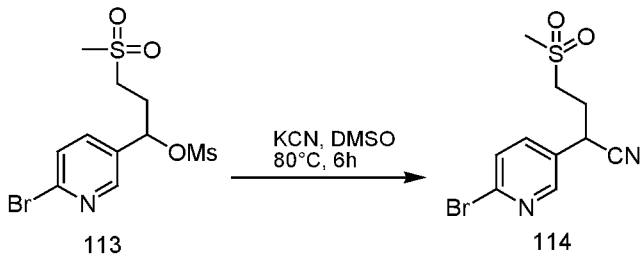


111 112

To a stirred solution of 2,5-dibromopyridine (0.30 g, 1.02 mmol) in DCM (5.0 mL) at 0°C was added MsCl (0.151 g, 1.32 mmol) under nitrogen. To resultant reaction mixture TEA (0.153 g, 1.52 mmol) solution in DCM (1.0 mL) was added drop wise, stirred for 15 min at 0°C. Allow reaction mixture to increase temperature slowly to RT and progress of reaction was monitored by TLC. On completion, quenched with water, extracted with ethyl acetate. The aqueous layer was basified with bicarbonate till basic to pH-paper, and then extracted with ethyl acetate, dried over sodium sulphate, concentrated under reduced pressure obtained 1-(6-bromopyridin-3-yl)-3-(methylsulfonyl)propyl methanesulfonate (0.320g, 84.43%) as crude yellow oily mass.

MS: 374.02 [M+1]

Step-4: Synthesis of 2-(6-bromopyridin-3-yl)-4-(methylsulfonyl)butanenitrile:

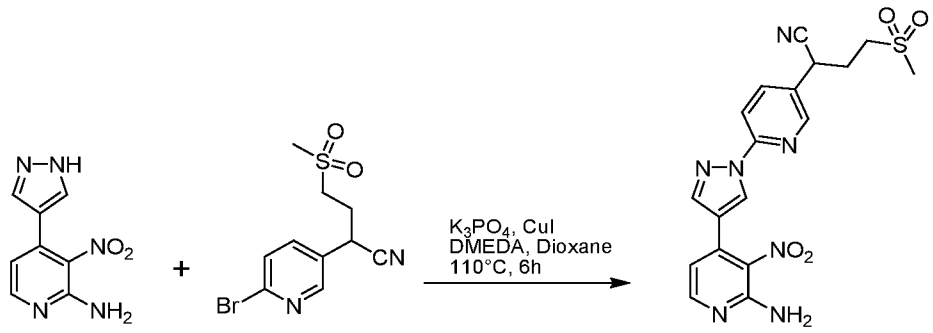


113 114

To a stirred solution of 2,5-dibromopyridine (0.320 g, 8.56 mmol) in DMSO (1.5 mL) at RT was added potassium cyanide (0.067 g, 10.27 mmol) under nitrogen and stirred for 1h at 80°C. Progress of reaction was monitored by TLC. After completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 2-3% MeOH in DCM as eluent to obtain 2-(6-bromopyridin-3-yl)-4-(methylsulfonyl)butanenitrile (0.120 g, 46.15 %) as dark brown sticky mass.

MS: 305.01 [M+1]

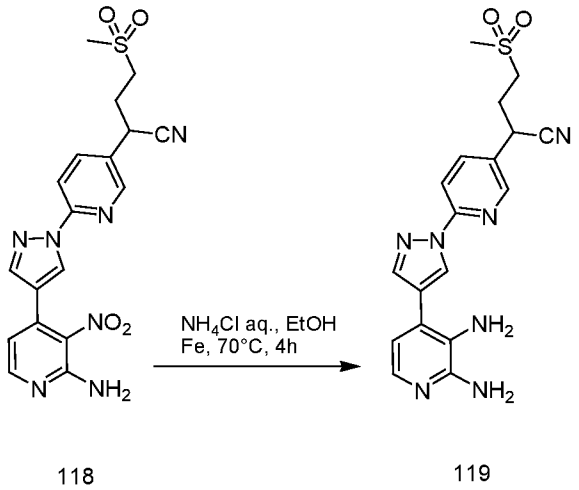
Step-5: Synthesis of 2-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4-(methylsulfonyl)butanenitrile



To a stirred solution of 3-nitro-4-(1H-pyrazol-4-yl) pyridin-2-amine (0.07g, 0.34 mmol) and compound 2-(6-bromopyridin-3-yl)-4-(methylsulfonyl)butanenitrile (0.155g, 0.51 mmol) in Dioxane (5 ml) was added K_3PO_4 (0.166g, 0.78 mmol) followed by CuI (0.006g, 0.034 mmol) and DMEDA (0.015g, 0.175 mmol). Reaction was heated at 110°C for 6h. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 2-3% MeOH in DCM to obtained 2-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4-(methylsulfonyl)butanenitrile (0.030 g, 20.54 %) as yellow solid.

MS: 428.1 [M+1]

Step-6: Synthesis of 2-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4-(methylsulfonyl)butanenitrile

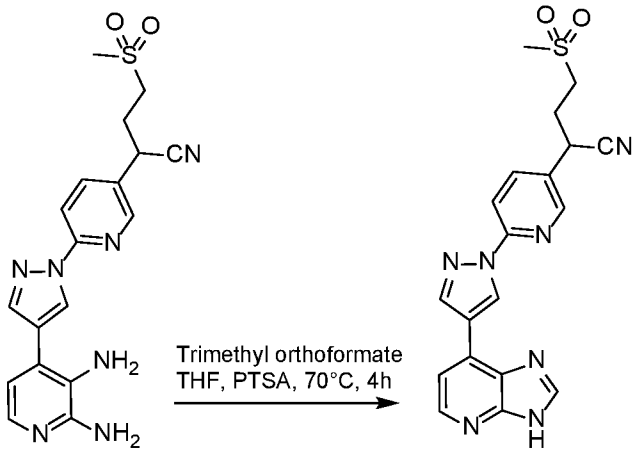


To a stirred solution of 2-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4-(methylsulfonyl)butanenitrile (0.030g, 0.070 mmol) in EtOH (3.0 mL), NH_4Cl (1.5 mL) was

added at room temperature. To resultant reaction mixture, Fe powder (0.019 g, 0.35 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, reaction mixture was diluted with H_2O: EtOAc (50 mL, 5:5) and pass over celite to remove inorganic impurities from the reaction mixture. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to obtained pure 4-(1-(5-(2,2,2- trifluoro-1- methoxy ethyl) pyridin-2-yl)-1H-pyrazol-4-yl) pyridine -2,3-diamine (0.015g, 53.57%) as dark brown solid mass.

MS: 398.2 [M+1]

Step-7: Synthesis of 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4-(methylsulfonyl)butanenitrile

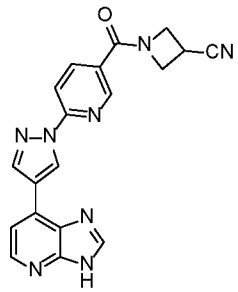


120 1116

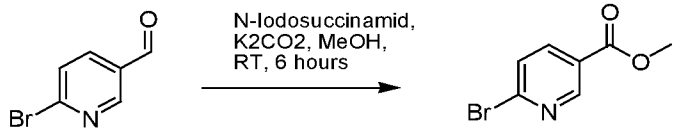
To a stirred solution of 4-(1-(5-(2,2,2-trifluoro-1- methoxy ethyl) pyridin-2-yl)-1H-pyrazol-4-yl) pyridine -2,3-diamine (0.015g, 0.037 mmol) in THF (1.0 mL), Trimethyl orthoformate (1.5 mL) was added. To resultant reaction mixture, PTSA (0.0012 g, 0.018 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with 10% MeOH in DCM. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 3% to 5% MeOH in DCM to obtained 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4-(methylsulfonyl)butanenitrile (0.004 g, 25.92%) as off white solid.

MS: 408.0 [M+1]

Synthesis of Compound No. 1089: 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)nicotinoyl)azetidine-3-carbonitrile



Step-1: Synthesis of Methyl 6-bromopyridine-3-carboxylate

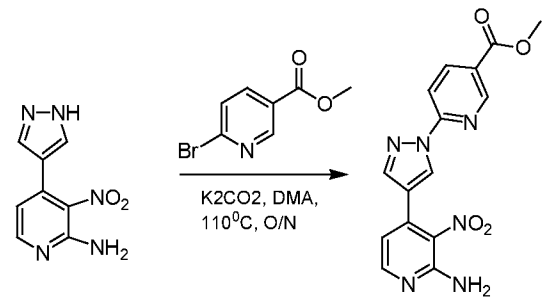


121 122

To a stirred solution of 6-bromopyridine-3-carbaldehyde (1.5 g, 0.810 mmol) in methanol (45 mL) at RT was added N-Iodosuccinimide (2.72 g, 1.210 mmol) and base potassium carbonate (1.66g, 1.210mmol) under dark and stirred for 6h at same temperature. Progress of reaction was monitored by TLC. After reaction completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with ethyl acetate. The organic layer was washed with saturated sodium thiosulfate solution, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 8-12% ethyl acetate in hexane as eluent to obtain Methyl 6-bromopyridine-3-carboxylate (1.05 g, 59.8 %) as white solid.

MS: 215.0 [M+1]

Step-2: Synthesis of methyl 6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridine-3-carboxylate

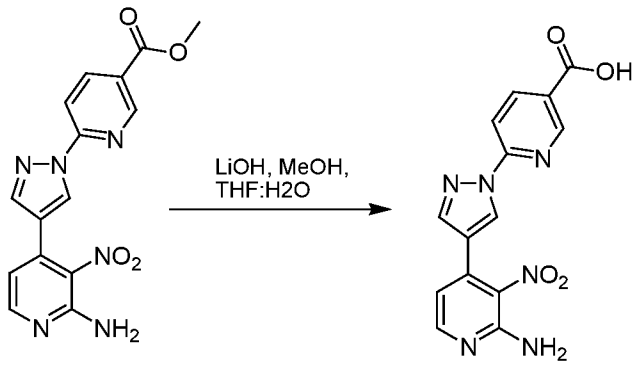


123 124

To a stirred solution of 3-nitro-4-(1H-pyrazol-4-yl) pyridin-2-amine (0.300g, 0.138 mmol) and compound Methyl 6-bromopyridine-3-carboxylate (0.44g, 0.207 mmol) in DMA (7 ml) was added K_2CO_3 (0.381g, 0.276 mmol) at RT. Reaction was heated at 110°C for 16h. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 40-60% acetone in n-hexane to obtained methyl 6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridine-3-carboxylate (0.210 g, 42.85 %) as yellow solid.

MS: 341.09 [M+1]

Step-3: 6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridine-3-carboxylic acid

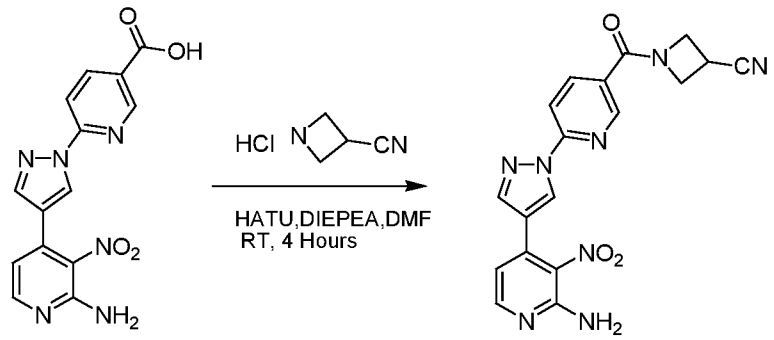


125 126

To a stirred solution of methyl 6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridine-3-carboxylate (0.2 g, 0.058 mmol) in mixture of THF: MeOH: H_2O (18 mL, 5:3:1) was added LiOH (0.044g, 0.117 mmol). And allowed to stir for 2h at room temperature. On completion, all volatiles were evaporated under reduced pressure. Reaction mass diluted with water, acidify with 6N HCl adjusted pH at 6 and extracted with EtOAc. Organic portions were combined, dried over Na_2SO_4, evaporated under reduced pressure to obtain 6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridine-3-carboxylic acid (0.170g, 89%) as yellow solid.

MS: 327[M+1]

Step-4: 1-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)nicotinoyl)azetidine-3-carbonitrile

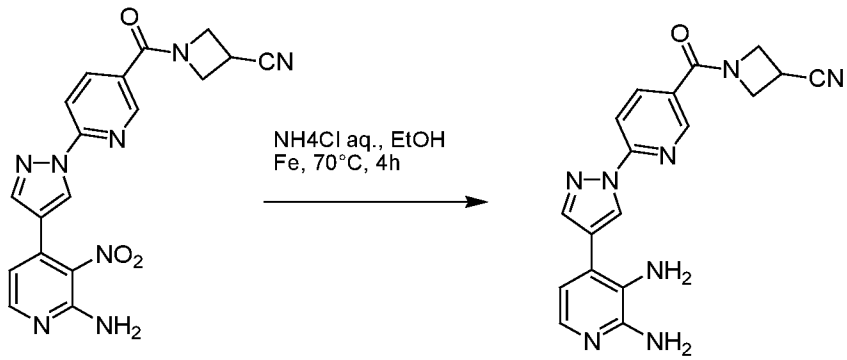


127 128

To a stirred solution of 6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridine-3-carboxylic acid (0.080g, 0.0271mmol) and Azetidine-3-carbonitrile hydrochloride (0.039g, 0.049mmol) in DMF (3 mL) were added HATU (0.139g, 0.036mmol, and DIPEA (0.063g, 0.049 mmol). Then reaction mixture was stirred at room temperature for 6h. Reaction was monitored by TLC. On completion, reaction was quenched with water, extracted with ethyl acetate. Organic layer was washed with water, brine, dried over sodium sulphate and evaporated under reduced pressure to give crude product. Purification of the crude was done by silica gel (100-200 Mesh) column chromatography; eluent 4% MeOH in DCM to obtain 1-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)nicotinoyl)azetidine-3-carbonitrile (0.055g, 58%) as light yellow solid.

MS: 391.09[M+1]

Step-5: 1-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)nicotinoyl)azetidine-3-carbonitrile

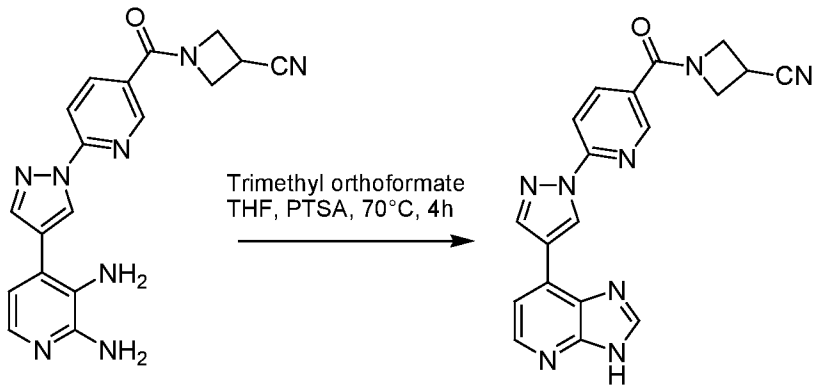


129 130

To a stirred solution of 1-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)nicotinoyl)azetidine-3-carbonitrile (0.050g, 0.012 mmol) in EtOH (3.0 mL), NH_4Cl (2.5 mL) was added at room temperature. To resultant reaction mixture, Fe powder (0.033 g, 0.064 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, reaction mixture was diluted with H_2O: EtOAc (50 mL, 5:5) and pass over celite to remove inorganic impurities from the reaction mixture. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to obtained 1-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)nicotinoyl)azetidine-3-carbonitrile (0.035 g, 76 %) as dark brown solid mass.

MS: 361.2 [M+1]

Step-6: 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)nicotinoyl)azetidine-3-carbonitrile

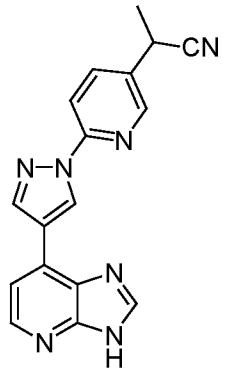


131 1089

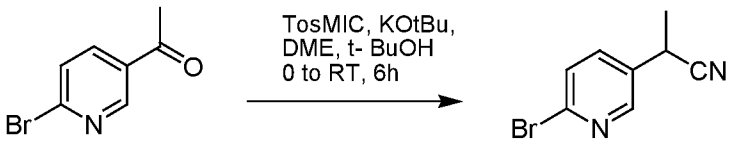
To a stirred solution of 1-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)nicotinoyl)azetidine-3-carbonitrile (0.035g, 0.097 mmol) in THF (1.0 mL), trimethyl orthoformate (1.5 mL) was added. To resultant reaction mixture, PTSA (0.003 g, 0.0017 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with 10% MeOH in DCM. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 5% to 6% MeOH in DCM to obtained 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)nicotinoyl)azetidine-3-carbonitrile (0.018 g, 51.42%) as off white solid.

MS: 371.1[M+1]

Synthesis of Compound No. 1107: 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)propanenitrile



Step-1: Synthesis of 2-(6-bromopyridin-3-yl)propanenitrile:



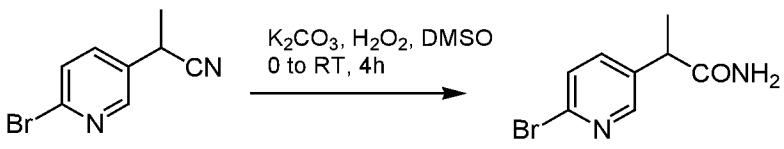
132 133

To a stirred solution of 1-(6-bromopyridin-3-yl)ethanone (0.4 g, 0.20 mmol) in DME (12 mL) at 0°C under inert condition was added TosMIC (0.585g 0.30 mmol). A solution of base potassium ter-butoxide (0.336g, 0.30 mmol) in tert-butanol was then added drop wise to the reaction mixture. After addition mixture was stirred for 6h at room temprature. Progress of reaction was monitored by TLC. After completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with ethyl acetate. The organic layer

was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 15% ethyl acetate in hexane as eluent to obtain 2-(6-bromopyridin-3-yl)propanenitrile (0.240 g, 57.14 %) as colourless oil.

MS: 211 [M+1]

Step-2: Synthesis of 2-(6-bromopyridin-3-yl)propanamide

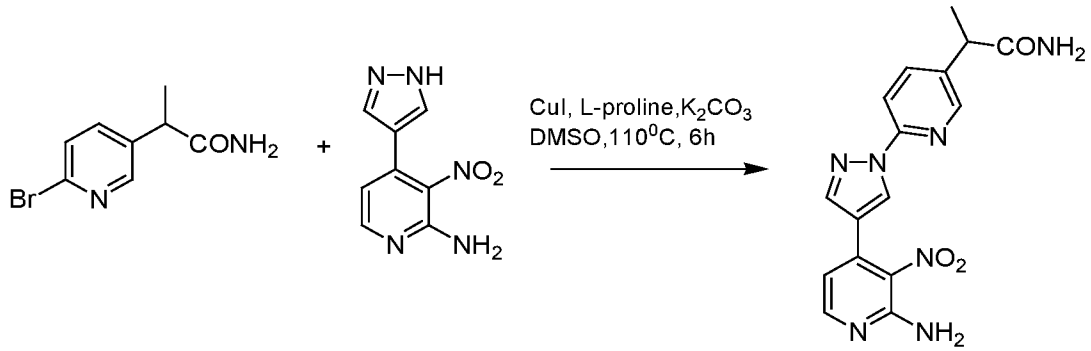


134 135

To a stirred solution of 2-(6-bromopyridin-3-yl)propanenitrile (0.240g, 0.114 mmol) and DMSO (4 ml) at 0^0C under N_2 added base potassium carbonate (0.315g, 0.228 mmol). Added hydrogen peroxide (0.7 ml) dropwise at 0^0C and the resultant mixture was stirred at RT for 4h. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give pure product 2-(6-bromopyridin-3-yl)propanamide (0.230 g, 88.46%) as off white solid.

MS: 228 [M+1]

Step-3: Synthesis of 2-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)propanamide:

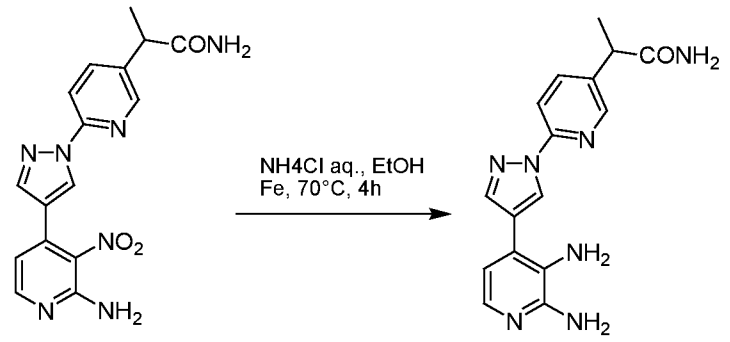


136 137 138

To a stirred solution of 3-nitro-4-(1H-pyrazol-4-yl) pyridin-2-amine (0.160g, 0.078 mmol) and compound 2-(6-bromopyridin-3-yl)propanamide (0.200g, 0.078 mmol) in DMSO (5 ml) was added K_2CO_3 (0.215g, 0.156 mmol) followed by CuI (0.029g, 0.00156 mmol) and L-proline (0.017g, 0.00156 mmol). Reaction was heated at 110°C for 6h. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 6-7% MeOH in DCM to obtained 2-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)propanamide (0.140 g, 45.45 %) as yellow solid.

MS: 354.1 [M+1]

Step-4: Synthesis of 2-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)propanamide

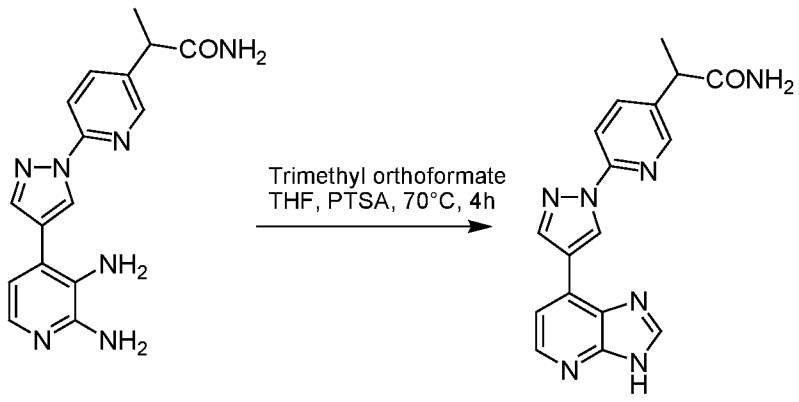


139 140

To a stirred solution of 2-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)propanamide (0.140g, 0.039 mmol) in EtOH (7.0 mL), NH_4Cl (2.0 mL) was added at room temperature. To the resultant reaction mixture, Fe powder (0.105 g, 0.198 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, reaction mixture was diluted with H_2O: EtOAc (50 mL, 5:5) and pass over celite to remove inorganic impurities from the reaction mixture. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to obtained pure 2-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)propanamide (0.090g, 70%) as dark brown solid mass.

MS: 324.2 [M+1]

Step-5: Synthesis of 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)propanamide:

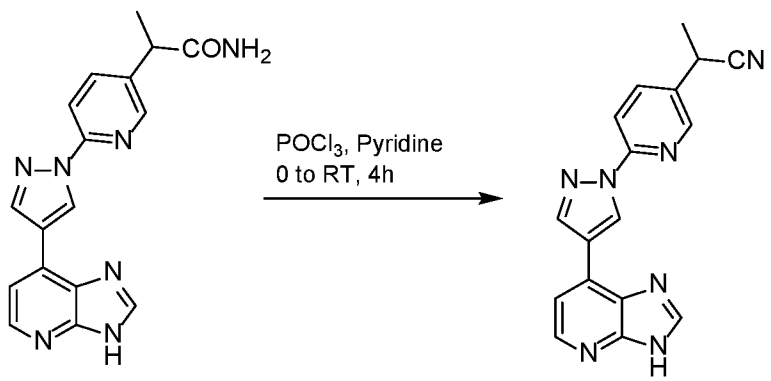


141 142

To a stirred solution of 2-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)propanamide (0.090g, 0.0278 mmol) in THF (1.0 mL), Trimethyl orthoformate (1.5 mL) was added. To resultant reaction mixture, PTSA (0.0095 g, 0.0055 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with 10% MeOH in DCM. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 8 to 9% MeOH in DCM to obtained 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)propanamide (0.048 g, 52.17%) as off white solid.

MS: 334.1 [M+1]

Step-6: Synthesis of 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)propanenitrile :

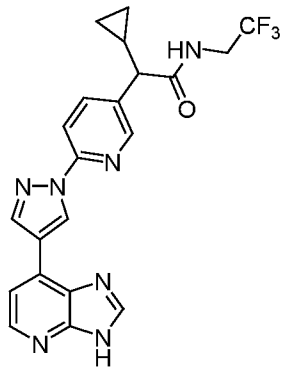


143 1107

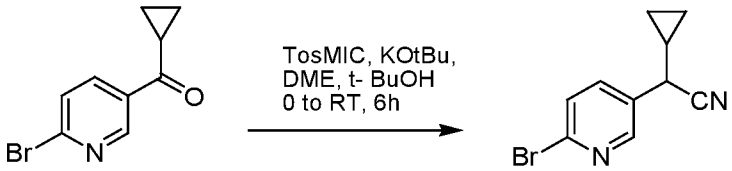
To a stirred solution of 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)propanamide (0.040g, 0.0120 mmol) in pyridine (3.0 mL), added $POCl_3$ (0.091g, 0.60mmol) dropwise at 0^0C. After addition stirred for 4h at room temprature. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with 10% MeOH in DCM. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 4 to 6% MeOH in DCM to obtained 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)propanenitrile (0.021 g, 56.7%) as off white solid.

MS: 316.1 [M+1]

Synthesis of Compound No. 1167: 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-cyclopropyl-N-(2,2,2-trifluoroethyl)acetamide



Step-1: Synthesis of 2-(6-bromopyridin-3-yl)-2-cyclopropylacetonitrile:

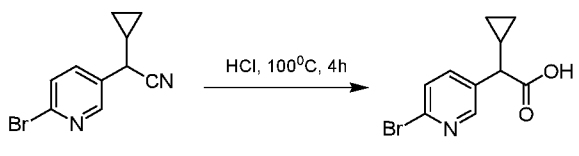


144 145

To a stirred solution of (6-bromopyridin-3-yl)(cyclopropyl)methanone (1.0 g, 0.442 mmol) in DME (12 mL) at 0°C under inert condition was added TosMIC (1.29g 0.663 mmol). A solution of base potassium ter-butoxide (0.991g, 0.884 mmol) in tert-butanol (1.0 ml) was then added drop wise to the reaction mixture. After addition mixture was stirred for 6h at room temprature. Progress of reaction was monitored by TLC. After completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 15% ethyl acetate in hexane as eluent to obtain 2-(6-bromopyridin-3-yl)-2-cyclopropylacetonitrile (0.6 g, 56.60 %) as colourless oil.

MS: 239 [M+2]

Step-2: Synthesis of 2-(6-bromopyridin-3-yl)-2-cyclopropylacetic acid:

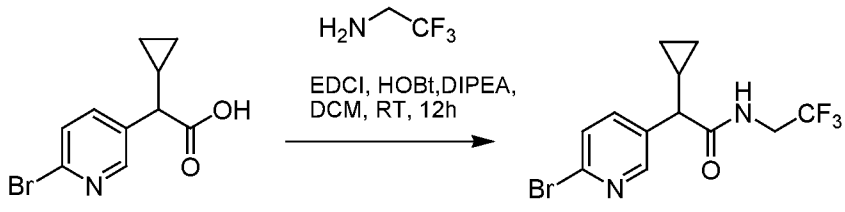


146 147

To a stirred solution of 2-(6-bromopyridin-3-yl)-2-cyclopropylacetonitrile (0.500g, 0.210 mmol) was added 4M HCl (5.0 mL) at room temprature. The resultant reaction mixture was stirred for 4h at 100^0C. Completion of reaction was monitored by TLC. On completion, quenched with water, extracted with ethyl acetate. The combined organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give pure desired product 2-(6-bromopyridin-3-yl)-2-cyclopropylacetic acid (0.320 g, 59.25%) as sticky oil.

MS: 258 [M+2]

Step-3: Synthesis of 2-(6-bromopyridin-3-yl)-2-cyclopropyl-N-(2,2,2-trifluoroethyl)acetamide:

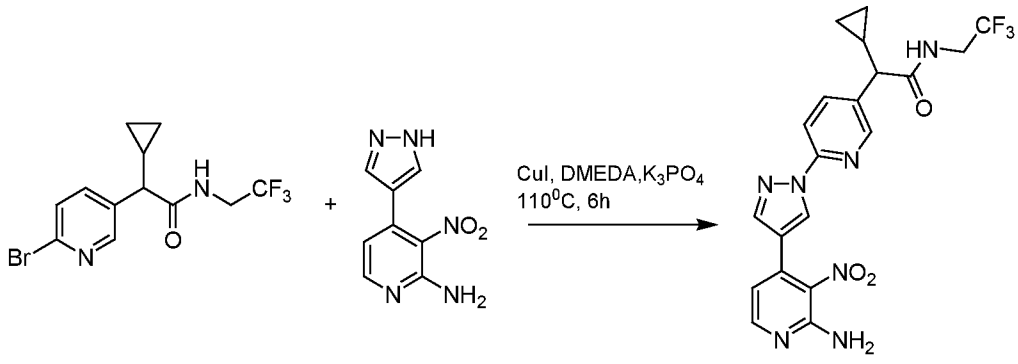


148 149

To a stirred solution of 2-(6-bromopyridin-3-yl)-2-cyclopropylacetic acid (0.32g, 0.125mmol) and Azetidine-3-carbonitrile hydrochloride (0.185g, 0.187mmol) in DMF (3 mL) were added EDCI (0.357g, 0.187mmol), HOBT (0.252g, 0.187mmol) and DIPEA (0.322g, 0.250 mmol). Then reaction mixture was stirred at room temperature for 12h. Reaction was monitored by TLC. On completion, reaction was quenched with water, extracted with ethyl acetate. Organic layer was washed with water, brine, dried over sodium sulphate and evaporated under reduced pressure to give crude product. Purification of the crude was done by silica gel (100-200 Mesh) column chromatography; eluent 30% ethyl acetate in hexane to obtain 2-(6-bromopyridin-3-yl)-2-cyclopropyl-N-(2,2,2-trifluoroethyl)acetamide (0.260g, 61.90%) as off white solic.

MS: 339.09[M+2]

Step-4: Synthesis of 2-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-cyclopropyl-N-(2,2,2-trifluoroethyl)acetamide

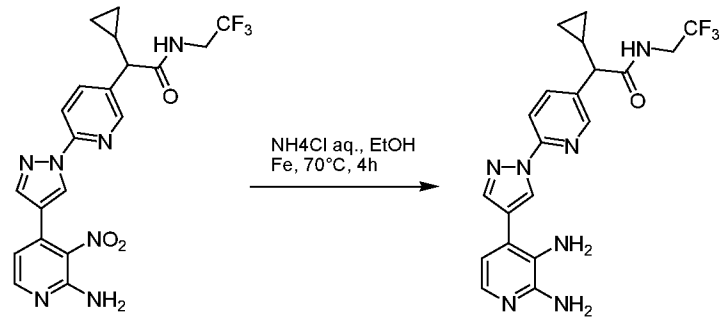


150 151 152

To a stirred solution of 3-nitro-4-(1H-pyrazol-4-yl) pyridin-2-amine (0.100g, 0.0487 mmol) and compound 2-(6-bromopyridin-3-yl)-2-cyclopropyl-N-(2,2,2-trifluoroethyl)acetamide (0.163g, 0.0487 mmol) in Dioxane (5 ml) was added K_3PO_4 (0.206g, 0.0974 mmol) followed by CuI (0.018g, 0.00974 mmol) and DMEDA (0.085g, 0.0974 mmol). Reaction was heated at 110°C for 6h. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 4-6% MeOH in DCM to obtained 2-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-cyclopropyl-N-(2,2,2-trifluoroethyl)acetamide (0.130 g, 59 %) as yellow solid.

MS: 462.1 [M+1]

Step-5: Synthesis 2-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-cyclopropyl-N-(2,2,2-trifluoroethyl)acetamide

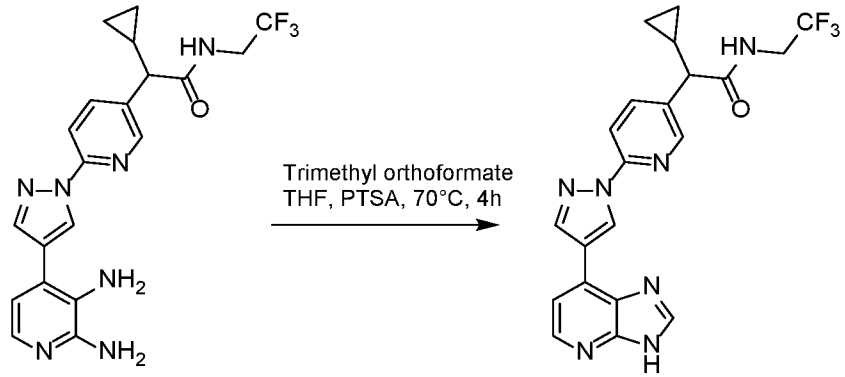


153 154

To a stirred solution of 2-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-cyclopropyl-N-(2,2,2-trifluoroethyl)acetamide (0.080g, 0.0173 mmol) in EtOH (7.0 mL), NH_4Cl (2.0 mL) was added at room temperature. To the resultant reaction mixture, Fe powder (0.045 g, 0.0867 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, reaction mixture was diluted with H_2O: EtOAc (50 mL, 5:5) and pass over celite to remove inorganic impurities from the reaction mixture. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to obtained pure 2-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-cyclopropyl-N-(2,2,2-trifluoroethyl)acetamide (0.061g, 82.43%) as dark brown solid mass.

MS: 432.2 [M+1]

Step-6: Synthesis of 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-cyclopropyl-N-(2,2,2-trifluoroethyl)acetamide:

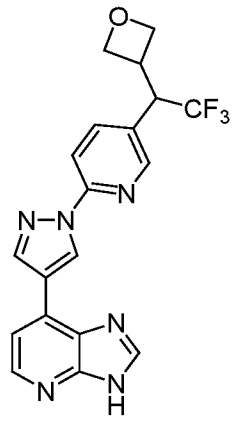


155 1167

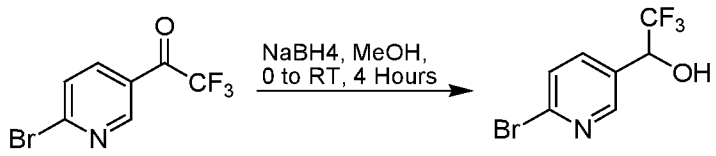
To a stirred solution of 2-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-cyclopropyl-N-(2,2,2-trifluoroethyl)acetamide ((0.060g, 0.0139 mmol) in THF (1.0 mL), Trimethyl orthoformate (1.5 mL) was added. To resultant reaction mixture, PTSA (0.0046 g, 0.0027 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with 10% MeOH in DCM. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 7 to 8% MeOH in DCM to obtained 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-cyclopropyl-N-(2,2,2-trifluoroethyl)acetamide (0.035 g, 57.37%) as off white solid.

MS: 442.1 [M+1]

Synthesis of Compound No. 1136:- 7-(1-(5-(2,2,2-trifluoro-1-(oxetan-3-yl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine



Step-1: Synthesis of 1-(6-bromopyridin-3-yl)-2,2,2-trifluoroethanol

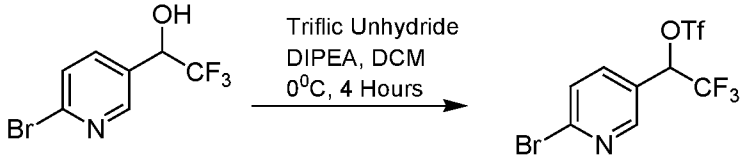


156 157

To a stirred solution of 1-(6-bromopyridin-3-yl)-2,2,2-trifluoroethanone (2.5g, 0.984 mmol) in MeOH (50 mL), $NaBH_4$ (0.744g, 1.962 mmol) was added at 0°C. Reaction was allowed to stir at room temperature for 4h. Reaction was monitored by TLC. On completion, reaction was quenched with water, extracted with EtOAc. The organic layer was washed with water, dried over Na_2SO_4, evaporated under reduced pressure to give 1-(6-bromopyridin-3-yl)-2,2,2-trifluoroethanol (2.3g, 91%) as white solid.

MS: 256.2 [M+1]

Step-2: synthesis of 1-(6-bromopyridin-3-yl)-2,2,2-trifluoroethyl trifluoromethanesulfonate



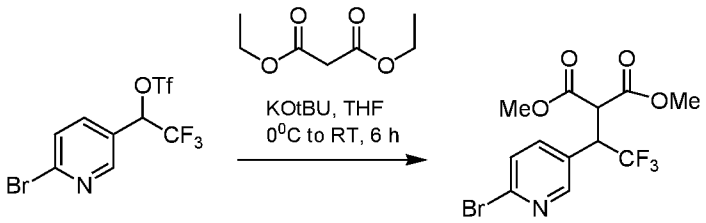
158 159

To a stirred solution of 1-(6-bromopyridin-3-yl)-2,2,2-trifluoroethanol (2.3 g, 0.898 mmol) in DCM (46 mL), DIPEA (2.31 g, 1.796 mmol) was added at 0°C. To resultant reaction mass

triflic anhydride (3.7 g, 1.347 mmol) was added dropwise at 0^0C in 10 minute and stirred reaction mixture at same temprature 4h. Completion of reaction was monitored by TLC. On completion, quenched with water, extracted with DCM. The organic layer was washed with water, brine, dried over sodium sulphate, concentrated under reduced pressure to obtained crude reaction mass. Purification of the crude was done *via* silica gel (100-200 Mesh) column chromatography and desired compound eluted at 10% acetone/n-Hexane to obtained 1-(6-bromopyridin-3-yl)-2,2,2-trifluoroethyl trifluoromethanesulfonate (2.5 g, 72%) as white solid.

MS: 388 [M+1]

Step-3: Synthesis of diethyl 2-(1-(6-bromopyridin-3-yl)-2,2,2-trifluoroethyl)malonate

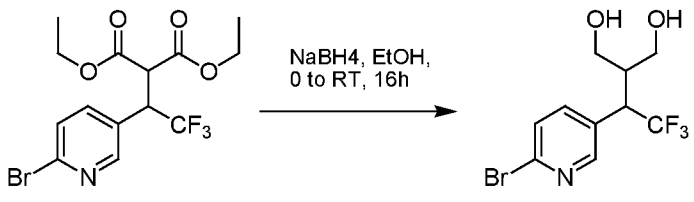


160 161

To a stirred solution of 1-(6-bromopyridin-3-yl)-2,2,2-trifluoroethyl trifluoromethanesulfonate (2.4g, 0.620 mmol) in THF (50 mL), Diethyl malonate (1.63 g, 1.240 mmol) was added at room temperature and cooled it to 10^0C. Added base potassium ter-butoxide (1.38g, 1.240 mmol) lot wise at 10^0C and stirring continued at room temprature for 6h. Completion of reaction was monitored by TLC. On completion, quenched with water, extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate, concentrated under reduced pressure to obtained crude reaction mass. Purification of the crude was done *via* silica gel (100-200 Mesh) column chromatography and desired compound eluted at 15% ethyl acetate/n-Hexane to obtained diethyl 2-(1-(6-bromopyridin-3-yl)-2,2,2-trifluoroethyl)malonate (1.6 g, 70%) as yellow oil.

MS: 398.2[M+1]

Step-4: Synthesis of 2-(1-(6-bromopyridin-3-yl)-2,2,2-trifluoroethyl)propane-1,3-diol

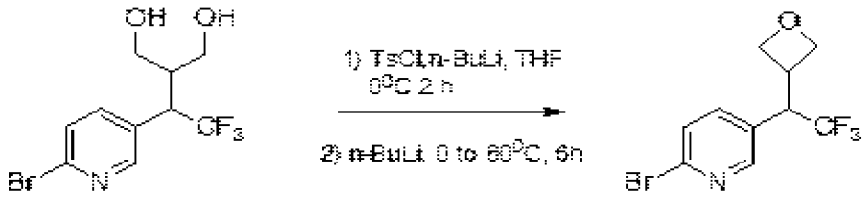


162 163

To a stirred solution of diethyl 2-(1-(6-bromopyridin-3-yl)-2,2,2-trifluoroethyl)malonate (1.6g, 0.402 mmol) in EtOH (32 mL), $NaBH_4$ (0.450g, 1.206 mmol) was added at 0°C. Reaction was allowed to stir at room temperature for 16h. Reaction was monitored by TLC. On completion, reaction was quenched with water, extracted with EtOAc. The organic layer was washed with water, dried over Na_2SO_4, evaporated under reduced pressure to obtain crude reaction mass. Purification of the crude was done *via* silica gel (100-200 Mesh) column chromatography and desired compound eluted at 30% acetone/n-Hexane to obtained **2**-(1-(6-bromopyridin-3-yl)-2,2,2-trifluoroethyl)propane-1,3-diol (0.460g, 35%) as clear oil.

MS: 314 [M+1]

Step-5: Synthesis of 2-bromo-5-(2,2,2-trifluoro-1-(oxetan-3-yl)ethyl)pyridine

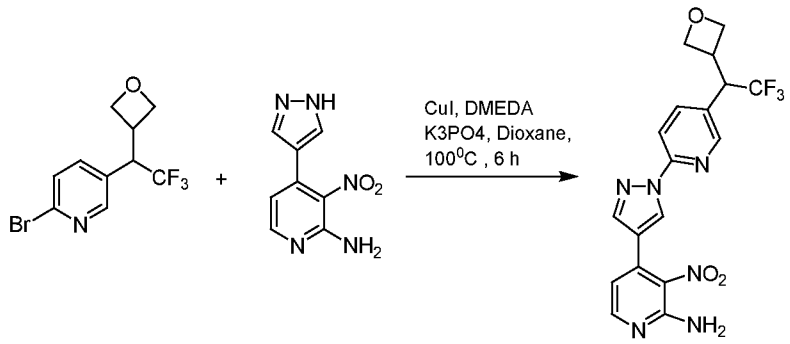


164 165

To a stirred solution of 2-(1-(6-bromopyridin-3-yl)-2,2,2-trifluoroethyl)propane-1,3-diol (0.450g, 0.143 mmol) in anhydrous THF (20 mL) at 0^0C under N_2. Added n-Butyl lithium (1.6M in hexane) (0.890 mL, 0.143 mmol) dropwise at 0^0C and stirred it for 30 minute. A solution of p-toluenesulfonyl chloride (0.271g. 0.143 mmol) in anhydrous THF was added slowly. The mixture was stirred at 0^0C for 1h, and a second batch of n-Butyl lithium (1.6M in hexane) (0.890 mL, 0.143 mmol) was added dropwise. After addition the mixture was heated at 60^0C and stirred for 4h. Completion of reaction was monitored by TLC. After reaction completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with ethyl acetate. Combined organic layer was dried over sodium sulphate, concentrated under reduced pressure obtained crude product. Purification of the crude was done *via* silica gel (100-200 Mesh) column chromatography and desired compound eluted at 10% acetone/n-Hexane to obtained 2-bromo-5-(2,2,2-trifluoro-1-(oxetan-3-yl)ethyl)pyridine (0.130g, 31%) as clear oil.

MS: 296.1 [M+1]

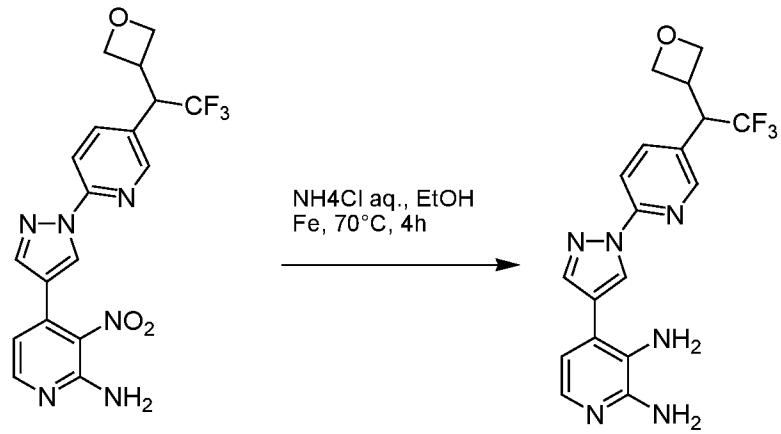
Step-6: Synthesis of 4-(1-(5-(2,2,2-trifluoro-1-(oxetan-3-yl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine



To a stirred solution of 3-nitro-4-(1H-pyrazol-4-yl) pyridin-2-amine (0.088g, 0.0429 mmol) and compound 2-bromo-5-(2,2,2-trifluoro-1-(oxetan-3-yl)ethyl)pyridine (0.128g, 0.0429 mmol) in Dioxane (5 ml) was added K_3PO_4 (0.182g, 0.0864 mmol) followed by CuI (0.016g, 0.00864 mmol) and DMEDA (0.076g, 0.0864 mmol). Reaction was heated at 110°C for 6h. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 4-5% MeOH in DCM to obtained 4-(1-(5-(2,2,2-trifluoro-1-(oxetan-3-yl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine (0.085 g, 47.22 %) as yellow solid.

MS: 421.1 [M+1]

Step-7: Synthesis of 4-(1-(5-(2,2,2-trifluoro-1-(oxetan-3-yl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)pyridine-2,3-diamine

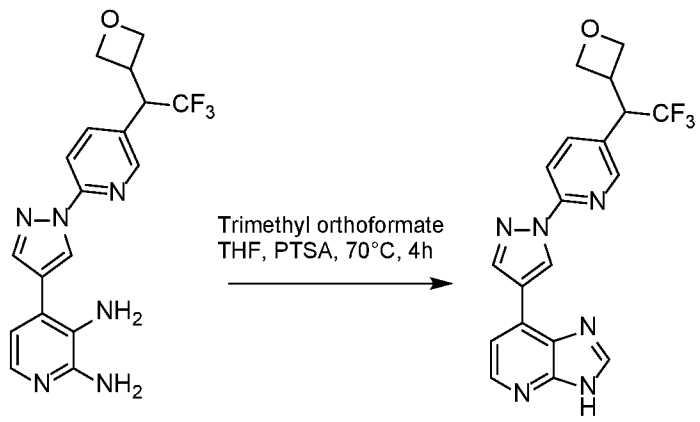


169 170

To a stirred solution of 4-(1-(5-(2,2,2-trifluoro-1-(oxetan-3-yl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine (0.050g, 0.0119 mmol) in EtOH (3.0 mL), NH_4Cl (1.5 mL) was added at room temperature. To resultant reaction mixture, Fe powder (0.031 g, 0.0591 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, reaction mixture was diluted with H_2O: EtOAc (50 mL, 5:5) and pass over celite to remove inorganic impurities from the reaction mixture. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to obtained pure 4-(1-(5-(2,2,2-trifluoro-1-(oxetan-3-yl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)pyridine-2,3-diamine (0.032g, 69.56%) as dark brown solid mass.

MS: 391.2 [M+1]

Step-8: Synthesis of 7-(1-(5-(2,2,2-trifluoro-1-(oxetan-3-yl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine

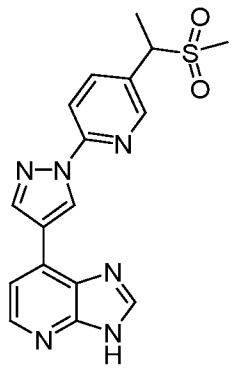


171 1136

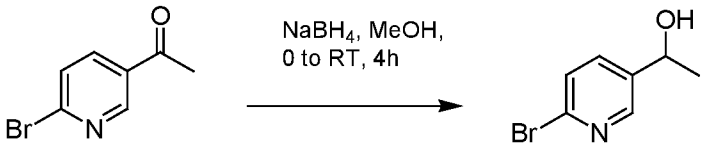
To a stirred solution of 4-(1-(5-(2,2,2-trifluoro-1-(oxetan-3-yl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)pyridine-2,3-diamine (0.030g, 0.0076 mmol) in THF (1.0 mL), Trimethyl orthoformate (1.5 mL) was added. To resultant reaction mixture, PTSA (0.004 g, 0.0015 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with 10% MeOH in DCM. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 3% to 5% MeOH in DCM to obtained 7-(1-(5-(2,2,2-trifluoro-1-(oxetan-3-yl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine (0.021 g, 70%) as off white solid.

MS: 401.0 [M+1]

Synthesis of Compound No. 1158:7-(1-(5-(1-(methylsulfonyl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine



Step-1: Synthesis of 1-(6-bromopyridin-3-yl)ethanol :

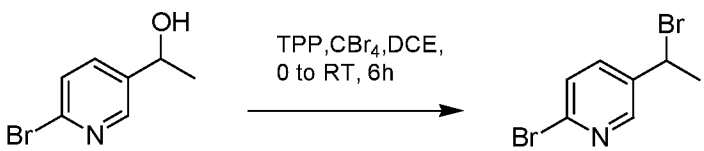


172 173

To a stirred solution of 1-(6-bromopyridin-3-yl)ethanone (0.5g, 0.250 mmol) in MeOH (20 mL), $NaBH_4$ (0.190g, 0.500 mmol) was added at 0°C. Reaction was allowed to stir at room temperature for 4h. Reaction was monitored by TLC. On completion, reaction was quenched with water, extracted with EtOAc. The organic layer was washed with water, dried over Na_2SO_4, evaporated under reduced pressure to obtain crude reaction mass. Purification of the crude was done *via* silica gel (100-200 Mesh) column chromatography and desired compound eluted at 25% ethyl acetate/n-Hexane to obtained 1-(6-bromopyridin-3-yl)ethanol (0.450g, 89.10%) as clear oil.

MS: 202.1 [M+1]

Step-2: Synthesis of 2-bromo-5-(1-bromoethyl)pyridine

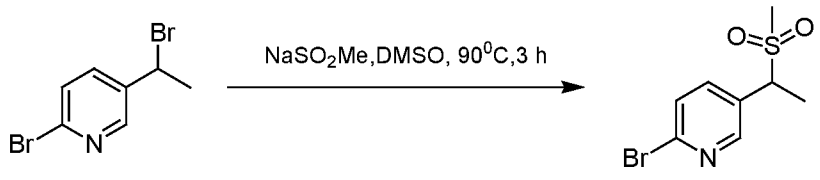


174 175

To a stirred solution of 1-(6-bromopyridin-3-yl)ethanol (0.400 g, 0.198 mmol) in DCE (20 mL), TPP (0.778 g, 0.297 mmol) was added and then added carbontetrabromide (0.932 g, 0.297 mmol) portion-wise at 0°C. The resultant reaction mixture was stirred at room temprature for 6h. Completion of reaction was monitored by TLC. After completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with DCM. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude product was purified by silica gel (100-200 mesh) column chromatography using 12% ethyl acetate in hexane as eluent to obtain 2-bromo-5-(1-bromoethyl)pyridine (0.290 g, 55.98 %) as white solid.

MS: 263.1 [M+1]

Step-3: Synthesis of 2-bromo-5-(1-(methylsulfonyl)ethyl)pyridine :

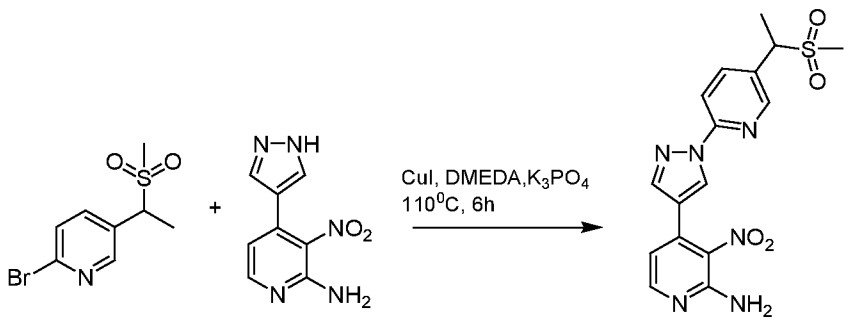


176 177

To a stirred solution of 2-bromo-5-(1-bromoethyl)pyridine (0.280g, 0.106 mmol) in DMSO (3.0 mL), sodium mathanesulfinate (0.163g, 0160 mmol) was added. To resultant reaction mixture was added stirred for 3h at 90°C. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give pure desired product 2-bromo-5-(1-(methylsulfonyl)ethyl)pyridine (0.155 g, 55.35%) as clear oil.

MS: 263 [M+1]

Step-4: Synthesis of 4-(1-(5-(1-(methylsulfonyl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine

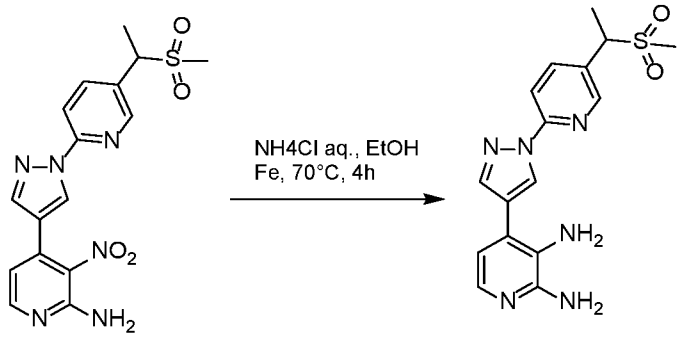


178 179 180

To a stirred solution of 3-nitro-4-(1H-pyrazol-4-yl) pyridin-2-amine (0.117g, 0.057 mmol) and compound 2-bromo-5-(1-(methylsulfonyl)ethyl)pyridine (0.150g, 0.057 mmol) in Dioxane (7 ml) was added K_3PO_4 (0.241g, 0.114 mmol) followed by CuI (0.021g, 0.0114 mmol) and DMEDA (0.100g, 0.114 mmol). Reaction was heated at 110°C for 6h. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 5-6% MeOH in DCM to obtained 4-(1-(5-(1-(methylsulfonyl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine (0.095 g, 42.79 %) as yellow solid.

MS: 389.1 [M+1]

Step-5: Synthesis of 4-(1-(5-(1-(methylsulfonyl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)pyridine-2,3-diamine:

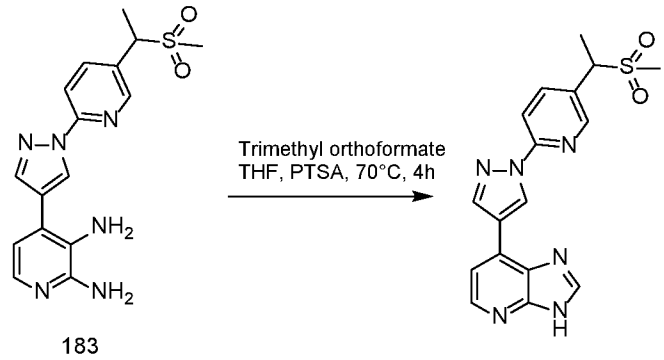


181 182

To a stirred solution of 4-(1-(5-(1-(methylsulfonyl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine (0.095g, 0.024 mmol) in EtOH (7.0 mL), NH_4Cl (2.0 mL) was added at room temperature. To the resultant reaction mixture, Fe powder (0.064 g, 0.122 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, reaction mixture was diluted with H_2O: EtOAc (50 mL, 5:5) and pass over celite to remove inorganic impurities from the reaction mixture. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to obtained pure 4-(1-(5-(1-(methylsulfonyl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)pyridine-2,3-diamine (0.060g, 68.96%) as dark brown solid mass.

MS: 359.2 [M+1]

Step-6: Synthesis of 7-(1-(5-(1-(methylsulfonyl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine:

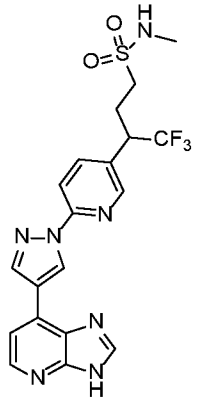


183 1158

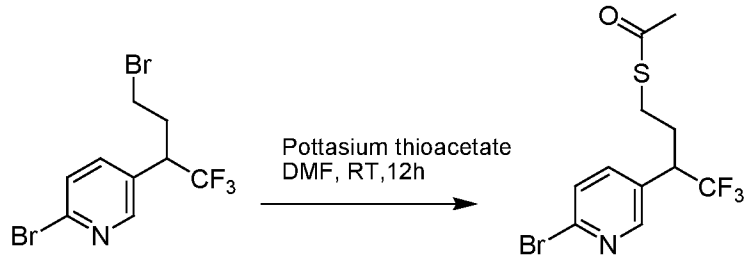
To a stirred solution of 4-(1-(5-(1-(methylsulfonyl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)pyridine-2,3-diamine (0.060g, 0.0136 mmol) in THF (1.0 mL), Trimethyl orthoformate (1.5 mL) was added. To resultant reaction mixture, PTSA (0.0046 g, 0.0027 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with 10% MeOH in DCM. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 7 to 8% MeOH in DCM to obtained 7-(1-(5-(1-(methylsulfonyl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine (0.027 g, 44.26%) as off white solid.

MS: 369.1 [M+1]

Synthesis of Compound No. 1142: 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutane-1-sulfonamide



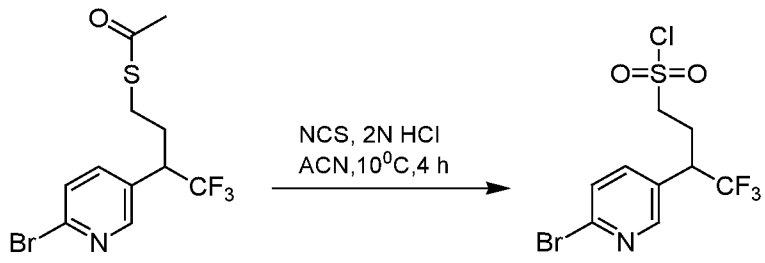
Step-1: Synthesis of S-3-(6-bromopyridin-3-yl)-4,4,4-trifluorobutyl ethanethioate:



184 185

To a stirred solution of 2-bromo-5-(4-bromo-1,1,1-trifluorobutan-2-yl)pyridine (0.300 g, 0.086 mmol) in DMF (5 mL) was added potassium tioacetate (0.197, 0.172 mmol) under nitrogen and stirred for 12h at room temperature. Progress of reaction was monitored by TLC. After reaction completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with diethyl ether. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 18% ethyl acetate in hexane as eluent to obtain S-3-(6-bromopyridin-3-yl)-4,4,4-trifluorobutyl ethanethioate (0.200 g, 68.96 %) as black solid.

Step-2: Synthesis of 3-(6-bromopyridin-3-yl)-4,4,4-trifluorobutane-1-sulfonyl chloride

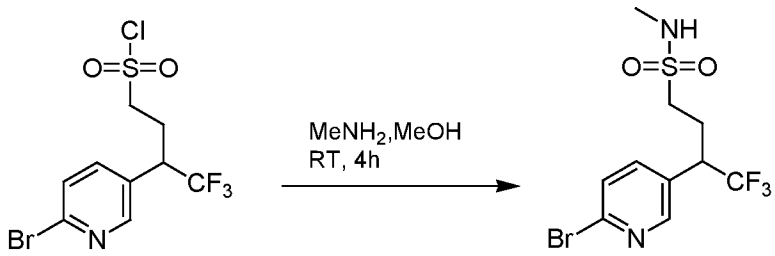


186 187

To a stirred solution of N-chlorosuccinamide (0.470g, 0.350 mmol) and 2N HCl (0.5 ml) in ACN at 0^0C under N_2 added solution of S-3-(6-bromopyridin-3-yl)-4,4,4-trifluorobutyl ethanethioate (0.300g, 0.877 mmol) in ACN dropwise. The resultant mixture was stirred at RT for 4h at room temprature. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 9 to 15% EA/Hexane to 3-(6-bromopyridin-3-yl)-4,4,4-trifluorobutane-1-sulfonyl chloride (0.225 g, 72.58%) as yellow oil.

MS: 366 [M+1]

Step-3: Synthesis of 3-(6-bromopyridin-3-yl)-4,4,4-trifluoro-N-methylbutane-1-sulfonamide

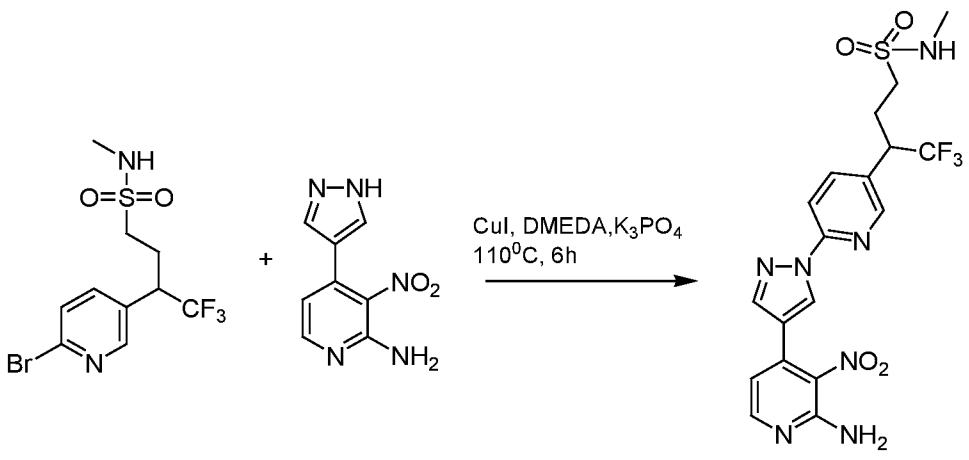


188 189

To a stirred solution of 3-(6-bromopyridin-3-yl)-4,4,4-trifluorobutane-1-sulfonyl chloride (0.150g, 0.0409 mmol) in MeOH (7 mL), base trimethylamine (0.124g, 0.122 mmol) was added. Then add methylamine. HCl (0.082g, 0.122 mmol) was added at room temprature. Reaction was stirred at room temperature for 4h. Reaction was monitored by TLC. On completion, reaction was quenched with water, extracted with EtOAc. The organic layer was washed with water, dried over Na_2SO_4, evaporated under reduced pressure to obtain pure compound 3-(6-bromopyridin-3-yl)-4,4,4-trifluoro-N-methylbutane-1-sulfonamide (0.130g, 87.83%) as clear oil.

MS: 361 [M+1]

Step-4: Synthesis of 3-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutane-1-sulfonamide

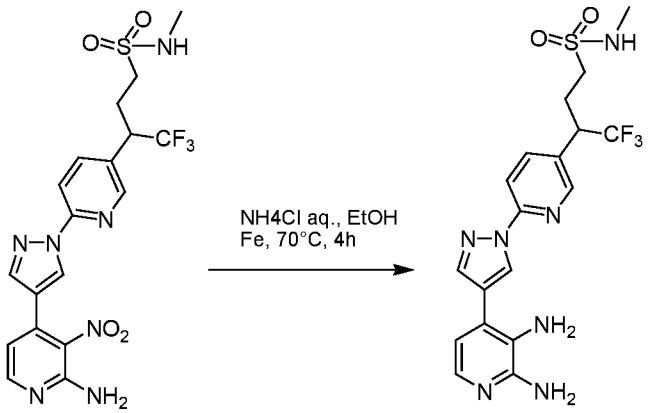


190 191 192

To a stirred solution of 3-nitro-4-(1H-pyrazol-4-yl) pyridin-2-amine (0.073g, 0.036 mmol) and compound 3-(6-bromopyridin-3-yl)-4,4,4-trifluoro-N-methylbutane-1-sulfonamide (0.130g, 0.036 mmol) in Dioxane (5 ml) was added K_3PO_4 (0.152g, 0.072 mmol) followed by CuI (0.013g, 0.0072 mmol) and DMEDA (0.0066g, 0.072 mmol). Reaction was heated at 110°C for 6h. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 6-7% MeOH in DCM to obtained 3-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutane-1-sulfonamide (0.09 g, 45 %) as yellow solid.

MS: 486.1 [M+1]

Step-5: Synthesis of 3-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutane-1-sulfonamide

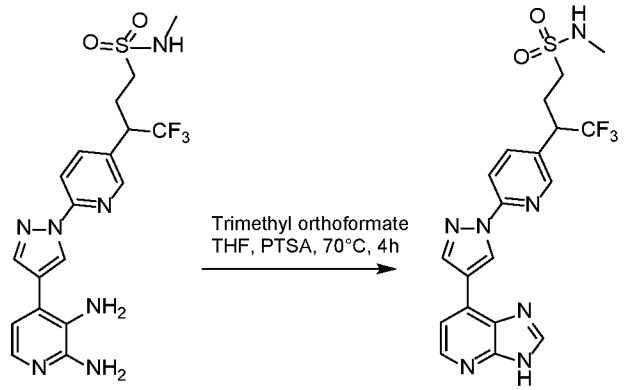


193 194

To a stirred solution of 3-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutane-1-sulfonamide (0.070g, 0.0144 mmol) in EtOH (7.0 mL), NH_4Cl (2.0 mL) was added at room temperature. To the resultant reaction mixture, Fe powder (0.40 g, 0.76 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, reaction mixture was diluted with H_2O: EtOAc (50 mL, 5:5) and pass over celite to remove inorganic impurities from the reaction mixture. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to obtained pure 3-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutane-1-sulfonamide (0.045g, 69.23%) as dark brown solid mass.

MS: 456.2 [M+1]

Step-6: Synthesis of 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutane-1-sulfonamide:

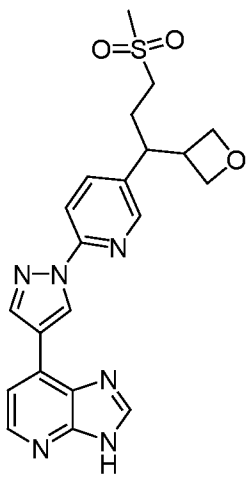


195 1142

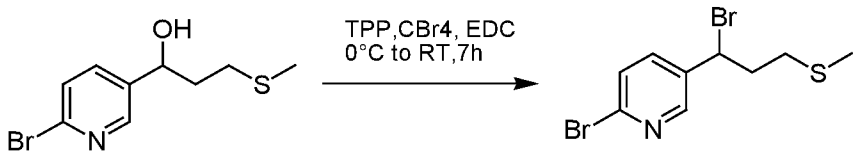
To a stirred solution of 3-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutane-1-sulfonamide (0.045g, 0.0098 mmol) in THF (1.0 mL), Trimethyl orthoformate (1.5 mL) was added. To resultant reaction mixture, PTSA (0.0034 g, 0.0019 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with 10% MeOH in DCM. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 8 to 9% MeOH in DCM to obtained 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutane-1-sulfonamide (0.021 g, 46.66%) as off white solid.

MS: 466.1 [M+1]

Synthesis of Compound No. 1160: 7-(1-(5-(3-(methylsulfonyl)-1-(oxetan-3-yl)propyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine



Step-1: Synthesis of 2-bromo-5-(1-bromo-3-(methylthio)propyl)pyridine:

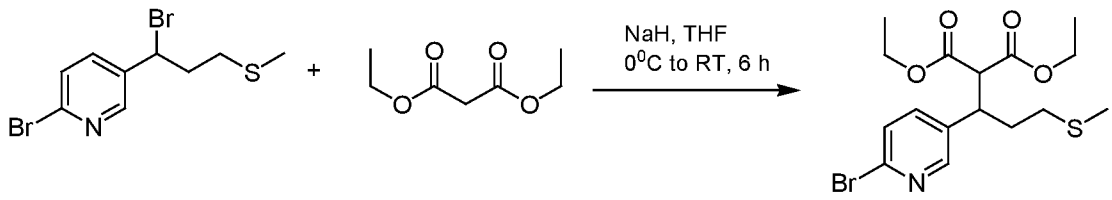


196 197

To a stirred solution of 1-(6-bromopyridin-3-yl)-3-(methylthio)propan-1-ol (3.5 g, 1.33 mmol) in DCE (70 mL), TPP (4.5 g, 1.73 mmol) was added and then added carbontetrabromide (5.7 g, 1.73 mmol) portion-wise at 0°C. The resultant reaction mixture was stirred at room temprature for 7h. Completion of reaction was monitored by TLC. After reaction completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with DCM. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude product was purified by silica gel (100-200 mesh) column chromatography using 4% ethyl acetate in hexane as eluent to obtain 2-bromo-5-(1-bromo-3-(methylthio)propyl)pyridine (2.65 g, 61.05 %) as yellow oil.

MS: 326.1 [M+1]

Step-2: Synthesis of diethyl 2-(1-(6-bromopyridin-3-yl)-3-(methylthio)propyl)malonate :

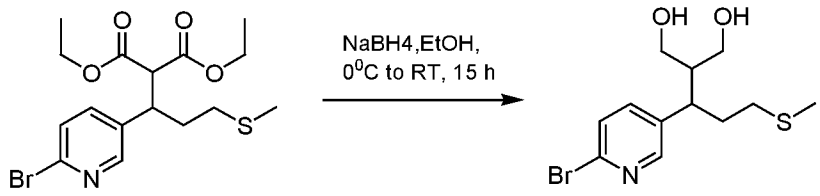


198 199 200

To a stirred solution of 2-bromo-5-(1-bromo-3-(methylthio)propyl)pyridine (2.34g, 0.720 mmol) in THF (50 mL), Diethyl malonate (1.72 g, 1.08 mmol) was added at room temperature and cooled it to 10^0C. Added base sodium hydride (0.420g, 1.08 mmol) lot wise at 10^0C and stirring continued at room temprature for 6h. Completion of reaction was monitored by TLC. On completion, quenched with water, extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate, concentrated under reduced pressure to obtained crude reaction mass. Purification of the crude was done *via* silica gel (100-200 Mesh) column chromatography and desired compound eluted at 15% ethyl acetate/n-Hexane to obtained diethyl 2-(1-(6-bromopyridin-3-yl)-3-(methylthio)propyl)malonate (1.05 g, 37.5%) as yellow oil.

MS: 404.2[M+1]

Step-3: Synthesis of 2-(1-(6-bromopyridin-3-yl)-3-(methylthio)propyl)propane-1,3-diol :

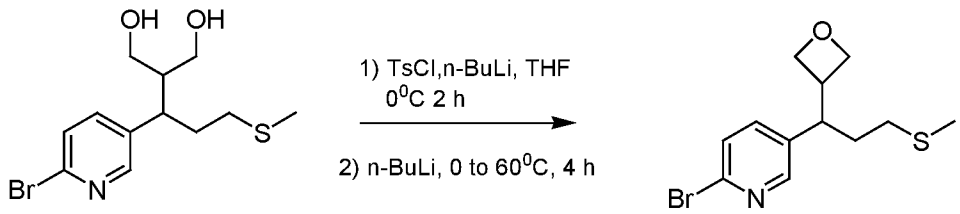


201 202

To a stirred solution of diethyl 2-(1-(6-bromopyridin-3-yl)-3-(methylthio)propyl)malonate (1.05g, 0.259 mmol) in EtOH (20 mL), $NaBH_4$ (0.290g, 0.777 mmol) was added at 0°C. Reaction was allowed to stir at room temperature for 16h. Reaction was monitored by TLC. On completion, reaction was quenched with water, extracted with EtOAc. The organic layer was washed with water, dried over Na_2SO_4, evaporated under reduced pressure to obtain crude reaction mass. Purification of the crude was done *via* silica gel (100-200 Mesh) column chromatography and desired compound eluted at 30% acetone/n-Hexane to obtained 2-(1-(6-bromopyridin-3-yl)-3-(methylthio)propyl)propane-1,3-diol (0.500g, 60.16%) as clear oil.

MS: 320 [M+1]

Step-4: Synthesis of 2-bromo-5-(3-(methylthio)-1-(oxetan-3-yl)propyl)pyridine :



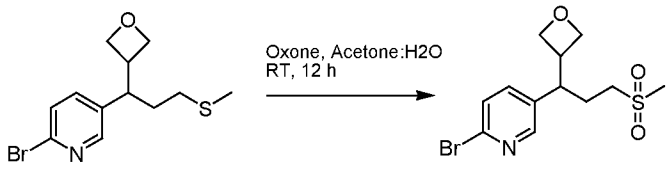
203 204

To a stirred solution of 2-(1-(6-bromopyridin-3-yl)-3-(methylthio)propyl)propane-1,3-diol (0.470g, 0.146 mmol) in anhydrous THF (30 mL) at 0°C under N_2. Added n-Butyl lithium (1.6M in hexane) (0.908 mL, 0.146 mmol) dropwise at 0°C and stirred it for 30 minute. A solution of p-toluenesulfonyl chloride (0.277g. 0.146 mmol) in anhydrous THF was added slowly. The mixture was stirred at 0°C for 1h, and a second batch of n-Butyl lithium (1.6M in hexane) (0.908 mL, 0.146 mmol) was added dropwise. After addition the mixture was heated at 60°C and stirred for 4h. Completion of reaction was monitored by TLC. After reaction completion reaction mass was quenched with ice cold water. Phases separated and aqueous

layer was extracted with ethyl acetate. Combined organic layer was dried over sodium sulphate, concentrated under reduced pressure obtained crude product. Purification of the crude was done *via* silica gel (100-200 Mesh) column chromatography and desired compound eluted at 11% acetone/n-Hexane to obtained 2-bromo-5-(3-(methylthio)-1-(oxetan-3-yl)propyl)pyridine (0.160g, 36.1%) as clear oil.

MS: 302.1 [M+1]

Step-5: Synthesis of 2-bromo-5-(3-(methylsulfonyl)-1-(oxetan-3-yl)propyl)pyridine :

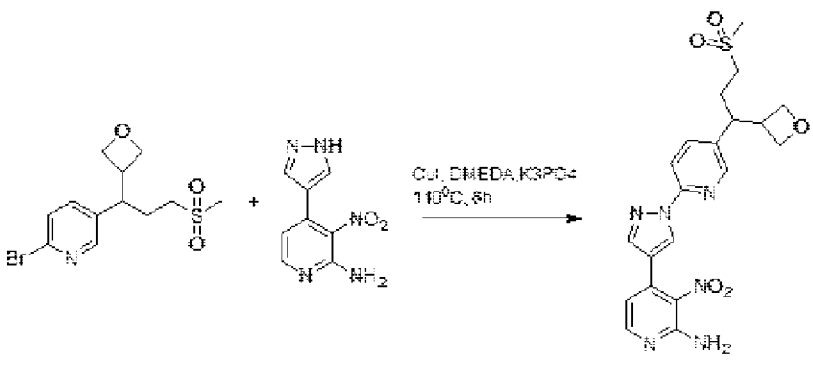


205 206

To a stirred solution of 2-bromo-5-(3-(methylthio)-1-(oxetan-3-yl)propyl)pyridine (0.160 g, 0.0520 mmol) in Acetone:H_2O (20 mL, 7:3) at 0^{0}C was added oxone (0.487 g, 0.158 mmol) under nitrogen and stirred for 12h at same temperature. Progress of reaction was monitored by TLC. After reaction completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 3% MeOH in DCM as eluent to obtain 2-bromo-5-(3-(methylsulfonyl)-1-(oxetan-3-yl)propyl)pyridine (0.130 g, 73.86 %) as colourless oil.

MS: 334.0 [M+1]

Step-6: Synthesis of 4-(1-(5-(3-(methylsulfonyl)-1-(oxetan-3-yl)propyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine :

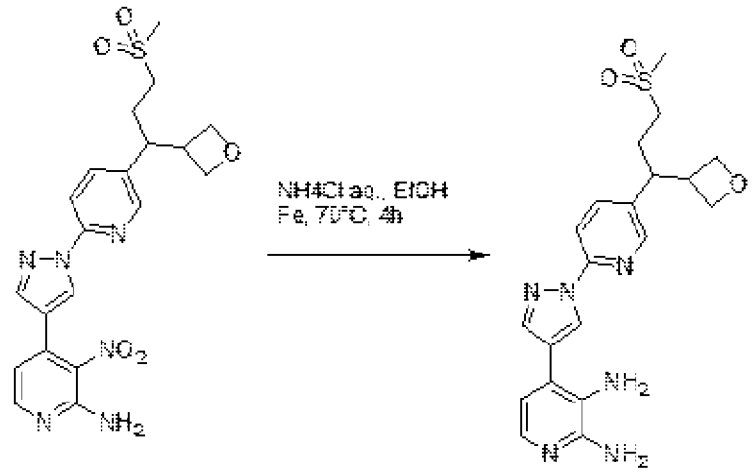


207 208 209

To a stirred solution of 3-nitro-4-(1H-pyrazol-4-yl) pyridin-2-amine (0.079g, 0.0389 mmol) and compound 2-bromo-5-(3-(methylsulfonyl)-1-(oxetan-3-yl)propyl)pyridine (0.130g, 0.0389 mmol) in Dioxane (5 ml) was added K_3PO_4 (0.164g, 0.0778 mmol) followed by CuI (0.014g, 0.0077 mmol) and DMEDA (0.068g, 0.0778 mmol). Reaction was heated at 110°C for 6h. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 4-5% MeOH in DCM to obtained 4-(1-(5-(3-(methylsulfonyl)-1-(oxetan-3-yl)propyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine (0.085 g, 47.22 %) as yellow solid.

MS: 459.1 [M+1]

Step-7: Synthesis of 4-(1-(5-(3-(methylsulfonyl)-1-(oxetan-3-yl)propyl)pyridin-2-yl)-1H-pyrazol-4-yl)pyridine-2,3-diamine

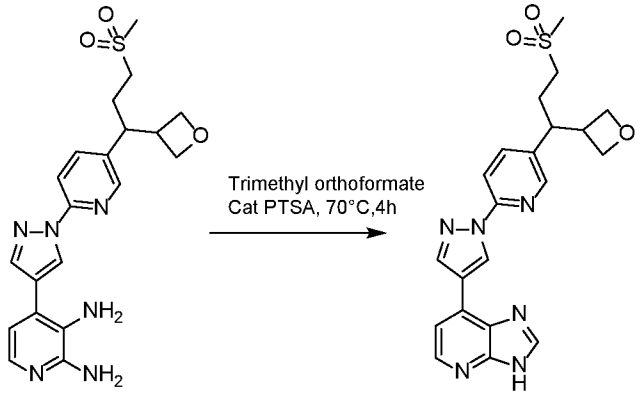


210 211

To a stirred solution of 4-(1-(5-(3-(methylsulfonyl)-1-(oxetan-3-yl)propyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine (0.060g, 0.0131 mmol) in EtOH (7.0 mL), NH_4Cl (2.0 mL) was added at room temperature. To the resultant reaction mixture, Fe powder (0.034 g, 0.06591 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, reaction mixture was diluted with H_2O: EtOAc (50 mL, 5:5) and pass over celite to remove inorganic impurities from the reaction mixture. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to obtained pure 4-(1-(5-(3-(methylsulfonyl)-1-(oxetan-3-yl)propyl)pyridin-2-yl)-1H-pyrazol-4-yl)pyridine-2,3-diamine (0.045g, 80.35%) as dark brown solid mass.

MS: 429.2 [M+1]

Step-8: Synthesis of 7-(1-(5-(3-(methylsulfonyl)-1-(oxetan-3-yl)propyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine :

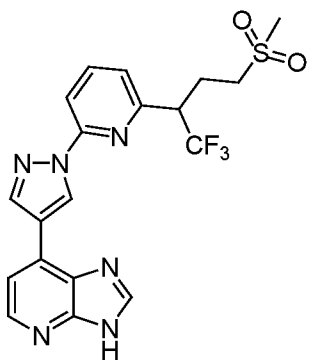


212 1160

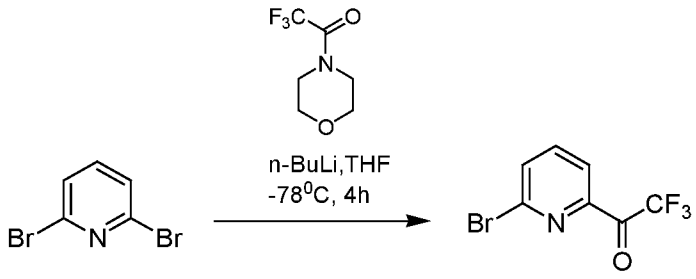
To a stirred solution of 4-(1-(5-(3-(methylsulfonyl)-1-(oxetan-3-yl)propyl)pyridin-2-yl)-1H-pyrazol-4-yl)pyridine-2,3-diamine (0.045g, 0.0105 mmol) in THF (1.0 mL), Trimethyl orthoformate (1.5 mL) was added. To resultant reaction mixture, PTSA (0.0036 g, 0.0021 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with 10% MeOH in DCM. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 6 to 7% MeOH in DCM to obtained 7-(1-(5-(3-(methylsulfonyl)-1-(oxetan-3-yl)propyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine (0.025 g, 54%) as off white solid.

MS: 439.0 [M+1]

Synthesis of Compound No. 1175: 7-(1-(6-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine



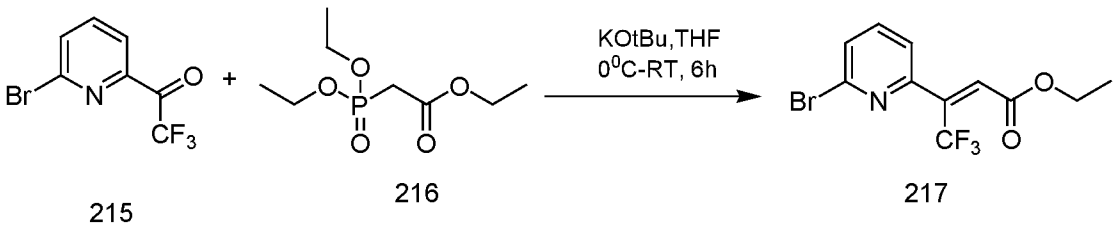
Step-1: Synthesis of 1-(6-bromopyridin-2-yl)-2,2,2-trifluoroethanone:



213 214

To a stirred solution of 2,6-dibromopyridine (5.0 g, 2.12 mmol) in THF (50 mL) at -78°C was added n-Butyl lithium (2.5M in hexane) (12.5 mL, 3.18 mmol) under nitrogen and stirred for 1h at same temperature. 2,2,2-trifluoro-1-morpholinoethanone (5.06 g, 2.76 mmol) was then added drop wise to the reaction mixture, stirred for 1h at -78°C. Progress of reaction was monitored by TLC. After reaction completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with diethyl ether. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 18% ethyl acetate in hexane as eluent to obtain 1-(6-bromopyridin-2-yl)-2,2,2-trifluoroethanone (3.5 g, 64.81 %) as colourless oil.

Step-2: Synthesis of (E/Z)-ethyl 3-(6-bromopyridin-2-yl)-4,4,4-trifluorobut-2-enoate



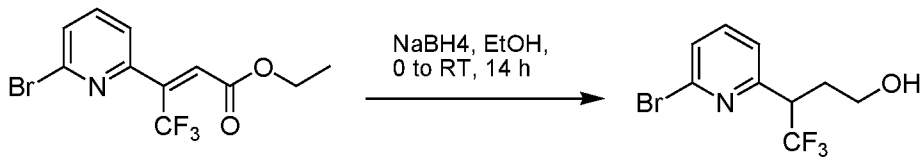
215 216 217

To a stirred solution of Triethyl phosphonoacetate (3.9g, 1.77 mmol) and THF (60 ml) at 0^0C under N_2 added base potassium ter-butoxide (1.98g, 1.77 mmol) lotwise. The resultant mixture was stirred at RT for 1h for anion generation. A solution of 1-(6-bromopyridin-2-yl)-2,2,2-trifluoroethanone (3.0 g, 1.18 mmol) in THF (15 ml) was added slowly. After addition stirred mixture for 6h at RT. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography:

eluent at 9 to 15% EA/Hexane to obtained (E/Z)-ethyl 3-(6-bromopyridin-2-yl)-4,4,4-trifluorobut-2-enoate (1.5 g, 40%) as yellow oil.

MS: 324 [M+1]

Step-3: Synthesis of 3-(6-bromopyridin-2-yl)-4,4,4-trifluorobutan-1-ol :

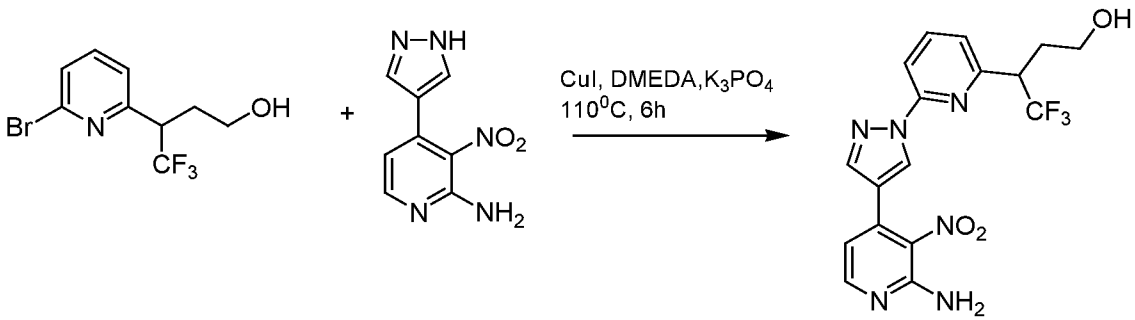


218 219

To a stirred solution of (E/Z)-ethyl 3-(6-bromopyridin-2-yl)-4,4,4-trifluorobut-2-enoate (1.5g, 462 mmol) in EtOH (30 mL), $NaBH_4$ (0.520g, 1380 mmol) was added at 0°C. Reaction was allowed to stir at room temperature for 14h. Reaction was monitored by TLC. On completion, reaction was quenched with water, extracted with EtOAc. The organic layer was washed with water, dried over Na_2SO_4, evaporated under reduced pressure to obtain crude reaction mass. Purification of the crude was done *via* silica gel (100-200 Mesh) column chromatography and desired compound eluted at 30% ethyl acetate/n-Hexane to obtained 3-(6-bromopyridin-2-yl)-4,4,4-trifluorobutan-1-ol (0.610g, 46.5%) as clear oil.

MS: 284 [M+1]

Step-4: Synthesis of 3-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-2-yl)-4,4,4-trifluorobutan-1-ol



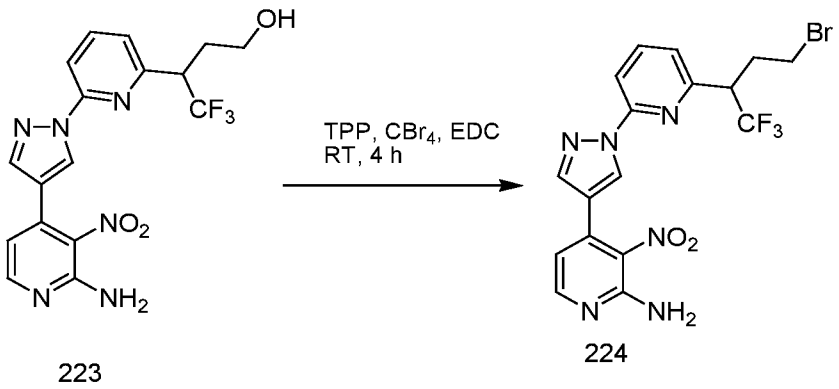
220 221 222

To a stirred solution of 3-nitro-4-(1H-pyrazol-4-yl) pyridin-2-amine (0.253g, 123 mmol) and compound 3-(6-bromopyridin-2-yl)-4,4,4-trifluorobutan-1-ol (0.350g, 123 mmol) in Dioxane (5 ml) was added K_3PO_4 (0.521g, 246 mmol) followed by CuI (0.046g, 0.246 mmol) and

DMEDA (0.216g, 246 mmol). Reaction was heated at 110°C for 6h. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 6-7% MeOH in DCM to obtained 3-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-2-yl)-4,4,4-trifluorobutan-1-ol (0.250 g, 50 %) as yellow solid.

MS: 409.1 [M+1]

Step-5: Synthesis of 4-(1-(6-(4-bromo-1,1,1-trifluorobutan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine

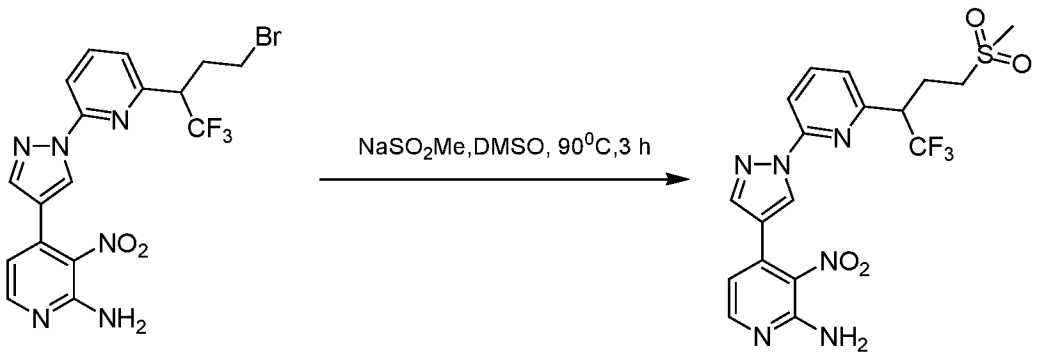


223 224

To a stirred solution of 3-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-2-yl)-4,4,4-trifluorobutan-1-ol (0.120 g, 0.29 mmol) in DCE (10 mL), TPP (0.115 g, 0.44 mmol) was added and then added carbontetrabromide (0.145 g, 0.44 mmol) portion-wise at 0°C. The resultant reaction mixture was stirred at room temprature for 7h. Completion of reaction was monitored by TLC. After completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with DCM. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude product was purified by silica gel (100-200 mesh) column chromatography using 2 to 3% methanol in DCMA as eluent to obtain 4-(1-(6-(4-bromo-1,1,1-trifluorobutan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine (0.065 g, 47.05 %) as yellow solid.

MS: 471.1 [M+1]

Step-6: Synthesis of 4-(1-(6-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine:

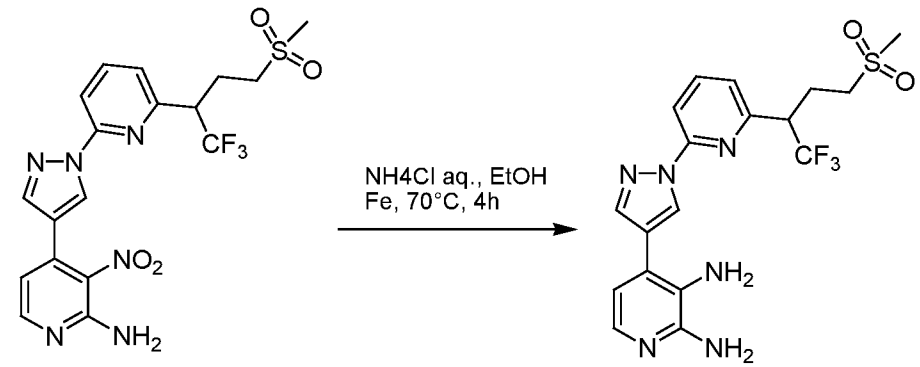


225 226

To a stirred solution of 4-(1-(6-(4-bromo-1,1,1-trifluorobutan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine (0.065g, 0.130 mmol) in DMSO (3.0 mL), sodium mathanesulfinate (0.027g, 0.20 mmol) was added. To resultant reaction mixture was added stirred for 3h at 90°C. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 6 to 7% MeOH/DCM to obtained 4-(1-(6-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine (0.052 g, 81.20%) as yellow solid.

MS: 471[M+1]

Step-7: Synthesis of 4-(1-(6-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)pyridine-2,3-diamine:



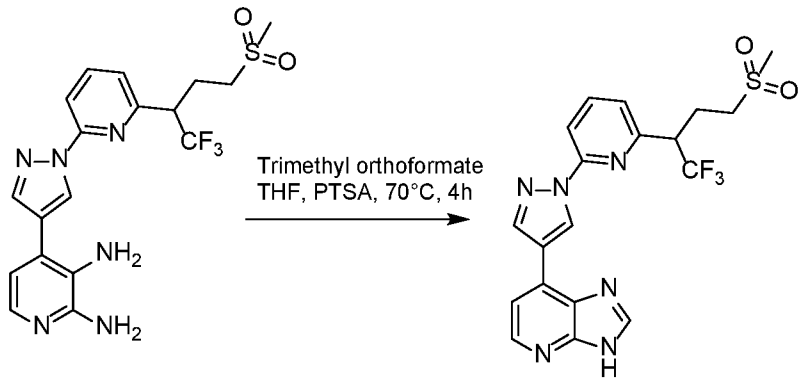
227 228

-

To a stirred solution of 4-(1-(6-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine (0.052g, 0.11 mmol) in EtOH (7.0 mL), NH_4Cl (2.0 mL) was added at room temperature. To the resultant reaction mixture, Fe powder (0.029 g, 0.55 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, reaction mixture was diluted with H_2O: EtOAc (50 mL, 5:5) and pass over celite to remove inorganic impurities from the reaction mixture. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to obtained pure 4-(1-(6-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)pyridine-2,3-diamine (0.036g, 75%) as dark brown solid mass.

MS: 441.2 [M+1]

Step-8: Synthesis of 7-(1-(6-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine :

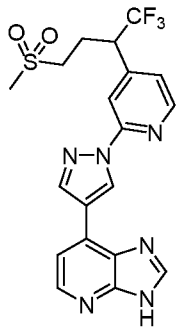


229 1175

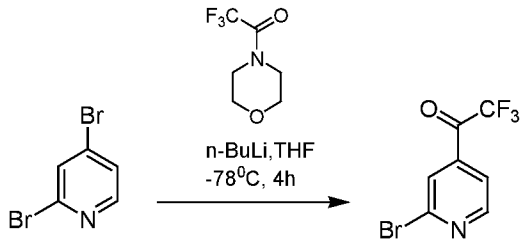
To a stirred solution of 4-(1-(6-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)pyridine-2,3-diamine (0.035g, 0.079 mmol) in THF (1.0 mL), Trimethyl orthoformate (1.5 mL) was added. To resultant reaction mixture, PTSA (0.0027 g, 0.015 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with 10% MeOH in DCM. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 8 to 9% MeOH in DCM to obtained 7-(1-(6-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine (0.021 g, 60%) as off white solid.

MS: 451.1 [M+1]

Synthesis of Compound No. 1176: 7-(1-(4-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine



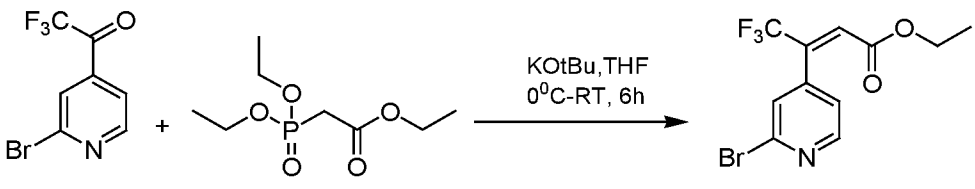
Step-1: Synthesis of 1-(2-bromopyridin-4-yl)-2,2,2-trifluoroethanone:



230 231

To a stirred solution of 2,4-dibromopyridine (5.0 g, 2.12 mmol) in THF (50 mL) at -78°C was added n-Butyl lithium (2.5M in hexane) (12.5 mL, 3.18 mmol) under nitrogen and stirred for 1h at same temperature. 2,2,2-trifluoro-1-morpholinoethanone (5.06 g, 2.76 mmol) was then added drop wise to the reaction mixture, stirred for 1h at -78°C. Progress of reaction was monitored by TLC. After reaction completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with diethyl ether. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 18% ethyl acetate in hexane as eluent to obtain 1-(2-bromopyridin-4-yl)-2,2,2-trifluoroethanone (3.5 g, 64.81 %) as colourless oil.

Step-2: Synthesis of (E/Z)-ethyl 3-(2-bromopyridin-4-yl)-4,4,4-trifluorobut-2-enoate

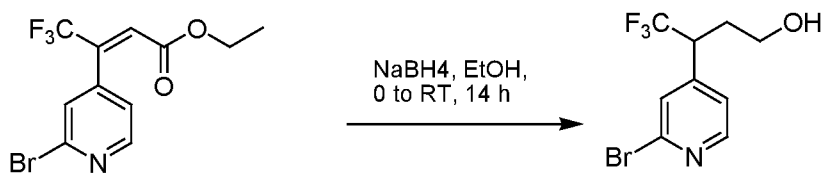


232 233 234

To a stirred solution of Triethyl phosphonoacetate (3.9g, 1.77 mmol) and THF (60 ml) at 0^0C under N_2 added base potassium ter-butoxide (1.98g, 1.77 mmol) lotwise. The resultant mixture was stirred at RT for 1h for anion generation. A solution of 1-(2-bromopyridin-4-yl)-2,2,2-trifluoroethanone (3.0 g, 1.18 mmol) in THF (15 ml) was added slowly. After addition stirred mixture for 6h at RT. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 9 to 15% EA/Hexane to obtained (E/Z)-ethyl 3-(2-bromopyridin-4-yl)-4,4,4-trifluorobut-2-enoate (1.5 g, 40%) as yellow oil.

MS: 324 [M+1]

Step-3: Synthesis of 3-(2-bromopyridin-4-yl)-4,4,4-trifluorobutan-1-ol:

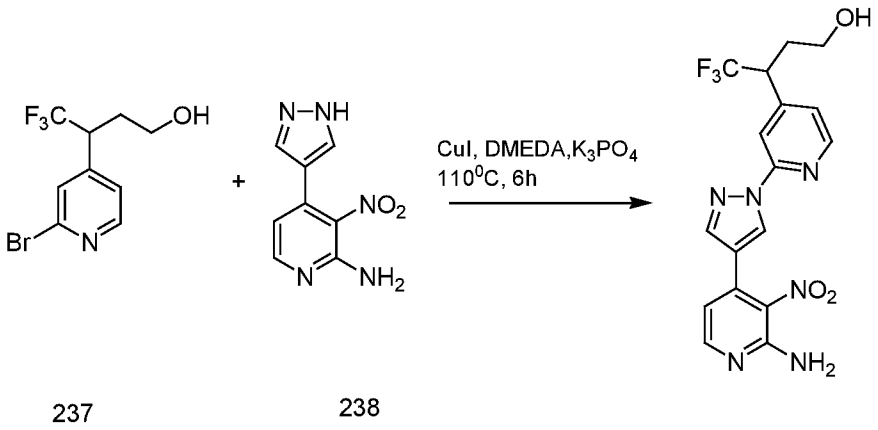


235 236

To a stirred solution of (E/Z)-ethyl 3-(6-bromopyridin-3-yl)-4,4,4-trifluorobut-2-enoate (1.5g, 462 mmol) in EtOH (30 mL), $NaBH_4$ (0.520g, 1380 mmol) was added at 0^oC. Reaction was allowed to stir at room temperature for 14h. Reaction was monitored by TLC. On completion, reaction was quenched with water, extracted with EtOAc. The organic layer was washed with water, dried over Na_2SO_4, evaporated under reduced pressure to obtain crude reaction mass. Purification of the crude was done *via* silica gel (100-200 Mesh) column chromatography and desired compound eluted at 30% ethyl acetate/n-Hexane to obtained 3-(2-bromopyridin-4-yl)-4,4,4-trifluorobutan-1-ol (0.610g, 46.5%) as clear oil.

MS: 284 [M+1]

Step-4: Synthesis of 3-(2-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-4-yl)-4,4,4-trifluorobutan-1-ol

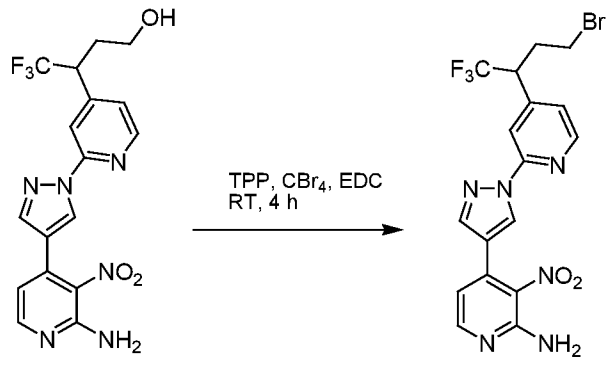


237 238 239

To a stirred solution of 3-nitro-4-(1H-pyrazol-4-yl) pyridin-2-amine (0.253g, 123 mmol) and compound 3-(2-bromopyridin-4-yl)-4,4,4-trifluorobutan-1-ol (0.350g, 123 mmol) in Dioxane (5 ml) was added K_3PO_4 (0.521g, 246 mmol) followed by CuI (0.046g, 0.246 mmol) and DMEDA (0.216g, 246 mmol). Reaction was heated at 110°C for 6h. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 6-7% MeOH in DCM to obtained 3-(2-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-4-yl)-4,4,4-trifluorobutan-1-ol (0.250 g, 50 %) as yellow solid.

MS: 409.1 [M+1]

Step-5: Synthesis of 4-(1-(4-(4-bromo-1,1,1-trifluorobutan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine

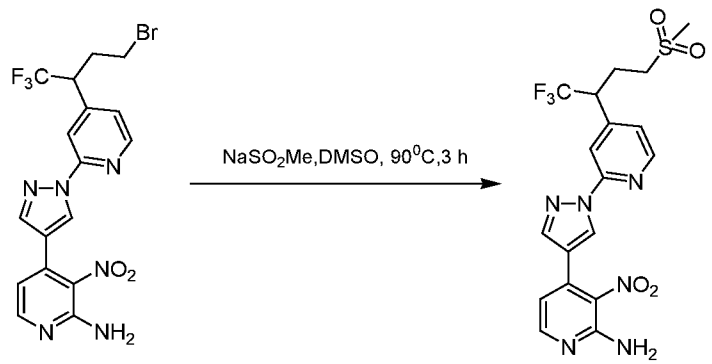


240 241

To a stirred solution of 3-(2-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-4-yl)-4,4,4-trifluorobutan-1-ol (0.120 g, 0.29 mmol) in DCE (10 mL), TPP (0.115 g, 0.44 mmol) was added and then added carbontetrabromide (0.145 g, 0.44 mmol) portion-wise at 0°C. The resultant reaction mixture was stirred at room temprature for 7h. Completion of reaction was monitored by TLC. After completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with DCM. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude product was purified by silica gel (100-200 mesh) column chromatography using 2 to 3% methanol in DCMA as eluent to obtain 4-(1-(4-(4-bromo-1,1,1-trifluorobutan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine (0.065 g, 47.05 %) as yellow solid.

MS: 471.1 [M+1]

Step-6: Synthesis of 4-(1-(4-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine:

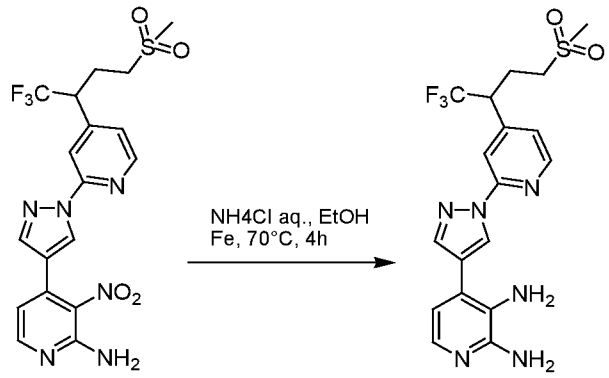


242 243

To a stirred solution of 4-(1-(4-(4-bromo-1,1,1-trifluorobutan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine (0.065g, 0.130 mmol) in DMSO (3.0 mL), sodium mathanesulfinate (0.027g, 0.20 mmol) was added. To resultant reaction mixture was added stirred for 3h at 90°C. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 6 to 7% MeOH/DCM to obtained 4-(1-(4-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine (0.052 g, 81.20%) as yellow solid.

MS: 471[M+1]

Step-7: Synthesis of 4-(1-(4-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)pyridine-2,3-diamine:

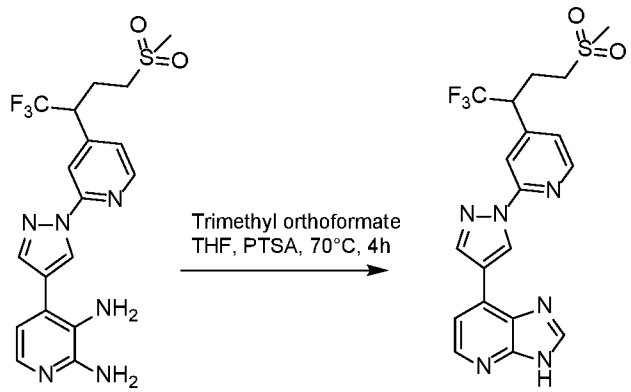


244 245

To a stirred solution of 4-(1-(4-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine (0.052g, 0.11 mmol) in EtOH (7.0 mL), NH_4Cl (2.0 mL) was added at room temperature. To the resultant reaction mixture, Fe powder (0.029 g, 0.55 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, reaction mixture was diluted with H_2O: EtOAc (50 mL, 5:5) and pass over celite to remove inorganic impurities from the reaction mixture. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to obtained pure 4-(1-(4-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)pyridine-2,3-diamine (0.036g, 75%) as dark brown solid mass.

MS: 441.2 [M+1]

Step-8: Synthesis of 7-(1-(4-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine:

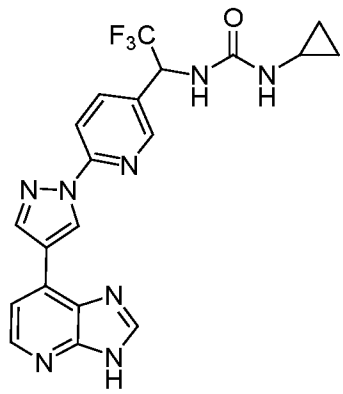


246 1176

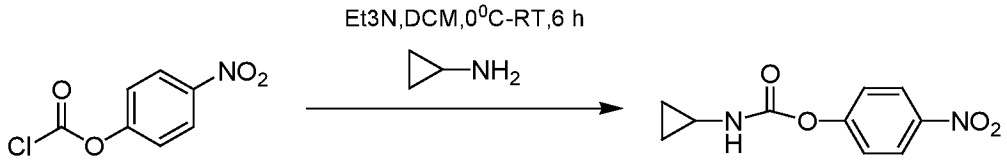
To a stirred solution of 4-(1-(5-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)pyridine-2,3-diamine ((0.035g, 0.079 mmol) in THF (1.0 mL), Trimethyl orthoformate (1.5 mL) was added. To resultant reaction mixture, PTSA (0.0027 g, 0.015 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with 10% MeOH in DCM. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 8 to 9% MeOH in DCM to obtained 7-(1-(4-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine (0.021 g, 60%) as off white solid.

MS: 451.1 [M+1]

Synthesis of Compound No. 1178: 1-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethyl)-3-cyclopropylurea



Step-1: Synthesis of 4-nitrophenyl cyclopropylcarbamate:



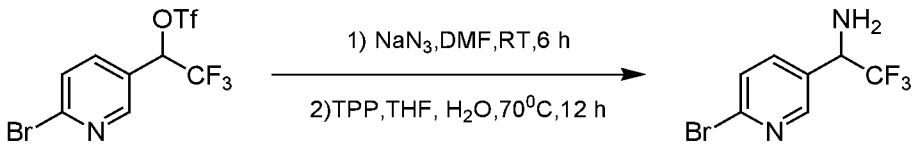
247 248

To a stirred solution of cyclopropanamine (2.0g, 3.508 mmol) in DCM (60.0 mL), trimethylamine (5.3 g , 5.26 mmol) was added followed by 4-nitrophenyl chloroformate (9.1 g , 4.55 mmol) at 0^0C. The resultant reaction mixture was stirred for 6h at room temperature. Completion of reaction was monitored by TLC. On completion solid fall out was directly

filtered on buckner and then washed with DCM to obtained pure product (1.2 g, 15.58%) as white solid

MS: 223 [M+1]

Step-2: Synthesis of 1-(6-bromopyridin-3-yl)-2,2,2-trifluoroethanamine



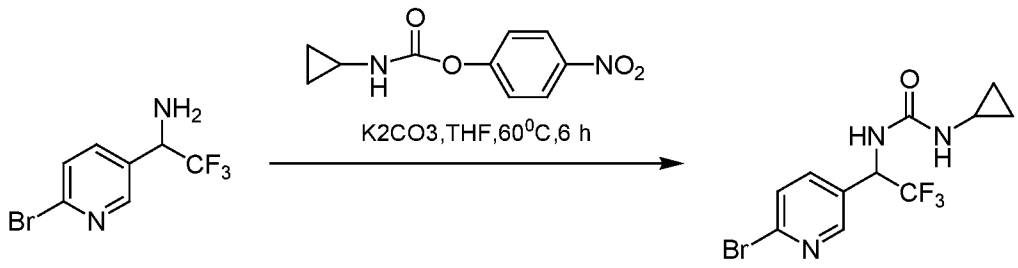
249 250

To a stirred solution of 1-(6-bromopyridin-3-yl)-2,2,2-trifluoroethyl trifluoromethanesulfonate (0.650g, 0.167 mmol) in DMF (5 ml) was added sodium azide (0.108g, 0.167 mmol) at room

temperature. Stirred reaction mixture at same temperature for 6h. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give pure intermediate. To solution of Azide intermediate (0.550g, 0.192 mmol) was added TPP (0.512g, 0.192 mmol) in THF:H_2O (8:2ml) at RT and then stirring continued at 60^0C for 12 h. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 20-30% acetone in hexane to obtained 1-(6-bromopyridin-3-yl)-2,2,2-trifluoroethanamine (0.160 g, 32 %) as yellow oil.

MS: 255.1 [M+1]

Step-3: Synthesis 1-(1-(6-bromopyridin-3-yl)-2,2,2-trifluoroethyl)-3-cyclopropylurea

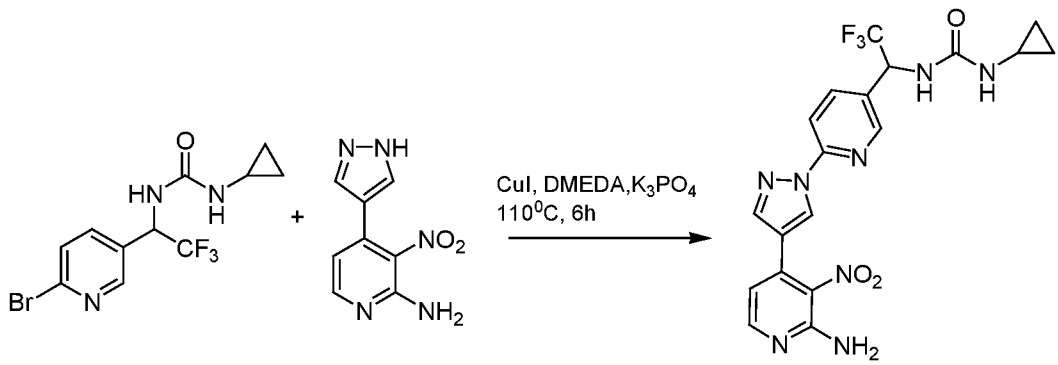


251 252

To a stirred solution of 1-(6-bromopyridin-3-yl)-2,2,2-trifluoroethanamine (0.200g, 0.078 mmol) in THF (10.0 mL), potassium carbonate (0.107 g , 0.078 mmol) was added followed by 4-nitrophenyl cyclopropylcarbamate (0.248 g , 0.011 mmol). The resultant reaction mixture was stirred for 6h at 60^0C. Completion of reaction was monitored by TLC. On completion, quenched with water, extracted with ethyl acetate. The combined organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 15 to 20 % Acetone/Hexane to obtained (0.120 g, 50.84%) as white solid.

MS: 338[M+1]

Step-4: Synthesis of 1-(1-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethyl)-3-cyclopropylurea

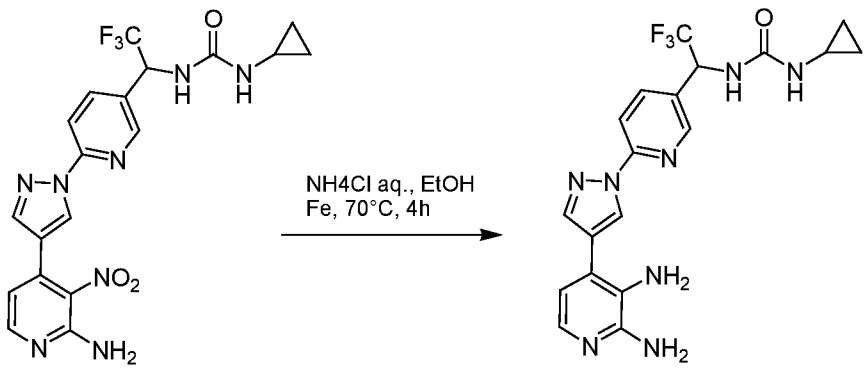


253 254 255

To a stirred solution of 3-nitro-4-(1H-pyrazol-4-yl) pyridin-2-amine (0.090g, 0.0443 mmol) and compound 1-(1-(6-bromopyridin-3-yl)-2,2,2-trifluoroethyl)-3-cyclopropylurea (0.150g, 0.0443 mmol) in Dioxane (5 ml) was added K_3PO_4 (0.122g, 0.0886 mmol) followed by CuI (0.016g, 0.00886 mmol) and DMEDA (0.077g, 0.0886 mmol). Reaction was heated at 110°C for 6h. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 9-10% MeOH in DCM to obtained 1-(1-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethyl)-3-cyclopropylurea (0.090 g, 45 %) as yellow solid.

MS: 463.1 [M+1]

Step-5: Synthesis 1-(1-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethyl)-3-cyclopropylurea

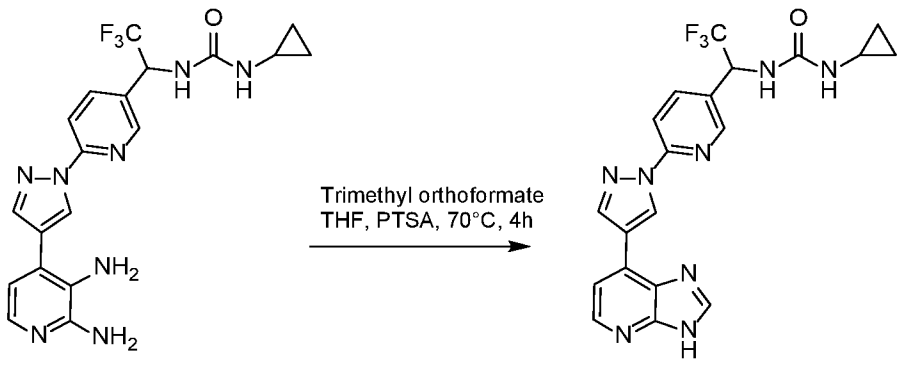


256 257

To a stirred solution of 1-(1-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethyl)-3-cyclopropylurea (0.085g, 0.0183 mmol) in EtOH (7.0 mL), NH_4Cl (2.0 mL) was added at room temperature. To the resultant reaction mixture, Fe powder (0.048 g, 0.0919 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, reaction mixture was diluted with H_2O: EtOAc (50 mL, 5:5) and pass over celite to remove inorganic impurities from the reaction mixture. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to obtained pure 1-(1-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethyl)-3-cyclopropylurea (0.045g, 56.96%) as dark brown solid mass.

MS: 433.2 [M+1]

Step-6: Synthesis of 1-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethyl)-3-cyclopropylurea:

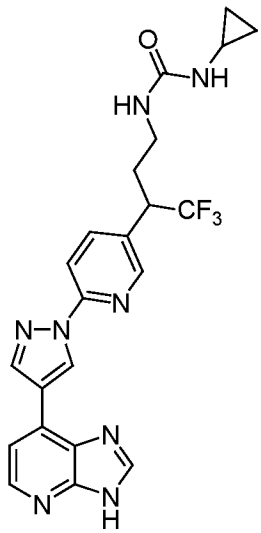


258 1178

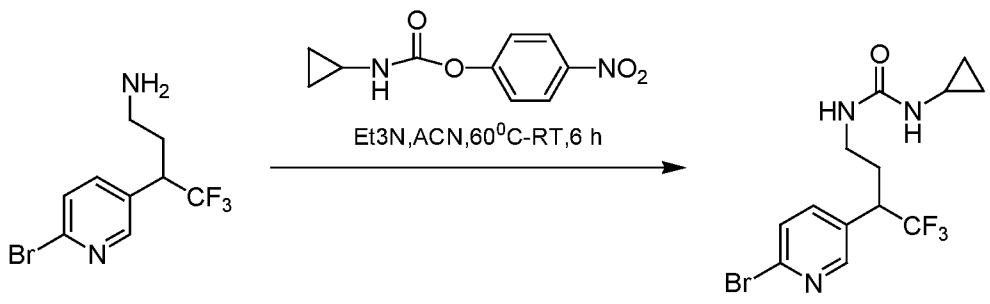
To a stirred solution of 1-(1-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethyl)-3-cyclopropylurea ((0.045g, 0.0104 mmol) in THF (1.0 mL), Trimethyl orthoformate (1.5 mL) was added. To resultant reaction mixture, PTSA (0.0035 g, 0.0020 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with 10% MeOH in DCM. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 10 to 11% MeOH in DCM to obtained 1-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethyl)-3-cyclopropylurea (0.023 g, 51%) as off white solid.

MS: 443.1 [M+1]

Synthesis of Compound No. 1179: 1-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)-3-cyclopropylurea



Step-1: Synthesis of 1-(3-(6-bromopyridin-3-yl)-4,4,4-trifluorobutyl)-3-cyclopropylurea :

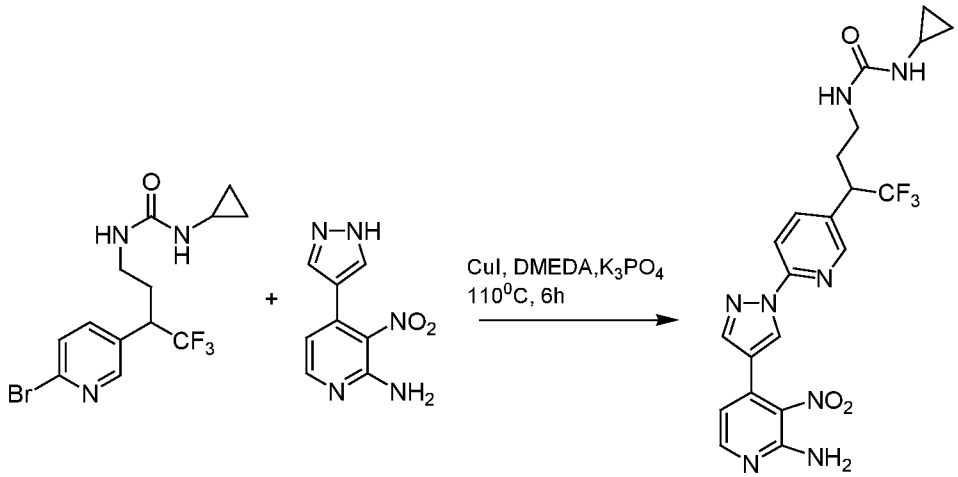


259 260

To a stirred solution of 3-(6-bromopyridin-3-yl)-4,4,4-trifluorobutan-1-amine (0.130g, 0.045 mmol) in ACN (10.0 mL), trimethylamine (0.136 g , 0.135 mmol) was added followed by 4-nitrophenyl cyclopropylcarbamate (0.152 g , 0.068 mmol). The resultant reaction mixture was stirred for 6h at 60^0C. Completion of reaction was monitored by TLC. On completion, quenched with water, extracted with ethyl acetate. The combined organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 25 to 30 % Acetone/Hexane to obtained (0.140 g, 83.83%) as sticky oil.

MS: 367[M+2]

Step-2: Synthesis of 1-(3-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)-3-cyclopropylurea

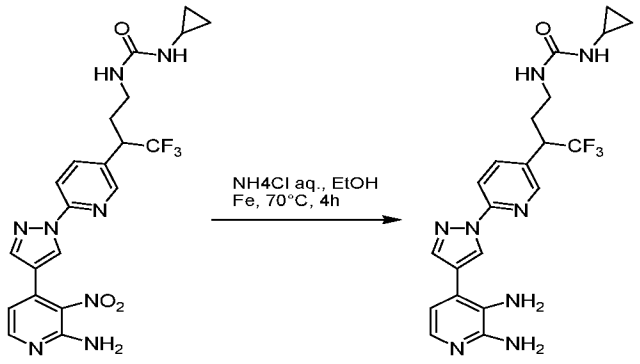


261 262 263

To a stirred solution of 3-nitro-4-(1H-pyrazol-4-yl) pyridin-2-amine (0.073g, 0.0356 mmol) and compound 1-(3-(6-bromopyridin-3-yl)-4,4,4-trifluorobutyl)-3-cyclopropylurea (0.130g, 0.0356 mmol) in Dioxane (5 ml) was added K_3PO_4 (0.150g, 0.0712 mmol) followed by CuI (0.013g, 0.00712 mmol) and DMEDA (0.062g, 0.0712 mmol). Reaction was heated at 110°C for 6h. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 7-8% MeOH in DCM to obtained 1-(3-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)-3-cyclopropylurea (0.080 g, 45.97 %) as yellow solid.

MS: 491.1 [M+1]

Step-3: Synthesis 1-(3-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)-3-cyclopropylurea

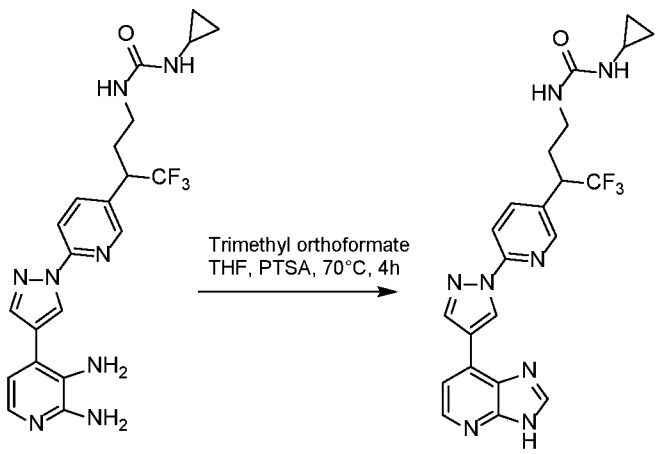


264 265

To a stirred solution of 1-(3-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)-3-cyclopropylurea (0.060g, 0.0122 mmol) in EtOH (7.0 mL), NH_4Cl (2.0 mL) was added at room temperature. To the resultant reaction mixture, Fe powder (0.032 g, 0.0612 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, reaction mixture was diluted with H_2O: EtOAc (50 mL, 5:5) and pass over celite to remove inorganic impurities from the reaction mixture. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to obtained pure 1-(3-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)-3-cyclopropylurea (0.042g, 75%) as dark brown solid mass.

MS: 461.2 [M+1]

Step-4: Synthesis of 1-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)-3-cyclopropylurea:

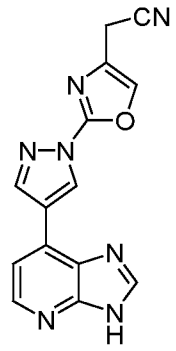


266 1179

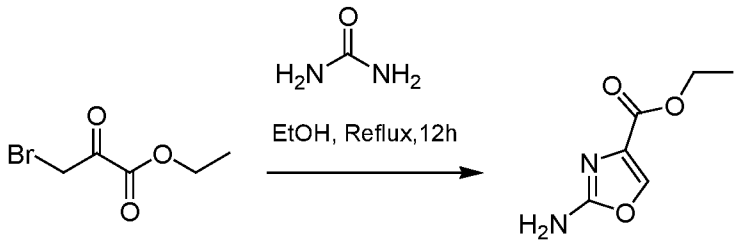
To a stirred solution of 1-(3-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)-3-cyclopropylurea ((0.042g, 0.0091 mmol) in THF (1.0 mL), Trimethyl orthoformate (1.5 mL) was added. To resultant reaction mixture, PTSA (0.0031 g, 0.0018 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with 10% MeOH in DCM. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 8 to 9% MeOH in DCM to obtained 1-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)-3-cyclopropylurea (0.021 g, 48.83%) as off white solid.

MS: 471.1 [M+1]

Synthesis of Compound No. 1075: 2-(2-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)oxazol-4-yl)acetonitrile



Step-1: Synthesis of ethyl 2-aminooxazole-4-carboxylate



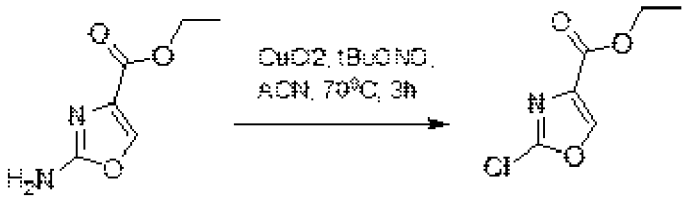
267 268

To a stirred solution of ethyl 3-bromo-2-oxopropanoate (1.0 g, 5.128 mmol) in ethanol (20 mL**),** urea (0.462g, 7.692 mmol) was added at room temprature. The resultant reaction mixture was stirred at reflux temprature for overnight. Completion of reaction was monitored by TLC. On completion, quenched with ice water, extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate, concentrated under reduced pressure

obtained crude reaction mass. Purification of the crude was done *via* silica gel (100-200 Mesh) column chromatography and desired compound eluted at 40% ethyl acetate/n-Heaxane to obtained ethyl 2-aminooxazole-4-carboxylate (0.700g, 87.5%) as cream colour solid.

MS: 157.2 [M+1]

Step-2: synthesis of ethyl 2-chlorooxazole-4-carboxylate:

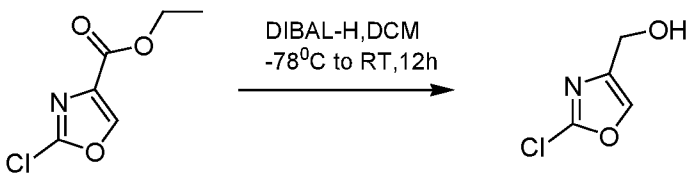


269 270

To a stirred solution of $CuCl_2$ (1.29 g, 9.609 mmol) in ACN (20 mL), ter-butylnitrile (0.991 g, 9.609 mmol) was added at room temperature. To resultant reaction mass was heated at 65^0C. Added compound ethyl 2-aminooxazole-4-carboxylate (1.0 g, 6.406 mmol) was added portion wise at 65^0C and stirring continued for 2h. Completion of reaction was monitored by TLC. Reaction mixture was cooled to 0^0C and acidify with 6N HCl and extracted with ether. The organic layer was washed with water, brine, dried over sodium sulphate, concentrated under reduced pressure to obtained crude reaction mass. Purification of the crude was done *via* silica gel (100-200 Mesh) column chromatography and desired compound eluted at 18% ethyl acetate/n-Hexane to obtained ethyl 2-chlorooxazole-4-carboxylate (0500 g, 44.6%) as brown solid.

MS: 176 [M+1]

Step-3: Synthesis of (2-chlorooxazol-4-yl) methanol



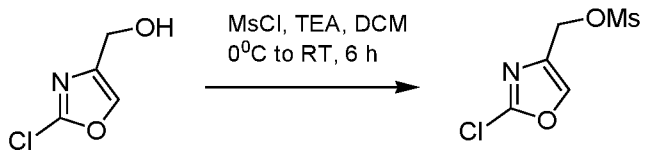
271 272

To a stirred solution of ethyl 2-chlorooxazole-4-carboxylate (0.400g, 2.271 mmol) in DCM (10 mL) cooled it to -78^0C under inert condition. Added DIBAL-H (3.4 ml, 3.410 mmol) at -78^0C and stirring continued for 1h for same temprature. After that stirred it at room temperature

for 16h. Completion of reaction was monitored by TLC. Reaction mixture was quenched with crushed ice, followed by 1N HCl, extracted with ether. The organic layer was washed with water, brine, dried over sodium sulphate, concentrated under reduced pressure to obtained crude (2-chlorooxazol-4-yl)methanol (0.250g, 82.5%) as yellow liquid, which is used as such for next step.

MS: 134.1[M+1]

Step-4: Synthesis of (2-chlorooxazol-4-yl) methyl methanesulfonate

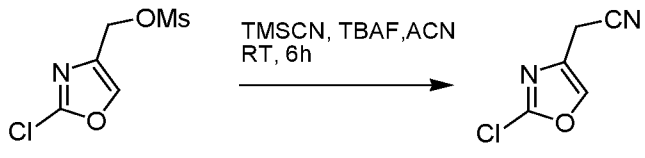


273 274

To a stirred solution of (2-chlorooxazol-4-yl) methanol (0.10g, 0.749 mmol) in DCM (10 mL), base triethylamine (0.114g, 1.123 mmol) was added at room temperature and cooled it to 0^0C. Added mesyl chloride (0.103g, 0.898 mmol) dropwise at 0^0C and stirring continued for 6h. Completion of reaction was monitored by TLC. On completion, quenched with water, extracted with DCM. Combine organic layer was dried over sodium sulphate, concentrated under reduced pressure obtained pure (2-chlorooxazol-4-yl)methyl methanesulfonate (0.155g, 97.77%) as off white solid.

MS: 211.1 [M+1]

Step-5: Synthesis of 2-(2-chlorooxazol-4-yl)acetonitrile



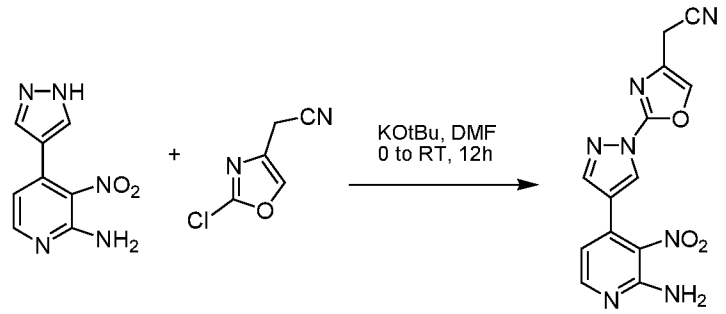
275 276

To a stirred solution of (2-chlorooxazol-4-yl)methyl methanesulfonate (0.500g, 2.362 mmol) in ACN (10 mL), TBAF 1M in THF (4.72 ml, 4.725 mmol) was added at room temperature and then added TMSCN (0.469g, 4.725 mmol). Stirred resultant reaction mixture for 6h at room temprature. Completion of reaction was monitored by TLC. On completion, quenched with water, extracted with ethyl acetate, dried over sodium sulphate, concentrated under reduced pressure to obtained crude reaction mass. Purification of the crude was done *via* silica gel (100-

200 Mesh) column chromatography and desired compound eluted at 18% ethyl acetate/n-Hexane to obtained pure 2-(2-chlorooxazol-4-yl)acetonitrile (0.210g, 62.31%) as white solid.

MS: 143.2 [M+1]

Step-6: Synthesis of 2-(2-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)oxazol-4-yl)acetonitrile

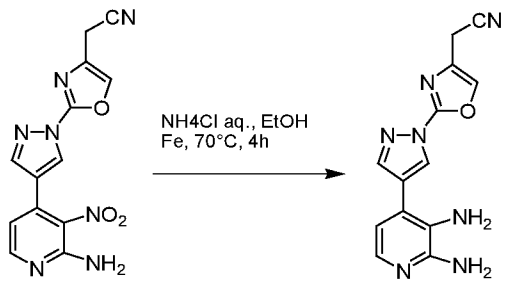


277 278 279

To a stirred solution of 3-nitro-4-(1H-pyrazol-4-yl) pyridin-2-amine (0.040g, 0.195 mmol), DMF (4 ml), potassium ter-butoxide (0.022g, 0.195 mmol) and compound 2-(2-chlorooxazol-4-yl)acetonitrile (0.028g, 0.39 mmol) was added at room temprature. Reaction was heated at 80°C for 12h. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 5-6% MeOH in DCM to obtained 2-(2-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)oxazol-4-yl)acetonitrile (0.030 g, 49.45 %) as yellow solid.

MS: 312.1 [M+1]

Step-7 : Synthesis of 2-(2-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)oxazol-4-yl)acetonitrile

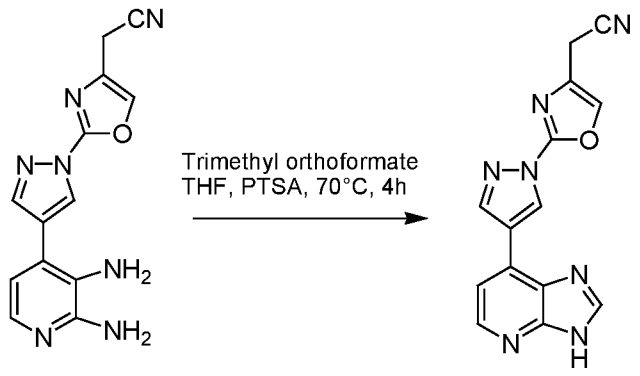


280 281

To a stirred solution of 2-(2-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)oxazol-4-yl)acetonitrile (0.030g, 0.096 mmol) in EtOH (3.0 mL), NH_4Cl (2.5 mL) was added at room temperature. To resultant reaction mixture, Fe powder (0.017 g, 0.48 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, reaction mixture was diluted with H_2O: EtOAc (50 mL, 5:5) and pass over celite to remove inorganic impurities from the reaction mixture. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to obtained 2-(2-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)oxazol-4-yl)acetonitrile (0.025 g, 92 %) as dark brown solid mass.

MS: 283.2 [M+1]

Step-8: Synthesis of 2-(2-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)oxazol-4-yl)acetonitrile

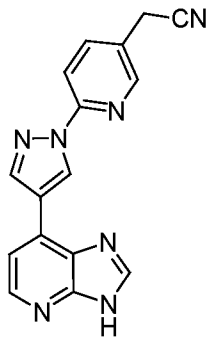


282 1075

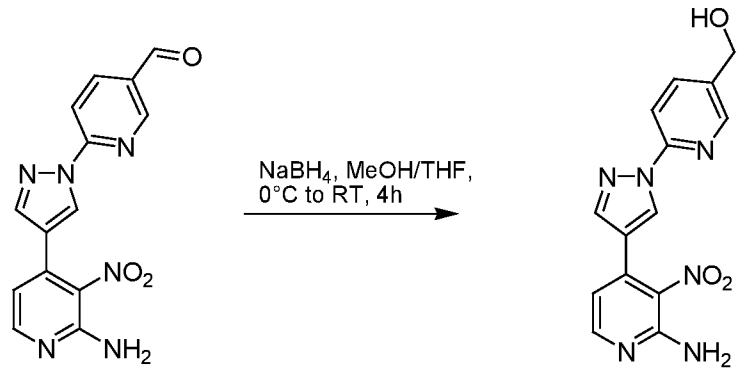
To a stirred solution of 2-(2-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)oxazol-4-yl)acetonitrile (0.025g, 0.088 mmol) in THF (1.0 mL), trimethyl orthoformate (1.5 mL) was added. To resultant reaction mixture, PTSA (0.003 g, 0.0017 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with 10% MeOH in DCM. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 6 to 7% MeOH in DCM to obtained 2-(2-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)oxazol-4-yl)acetonitrile (0.011 g, 44%) as off white solid.

MS: 293.1[M+1]

Synthesis of Compound No. 1078: 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)acetonitrile



Step-1: Synthesis of (6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)methanol:

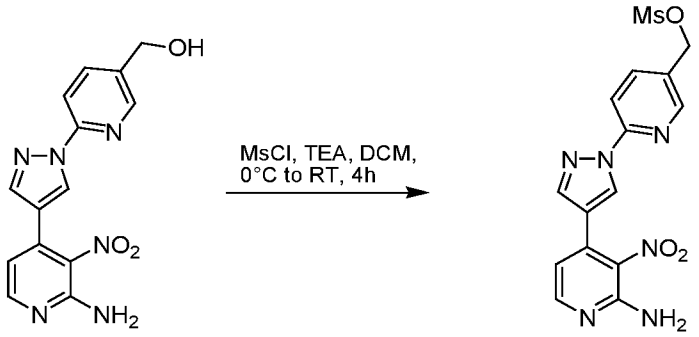


283 284

To a stirred solution solution of 6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridine-3-carbaldehyde (0.50 g, 1.612 mmol) in methanol/THF (10 mL, 1:1) was added sodium borohydride (0.069 g, 1.612 mmol) at 0°C and the mixture was stirred at room temperature for 3h. Progress of reaction was monitored by TLC. After reaction completion water (10 mL) was added to the reaction mixture and the product extracted with ethyl acetate. The organic layer was dried over sodium sulphate, concentrated under reduced pressure to give (6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)methanol (0.5 g, 100%) as yellow solid.

MS: 313.28 [M+1]

Step-2: Synthesis of (6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)methyl methanesulfonate

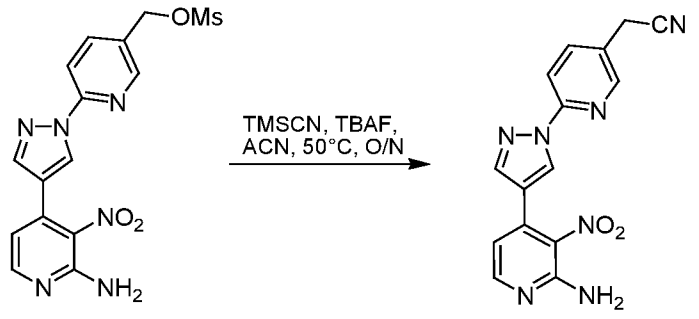


285 286

To a stirred solution of (6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)methanol (0.15 g, 0.480 mmol) in DCM (5.0 mL) at 0°C was added MsCl (0.06 g, 0.528 mmol) under nitrogen. To resultant reaction mixture TEA (0.063 g, 0.629 mmol) solution in DCM (1.0 mL) was added drop wise, stirred for 15 min at 0°C and then warmed to RT and progress of reaction was monitored by TLC. On completion, quenched with water, extracted with ethyl acetate. Organic layer was dried over sodium sulphate, concentrated under reduced pressure to obtain (6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl) pyridin-3-yl) methyl methanesulfonate (0.19 g, 100 %) as crude yellow oily mass.

MS: 391.37 [M+1]

Step-3: synthesis of 2-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)acetonitrile



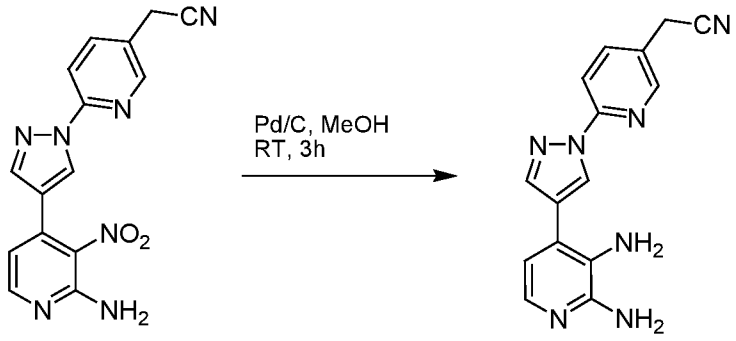
287 288

To a stirred solution of (6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl) pyridin-3-yl) methyl methanesulfonate (0.25 g, 0.641 mmol) in ACN (5 mL) at 0°C was added TMSCN (0.13 g, 1.282 mmol) under nitrogen followed by TBAF (1M solution in THF, 1.3 mL, 1.282 mmol) and the resulted solution heated overnight at 50°C. Progress of reaction was monitored by TLC. After reaction completion reaction mass was cooled to 0°C and quenched with 1M HCl. Product

was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 1% MeOH/DCM as eluent to obtain 2-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)acetonitrile (0.08 g, 40 %) as yellow oil.

MS: 322.29 [M+1]

Step-4: Synthesis of 2-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)acetonitrile

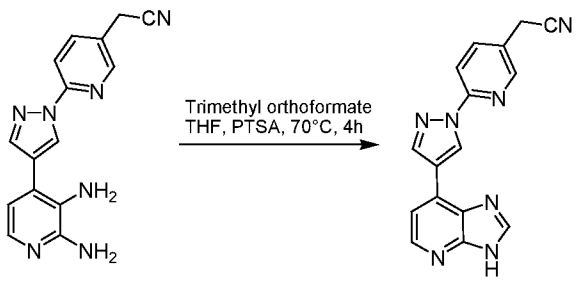


289 290

To a stirred solution of 2-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)acetonitrile (0.05 g, 0.1557 mmol) in methanol (5 mL) was hydrogenated by 10% Pd/C (0.005 g, 10 % wt/wt) using hydrogen balloon. Progress of the reaction was monitored by TLC. After reaction completion reaction mass filtered through celite and filtrate was evaporated under reduced pressure to give 2-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)acetonitrile (0.044 g, 99 %) as brown solid.

MS: 292.31 [M+1]

Step-5: Synthesis of 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)acetonitrile

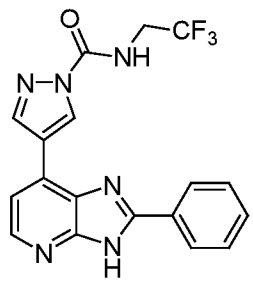


291 1078

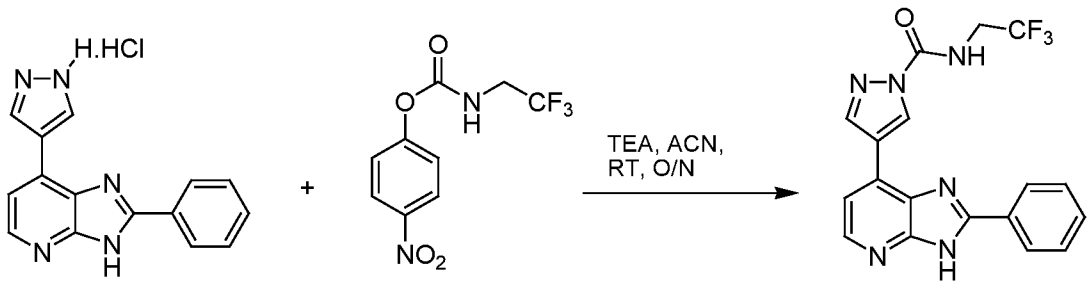
To a stirred solution of 2-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)acetonitrile (0.045 g, 0.1512 mmol) in THF (1.0 mL), trimethyl orthoformate (1.0 mL) was added. To resultant reaction mixture, PTSA (0.005 g, 0.0302 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, quenched with aq. sodium bicarbonate solution, extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 3% to 5% MeOH in DCM to obtain 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)acetonitrile (0.05 g, 10 %) as off white solid.

MS: 302.31 [M+1]

Synthesis of Compound No. 1094: N-(2,2,2-trifluoroethyl)-4-(2-phenyl-3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide



Step-1: Synthesis of N-(2,2,2-trifluoroethyl)-4-(2-phenyl-3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide:



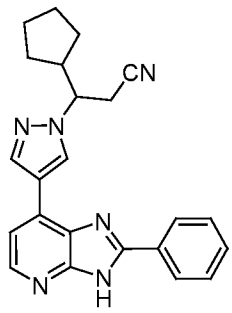
292 293 1094

To a stirred solution of tert-butyl 2-phenyl-7-(1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine hydrochloride (0.015 g, 0.05042 mmol) and 4-nitrophenyl 2,2,2-trifluoroethylcarbamate (0.013 g, 0.05042 mmol) in anhydrous ACN (3 mL) was added triethylamine (0.01 g, 0.1008 mmol) and stirred at RT overnight. Progress of reaction was monitored by TLC. After reaction completion reaction mass was quenched with ice cold water and extracted with ethyl acetate.

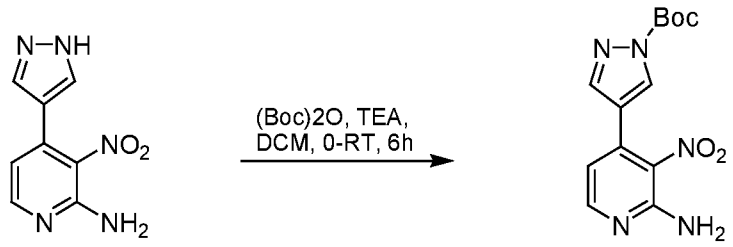
The organic layer was dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 2 % methanol in DCM as eluent to yield N-(2,2,2-trifluoroethyl)-4-(2-phenyl-3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide (0.004 g, 20 %) as white solid.

MS: 387.33 [M+1]

Synthesis of Compound No. 1180: 3-cyclopentyl-3-(4-(2-phenyl-3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)propanenitrile



Step-1: Synthesis of tert-butyl 4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazole-1-carboxylate:

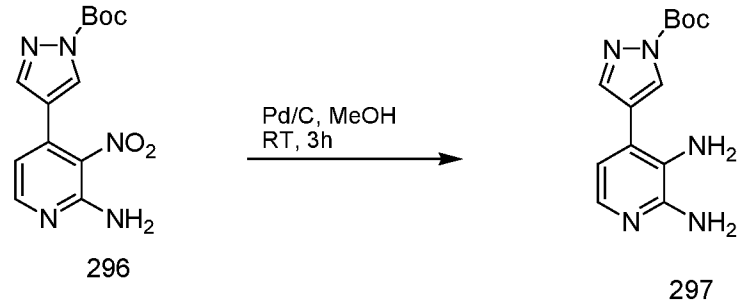


295 296

To a stirred solution of 3-nitro-4-(1H-pyrazol-4-yl)pyridin-2-amine (1 g, 4.878 mmol) in DCM (10 mL) was added TEA (2.0 mL, 14.634 mmol) dropwise at room temperature and reaction allowed to stir for 15 min. After 15 min Boc anhydride (1.59 g, 7.317 mmol) was added it and stirred for 6h. Reaction was monitored by TLC. On completion reaction was quenched with water, extracted with DCM. The organic layer was washed with water, $NaHCO_3$, brine, dried over Na_2SO_4, evaporated under reduced pressure. Crude was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 1% MeOH in DCM to obtain tert-butyl 4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazole-1-carboxylate (1.2 g, 81.0 %) as yellow solid.

MS: 306.29 [M+1]

Step-2: Synthesis of tert-butyl 4-(2,3-diaminopyridin-4-yl)-1H-pyrazole-1-carboxylate:

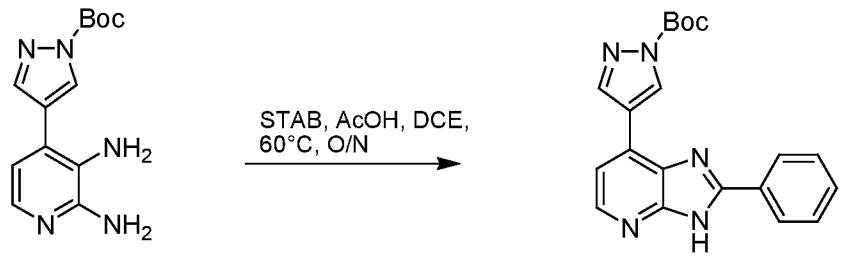


296 297

To a stirred solution of tert-butyl 4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazole-1-carboxylate (0.5 g, 1.639 mmol) in methanol (5 mL) was hydrogenated by 10% Pd/C (0.05 g, 10 % wt/wt) using hydrogen balloon. Progress of the reaction was monitored by TLC. After reaction completion reaction mass filtered through celite and filtrate was evaporated under reduced pressure to give tert-butyl 4-(2,3-diaminopyridin-4-yl)-1H-pyrazole-1-carboxylate (0.45 g, 99.8 %) as brown solid.

MS: 276.31 [M+1]

Step-3: Synthesis of tert-butyl 4-(2-phenyl-3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxylate:

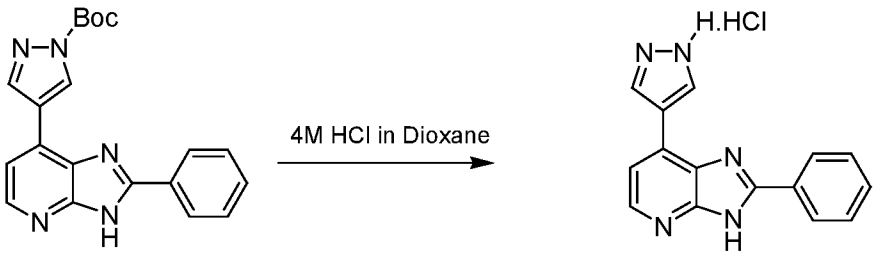


298 299

To a stirred solution of tert-butyl 4-(2,3-diaminopyridin-4-yl)-1H-pyrazole-1-carboxylate (0.4 g, 1.452 mmol) and benzaldehyde (0.15 g, 1.452 mmol) in DCE (5 mL) at 0°C was added AcOH (0.4 mL) and stirred for 30 min. Sodium triacetoxyborohydride (0.13 g, 2.179 mmol) was then added and the resulting mixture was heated overnight at 60°C. Progress of reaction was monitored by TLC. After reaction completion reaction mass was cooled to 0°C and quenched with ice water. Product was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 1% MeOH/DCM as eluent to obtain tert-butyl 4-(2-phenyl-3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxylate (0.3 g, 57.1 %) as white solid.

MS: 362.4 [M+1]

Step-4: Synthesis of tert-butyl 2-phenyl-7-(1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine hydrochloride :

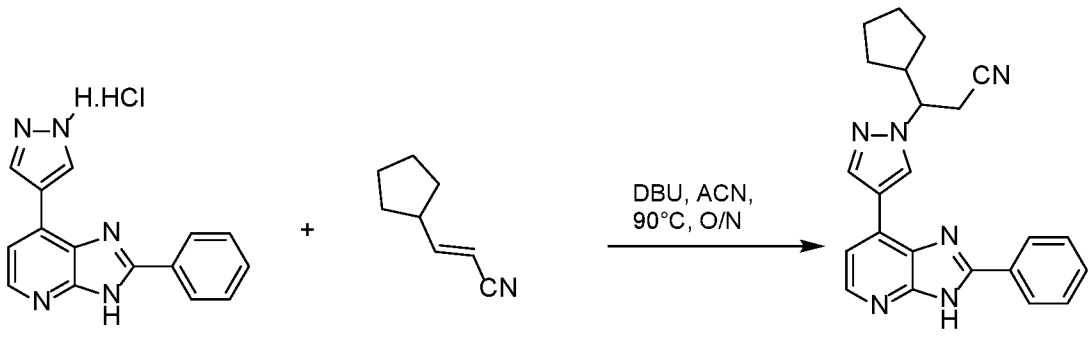


300 301

To tert-butyl 4-(2-phenyl-3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxylate (0.3 g, 0.831 mmol) was added 4 M HCl in Dioxane (3 mL) and stirred at room temperature for 3h. Progress of reaction was monitored by TLC. After reaction completion reaction mass was concentrated under reduced pressure, washed with diethyl ether and dried to give tert-butyl 2-phenyl-7-(1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine hydrochloride (0.25g, 100%) as white solid.

MS: 298.4 [M+1]

Step-5: Synthesis of 3-cyclopentyl-3-(4-(2-phenyl-3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)propanenitrile:



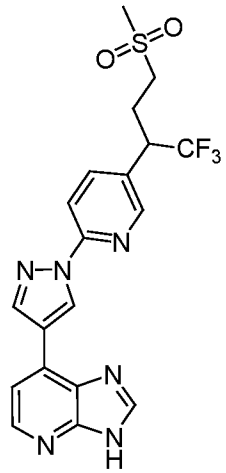
302 303 1180

To a stirred solution of tert-butyl 2-phenyl-7-(1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine hydrochloride (0.03 g, 0.115 mmol) and 3-cyclopentylacrylonitrile (0.015 g, 0.126 mmol) in anhydrous ACN (5 mL) was added DBU (0.052 g, 0.3448 mmol) and heated overnight at 90° C. Progress of reaction was monitored by TLC. After reaction completion reaction mass was

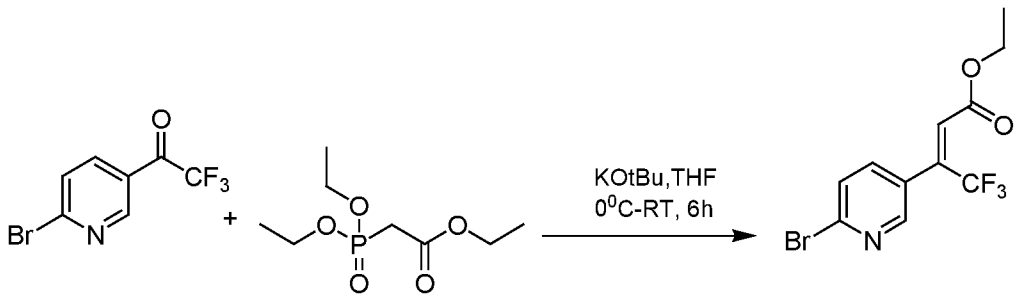
quenched with ice cold water and extracted with ethyl acetate. The organic layer was dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 3 % methanol in DCM as eluent to yield 3-cyclopentyl-3-(4-(2-phenyl-3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)propanenitrile (0.005 g, 11.3 %) as white solid.

MS: 383.46 [M+1]

Synthesis of Compound No. 1174: 7-(1-(6-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine



Step-1: Synthesis of (E/Z)-ethyl 3-(6-bromopyridin-3-yl)-4,4,4-trifluorobut-2-enoate



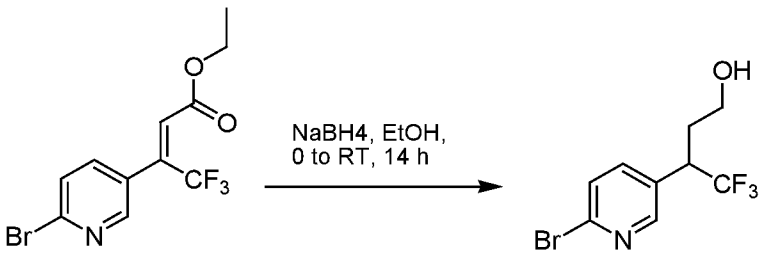
304 305 306

To a stirred solution of Triethyl phosphonoacetate (3.9g, 1.77 mmol) and THF (60 ml) at 0^0C under N_2 added base potassium ter-butoxide (1.98g, 1.77 mmol) lotwise. The resultant mixture was stirred at RT for 1h for anion generation. A solution of 1-(6-bromopyridin-3-yl)-2,2,2-trifluoroethanone (3.0 g, 1.18 mmol) in THF (15 ml) was added slowly. After addition stirred mixture for 6h at RT. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude

desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 9 to 15% EA/Hexane to obtained (E/Z)-ethyl 3-(6-bromopyridin-2-yl)-4,4,4-trifluorobut-2-enoate (1.5 g, 40%) as yellow oil.

MS: 324 [M+1]

Step-2: Synthesis of 3-(6-bromopyridin-3-yl)-4,4,4-trifluorobutan-1-ol:

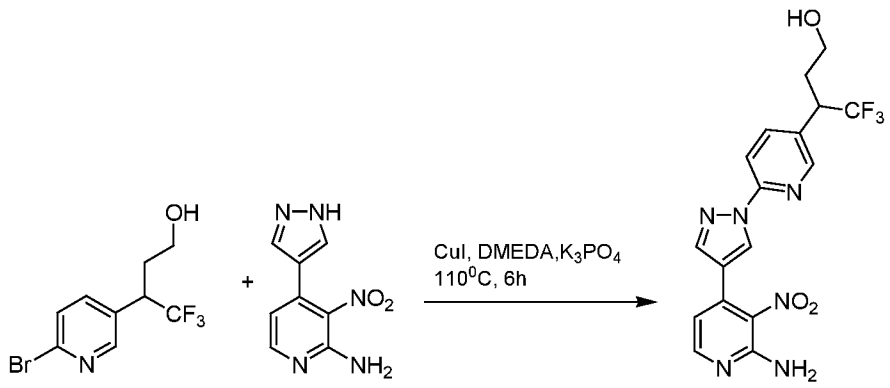


307 308

To a stirred solution of (E/Z)-ethyl 3-(6-bromopyridin-3-yl)-4,4,4-trifluorobut-2-enoate (1.5g, 462 mmol) in EtOH (30 mL), $NaBH_4$ (0.520g, 1380 mmol) was added at 0°C. Reaction was allowed to stir at room temperature for 14h. Reaction was monitored by TLC. On completion, reaction was quenched with water, extracted with EtOAc. The organic layer was washed with water, dried over Na_2SO_4, evaporated under reduced pressure to obtain crude reaction mass. Purification of the crude was done *via* silica gel (100-200 Mesh) column chromatography and desired compound eluted at 30% ethyl acetate/n-Hexane to obtained3-(6-bromopyridin-3-yl)-4,4,4-trifluorobutan-1-ol (0.610g, 46.5%) as clear oil.

MS: 284 [M+1]

Step-3: Synthesis of 3-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutan-1-ol

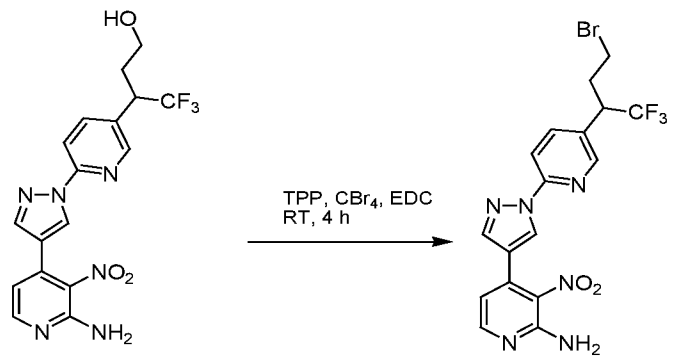


309 310 311

To a stirred solution of 3-nitro-4-(1H-pyrazol-4-yl) pyridin-2-amine (0.253g, 123 mmol) and compound 3-(6-bromopyridin-3-yl)-4,4,4-trifluorobutan-1-ol (0.350g, 123 mmol) in Dioxane (5 ml) was added K_3PO_4 (0.521g, 246 mmol) followed by CuI (0.046g, 0.246 mmol) and DMEDA (0.216g, 246 mmol). Reaction was heated at 110°C for 6h. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 6-7% MeOH in DCM to obtained 3-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutan-1-ol (0.250 g, 50 %) as yellow solid.

MS: 409.1 [M+1]

Step-4: Synthesis of 4-(1-(5-(4-bromo-1,1,1-trifluorobutan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine

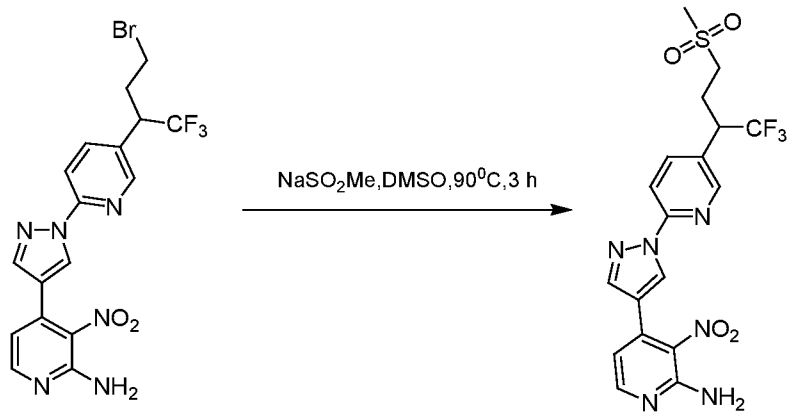


312 313

To a stirred solution of 3-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutan-1-ol (0.120 g, 0.29 mmol) in DCE (10 mL), TPP (0.115 g, 0.44 mmol) was added and then added carbontetrabromide (0.145 g, 0.44 mmol) portion-wise at 0°C. The resultant reaction mixture was stirred at room temprature for 7h. Completion of reaction was monitored by TLC. After completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with DCM. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude product was purified by silica gel (100-200 mesh) column chromatography using 2 to 3% methanol in DCMA as eluent to obtain 4-(1-(5-(4-bromo-1,1,1-trifluorobutan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine (0.065 g, 47.05 %) as yellow solid.

MS: 471.1 [M+1]

Step-5: Synthesis of 4-(1-(5-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine:

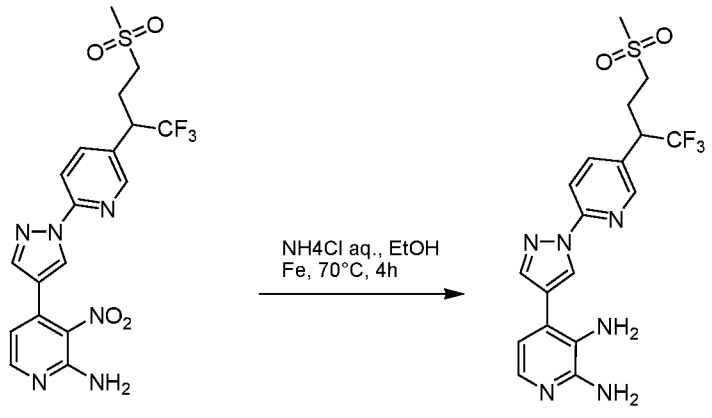


314 315

To a stirred solution of 4-(1-(5-(4-bromo-1,1,1-trifluorobutan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine (0.065g, 0.130 mmol) in DMSO (3.0 mL), sodium mathanesulfinate (0.027g, 0.20 mmol) was added. To resultant reaction mixture was added stirred for 3h at 90°C. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 6 to 7% MeOH/DCM to obtained 4-(1-(5-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine (0.052 g, 81.20%) as yellow solid.

MS: 471[M+1]

Step-6: Synthesis of 4-(1-(5-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)pyridine-2,3-diamine:

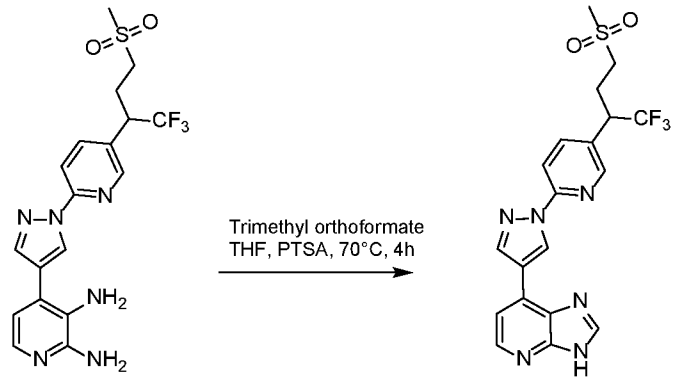


316 317

To a stirred solution of 4-(1-(5-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3-nitropyridin-2-amine (0.052g, 0.11 mmol) in EtOH (7.0 mL), NH_4Cl (2.0 mL) was added at room temperature. To the resultant reaction mixture, Fe powder (0.029 g, 0.55 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, reaction mixture was diluted with H_2O: EtOAc (50 mL, 5:5) and pass over celite to remove inorganic impurities from the reaction mixture. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to obtained pure 4-(1-(5-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)pyridine-2,3-diamine (0.036g, 75%) as dark brown solid mass.

MS: 441.2 [M+1]

Step-7: Synthesis of 7-(1-(5-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine:

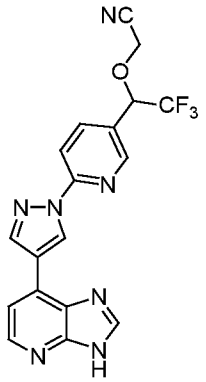


318 1174

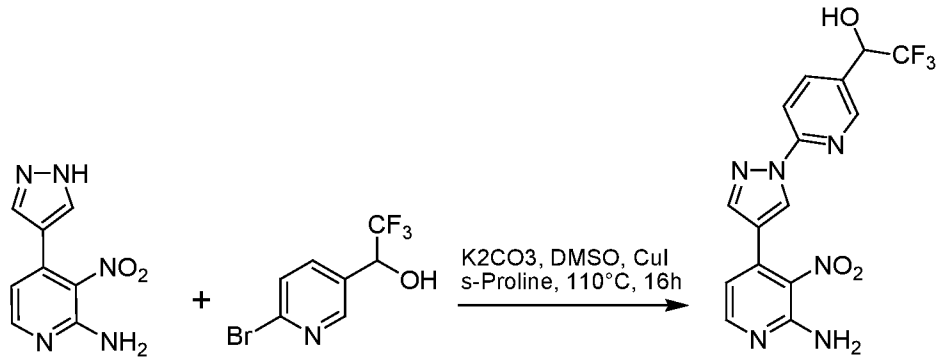
To a stirred solution of 4-(1-(5-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)pyridine-2,3-diamine (0.035g, 0.079 mmol) in THF (1.0 mL), Trimethyl orthoformate (1.5 mL) was added. To resultant reaction mixture, PTSA (0.0027 g, 0.015 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with 10% MeOH in DCM. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 8 to 9% MeOH in DCM to obtained 7-(1-(5-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine (0.021 g, 60%) as off white solid.

MS: 451.1 [M+1]

Synthesis of Compound No. 1157: 2-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethoxy)acetonitrile



Step-1: Synthesis of 1-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethanol

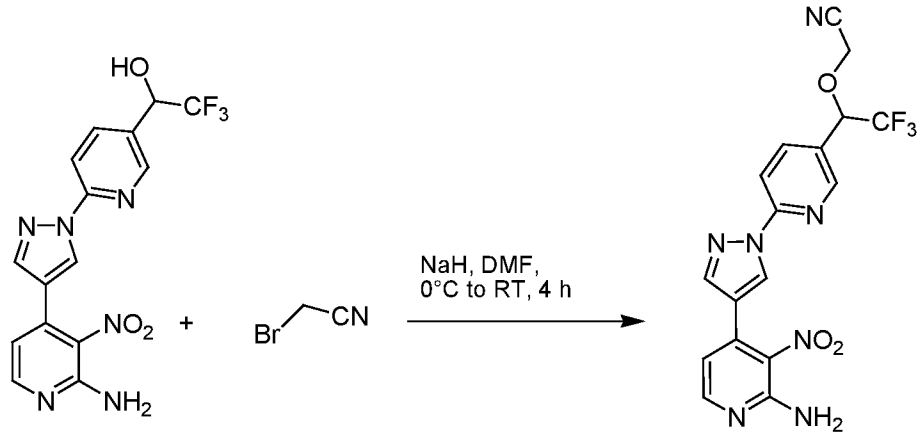


319 320 321

To a stirred solution of 3-nitro-4-(1H-pyrazol-4-yl) pyridin-2-amine (0.500 g, 2.439 mmol) and compound 1-(6-bromopyridin-3-yl)-2,2,2-trifluoroethanol (0.68 g, 2.682 mmol) in DMSO (5 ml) was added K_2CO_3 (1.0 g, 7.317 mmol) followed by CuI (0.045 g, 0.243 mmol) and s-Proline (0.146 g, 1.219 mmol). Reaction was heated at 110°C for 16h. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 2-3% MeOH in DCM to obtained 1-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethanol (0.35 g, 37.8 %) as yellow solid.

MS: 381.28 [M+1]

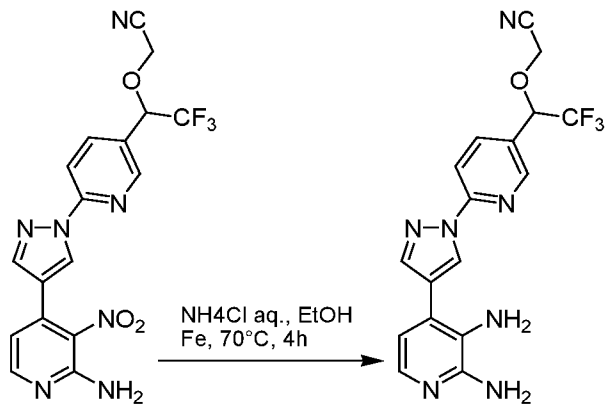
Step-2: synthesis of 2-(1-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethoxy)acetonitrile



322 323

To a stirred solution of 1-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethanol (0.3 g, 0.7894 mmol) in DMF (10 mL) at 0°C was added NaH (0.31 g, 0.7894 mmol) under nitrogen and stirred for 30 min. at same temperature. To resultant reaction mass 2-bromoacetonitrile (0.094 g, 0.7894 mmol) was added and stirred for 4h at RT. Progress of reaction was monitored by TLC. After reaction completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 1 % Methanol in DCM as eluent to obtain 2-(1-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethoxy)acetonitrile (0.14 g, 42.4 %) as yellow solid.
MS: 420.32 [M+1]

Step-3: Synthesis of 2-(1-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethoxy)acetonitrile

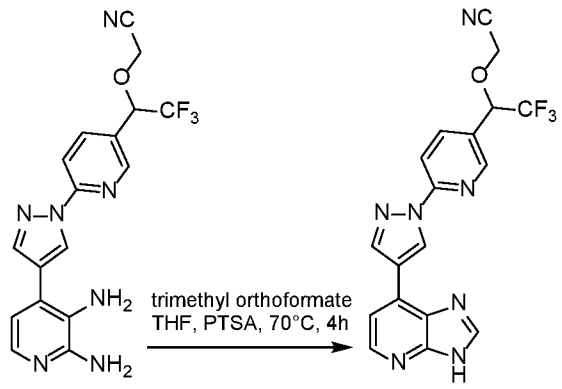


324 325

To a stirred solution of 2-(1-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethoxy)acetonitrile (0.050g, 0.119 mmol) in EtOH (10 mL), NH4Cl (2.5 mL) was added at room temperature. To resultant reaction mixture, Fe powder (0.033 g, 0.59 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, reaction mixture was diluted with H_2O: EtOAc (50 mL, 5:5) and filtered through celite to remove inorganic impurities from the reaction mixture. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to obtained pure 2-(1-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethoxy)acetonitrile (0.040 g, 86.9 %) as dark brown solid mass.

MS: 389.33 [M+1]

Step-4: Synthesis of 2-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethoxy)acetonitrile

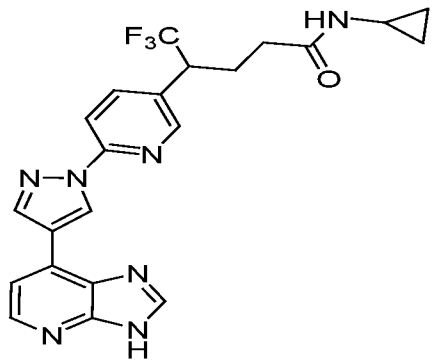


326 1157

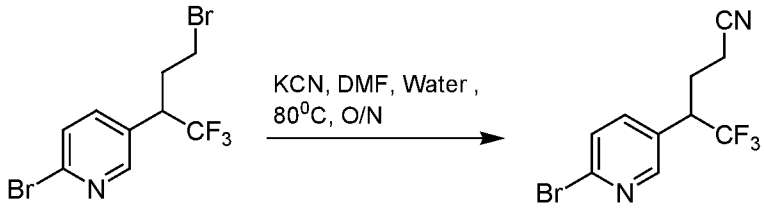
To a stirred solution of 2-(1-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethoxy)acetonitrile (0.040g, 0.102 mmol) in THF (3.0 mL), trimethyl orthoformate (1.5 mL) was added. To resultant reaction mixture, PTSA (0.003 g, 0.0205 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography using 3% to 5% MeOH in DCM as eluent to obtain 2-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethoxy)acetonitrile (0.008 g, 19.5 %) as off white solid.

MS: 400.33 [M+1]

Synthesis of Compound No. 1150: 4-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-N-cyclopropyl-5,5,5-trifluoropentanamide



Step-1: Synthesis of 4-(6-bromopyridin-3-yl)-5,5,5-trifluoropentanenitrile

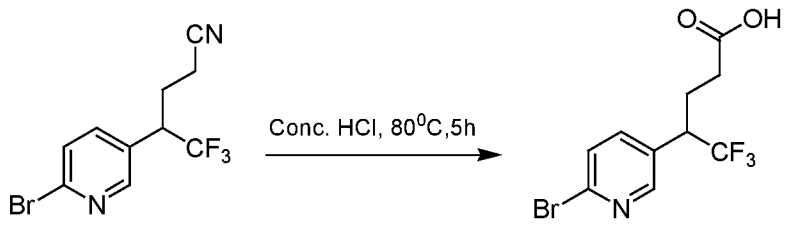


327 328

To a stirred solution of 2-bromo-5-(4-bromo-1,1,1-trifluorobutan-2-yl)pyridine (2.0 g, 5.797 mmol) in DMSO (10 mL) and water (2 mL)at RT was added potassium cyanide (0.75 g, 11.594 mmol) under nitrogen and heated overnight at 80°C. Progress of reaction was monitored by TLC. After completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 15 % acetone in hexane as eluent to obtain 4-(6-bromopyridin-3-yl)-5,5,5-trifluoropentanenitrile (1.1 g, 65.08 %) as dark brown sticky mass.

MS: 293.08 [M+1]

Step-2: Synthesis of 4-(6-bromopyridin-3-yl)-5,5,5-trifluoropentanoic acid

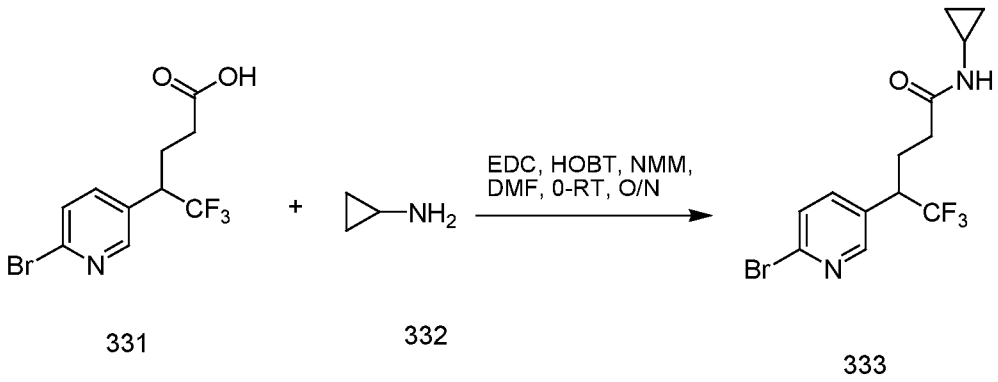


329 330

Conc. HCl (10 mL) was added to 4-(6-bromopyridin-3-yl)-5,5,5-trifluoropentanenitrile (1.0 g, 3.412 mmol) in a sealed tube and heated to 80°C for 5h. Progress of reaction was monitored by TLC. After completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure to obtain 4-(6-bromopyridin-3-yl)-5,5,5-trifluoropentanoic acid (0.6 g, 56.6 %) as dark brown sticky mass.

MS: 312.08 [M+1]

Step-3: Synthesis of 4-(6-bromopyridin-3-yl)-N-cyclopropyl-5,5,5-trifluoropentanamide

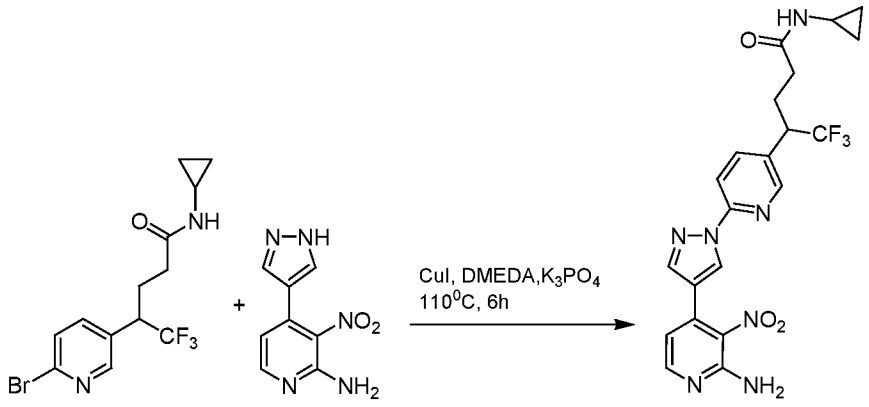


331 332 333

To a stirred solution of 4-(6-bromopyridin-3-yl)-5,5,5-trifluoropentanoic acid (0.15 g, 0.4823 mmol) and cyclopropylamine (0.033 g, 0.5787 mmol) in DMF (5 mL) was added EDCI (0.110 g, 0.5787 mmol), HOBT (0.097 g, 0.723 mmol) and NMM (0.146 g, 1.446 mmol) at 10°C. The resulting reaction mixture was stirred at room temperature for 16h. Reaction was monitored by TLC. On completion reaction was quenched with water, extracted with ethyl acetate. Organic layer was washed with water, brine, dried over sodium sulphate, concentrated under reduced pressure to obtain 4-(6-bromopyridin-3-yl)-N-cyclopropyl-5,5,5-trifluoropentanamide as crude (0.150 g, 88.8%) as yellow oil.

MS: 351.16 [M+1]

Step-4: Synthesis of 4-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-N-cyclopropyl-5,5,5-trifluoropentanamide

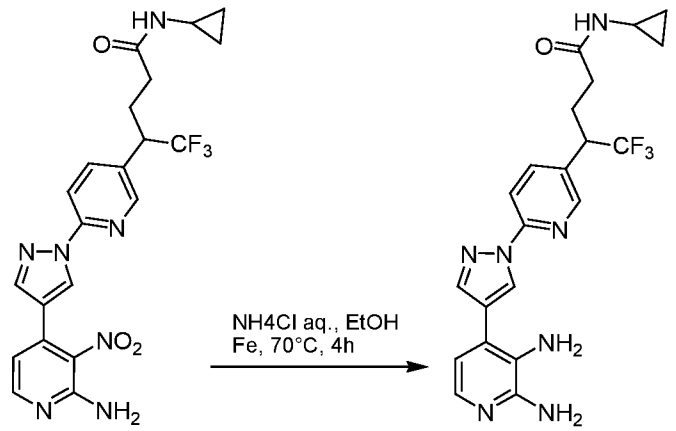


334 335 336

To a stirred solution of 3-nitro-4-(1H-pyrazol-4-yl) pyridin-2-amine (0.06 g, 0.292 mmol) and compound 4-(6-bromopyridin-3-yl)-N-cyclopropyl-5,5,5-trifluoropentanamide (0.150 g, 0.536 mmol) in Dioxane (5 ml) was added K_3PO_4 (0.124 g, 0.585 mmol) followed by CuI (0.011 g, 0.0585 mmol) and DMEDA (0.128 g, 1.463 mmol). Reaction was heated at 110°C for 6h. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography using 2 % MeOH in DCM as eluent to obtain 4-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-N-cyclopropyl-5,5,5-trifluoropentanamide (0.05 g, 35.9 %) as yellow solid.

MS: 476.42 [M+1]

Step-5: Synthesis of 4-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-N-cyclopropyl-5,5,5-trifluoropentanamide

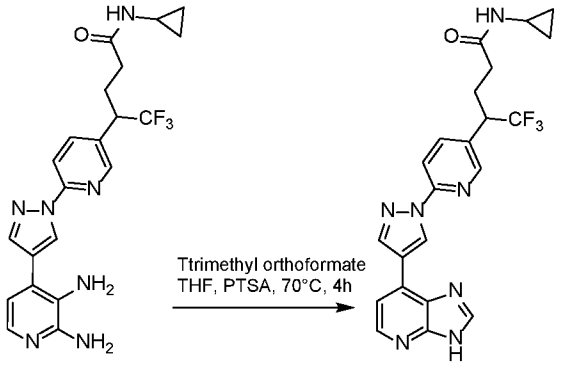


337 338

To a stirred solution of 4-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-N-cyclopropyl-5,5,5-trifluoropentanamide (0.050g, 0.105 mmol) in EtOH (10 mL), NH4Cl (2.5 mL) was added at room temperature. To resultant reaction mixture, Fe powder (0.029 g, 0.526 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, reaction mixture was diluted with H_2O: EtOAc (50 mL, 5:5) and filtered through celite to remove inorganic impurities from the reaction mixture. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to obtained pure 4-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-N-cyclopropyl-5,5,5-trifluoropentanamide (0.040 g, 85.4 %) as dark brown solid mass.

MS: 446.44 [M+1]

Step-6: Synthesis of 4-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-N-cyclopropyl-5,5,5-trifluoropentanamide

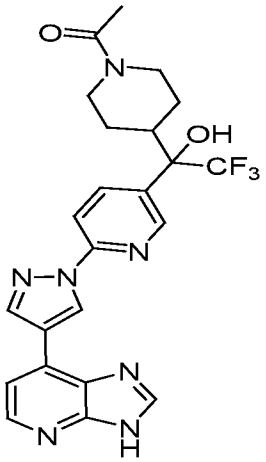


339 1150

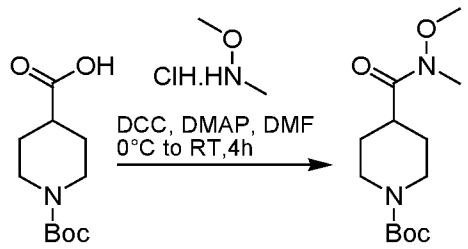
To a stirred solution of 4-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-N-cyclopropyl-5,5,5-trifluoropentanamide (0.040g, 0.0898 mmol) in THF (3.0 mL), trimethyl orthoformate (1.5 mL) was added. To resultant reaction mixture, PTSA (0.003 g, 0.0179 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography using 3% to 5% MeOH in DCM as eluent to obtain 4-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-N-cyclopropyl-5,5,5-trifluoropentanamide (0.020 g, 49.0 %) as off white solid.

MS: 456.44 [M+1]

Synthesis of Compound No. 1131: 1-(4-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-hydroxyethyl)piperidin-1-yl)ethanone



Step-1: Synthesis of N-methoxy-N-methyl cyclopropane carboxamide:

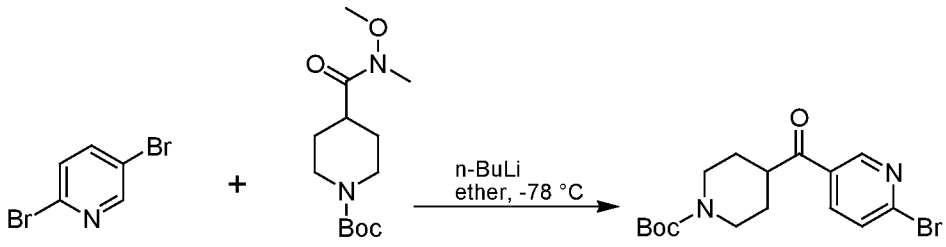


340 341

To a stirred solution of 1-(tert-butoxy carbonyl)piperidine-4-carboxylic acid (10.0 g, 43.66 mmol) and N-methoxy methanamine hydrochloride (5.56 g, 56.76 mmol) in DMF (35 mL), DCC (13.51g, 65.49 mmol) and DMAP (1.60g, 13.98 mmol) was added successively at 0°C and allow to stirred for 30 min. Resultant reaction mass was allow to warm to RT and stirred for 4h. Completion of reaction was monitored by TLC. On completion, quenched reaction mixture with 1N HCl water and extracted with EtOAc. The organic layer was washed with bicarbonate water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 20% acetone in n-hexane to obtained tert-butyl 4-(N-methoxy-N-methylcarbamoyl)piperidine-1-carboxylate (7.45g, 60%) as colourless oily mass.

MS: 273.1 [M+1]

Step-2: Synthesis of tert-butyl 4-(6-bromonicotinoyl)piperidine-1-carboxylate:

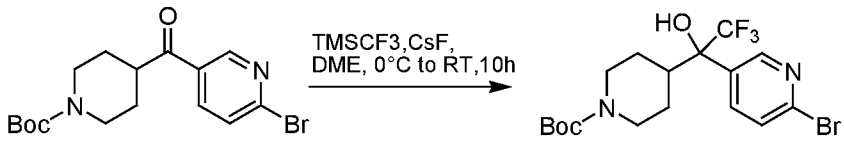


342 343 344

To a stirred solution of 2,5-dibromopyridine (5.0 g, 21.18 mmol) in diethyl ether (100 mL) at -78°C was added n-Butyl lithium (2.5M in hexane) (8.47 mL, 21.18 mmol) under nitrogen and stirred for 1h at same temperature. tert-butyl 4-(N-methoxy-N-methylcarbamoyl)piperidine-1-carboxylate (6.36 g, 23.29 mmol) was then added drop wise to the reaction mixture, stirred for 1h at -78°C. Progress of reaction was monitored by TLC. After reaction completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with 10% MeOH in DCM. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure to obtained tert-butyl 4-(6-bromonicotinoyl)piperidine-1-carboxylate (5.8 g, 67.12%) as colourless oily mass.

MS: 371.0 [M+1]

Step-3: Synthesis of tert-butyl 4-(1-(6-bromopyridin-3-yl)-2,2,2-trifluoro-1-hydroxyethyl)piperidine-1-carboxylate

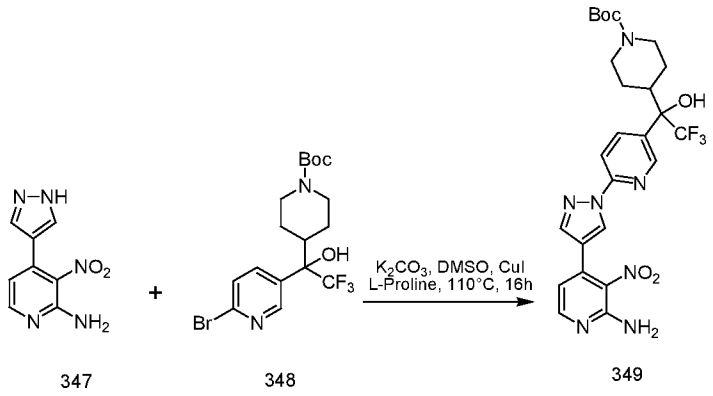


345 346

To a stirred solution of tert-butyl 4-(6-bromonicotinoyl)piperidine-1-carboxylate (1 g, 2.71 mmol) in DME (50 mL), TMSCF3 (0.77 g, 5.43 mmol) was added at 0°C under nitrogen followed by CsF (0.82 g, 5.43 mmol) added portion wise to reaction mixture. Allow to warm reaction mixture to RT and stirred for 10h. On completion, reaction mixture quenched with 0.1 N HCL and extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 10 % Acetone in Hexane as eluent to obtain tert-butyl 4-(1-(6-bromopyridin-3-yl)-2,2,2-trifluoro-1-hydroxyethyl)piperidine-1-carboxylate (0.52 g, 45.45%) as white colour solid.

MS: 440 [M+2]

Step-4: Synthesis of tert-butyl 4-(1-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-hydroxyethyl)piperidine-1-carboxylate

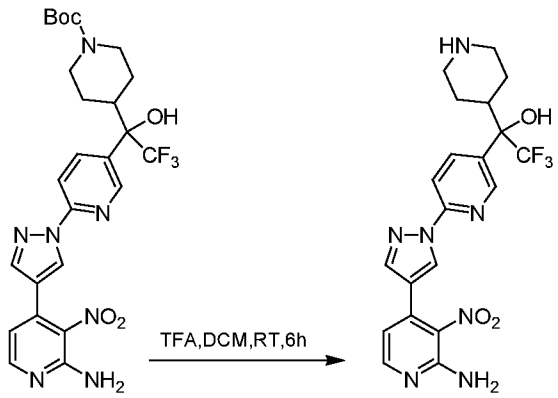


347 348 349

To a stirred solution of 3-nitro-4-(1H-pyrazol-4-yl) pyridin-2-amine (0.20g, 0.975 mmol) and compound 4-(1-(6-bromopyridin-3-yl)-2,2,2-trifluoro-1-hydroxyethyl)piperidine-1-carboxylate (0.428 g, 0.975 mmol) in DMSO (6 ml) was added K_2CO_3 (0.403 g, 2.92 mmol) followed by CuI (0.016g, 0.0975 mmol) and L-Proline (0.056g, 0.487 mmol). Reaction was heated at 110°C for 16h. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 40-60% acetone in n-hexane to obtained tert-butyl 4-(1-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-hydroxyethyl)piperidine-1-carboxylate (0.075 g, 15.12 %) as yellow solid

MS: 564.02 [M+1]

Step-5: Synthesis of 1-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(piperidin-4-yl)ethanol

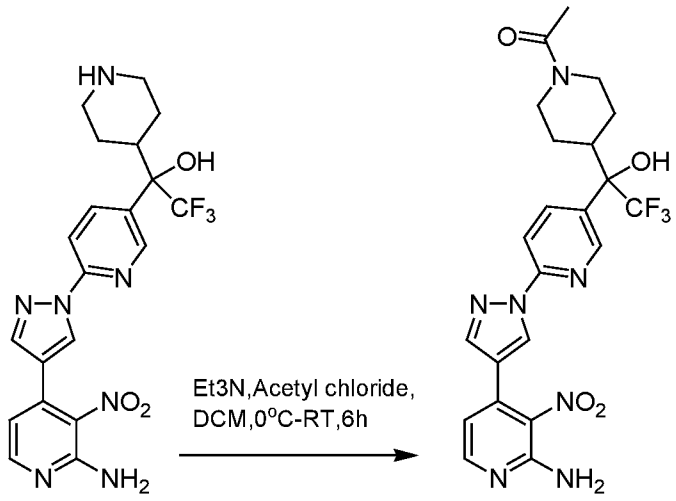


350 351

To a stirred solution of tert-butyl 4-(1-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl) pyridin-3-yl)-2,2,2-trifluoro-1-hydroxyethyl)piperidine-1-carboxylate (0.075 g, 13.51 mmol) in DCM (50 mL), TFA(0.2 g, 13.51 mmol) was added dropwise at RT under nitrogen. Allow to warm reaction mixture to RT and stirred for 6h. On completion, reaction mixture quenched with bicarbonate solution and extracted with 10% MeOH in DCM. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 4-5% MeOH in DCM as eluent to obtain (6-bromopyridin-3-yl)(piperidin-4-yl)methanone (43 g, 74.52%) as yellow solid.

MS: 364.16 [M+1]

Step-6: Synthesis of 1-(4-(1-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl) pyridin-3-yl)-2,2,2-trifluoro-1hydroxyethyl)piperidin-1-yl)ethanone



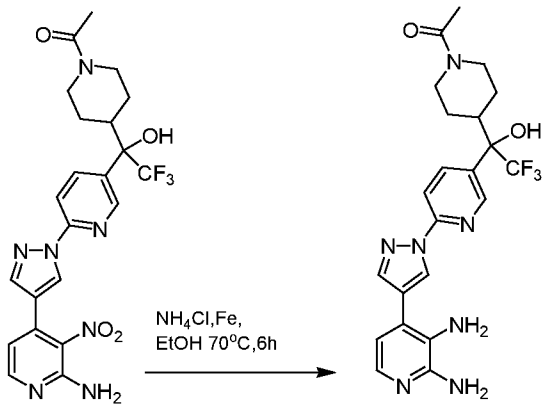
352 353

To a stirred solution of (6-bromopyridin-3-yl)(piperidin-4-yl)methanone1-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(piperidin-4-yl)ethanol (0.040 g, 0.109mmol) in dry DCM (5 mL) at 0°C was added Et3N (0.033 g, 0.329 mmol) under nitrogen. To resultant reaction mixture Acetyl Chloride (0.005 g, 0.109 mmol) was added drop wise to the reaction mixture, stirred for 1h at 0°C. Allow to warm to RT and Stirred for 1h. Progress of reaction was monitored by TLC. After reaction completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) on flash column chromatography using 2-3% MeOH in DCM as eluent to obtain 1-(4-(1-(6-(4-(2-amino-3-

nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1hydroxyethyl)piperidin-1-yl)ethanone (0.035 g, 63.63 %) as yellow solid.

MS: 506.01 [M+1]

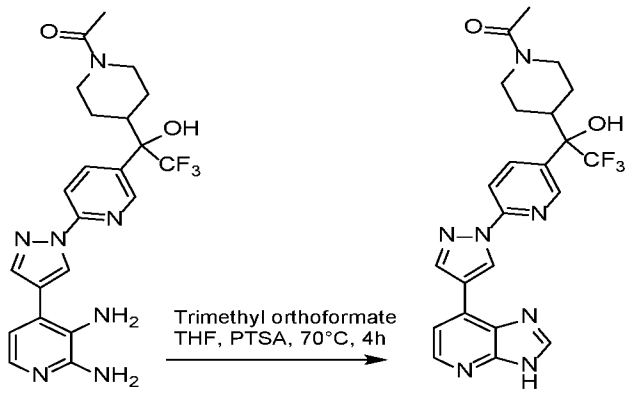
Step-7: Synthesis of 1-(4-(1-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-hydroxyethyl)piperidin-1-yl)ethenone



354 355

To a stirred solution of 1-(4-(1-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl) pyridin-3-yl)-2, 2, 2-trifluoro-1hydroxyethyl) piperidin-1-yl) ethanone (0.035g, 0.0693 mmol) in EtOH (3.0 mL), NH_4Cl (2.5 mL) was added at room temperature. To resultant reaction mixture, Fe powder (0.019 g, 0.346 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, reaction mixture was diluted with H_2O: EtOAc (50 mL, 5:5) and pass over celite to remove inorganic impurities from the reaction mixture. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to obtained 1-(4-(1-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-hydroxyethyl)piperidin-1-yl)ethanone (0.025 g, 78.12 %) as dark brown solid mass.
MS: 476.19 [M+1]

tep-8: Synthesis of 1-(4-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-hydroxyethyl)piperidin-1-yl)ethenone

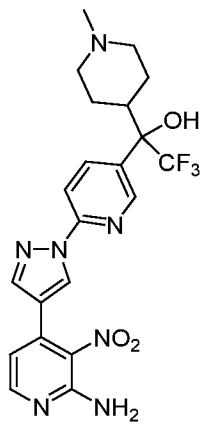


356 1131

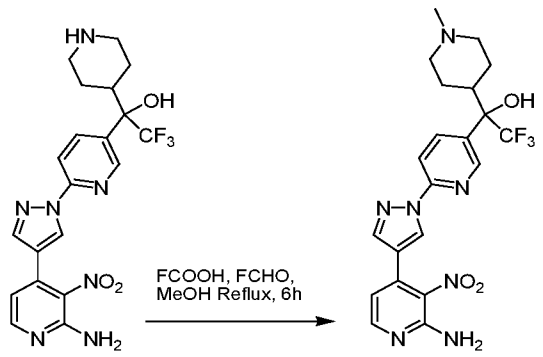
To a stirred solution 1-(4-(1-(6-(4-(2, 3-diaminopyridin-4-yl)-1H-pyrazol-1-yl) pyridin-3-yl)-2, 2, 2-trifluoro-1-hydroxyethyl) piperidin-1-yl) ethanone 0.025g, 0.05263 mmol) in THF (1.0 mL), trimethyl orthoformate (1.5 mL) was added. To resultant reaction mixture, PTSA (0.003 g, 0.0052 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with 10% MeOH in DCM. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) on flash column chromatography using 5-6% MeOH in DCM as eluent to obtained 1-(4-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-hydroxyethyl)piperidin-1-yl)ethanone (0.006 g, 17.41%) as off white solid.

MS: 486.02 [M+1]

Synthesis of Compound No. 1133: 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-methylpiperidin-4-yl)ethanol



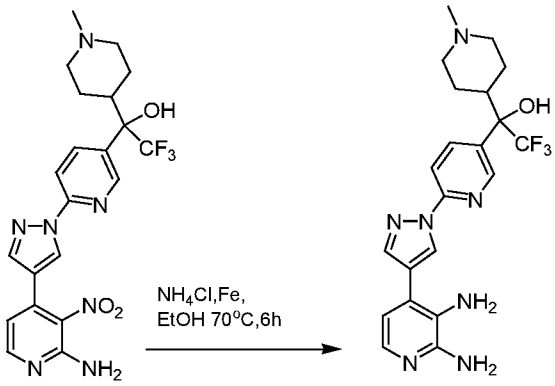
Step-1: Synthesis of 1-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-methylpiperidin-4-yl)ethanol



357 358

To a stirred solution of 1-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(piperidin-4-yl)ethanol (0.110 g, 0.023mmol) in dry methanol (5 mL) at room temprature was added formic acid (0.030 g, 0.071 mmol) and formaldehyde (0.021 g, 0.071 mmol) under nitrogen. Stirred reaction mixture at 70^0C for 6h. Progress of reaction was monitored by TLC. After reaction completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) on flash column chromatography using 5-6% MeOH in DCM as eluent to obtain 1-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-methylpiperidin-4-yl)ethanol (0.060 g, 53.63 %) as yellow solid.
MS: 478.01 [M+1]

Step-2: 1-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-methylpiperidin-4-yl)ethanol

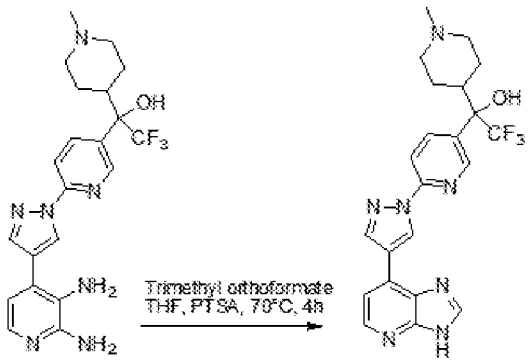


359 360

To a stirred solution of 1-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-methylpiperidin-4-yl)ethanol (0.060g, 0.0125 mmol) in EtOH (7.0 mL), NH_4Cl (2.5 mL) was added at room temperature. To resultant reaction mixture, Fe powder (0.033 g, 0.062 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, reaction mixture was diluted with H_2O: EtOAc (50 mL, 5:5) and pass over celite to remove inorganic impurities from the reaction mixture. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to obtained 1-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-methylpiperidin-4-yl)ethanol (0.040 g, 71.4 %) as dark brown solid mass.

MS: 448.19 [M+1]

Step-3: Synthesis of 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-methylpiperidin-4-yl)ethanol

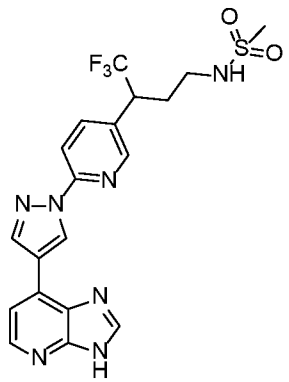


361 1133

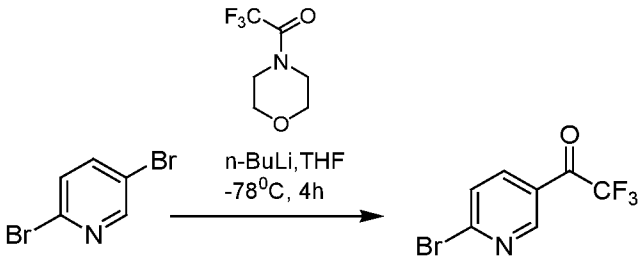
To a stirred solution 1-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-methylpiperidin-4-yl)ethanol 0.040g, 0.0089 mmol) in THF (1.0 mL), trimethyl orthoformate (2.0 mL) was added. To resultant reaction mixture, PTSA (0.003 g, 0.0052 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with 10% MeOH in DCM. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) on flash column chromatography using 5-6% MeOH in DCM as eluent to obtained 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-methylpiperidin-4-yl)ethanol (0.014 g, 34.41%) as off white solid.

MS: 458.02 [M+1]

Synthesis of Compound No. 1146: N-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)methanesulfonamide



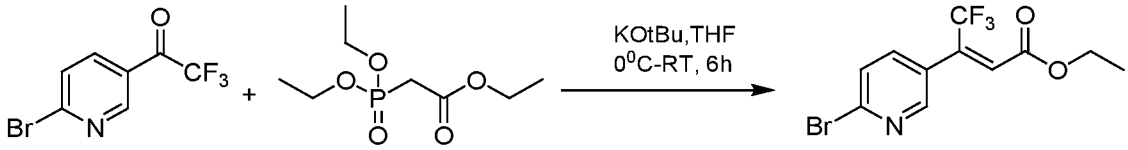
Step-1: Synthesis of 1-(6-bromopyridin-3-yl)-2,2,2-trifluoroethanone:



362 363

To a stirred solution of 2,5-dibromopyridine (5.0 g, 2.12 mmol) in THF (50 mL) at -78°C was added n-Butyl lithium (2.5M in hexane) (12.5 mL, 3.18 mmol) under nitrogen and stirred for 1h at same temperature. 2,2,2-trifluoro-1-morpholinoethanone (5.06 g, 2.76 mmol) was then added drop wise to the reaction mixture, stirred for 1h at -78°C. Progress of reaction was monitored by TLC. After reaction completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with diethyl ether. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 18% ethyl acetate in hexane as eluent to obtain 1-(6-bromopyridin-2-yl)-2,2,2-trifluoroethanone (3.5 g, 64.81 %) as colourless oil.

Step-2: Synthesis of (E/Z)-ethyl 3-(6-bromopyridin-3-yl)-4,4,4-trifluorobut-2-enoate

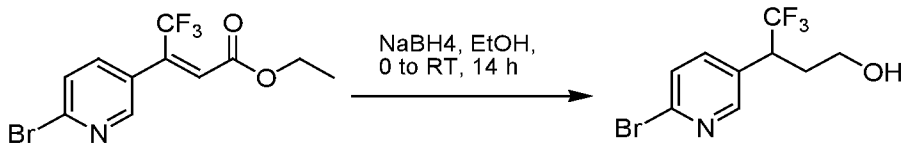


364 365 366

To a stirred solution of Triethyl phosphonoacetate (3.9g, 1.77 mmol) and THF (60 ml) at 0^0C under N_2 added base potassium ter-butoxide (1.98g, 1.77 mmol) lotwise. The resultant mixture was stirred at RT for 1h for anion generation. A solution of 1-(6-bromopyridin-3-yl)-2,2,2-trifluoroethanone (3.0 g, 1.18 mmol) in THF (15 ml) was added slowly. After addition stirred mixture for 6h at RT. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 9 to 15% EA/Hexane to obtained (E/Z)-ethyl 3-(6-bromopyridin-3-yl)-4,4,4-trifluorobut-2-enoate (1.5 g, 40%) as yellow oil.

MS: 324 [M+1]

Step-3: Synthesis of 3-(6-bromopyridin-3-yl)-4,4,4-trifluorobutan-1-ol :

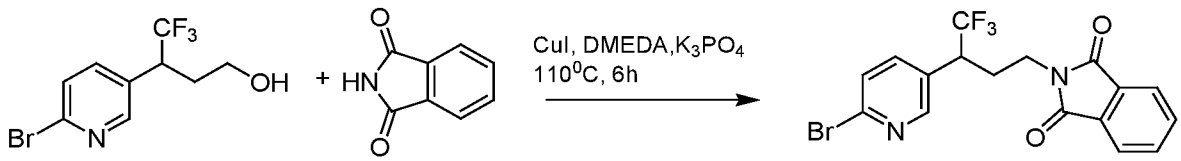


367 368

To a stirred solution of (E/Z)-ethyl 3-(6-bromopyridin-3-yl)-4,4,4-trifluorobut-2-enoate (1.5g, 462 mmol) in EtOH (30 mL), $NaBH_4$ (0.520g, 1380 mmol) was added at 0^oC. Reaction was allowed to stir at room temperature for 14h. Reaction was monitored by TLC. On completion, reaction was quenched with water, extracted with EtOAc. The organic layer was washed with water, dried over Na_2SO_4, evaporated under reduced pressure to obtain crude reaction mass. Purification of the crude was done *via* silica gel (100-200 Mesh) column chromatography and desired compound eluted at 30% ethyl acetate/n-Hexane to obtained 3-(6-bromopyridin-3-yl)-4,4,4-trifluorobutan-1-ol (0.610g, 46.5%) as clear oil.

MS: 284 [M+1]

Step-4: Synthesis of 2-(3-(6-bromopyridin-3-yl)-4,4,4-trifluorobutyl)isoindoline-1,3-dione

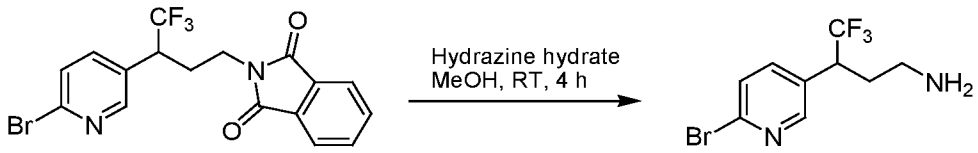


369 370 371

To ice cooled a stirred solution of isoindoline-1,3-dione (0.774 g, 5.28 mmol) and compound 3-(6-bromopyridin-2-yl)-4,4,4-trifluorobutan-1-ol (1 g, 3.53 mmol) and TPP (1.3g, 5.28 mmol) in THF (10 ml) was added DEAD (0.919 g, 5.28 mmol). Reaction was stirred at RT for 16h. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 20 % Acetone in Hexane to obtained 2-(3-(6-bromopyridin-3-yl)-4,4,4-trifluorobutyl)isoindoline-1,3-dione (0.600 g, 42 %) as yellowish colour free flow solid.

MS: 409.1 [M+1]

Step-5: Synthesis of 3-(6-bromopyridin-3-yl)-4,4,4-trifluorobutan-1-amine

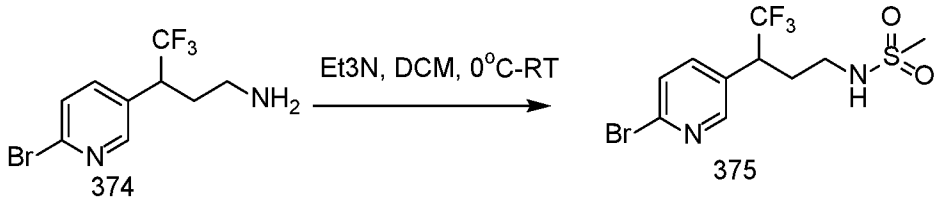


372 373

To a stirred solution of 2-(3-(6-bromopyridin-3-yl)-4, 4,4-trifluorobutyl) isoindoline-1,3-dione (0.500 g, 0.29 mmol) in MeOH (10 mL), Hydrazine hydrate (3ml) was added dropwise at 0°C. The resultant reaction mixture was stirred at room temprature for 4h. Completion of reaction was monitored by TLC. After completion reaction mass was quenched with 1N NaOH solution. Phases separated and aqueous layer was extracted with DCM. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Obtain 3-(6-bromopyridin-3-yl)-4,4,4-trifluorobutan-1-amine (0.200 g, 47.05 %) as reddish semi solid used as such in next step.

MS: 284.09 [M+1]

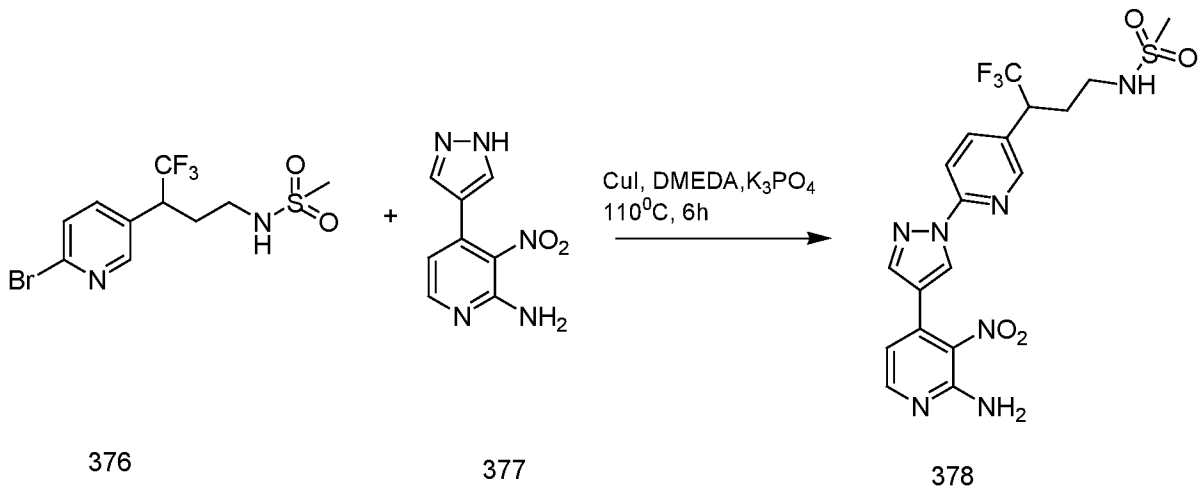
Step-:6 Synthesis of:



To an ice cooled stirred solution of 3-(6-bromopyridin-3-yl)-4, 4,4-trifluorobutan-1-amine (0.080g, 0.282 mmol) in DCM (4.0 mL), trimethylamine (0.057 ml , 0.424 mmol) was added followed by MsCl (0.035 g , 0.252 mmol) . To resultant reaction mixture was added stirred for 3h at RT. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with dichloromethane. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 10 to 15 % Acetone/Hexane to obtained (0.070 g, 81.20%) as reddish semi solid.

MS: 363[M+2]

Step-7: Synthesis of N-(3-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)methanesulfonamide



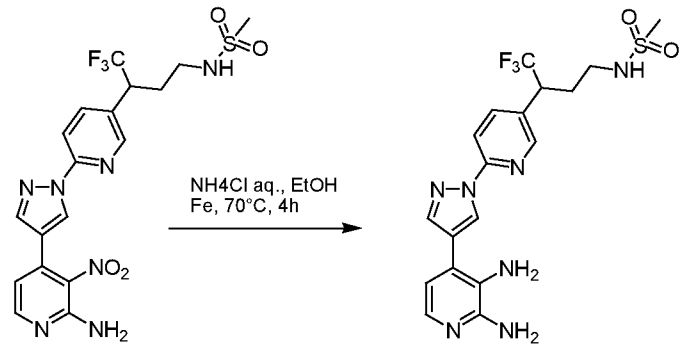
376 377 378

To a stirred solution of 3-nitro-4-(1H-pyrazol-4-yl) pyridin-2-amine (0.040 g, 0.195 mmol) and compound N-(3-(6-bromopyridin-3-yl)-4,4,4-trifluorobutyl)methanesulfonamide (0.070g, 0.195 mmol) in Dioxane (5 ml) was added K_3PO_4 (0.080g, 0.585 mmol) followed by CuI (0.005g, 0.0195 mmol) and DMEDA (0.017g, 0.195 mmol). Reaction was heated at 110°C for

6h. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 6-7% MeOH in DCM to obtained N-(3-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)methanesulfonamide (0.035 g, 50 %) as yellow solid.

MS: 466.1 [M+1]

Step-8: Synthesis of N-(3-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)methanesulfonamide

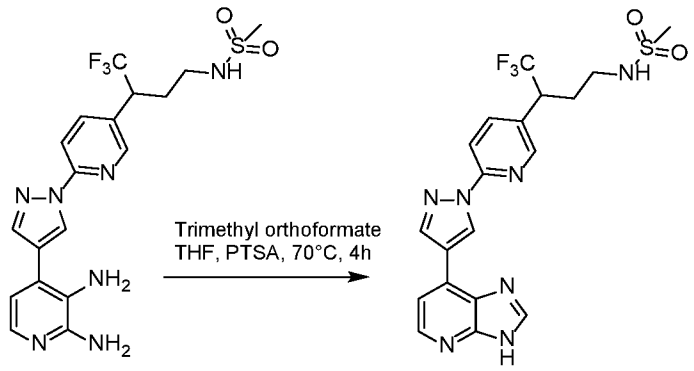


379 380

To a stirred solution of N-(3-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)methanesulfonamide (0.035 g, 0.11 mmol) in EtOH (7.0 mL), NH_4Cl (2.0 mL) was added at room temperature. To the resultant reaction mixture, Fe powder (0.029 g, 0.55 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, reaction mixture was diluted with H_2O: EtOAc (50 mL, 5:5) and pass over celite to remove inorganic impurities from the reaction mixture. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to obtained pure N-(3-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)methanesulfonamide (0.025 g, 75%) as dark brown solid mass.

MS: 456.2 [M+1]

Step-9: Synthesis of N-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)methanesulfonamide:

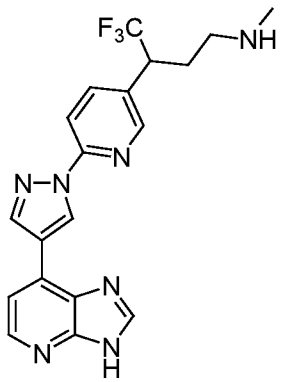


381 1146

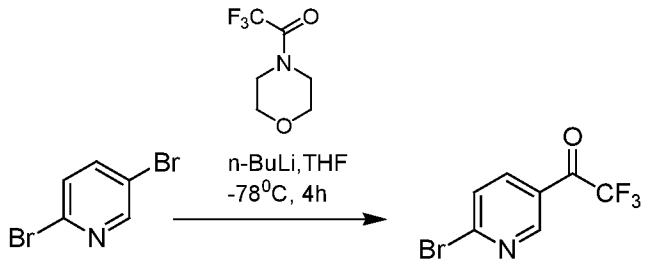
To a stirred solution of N-(3-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)methanesulfonamide ((0.025 g, 0.079 mmol) in THF (1.0 mL), Trimethyl orthoformate (1.5 mL) was added. To resultant reaction mixture, PTSA (0.0027 g, 0.015 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with 10% MeOH in DCM. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 8 to 9% MeOH in DCM to obtained N-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)methanesulfonamide (0.006 g, 60%) as off white solid.

MS: 466.45 [M+1]

Synthesis of Compound No. 1152: 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutan-1-amine



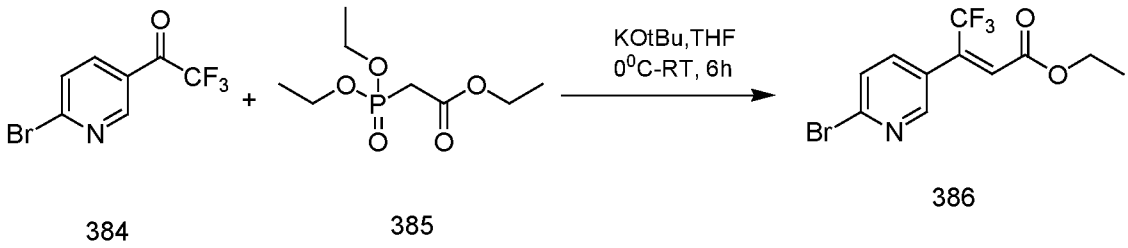
Step-1: Synthesis of 1-(6-bromopyridin-3-yl)-2,2,2-trifluoroethanone



382 383

To a stirred solution of 2, 5-dibromopyridine (5.0 g, 2.12 mmol) in THF (50 mL) at -78°C was added n-Butyl lithium (2.5M in hexane) (12.5 mL, 3.18 mmol) under nitrogen and stirred for 1h at same temperature. 2,2,2-trifluoro-1-morpholinoethanone (5.06 g, 2.76 mmol) was then added drop wise to the reaction mixture, stirred for 1h at -78°C. Progress of reaction was monitored by TLC. After reaction completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with diethyl ether. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 18% ethyl acetate in hexane as eluent to obtain 1-(6-bromopyridin-2-yl)-2,2,2-trifluoroethanone (3.5 g, 64.81 %) as colourless oil.

Step-2: Synthesis of (E/Z)-ethyl 3-(6-bromopyridin-3-yl)-4,4,4-trifluorobut-2-enoate

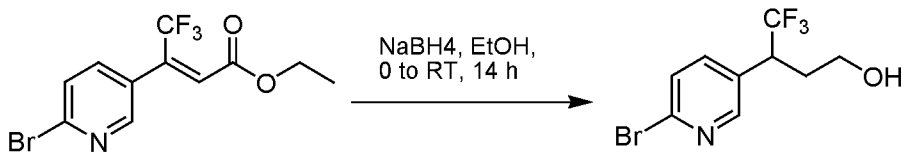


384 385 386

To a stirred solution of Triethyl phosphonoacetate (3.9g, 1.77 mmol) and THF (60 ml) at 0°C under N_2 added base potassium ter-butoxide (1.98g, 1.77 mmol) lotwise. The resultant mixture was stirred at RT for 1h for anion generation. A solution of 1-(6-bromopyridin-3-yl)-2,2,2-trifluoroethanone (3.0 g, 1.18 mmol) in THF (15 ml) was added slowly. After addition stirred mixture for 6h at RT. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 9 to 15% EA/Hexane to obtained (E/Z)-ethyl 3-(6-bromopyridin-3-yl)-4,4,4-trifluorobut-2-enoate (1.5 g, 40%) as yellow oil.

MS: 254 [M+2]

Step-3: Synthesis of 3-(6-bromopyridin-3-yl)-4,4,4-trifluorobutan-1-ol :

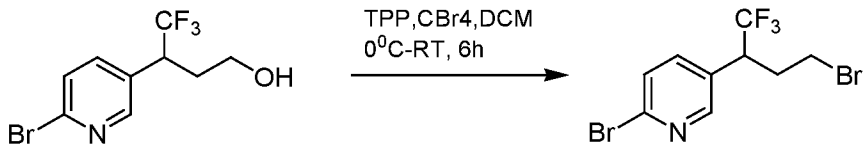


387 388

To a stirred solution of (E/Z)-ethyl 3-(6-bromopyridin-3-yl)-4,4,4-trifluorobut-2-enoate (1.5g, 462 mmol) in EtOH (30 mL), $NaBH_4$ (0.520g, 1380 mmol) was added at 0°C. Reaction was allowed to stir at room temperature for 14h. Reaction was monitored by TLC. On completion, reaction was quenched with water, extracted with EtOAc. The organic layer was washed with water, dried over Na_2SO_4, evaporated under reduced pressure to obtain crude reaction mass. Purification of the crude was done *via* silica gel (100-200 Mesh) column chromatography and desired compound eluted at 30% ethyl acetate/n-Hexane to obtained 3-(6-bromopyridin-3-yl)-4,4,4-trifluorobutan-1-ol (0.610g, 46.5%) as clear oil.

MS: 284 [M+1]

Step-4: Synthesis of 2-bromo-5-(4-bromo-1,1,1-trifluorobutan-2-yl)pyridine

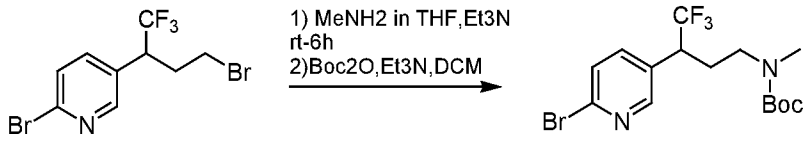


389 390

To a stirred solution of 3-(6-bromopyridin-3-yl)-4,4,4-trifluorobutan-1-ol (0.500 g, 1.76 mmol) in DCM (20 mL), TPP (0.922 g, 3.52 mmol) was added and then added carbontetrabromide (1.16 g, 3.521 mmol) portion-wise at 0°C. The resultant reaction mixture was stirred at room temperature for 7h. Completion of reaction was monitored by TLC. After completion reaction mass was quenched with ice cold water. Phases separated and aqueous layer was extracted with DCM. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude product was purified by silica gel (100-200 mesh) column chromatography using 5 to 7% Acetone in Hexane as eluent to obtain 2-bromo-5-(4-bromo-1,1,1-trifluorobutan-2-yl)pyridine (0.300 g, 47.05 %) as reddish colour semi solid.

MS: 346.97 [M+1]

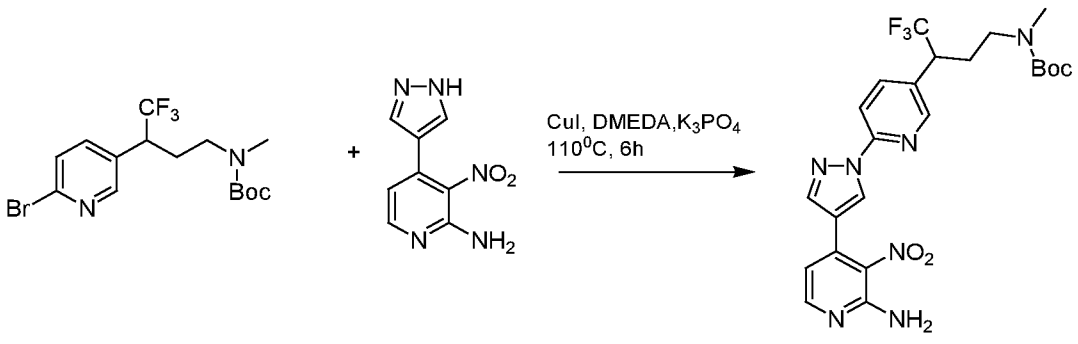
Step-5: Synthesis of tert-butyl 3-(6-bromopyridin-3-yl)-4,4,4-trifluorobutylmethylcarbamate



391 392

To a stirred solution of 2-bromo-5-(4-bromo-1, 1, 1-trifluorobutan-2-yl) pyridine (0.300 g, 0.867 mmol) in THF (10 mL), methyl amine in THF (3ml) followed by Et_3N (0.262 g, 2.60 mmol) was added at 0°C. The resultant reaction mixture was stirred at room temprature for 4h. Completion of reaction was monitored by TLC. After completion reaction mass was quenched with water. Phases separated and aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Obtain 3-(6-bromopyridin-3-yl)-4, 4,4-trifluoro-N-methylbutan-1-amine (93.75 %), (0.240 g,0.8080 mmol) was dissolved in DCM (10 mL), Boc Anhydride (0.264 g, 1.21 mmol) followed by Et_3N (0.204 g, 2.02 mmol) was added at 0°C. The resultant reaction mixture was stirred at room temperature for 6h. Completion of reaction was monitored by TLC. After completion reaction mass was quenched with water. Phases separated and aqueous layer was extracted with DCM. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Obtain tert-butyl 3-(6-bromopyridin-3-yl)-4,4,4-trifluorobutylmethylcarbamate (0.200 g, 49.05 %) as off white solid used as such in next step. MS: 397.09 [M+1]

Step-6: Synthesis of tert-butyl 3-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutylmethylcarbamate

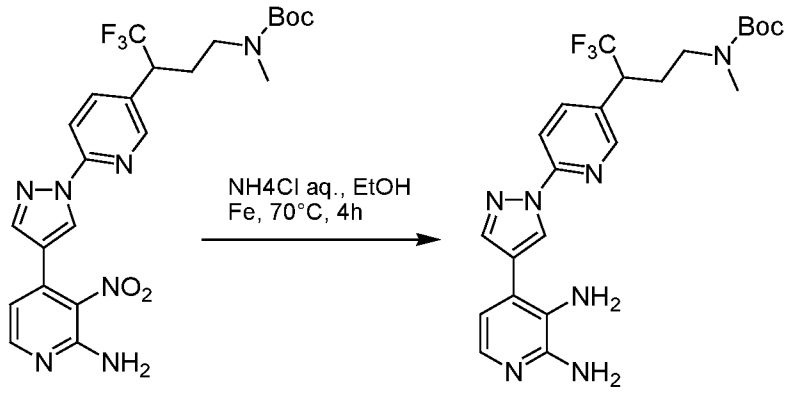


393 394 395

To a stirred solution of 3-nitro-4-(1H-pyrazol-4-yl) pyridin-2-amine (0.100 g, 0.487 mmol) and compound tert-butyl 3-(6-bromopyridin-3-yl)-4,4,4-trifluorobutylmethylcarbamate(0.193g,0.48 mmol) in Dioxane (5 ml) was added K_3PO_4 (0.305g, 1.44 mmol) followed by CuI (0.009g, 0.048mmol) and DMEDA (0.042 g,0.48 mmol). Reaction was heated at 110°C for 6h. Reaction was monitored by TLC. On completion reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 3-5% MeOH in DCM to obtained tert-butyl 3-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-tyrifluorobutylmethylcarbamate (0.070 g, 50 %) as yellow solid.

MS: 522.1 [M+1]

Step-7: Synthesis of tert-butyl 3-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutylmethylcarbamate:

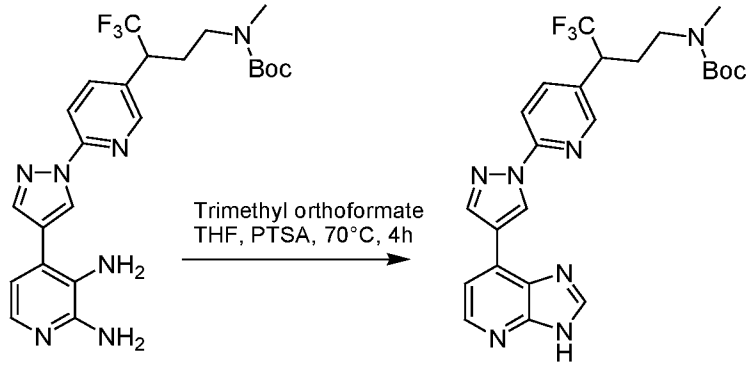


396 397

To a stirred solution tert-butyl 3-(6-(4-(2-amino-3-nitropyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutylmethylcarbamate (0.052g, 1.91 mmol) in EtOH (7.0 mL), NH_4Cl (2.0 mL) was added at room temperature. To the resultant reaction mixture, Fe powder (0.52 g, 9.51 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, reaction mixture was diluted with H_2O: EtOAc (50 mL, 5:5) and pass over celite to remove inorganic impurities from the reaction mixture. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to obtained pure tert-butyl 3-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutylmethylcarbamate (0.036g, 75%) as dark brown solid mass.

MS: 492.2 [M+1]

Step-8: Synthesis of tert-butyl 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutylmethylcarbamate:

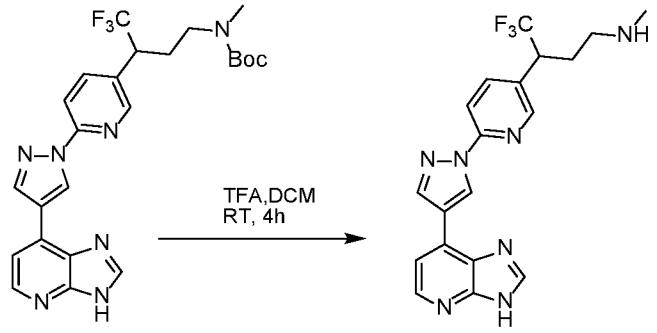


398 399

To a stirred solution of tert-butyl 3-(6-(4-(2,3-diaminopyridin-4-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutylmethylcarbamate (0.035g, 0.079 mmol) in THF (1.0 mL), Trimethyl orthoformate (1.5 mL) was added. To resultant reaction mixture, PTSA (0.0027 g, 0.015 mmol) was added and stirred for 4h at 70°C. Completion of reaction was monitored by TLC. On completion, quenched with bicarbonate water, extracted with 10% MeOH in DCM. The organic layer was washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure to give crude desired product that was purified by silica gel (100 to 200 Mesh) column chromatography: eluent at 8 to 9% MeOH in DCM to obtained tert-butyl 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutylmethylcarbamate (0.021 g, 60%) as off white solid.

MS: 502.1 [M+1]

Step-9: Synthesis 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutan-1-amine:



400 1152

To a stirred solution of tert-butyl 3-(6-(4-(3H-imidazo [4, 5-b] pyridin-7-yl)-1H-pyrazol-1-yl) pyridin-3-yl)-4, 4, 4-trifluorobutylmethylcarbamate (0.021 g, 0.0419 mmol) in DCM (50 mL), TFA (0.004 g, 0.0419 mmol) was added dropwise at RT under nitrogen. Allow to warm reaction

mixture to RT and stirred for 6h. On completion, reaction mixture quenched with bicarbonate solution and extracted with 10% MeOH in DCM. The organic layer was washed with brine, dried over sodium sulphate and concentrated under reduced pressure. Crude was purified by silica gel (100-200 mesh) column chromatography using 4-5% MeOH in DCM as eluent to obtain 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutan-1-amine (0.05 g, 31.25%) as off-white solid.

MS: 402.1 [M+1]

The compounds of the present invention were tested for their activity and were found to be active. The assays and results are presented here below.

Biological Example 1: JAK Biochemical Assay.

Recombinant JAK1, JAK2, JAK3 and TYK2 (Carna Biosciences) were used to develop biochemical assays in 50 mM HEPES pH 7.5, 1 mM EGTA, 10 mM $MgCl_2$, 2 mM DTT and 0.01% Tween-20. Amount of enzyme, substrate (ULigh-JAK-1 (Tyr1023) Peptide and ATP concentrations to be used was determined for each kinase assay by respective titration and Km studies. Biochemical assay was developed by LANCE Ultra TR-FRET technology (Perkin Elmer). Enzyme and compounds were incubated at 22°C for 60 minutes in a white 384 well optiplate (Perkin Elmer). Substrate and ATP were added to the above mix and incubated further for 90 minutes. Reaction is terminated by adding EDTA and detection antibody (Europium-anti-phospho-tyrosine (PT66) Antibody) was added. Assay read out was measured in TR-FRET mode in BMG FLUOstar multimode reader. Upon irradiation at 320 nm, the energy from the Eu donor is transferred to the ULight acceptor dye which, in turn, generates light at 665 nm. The intensity of the light emission is proportional to the level of ULight substrate phosphorylation. Compounds which interfere with JAK enzyme activity show a lesser substrate phosphorylation and values are projected in terms of % inhibition in comparison to vehicle control.

Biological Example 2: JAK cellular assays - STAT3 and STAT5 phosphorylation by IL-6 and GMCSF

TF-1 cells were starved overnight in OptiMEM medium with 0.5% charcoal stripped fetal bovine serum, 0.1mM nonessential amino acids (NEAA), 1mM sodium pyruvate and without phenol red in CO_2 incubator maintained at 37°c. Next day, cells were resuspended in RPMI without phenol red and dispensed into a 96 well plate at a final cell density of 1,20,000 cells per well. Compounds were diluted in DMSO and added to cells and incubated for 30 minutes in CO_2 incubator maintained at 37°c. Final DMSO concentration in cell based assay was 0.2%.

Human recombinant cytokines, IL-6 (30ng/ml) and GMCSF (5ng/ml) were added to the plate containing cells along with compound and incubated for 20 minutes with gentle tapping at every 5 minutes once. Compound mediated effects on STAT3 and STAT5 phosphorylation was measured in the lysates prepared by using CISBIO pSTAT3 and pSTAT5 detection kits by HTRF method. Background signal obtained from cells which were not activated with cytokines, was subtracted from vehicle controls and compound treated wells. Percentage inhibition of pSTAT3/5 levels by compounds were calculated from vehicle controls, which were considered as 100% pSTAT3/5 controls.

Biological Example 3: STAT5 phosphorylation by IL-2

HT-2 cells were starved overnight in RPMI phenol red with 10% fetal bovine serum for 4 hours in CO_2 incubator maintained at 37°c. Compounds were diluted in DMSO and added to 96 well plate containing a final density of 1,20,000 cells per well. Cells and compounds are incubated for 30 minutes in CO_2 incubator maintained at 37°c and final DMSO concentration in cell based assay was 0.2%. Human recombinant cytokine, IL-2 (50U/ml) was added to the plate containing cells and compound and incubated for 20 minutes with gentle tapping / shaking at every 5 minutes once. Compound mediated effects on STAT5 phosphorylation was measured in the lysates prepared by using CISBIO pSTAT5 detection kit by HTRF method. Background signal obtained from cells which were not activated with cytokines, was subtracted from vehicle controls and compound treated wells. Percentage inhibition of pSTAT5 levels by compounds were calculated from vehicle controls, which were considered as 100% pSTAT5 controls.

Biological Example 4: IFN-γ production in NK 92 cells by IL-12

NK 92 cells were cultured in medium without IL-2 for overnight. Next day, 5000 cells per well NK 92 cells were seeded in a 96 well plate. Compounds were added to cells and incubated for 1 hour. Later IL-12, 10U/ml was added to cells and incubated for overnight. Supernatant was collected from the wells and IFN-γ secretion was measured by using human IFN-γ ELISA kit. Absorbance was measured at 450nm in BMG FLUOstar. Background signal obtained from cells which were not activated with cytokines, was subtracted from vehicle controls and compound treated wells. Percentage inhibition of IFN-γ secretion by compounds were calculated from vehicle controls, which were considered as 100% IFN-γ secretion.

The compounds of the present invention have been tested as per Biological examples 1 to 4 and the result are in Table 2 below

Table 2: Activity of the compounds of the present invention.

S. No.	Biochemical Assay (µM)				Cell Based Assay (µM)			
	JAK1	JAK2	JAK3	TYK 2	TF-1/IL-6/ pSTAT3	TF-1/GMCSF / pSTAT5	HT-2/IL-2/ pSTAT5	NK-92/IL-2/ IFN-γ
1001.	>10	>10	>10	>10				
1002.	<0.5	<0.5	<0.5	>0.5	>10	>10		
1003.	0.021	0.036	0.175	0.182	>10			
1004.	>10	>10	>10	>10				
1005.	0.5	0.5	0.5	>1	>10			
1006.	0.5	0.5	0.5	>1				
1007.	>0.5	>0.5	>1	>1	>10			
1008.	>1	>1	>1	>10				
1009.	>10	>0.5	>1	>10				
1010.	<0.5	<0.5	>0.5	>1				
1011.	0.5	>1	>1	>1	>10	>10	>10	
1012.	0.5	0.5	>1	1				
1013.	>10	>10	>10	>10				
1014.	0.5	1	>1	>1	>10	>10	>10	
1015.	1	>1	>1	>1				
1016.	>10	>10	>10	>10				
1017.	>1	>1	>10	>10				
1018.	>10	>10	>10	>10				
1019.	0.5	>1	>1	>1				
1020.	>10	>10	>10	>10				
1021.	1	>1	>1	>1				
1022.	<0.5	<0.5	<0.5	<0.5	>10			
1023.	>10	>10	>10	>10				
1024.	>1	>1	>1	>1				
1025.	>10	>10	>10	>10				
1026.	0.041	0.048	0.283	0.122	>1	>10		

1027.	0.028	0.044	0.146	0.096	>10	>10	>10	
1028.	>1	>1	>1	>1				
1029.	>10	>10	>10	>10				
1030.	0.039	0.066	0.43	0.093	10			
1031.	>1	>1	>1	>1				
1032.	<0.5	<0.5	<0.5	<0.5	>10			
1033.	0.5	0.5	>1	>1				
1034.	>1	>1	>10	>10				
1035.	>10	>10	>10	>10	>10			
1036.	>10	>10	>10	>10				
1037.	>0.5	>1	>1	>0.5	>10			
1038.	>0.5	>0.5	>0.5	>0.5	10			
1039.	<0.5	<0.5	0.5	<0.5	10			
1040.	0.5	0.5	0.5	>1				
1041.	>1	>1	>10	>1	>10			
1042.	>10	>1	>10	>10				
1043.	0.03	0.031	0.123	0.053	4.7	>10		
1044.	<0.5	<0.5	<0.5	<0.5	10			
1045.	>1	>1	>1	>1				
1046.	<0.5	<0.5	<0.5	<0.5	>10	>10		
1047.	<0.5	<0.5	<0.5	<0.5	4.9	10		
1048.	<0.5	<0.5	<0.5	<0.5	>10	>10		
1049.	<0.5	<0.5	<0.5	<0.5	<10	>10		
1050.	<0.5	<0.5	<0.5	<0.5	<10	>10		
1051.	<0.5	<0.5	>1	<0.5	<10	>10		
1052.	<0.5	<0.5	>0.5	<0.5	>10	>10		
1053.	<1	<1	1	>1	>10	>10		
1054.	>10	>0.5	>1	>1	>1	10		
1055.	>1	<0.5	>1	>0.5	>10	>10		
1056.	<0.5	<0.5	<0.5	>0.5	>10	>10		
1057.	>0.5	>0.5	>0.5	>1				
1058.	>1	>1	>10	>10	>10	>10		
1059.	>1	>1	>10	>10				
1060.	>0.5	>0.5	>0.5	>1				

1061.	>1	1	>1	>1	>10	>10		
1062.	<0.5	<0.5	<0.5	<0.5				
1063.	>0.5	<0.5	>0.5	<0.5				
1064.	<0.5	<0.5	<0.5	<0.5	>10			
1065.	>0.5	<0.5	>0.5	>0.5				
1066.	1	>0.5	>0.5	>0.5	>10			
1067.	>1	>0.5	>0.5	>10	>10	>10		
1068.	>1	>1	>1	>1	>10	>10		
1069.	>10	>1	>0.5	>1				
1070.	>0.5	<0.5	>0.5	>0.5	>10	>10		
1071.	>0.5	>0.5	>0.5	>0.5	>10			
1072.	>0.5	>0.5	>0.5	1	>10	>10		
1073.	>1	>0.5	>0.5	>0.5	>1	>10		
1074.	>10	>1	>1	>1	>10	>10		
1075.	0.046	0.19	<0.5	>1	3.1	>10		
1076.	0.037	0.085	<0.5	>1	6	>10		
1077.	>1	>1	>1	>10	>10	>10		
1078.	0.025	0.108	0.07	>1	1.05	>10	>1	>10
1079.	>10	>1	>1	>10				
1080.	0.068	<0.5	<0.5	>10	>1	>10		
1081.	<0.5	>0.5	<0.5	>10	>1	>10		
1082.	<0.5	<0.5	<0.5	>1	>1	>10		
1083.	>0.5	>0.5	<0.5	>1				
1084.	NA	NA	NA	NA	>1	>10		
1085.	>1	>1	>1	>10				
1086.	<0.5	>0.5	>0.5	>10	>10	>10		
1087.	>0.5	>1	>1	>10				
1088.	>1	>1	>1	>1				
1089.	>0.5	>0.5	>1	>1				
1090.	0.053	0.3	0.12	>1	>1	>10	>1	
1091.	>0.5	>1	>0.5	>10				
1092.	>1	>1	>1	>1				
1093.	>0.5	<0.5	<0.5	>10				
1094.	<0.5	<0.5	<0.5	<0.5	>1	>1		

1095.	<1	<1	<1	>10				
1096.	>10	>1	>1	>10				
1097.	>10	>0.5	>10	>1				
1098.	>1	>1	>1	>10				
1099.	<0.5	<0.5	<0.5	>1	>1	>10		
1100.	>0.5	>0.5	>0.5	>10	>10	>10		
1101.	>0.5	>0.5	>1	>10	>10	>10		
1102.	<0.5	>0.5	>0.5	>1	>10	>10		
1103.	>0.5	>0.5	>10	>10	>1	>10		
1104.	>1	<0.5	<0.5	>1				
1105.	>1	>0.5	>0.5	>10				
1106.	<0.5	<0.5	<0.5	>1	>1	>10		
1107.	<0.1	>0.1	<0.1	>1	>1	>10		
1108.	>0.1	>0.5	>0.1	>1	>10	>10		
1109.	<0.5	<0.5	<0.5	>10	>1	>10		
1110.	>0.1	>0.5	>0.1	>1				
1111.	<0.5	>0.5	<0.5	>10	>10	>10		
1112.	0.5	>0.5	>1	>1	10	>10		
1113.	>1	>0.1	>0.5	>1	>10	>10		
1114.	>0.1	>0.5	>0.1	>1				
1115.	>0.5	>0.5	>0.5	>1				
1116.	>0.1	>0.5	>0.1.	>1	>1	>10		
1117.	NA	NA	NA	NA	>1	>10		
1118.	>0.5	>0.5	>0.5	>1	>10	>10		
1119.	0.03	0.2	0.07	>1	1.3	>10	>1	10
1120.	>0.05	>0.1	>0.1	>1	>1	>10		
1121.	0.1	>0.1	>0.1	>1				
1122.	>0.1	>0.5	>0.5	>1	>1	>1	>1	
1123.	>0.1	>0.5	>0.1	>1	>1	10		
1124.	>1	>1	>0.5	>1				
1125.	0.004	0.023	0.009	0.15	0.27	>10	0.26	>10
1126.	0.003	0.036	0.007	>1	0.34	>1	<1	
1127.	>0.5	>1	>1	>1	>1	>10		
1128.	<0.1	>0.5	>0.5	>1	>1	>10		

1129.	<0.1	>0.1	<0.1	>1	>0.5	>10	>1	
1130.	>0.1	>0.1	>0.1	>1	>1	>10		
1131.	0.053	0.38	0.11	>1	>0.5	>10	>1	
1132.	0.1	>0.5	>0.1	>1				
1133.	<0.1	0.1	0.1	>1	0.6	>10	2.3	
1134.	<0.1	0.5	<0.1	>1	>1	>10		
1135.	<0.1	<0.1	<0.1	<0.1	>1	>10		
1136.	<0.1	<0.1	<0.1	>1	0.7	>1	0.8	
1137.	0.5	>0.5	>0.5	>1				
1138.	<0.1	>0.1	>0.1	>1	>1	>10		
1139.	>0.5	>0.5	>0.1	>1	1			
1140.	<0.1	<0.1	<0.1	>1				
1141.	<0.1	<0.1	<0.1	>1	<1	>10		
1142.	<0.1	0.1	<0.1	>1	>0.5	>1	>0.5	
1143.	<0.1	<0.1	<0.1	>1	0.47	<1	0.67	
1144.	0.1	0.5	>0.1	>1	>1	>10		
1145.	<0.1	>0.1	<0.1	>1	>0.5	>1	>1	
1146.	<0.1	<0.1	<0.1	<0.1	>0.1	>0.1	>0.1	
1147.	>0.5	>1	>1	>1				
1148.	<0.1	<0.1	<0.1	>1	>0.5		>1	
1149.	<0.1	>0.1	<0.1	>1	>0.5		>0.5	
1150.	<0.1	<0.1	<0.1	>1	>0.5	>1	>1	
1151.	<0.1	>0.1	>0.1	>1	>0.5	>1	>1	
1152.	<0.1	<0.1	<0.1	>0.5	>0.1		>0.1	
1153.	<0.1	<0.1	<0.1	>0.5	0.36	>1	2.1	
1154.	<0.1	<0.1	<0.1	>0.5	>0.5	>1	>0.5	
1155.	>0.1	>0.5	>0.1	>1				
1156.	>0.1	>0.5	>0.5	>1	>0.5		>1	
1157.	<0.1	<0.1	<0.1	>0.5	<1	>10		
1158.	<0.1	>0.1	>0.1	>1	>1	>1		
1159.	<0.1	>0.1	<0.1	>1				
1160.	>0.1	>0.5	>0.5	>1				
1161.	>1	>1	>0.5	>1				
1162.	>0.5	>0.5	>0.5	>1				

1163.	>0.5	>0.5	>0.5	>1				
1164.	>1	>1	>1	>1				
1165.	>1	>1	>1	>1				
1166.	>0.5	>1	>0.5	>1				
1167.	0.096	0.3	0.173	>10	10	>10		
1168.	>0.1	>0.5	>0.1	>1	>1		>1	
1169.	0.013	0.073	0.014	>1	0.45	>10	<1	>10
1170.	>0.1	>0.1	>0.05	>1	>10	>10		
1171.	>1	>1	>1	>1	>10	>10		
1172.	0.5	0.5	<0.1	>1				
1173.	<0.1	<0.1	<0.1	>1	10	>10		
1174.	0.018	0.108	0.055	>1	0.3	>10	1.3	
1175.	>1	>1	>1	>1				
1176.	>1	>1	>1	>1				
1177.	>1	<0.5	>1	>0.5	>10	>10		
1178.	<0.1	<0.1	<0.1	>1	>1	1	>1	
1179	<0.1	<0.1	<0.1	>1	>1	>1	>1	
1180	<1	<1	<1	<1	>1	>1		
1181	<0.1	0.1	<0.1	>1	>0.5	>1	>1	
1182	0.015	0.1	0.041	>1	0.35	>1	0.9	>3
1183	>0.1	>0.5	>0.1	>1	1	>1		
1184	<0.1	>0.1	<0.1	>1	>0.8	>1	1.5	
1185	<0.1	>0.1	>0.1	>1	2	>1	>3	
1186	<0.1	>0.1	>0.1	>1	>0.8	>1	>1	
1187	<0.1	>0.1	<0.1	>1	>1	>1		
1188	<0.1	<0.1	<0.1	>1	>0.5	>1	>0.75	
1189	>0.5	>1	>1	>1				
1190	<0.1	<0.1	<0.1	>1	1		3.6	
1191	<0.1	<0.1	<0.1	>1	>1	>1		
1192	<0.1	<0.1	<0.1	>1	>0.8		>0.8	
1193	>0.1	>0.5	>0.1	>1				
1194	>0.5	>0.5	>0.5	>1				
1195	<0.1	<0.1	<0.1	>1	>0.5	>1		
1196	>0.1	>0.5	>0.1	>1				

1197	<0.1	<0.1	<0.1	>0.5	>0.3	>1		
1198	<0.1	<0.1	<0.1	>0.5	0.1	1	0.6	
1199	<0.1	>0.1	<0.1	>0.5				
1200	0.023	0.015	0.009	0.52	0.1	1	0.6	
1201	<0.1	>0.5	<0.1	>1	>0.5	>1		
1202	<0.1	>0.1	<0.1	>0.5	>0.5	>1		
1203	<0.1	<0.1	<0.1	>0.5	>0.1	>1	>0.5	
1204	<0.1	<0.1	<0.1	>1				
1205	<0.1	>0.1	>0.1	>1				
1206	>0.1	>0.1	>0.5	>1				
1207	0.005	0.01	0.005	>0.5	0.43		1.08	
1208	0.01	0.01	0.005	>0.5	>1			
1209	<0.1	<0.1	<0.1	>1	>0.75	>1		
1210	<0.1	<0.1	<0.1	>1	>0.75	>1		
1211	<0.1	>0.1	>0.1	>1				
1212	<0.1	<0.1	<0.1	>0.5	>0.75	>1		
1213	<0.1	<0.1	<0.1	>0.5	0.55		0.7	
1214	<0.1	<0.5	<0.1	>1	>1		>1	
1215	<0.1	<0.1	<0.1	>1	0.32		0.75	
1216	<0.1	<0.1	<0.1	>0.5	0.28		0.51	
1217	0.0026	0.007	0.006	0.08	>0.1		>0.5	
1218	NA	NA	NA	NA	>0.5			
1219	<0.1	<0.1	<0.1	>0.5	>0.75	>1		
1220	<0.1	<0.1	<0.1	>0.5	>1	>1		
1221	<0.1	<0.1	<0.1	>0.1	>0.75	>1		
1222	NA	NA	NA	NA	>0.8	>1		
1223	0.002	0.015	0.004	0.39	>0.1	>1	>0.5	
1224	0.001	0.03	0.001	>0.1	>0.75	>1		
1225	.0025	0.064	0.018	>1	0.16	>1	0.47	>3
1226	<0.01	>0.03	>0.03	>1	>0.5	>1	>0.75	
1227	<0.1	<0.1	<0.1	>0.1	>0.1	>0.75	>0.5	
1228	<0.1	<0.1	<0.1	>0.1	>0.5	>1	>0.5	
1229	<0.1	<0.1	<0.1	>1	>1		>1	
1230	<0.1	<0.1	<0.1	>0.5	>0.5		>0.5	

1231	.0003	0.005	0.003	0.1	0.05	1.5	0.15	>3
1232	0.003	0.023	0.015	0.2	0.09	>1	0.34	>3
1233	<0.1	<0.1	<0.1	<0.5	0.21	>1	>0.5	>3
1234	0.006	0.03	0.035	0.67	0.14	>1	0.47	>1
1235	0.001	>0.03	0.001	>1	0.36	>1	0.55	>1
1236	0.001	>0.03	>0.03	>0.1	>1		>0.75	
1237	0.001	0.01	0.005	0.1	0.19	>1	>0.5	>3
1238	0.003	>0.03	0.003	>0.1	>0.1	1	>0.1	
1239	0.006	0.056	0.023	0.06	0.05	0.26		
1240	>0.01	>0.03	>0.03	>1	>0.5	>1		
1241	<0.1	>0.1	<0.1	>1	>0.5	>1	>0.75	
1242	<0.1	<0.1	<0.1	>1	>1	>1	>1	
1243	<0.1	<0.1	<0.1	>1	>1	>1	>1	
1244	<0.1	>0.1	>0.1	>1	>1			
1245	>.001	>0.03	>.003	>1	>1			
1246	0.006	0.034	0.006	0.79	1.5		2	
1247	0.01	0.06	0.023	0.19	>1		>1	
1248	<0.1	<0.1	<0.1	>0.5	>0.75		>0.8	
1249	>0.5	>0.5	>0.5	>1				
1250	<0.1	<0.1	<0.1	>1	>1		>1	
1251	<0.1	<0.1	<0.1	>0.5	1		>2	
1252	<0.1	<0.1	<0.1	>0.5	1.1		1.63	

From Table 2, it can be clearly seen that the compounds of the present invention all possess activity as selective JAK1 inhibitor.

Biological Example 5: Comparison with existing JAK inhibitors

By way of illustration, certain exemplary compounds, were tested for their activity in comparison with existing JAK inhibitor. Example 1133, 1181 and 1215 was compared with the results of the existing JAK inhibitor under the same experimental condition, and the results are shown in Table 3

Table 3: Comparison of exemplary compounds of the present invention with known JAK inhibitors

Example	Biochemical IC50 (nM)				Cell based IC50 (μM)			
	JAK1	JAK2	JAK3	TYK2	TF-1/IL-6	TF-1/GM-CSF	HT-2/IL-2	NK-92/IL-12*
1133	8	152	100	850	0.6	>10	2.3	>10
1181	15	105	42	>1	0.35	>10	0.9	>10
1215	0.5	40	11	>100	0.3	>10	0.7	>10
Filgotinib	64	58	750	490	0.6	3.4	0.95	>10
Tofacitinib	1.2	1.7	0.34	33	0.033	0.24	0.019	3

* indicates IFN-γ detection from cell supernatants.

Data thus generated for compounds were compared with two reference standards, filgotinib – a JAK1 selective inhibitor, and tofacitinib – pan JAK inhibitor. Example 1133, 1181 and 1215 showed better potency as well as selectivity for JAK1 (7 to 80 fold selective for JAK1 vs JAK2; 3 to 22 fold selective for JAK1 vs JAK3) compared to filgotinib (0.9 fold JAK1 vs JAK2; 12 fold JAK1 vs JAK3). These compounds are also far superior in terms of JAK1 selectivity compared to a pan inhibitor such as tofacitinib.

Biological Example 6: Mouse model of Rheumatoid arthritis:

Rheumatoid arthritis (RA) is an autoimmune disease that can cause joint pain and damage throughout the body. Several cytokines such as IL-6 and IFN-γ activate the Janus kinase/signal transducers and activators of transcription (JAK/STAT) pathway. Inhibition of JAK/STAT pathway is considered as one of the therapeutic options for treatment of rheumatoid arthritis. Rodent models of arthritis can be used to evaluate the therapeutic potential of compounds dosed preventatively or therapeutically. These models include but are not limited to mouse or rat collagen-induced arthritis, rat adjuvant-induced arthritis, and collagen antibody-induced arthritis.

Compounds described herein are tested for JAK/STAT pathway inhibition driven efficacy in collagen induced mouse arthritis model. Compounds were orally dosed, QD for 21 days and at the end of the study, clinical symptoms, body weight and histopathology of ankle and paws were measured. Arthritis score was calculated for the compounds as well as reference standard, filgotinib. By way of exemplification, examples 1215, 1181 and 1133 showed very good efficacy and are better or comparable to filgotinib.

Biological Example 7: Mouse model of Imiquimod induced psoriasis:

Imiquimod (IMQ) induced dermatitis closely resembles human psoriasis lesions not only with regard to phenotypic and histological characteristics but also in the development of the lesions. IMQ is a ligand for toll-like receptor 7 (TLR7) and TLR8, and is a potent immune activator. IMQ's immunomodulatory effects in triggering psoriasis are attributed to stimulation of TLR7 and TLR8 on plasmacytoid dendritic cells (pDCs) and an upregulated type I interferon pathway. Migration of activated dermal dendritic cells to lymph nodes in skin triggers a sequence of events leading to late phase of psoriasis. Compounds described herein are tested for JAK inhibition driven efficacy in Imiquimod induced dermatitis in mice.

Female BALB/c mice were topically dosed with 3% cream formulation containing test compounds. After four hours of test compound administration, 5% Imiquimod was applied on back skin and right ear for five days. On day 6, post dosing with test compounds, the severity of psoriasis was monitored and graded following Psoriasis Area and Severity Index (PASI). Efficacies of the compounds were evaluated based on PASI score. Redness, thickness and scaling of back skin and ear were assessed among the groups for scoring.

Compounds of the present invention for instance, Example 1133, Example 1215 and filgotinib showed statistically significant decrease in cumulative psoriasis score compared to vehicle. There was a significant decrease in back skin thickness, ear thickness on administration of Example 1133, 1215 and filgotinib (3% topical, QD). Example 1215 showed better efficacy compared to 1133 and reference compound filgotinib. The data is represented by way of a Figure 1. From the figure, it can be clearly seen that there the exemplary compounds of the present invention show enhanced efficacy when compared to the compounds available in the market such Filgotinib.

Biological Example 9: Murine model of Oxazolone Induced Colitis:

The animal in which the colitis is produced can be any mammal and can include but is not limited to mouse, rat, guinea pig, hamster, rabbit, cat, dog, goat, monkey, and chimpanzee. The colitis can be produced in the animal by any method known in the art. A mouse model of oxazolone induced colitis was utilized to study the efficacy of JAK inhibitors. Oxazolone colitis has a histological resemblance to human ulcerative colitis. Pro-inflammatory cytokines elevated in ulcerative colitis rely on JAK family of tyrosine kinases for signal transduction. It has been proposed that JAK inhibition may be beneficial in the treatment of ulcerative colitis.

Male BALB/c mice were used in the study., 10-12 weeks, on day 1, 4% Oxazolone (in 4:1 acetone: olive oil formulation) or vehicle solution was applied between shoulders to

anesthetized animals. Seven days after skin sensitization, mice were fasted for 6 hours prior to intra-rectal administration of 1% oxazolone (in 1:1 ethanol:water formulation). Drug treatment or vehicle administration (PO, BID) was initiated on day 6, a day prior to intra-rectal oxazolone challenge. Animals were dosed with test compounds or vehicle till day 9. Disease activity index (DAI) was graded for each mouse by treatment-blinded experimenters. Body weight loss (0=none, 2=>5-10%, 4=>20%), stool consistency (0=normal, 2=soft without pellet, 4=severe diarrhoea) and rectal bleeding (0=no blood, 2=bloody stool, 4=adhesion of blood to anus& part of tail) were assessed for DAI score.

Below Table 4, mentions the scores of the compounds with respect to disease activity index parameters in comparison with vehicle treated group.

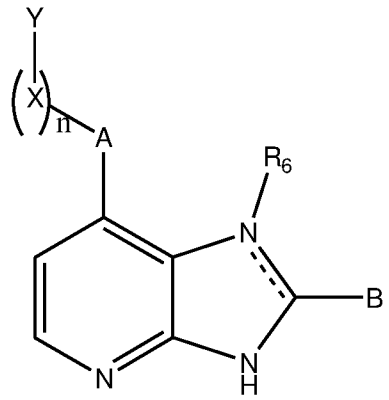
Table 4: Testing of exemplary compounds of the present invention in murine model of Oxazolone Induced Colitis:

	Stool Consistency Index	Rectal Bleeding Index	Body Weight Loss Index	Disease Activity Index
Vehicle	3 – 3.5	2.5 – 2.8	3.5 – 3.7	9 -10
1181	1.5 – 2.0	1.5 – 1.8	1.7 – 1.9	2-3
1215	1.0 – 1.2	0.2 – 0.4	0.2 – 0.3	1-2
Filgotinib	0.9 – 1.3	0.3 – 0.5	0.2 – 0.3	1-2

Compounds of the present invention such as example 1181, 1215 and filgotinib showed statistically significant decrease in disease activity index compared to vehicle. There was a significant decrease in stool consistency, rectal bleeding and body weight loss parameters on administration of Example 1181, 1215 and filgotinib (30mpk, PO, BID). Example 1215 showed better efficacy in comparison to the marketed compound Filgotinib.

We Claim:

1. 1H-imidazo[4,5-b]pyridin-2(3H)-one as selective inhibitor of JAK 1 their pharmaceutically acceptable salts and isomers of formula I:



Wherein;

A is a 5 membered or a 6 membered carbocycle or heterocycle comprising 1 to 3 heteroatom selected from the group comprising O, N, S optionally substituted with CH_3, F or Cl;

B is H or alkoxy or O, -CO-, optionally substituted 3 to 8 carbocyclic ring, 3 to 8 membered heterocyclic ring containing 1 to 3 heteroatoms selected from the group comprising O, N, S;

X is independently, H, $(CH_2)n$, -CO-, OCO, COO; $CO(CH_2)n$, $(NH_2)n$; $(CH_2)n(NH_2)n$; $(CH_2)n(NH_2)nCN$; CONH; $CONR_1R_2$, $CO(NH_2)n$; $(CH_2)nCO(NH_2)n$, $CO(NH_2)n(CH_2)CF_3$, $SO_2(CH_2)n$, $NH(CH_2)nCN$, unsubstituted or substituted 3-8 membered carbocylic ring or heterocyclic ring containing 1 to 3 heteroatoms selected from the group comprising O, N, S and SO_2, and substituents on the carboxylic or heterocyclic ring may be selected from Halogen, Alkoxy, CHMe, $-CH(CF_3)$, $-C(CF_3)(OH)$, $C(CF_3)(OMe)$, -CH(CN), CHOH, $CH(R_5)$,

Y may be absent or may be selected from H, R_1, R_2, halo, , C_1-C_6 Alkyl, C_1-C_6 Alkoxy CN, -CO-, COR_1, $(CH_2)n$, $-(CH_2)nCN$ -, CH_2CF_3, COOH, OR_1, NR_1R_2, $-COOR_1$, $-CON(R_1)_2$,$-SO_2(CH_2)n$,$-SO_2N(R_1)_2$, $-OCOR_1$, $CONHCH(CH_3)-CF_3$, CH_2CN, $CH_2SO_2CH_3$ $-NR_1COR_1$, -CONH, $CONR_1R_2$, $-CO(NH_2)n(CH_2)nSO_2$; $-CONH(CH_2)nOH$, $CONH(CH_2)nSO_2R_1R_2$, $-CONH-(CH_2)nCF_3$, $-CONH(CH_2)nCF_3$,$-NHCONH(CH_2)nCF_3$, $NHCONHR_1$, $-NHCOR_1R_2$, $NR_1CONR_1R_2$, $(NH_2)n$, $-NH_2CH_2$,

$NH_2CH_2CF_3$,-CH(CF_3)-(CH)n-CO-N-R_1R_2,CH(CF_3)-(CH)n-SO_2, (CH)n;CH(OH)(CF_3)(Heretocycle)R_1, optionally substituted 3 to 8 membered carbocyclic ring, or 3 to 8 membered saturated, mono-, fused- or bridged heterocyclic ring containing 1 to 3 heteroatoms, selected from the group comprising O, N, S or SO_2, optionally substituted 3 to 8 membered heterocyclic ring containing 1 to 3 heteroatoms, selected from the group comprising O, N, S or SO_2, wherein the substitution may independently be R_1 and R_2 at any position of the ring;$C_{1\text{-}6}$alk-aryl, Ar$C_{1\text{-}6}$alkyl;

R_1 and R_2 are independently selected from the group comprising H, halo, CN, CF_3, hydroxyl, Amino, SO_2, SO_2, C_1-C_6 Alkyl, SO_2-C_3-C_8-cycloalkyl, CH_2CN, CH_2CF_3, unsubstituted or substituted C_1-C_6 straight or branched alkyl wherein the substituents are selected from halo, OH, CN, C_1-C_6 alkoxy, optionally substituted NH_2, C_1-C_6 alkylsulfonyl, optionally substituted $CONH_2$, unsubstituted or substituted C_3-C_8 carbocyclyl or 3-8 membered heterocyclic ring with 1-3 heteroatoms selected from O, N and S, SO_2, C_1-C_6 straight or branched alkenyl, C_1-C_6 straight or branched alkynyl, , C_1-C_6 alkyloxy; C_1-C_6 alkylamino, C_1-C_6 alkylcarbonyl, C(O)-C_3-C_8-cycloalkyl, heteroalkyl, optionally substituted $CONH_2$, C_3–C_8 cycloalkyl, C_3–C_8cycloalkenyl, C_3–C_8heterocycloalkyl, C_3–C_8heterocycloalkenyl, carbocycyl, aryl, and heteroaryl, -CH(CF_3)-(CH)n-CO-N-R_3R_4, -CH(CF_3)-(CH)n-SO_2-NR_3R_4, CH(CF_3)-(CH)n-NR_3R_4, CH(CF_3)-NR_3R_4, CH(CF_3)-(CH)n-SO_2-CHR_3R_4, wherein cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, carbocyclyl, aryl and heteroaryl groups are optionally substituted;

R_3 and R_4 are H, independently CH_3, C_3–C_8 cycloalkyl;

R_5 is unsubstituted or substituted 3-8 membered carbocylic ring or heterocyclic ring containing 1 to 3 heteroatoms selected from the group comprising O, N, S, SO_2;

R_6, is independently H, C_1-C_6 straight or branched alkyl, halogen;

X can be connected to Y at any atom so as to arrive at chemically viable bond;

n is 0 to 3.

2. The compounds of formula I, as claimed in claim 1, selected from the group comprising:

1001. N-(2,2,2-trifluoroethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)benzamide;
1002. 1-(1,1,1-trifluoropropan-2-yl)-3-(4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)phenyl)urea;
1003. 1-(2,2,2-trifluoroethyl)-3-(4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)phenyl)urea;
1004. 1-(2,2,2-trifluoroethyl)-3-(5-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)pyrimidin-2-yl)urea;
1005. 1-(2,2,2-trifluoroethyl)-3-(5-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)pyridin-2-yl)urea;
1006. 1-(5-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)pyrazin-2-yl)-3-(2,2,2-trifluoroethyl)urea;
1007. N-(4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)phenyl)-3,3-dimethylazetidine-1-carboxamide;
1008. N-(4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)phenyl)morpholine-4-carboxamide;
1009. 1-(4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)phenyl)-3-(pyridin-4-yl)urea;
1010. 1-(4-(3H-imidazo[4,5-b]pyridin-7-yl)phenyl)-3-(2,2,2-trifluoroethyl)urea;
1011. N-(2,2,2-trifluoroethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)piperazine-1-carboxamide;
1012. N-(cyanomethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)piperazine-1-carboxamide;
1013. 4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-N-(2-(methylsulfonyl)ethyl)piperazine-1-carboxamide;
1014. 4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-N-(pyridin-4-yl)piperazine-1-carboxamide;
1015. N-(2-fluoropyridin-4-yl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)piperazine-1-carboxamide;
1016. N-(1-(methylsulfonyl)piperidin-4-yl)-4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)piperazine-1-carboxamide;
1017. N-(cyclopentylmethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)piperazine-1-carboxamide;

1018. 7-(4-(1,1-dioxidothiomorpholine-4-carbonyl)piperazin-1-yl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one;
1019. 4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-N-(2-methoxypyridin-4-yl)piperazine-1-carboxamide;
1020. N-(1,1-dioxidotetrahydro-2H-thiopyran-4-yl)-4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)piperazine-1-carboxamide;
1021. N-(1,1,1-trifluoropropan-2-yl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)piperazine-1-carboxamide;
1022. N-(2,2,2-trifluoroethyl)-4-(2-phenyl-3H-imidazo[4,5-b]pyridin-7-yl)piperazine-1-carboxamide;
1023. 7-(4-(3,3-dimethylazetidine-1-carbonyl)piperazin-1-yl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one;
1024. 4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-N-(2-methyl-4-(methylsulfonyl)phenyl)piperazine-1-carboxamide;
1025. N-(2,2,2-trifluoroethyl)-2-(4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)piperazin-1-yl)acetamide;
1026. N-(2,2,2-trifluoroethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1027. N-(cyanomethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1028. N-(2,2,2-trifluoroethyl)-3-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrrole-1-carboxamide;
1029. N-(2,2,2-trifluoroethyl)-4-(2,3-dihydro-1-methyl-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1030. N-(1,1,1-trifluoropropan-2-yl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1031. 7-(1-(4,4,4-trifluorobutanoyl)-1H-pyrazol-4-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one;
1032. N-(1-cyanocyclopropyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1033. N-(2-cyanopropan-2-yl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1034. N-(cyclopentylmethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1035. N-(cyanomethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide hydrochloride;
1036. N-(2,2,2-trifluoroethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1037. 7-(1-(3,3-dimethylazetidine-1-carbonyl)-1H-pyrazol-4-yl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one;
1038. N-(cyano(cyclopentyl)methyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1039. N-(2-cyano-1-cyclopentylethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1040. N-(2-cyanobutan-2-yl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1041. N-(1-cyclopentyl-2,2,2-trifluoroethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1042. 4-(1-ethyl-2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-N-(2,2,2-trifluoroethyl)-1H-pyrazole-1-carboxamide;
1043. N-(cyano(cyclopropyl)methyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1044. N-(1-cyano-2-methylpropyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1045. N-(2,2,2-trifluoroethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1046. N-(1-cyanopropan-2-yl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1047. N-((S)-1-cyano-2-methylpropyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1048. 1-(4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carbonyl)azetidine-3-carbonitrile;
1049. N-((R)-1-cyano-2-methylpropyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1050. N-(3-cyano-1,1,1-trifluoropropan-2-yl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1051. N-(2-cyano-1-cyclopropylethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1052. N-(1-cyanopropan-2-yl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1053. N-(1-cyanopropan-2-yl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1054. N-((R)-cyano(cyclopropyl)methyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1055. 1-(4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carbonyl)pyrrolidine-3-carbonitrile;
1056. N-(3-cyanocyclobutyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1057. 2-(1-(4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carbonyl)pyrrolidin-3-yl)acetonitrile;
1058. N-(1-(3-cyanoazetidin-1-yl)-1-oxopropan-2-yl)-4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1059. N-(2-(3-cyanoazetidin-1-yl)-2-oxoethyl)-4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1060. N-(2-(3-cyanoazetidin-1-yl)-2-oxoethyl)-4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1061. 3-(1-(4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carbonyl)pyrrolidin-3-yl)propanenitrile;
1062. N-(2-cyano-1-(tetrahydro-2H-pyran-4-yl)ethyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1063. N-(cyano(phenyl)methyl)-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1064. N-(2,2,2-trifluoroethyl)-4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1065. N-(2-cyano-1-(tetrahydro-2H-pyran-4-yl)ethyl)-4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1066. N-(2-cyanocyclohexyl)-4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1067. 1-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carbonyl)piperidine-4-carbonitrile;
1068. N-(1-(3-cyanoazetidin-1-yl)propan-2-yl)-4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;

1069. N-(1-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carbonyl)pyrrolidin-3-yl)propane-1-sulfonamide;
1070. N-(cyano(phenyl)methyl)-4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1071. N-(1-cyano-3-methoxypropyl)-4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1072. N-(1-cyano-3-(methylsulfonyl)propyl)-4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1073. N-((S)-1-cyano-2-methylpropyl)-4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1074. 1-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carbonyl)-4-methylpyrrolidine-3-carbonitrile;
1075. 2-(2-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)oxazol-4-yl)acetonitrile;
1076. 2-(2-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)thiazol-4-yl)acetonitrile;
1077. 7-(1-((oxazol-5-yl)methyl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1078. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)acetonitrile;
1079. 6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridine-3-carbonitrile;
1080. 7-(1-(5-((methylsulfonyl)methyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1081. 7-(1-(5-((oxetan-3-yl)methyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1082. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)acetonitrile hydrochloride;
1083. (6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)methanol;
1084. 7-(1-(5-(2,2,2-trifluoroethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1085. 7-(1-(5-(morpholinomethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1086. 4-((6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)methyl)thiomorpholine 1,1-dioxide;
1087. 1-((6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)methyl)azetidine-3-carbonitrile;

1088. 6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)-N-(cyanomethyl)pyridine-3-carboxamide;
1089. N-((6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)methyl)methanesulfonamide;
1090. N-((6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)methyl)methanesulfonamide;
1091. N-((6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)methyl)-2-cyanoacetamide;
1092. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-N-(2,2,2-trifluoroethyl)acetamide;
1093. 2-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)-N-(cyanomethyl)pyrimidine-5-carboxamide;
1094. N-(2,2,2-trifluoroethyl)-4-(2-phenyl-3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carboxamide;
1095. 4-(2-ethoxy-3H-imidazo[4,5-b]pyridin-7-yl)-N-(2,2,2-trifluoroethyl)-1H-pyrazole-1-carboxamide;
1096. 4-(2-cyclopropyl-3H-imidazo[4,5-b]pyridin-7-yl)-N-(2,2,2-trifluoroethyl)-1H-pyrazole-1-carboxamide;
1097. 3-(4-(2-(4-chloro-3-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)-tetrahydro-2H-pyran-4-carbonitrile;
1098. 4-(2-(1-acetylpiperidin-4-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-N-(2,2,2-trifluoroethyl)-1H-pyrazole-1-carboxamide;
1099. 2-(4-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)phenyl)acetonitrile;
1100. 2-(4-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)phenyl)-2-cyclopropylacetonitrile;
1101. 2-(4-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)phenyl)-2-morpholinoacetonitrile;
1102. N-(4-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)phenyl)-2-cyanoacetamide;
1103. 2-(4-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)-3-fluorophenyl)acetonitrile;
1104. 2-(4-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)-2-fluorophenyl)acetonitrile;

1105. 2-(4-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)-2-methoxyphenyl)acetonitrile;
1106. 2-(3-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)phenyl)acetonitrile;
1107. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)propanenitrile;
1108. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)propenamide;
1109. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)cyclopropanecarbonitrile;
1110. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-cyclopropylacetonitrile;
1111. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-(3,3-difluoroazetidin-1-yl)acetonitrile;
1112. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-morpholinoacetonitrile;
1113. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-(1,1-dioxidothiomorpholino)acetonitrile;
1114. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-(1-(methylsulfonyl)azetidin-3-yl)acetonitrile;
1115. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-(1-(methylsulfonyl)azetidin-3-yl)acetonitrile;
1116. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4-(methylsulfonyl)butanenitrile;
1117. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-2-yl)acetonitrile;
1118. 2-(2-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-4-yl)acetonitrile;
1119. 7-(1-(5-(2,2,2-trifluoro-1-methoxyethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1120. 7-(1-(5-(1-chloro-2,2,2-trifluoroethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1121. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-N,N-dimethylethanamine;

1122. 7-(1-(5-(1,1,1-trifluorobutan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1123. 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutanenitrile;
1124. 7-(1-(5-(2,2,2-trifluoro-1-isopropoxyethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1125. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1,1,1-trifluoropropan-2-ol;
1126. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-cyclopropyl-2,2,2-trifluoroethanol;
1127. 7-(1-(5-(1-cyclopropyl-2,2,2-trifluoro-1-methoxyethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1128. 7-(1-(5-(1,1,1,2-tetrafluoropropan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1129. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1,1,1-trifluoro-3-methylbutan-2-ol;
1130. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-cyclohexyl-2,2,2-trifluoroethanol;
1131. 1-(4-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-hydroxyethyl)piperidin-1-yl)ethenone;
1132. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-cyclopentyl-2,2,2-trifluoroethanol;
1133. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-methylpiperidin-4-yl)ethanol;
1134. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(tetrahydro-2H-pyran-4-yl)ethanol;
1135. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(piperidin-4-yl)ethan-1-ol;
1136. 7-(1-(5-(2,2,2-trifluoro-1-(oxetan-3-yl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1137. 7-(1-(5-(2,2,2-trifluoro-1-morpholinoethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1138. 7-(1-(5-(1,1,1-trifluoro-3-(methylsulfonyl)propan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1139. 7-(1-(5-(4-(cyclopropylsulfonyl)-1,1,1-trifluorobutan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1140. 7-(1-(5-(1-((methylsulfonyl)methoxy)-2,2,2-trifluoroethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1141. 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutane-1-sulfonamide;
1142. 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutane-1-sulfonamide;
1143. N-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)methanesulfonamide;
1144. 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N,N-dimethylbutanamide;
1145. 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutanamide;
1146. 1-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethyl)-3-cyclopropylurea;
1147. 7-(1-(5-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one;
1148. 4-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-5,5,5-trifluoro-N-methylpentanamide;
1149. N-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)cyclopropanecarboxamide;
1150. 4-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-N-cyclopropyl-5,5,5-trifluoropentanamide;
1151. N-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)cyclopentanecarboxamide;
1152. 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutan-1-amine;
1153. N-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)cyclopropanamine;
1154. 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutan-1-ol;
1155. 7-(1-(5-(1,1,1-trifluoro-4-methoxybutan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1156. 4-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-5,5,5-trifluoropentanenitrile;
1157. 2-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethoxy)acetonitrile;
1158. 7-(1-(5-(1-(methylsulfonyl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1159. (6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)(cyclopropyl)methanol;
1160. 7-(1-(5-(3-(methylsulfonyl)-1-(oxetan-3-yl)propyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1161. 7-(1-(5-(1-methoxy-3-(methylsulfonyl)propyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1162. 7-(1-(5-(1-fluoro-3-(methylsulfonyl)propyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1163. 7-(1-(5-(4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1164. (6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)(1-(methylsulfonyl)piperidin-4-yl)methanol;
1165. (6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)(1-methylpiperidin-4-yl)methanol;
1166. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-N-(2,2,2-trifluoroethyl)-2-hydroxyacetamide;
1167. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-cyclopropyl-N-(2,2,2-trifluoroethyl)acetamide;
1168. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-cyano-N-(2,2,2-trifluoroethyl)acetamide;
1169. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethanol;
1170. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-2-yl)-2,2,2-trifluoroethanol;
1171. 7-(1-(6-(2,2,2-trifluoro-1-methoxyethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1172. 1-(2-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-4-yl)-2,2,2-trifluoroethanol;

1173. 1-(5-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-2-yl)-2,2,2-trifluoroethanol;
1174. 7-(1-(5-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1175. 7-(1-(6-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1176. 7-(1-(4-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1177. 1-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazole-1-carbonyl)pyrrolidine-3-carbonitrile;
1178. 1-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethyl)-3-cyclopropylurea;
1179. 1-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)-3-cyclopropylurea;
1180. 3-cyclopentyl-3-(4-(2-phenyl-3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)propanenitrile;
1181. 7-(1-(5-((S)-1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1182. 7-(1-(5-((R)-1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1183. 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1,1,1-trifluoropropan-2-ol;
1184. 7-(1-(5-((R)-2,2,2-trifluoro-1-(oxetan-3-yl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1185. 7-(1-(5-((S)-2,2,2-trifluoro-1-(oxetan-3-yl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1186. 7-(1-(5-(1,1,1-trifluoro-4-(isopropylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1187. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-(methyl sulfonyl) 1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethanamine;
1188. 7-(1-(5-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-(cyclopropyl amino sulfonyl) 1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1189. 7-(1-(5-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-1H-imidazo[4,5-b]pyridin-2(3H)-one;

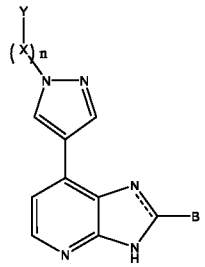
1190. 7-(1-(4-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)phenyl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1191. 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2-(trifluoromethyl)propan-1-ol;
1192. N-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethyl)-2-cyanoacetamide;
1193. 4-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-5,5,5-trifluoro-2-methylpentan-2-ol;
1194. 7-(1-(5-(3,3,3-trifluoro-2-((methylsulfonyl)methyl)propyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1195. N-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)-N-methylcyclopropanamine;
1196. 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-2,2-dimethylbutan-1-ol;
1197. N-(2-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethoxy)ethyl)cyclopropanamine;
1198. 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutan-1-amine;
1199. N-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)cyclohexanamine;
1200. 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutan-1-amine;
1201. 7-(1-(5-(1,1,1-trifluoro-4-morpholinobutan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1202. 1-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)azetidine-3-carbonitrile;
1203. 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-isopropylbutan-1-amine;
1204. 7-(1-(5-(4-(cyclopropylmethylsulfonyl)-1,1,1-trifluorobutan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1205. 7-(1-(5-(3-(cyclopropylmethylsulfonyl)-1,1,1-trifluoropropan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1206. 7-(1-(5-(1,1,1-trifluoro-3-morpholinopropan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1207. (S)-3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-isopropylbutan-1-amine;
1208. (R)-3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-isopropylbutan-1-amine;
1209. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-(Methyl sulfonyl)1H-pyrazol-1-yl)pyridin-3-yl)-3,3,3-trifluoropropan-1-amine;
1210. 4-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-5,5,5-trifluoro-N-isopropylpentanamide;
1211. 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N,N-diisopropylbutan-1-amine;
1212. N-(2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-3,3,3-trifluoropropyl)cyclopropanamine;
1213. (R)-3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutanamide;
1214. (S)-3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutanamide;
1215. (S)-4-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-5,5,5-trifluoro-N-isopropylpentanamide;
1216. 7-(1-(5-((S)-4-(cyclopropylsulfonyl)-1,1,1-trifluorobutan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1217. (S)-3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-N-methylbutan-1-amine,TFA salt;
1218. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-3,3,3-trifluoro-N-isopropylpropan-1-amine;
1219. 7-(1-(5-(1,1,1-trifluoro-4-(4-methylpiperazin-1-yl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1220. (4-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-hydroxyethyl)piperidin-1-yl)(cyclopropyl)methanone;
1221. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-(1-ethylpiperidin-4-yl)-2,2,2-trifluoroethanol;
1222. 7-(1-(5-(1,1,1-trifluoro-3-(4-methylpiperazin-1-yl)propan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1223. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1,1,1-trifluoro-4-(methylsulfonyl)butan-2-ol;

1224. 5-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-6,6,6-trifluorohexan-2-amine,TFA salt;
1225. (R)-1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-isopropylpyrrolidin-3-yl)ethanol;
1226. (S)-1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-isopropylpyrrolidin-3-yl)ethanol;
1227. 4-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-5,5,5-trifluoro-4-hydroxypentanenitrile;
1228. 2-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethoxy)-N-methylethanamine;
1229. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1,1,1-trifluoro-3-morpholinopropan-2-ol;
1230. 2-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1,1,1-trifluoro-4-morpholinobutan-2-ol;
1231. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-methylazetidin-3-yl)ethanol;
1232. (R)-1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-(1-ethylpyrrolidin-3-yl)-2,2,2-trifluoroethanol;
1233. (S)-1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-(1-ethylpyrrolidin-3-yl)-2,2,2-trifluoroethanol;
1234. (S)-1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-methylpyrrolidin-3-yl)ethanol;
1235. (R)-1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-methylpyrrolidin-3-yl)ethanol;
1236. 1-(3-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-hydroxyethyl)azetidin-1-yl)ethenone;
1237. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-isopropylazetidin-3-yl)ethanol;
1238. 4-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-5,5,5-trifluoro-4-hydroxy-N-isopropylpentanamide;
1239. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-1-(1-ethylazetidin-3-yl)-2,2,2-trifluoroethanol;
1240. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-isopropylpiperidin-4-yl)ethanol;

1241. N-(2-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoroethoxy)ethyl)propan-2-amine,TFA salt;
1242. (R)-1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-(oxetan-3-yl)pyrrolidin-3-yl)ethanol;
1243. (S)-1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-(oxetan-3-yl)pyrrolidin-3-yl)ethanol;
1244. 7-(1-(5-(2,2,2-trifluoro-1-methoxy-1-(1-methylpiperidin-4-yl)ethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;
1245. 3-(3-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-hydroxyethyl)azetidin-1-yl)-3-oxopropanenitrile;
1246. 3-(1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-hydroxyethyl)-N-methylazetidine-1-carboxamide;
1247. N-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)isobutyramide;
1248. N-(3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluorobutyl)-2-cyanoacetamide;
1249. 3-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-4,4,4-trifluoro-1-morpholinobutan-1-one;
1250. 1-(4-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-5,5,5-trifluoropentanoyl)azetidine-3-carbonitrile;
1251. (S)-1-(4-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)phenyl)-2,2,2-trifluoro-1-(1-isopropylpyrrolidin-3-yl)ethanol;
1252. (R)-1-(4-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)phenyl)-2,2,2-trifluoro-1-(1-isopropylpyrrolidin-3-yl)ethanol.

3. The 1H-imidazo[4,5-b]pyridin-2(3H)-one compounds as claimed in claim 1, their pharmaceutically acceptable salts and isomers of formula II:



Wherein;

B is H;

X is independently, H, $(CH_2)n$, -CO-, OCO, COO; $CO(CH_2)n$, $(NH_2)n$; $(CH_2)n(NH_2)n$; $(CH_2)n(NH_2)nCN$; CONH; $CONR_1R_2$, $CO(NH_2)n$; $(CH_2)nCO(NH_2)n$, $CO(NH_2)n(CH_2)CF_3$, $SO_2(CH_2)n$, $NH(CH_2)nCN$, unsubstituted or substituted 3-8 membered carbocylic ring or heterocyclic ring containing 1 to 3 heteroatoms selected from the group comprising O, N, S and SO_2, and substituents on the carboxylic or heterocyclic ring may be selected from Halogen, Alkoxy, CHMe, $-CH(CF_3)$, $-C(CF_3)(OH)$, $C(CF_3)(OMe)$, -CH(CN), CHOH, $CH(R_5)$,

H, R_1, R_2, halo, , C_1-C_6 Alkyl, C_1-C_6 Alkoxy CN, -CO-, COR_1, $(CH_2)n$, $-(CH_2)nCN$ -, CH_2CF_3, COOH, OR_1, NR_1R_2, $-COOR_1$, $-CON(R_1)_2$,$-SO_2(CH_2)n$,$-SO_2N(R_1)_2$, $-OCOR_1$, $CONHCH(CH_3)$-CF_3, CH_2CN, $CH_2SO_2CH_3$ $-NR_1COR_1$, -CONH, $CONR_1R_2$, $-CO(NH_2)n(CH_2)nSO_2$; $-CONH(CH_2)nOH$, $CONH(CH_2)nSO_2R_1R_2$, $-CONH-(CH_2)nCF_3$, $-CONH(CH_2)nCF_3$,$-NHCONH(CH_2)nCF_3$, $NHCONHR_1$, $-NHCOR_1R_2$, $NR_1CONR_1R_2$, $(NH_2)n$, $-NH_2CH_2$, $NH_2CH_2CF_3$,$-CH(CF_3)$-(CH)n-CO-N-R_1R_2,$CH(CF_3)$-(CH)n-SO_2, (CH)n;$CH(OH)(CF_3)$(Heretocycle)R_1, optionally substituted 3 to 8 membered carbocyclic ring, or 3 to 8 membered saturated, mono-, fused- or bridged heterocyclic ring containing 1 to 3 heteroatoms, selected from the group comprising O, N, S or SO_2, optionally substituted 3 to 8 membered heterocyclic ring containing 1 to 3 heteroatoms, selected from the group comprising O, N, S or SO_2, wherein the substitution may independently be R_1 and R_2 at any position of the ring;C_{1-6}alk-aryl, ArC_{1-6}alkyl;

R_1 and R_2 are independently selected from the group comprising H, halo, CN, CF_3, hydroxyl, Amino, SO_2, SO_2, C_1-C_6 Alkyl, SO_2-C_3-C_8-cycloalkyl, CH_2CN, CH_2CF_3, unsubstituted or substituted C_1-C_6 straight or branched alkyl wherein the substituents are selected from halo, OH, CN, C_1-C_6 alkoxy, optionally substituted NH_2, C_1-C_6 alkylsulfonyl, optionally substituted $CONH_2$, unsubstituted or substituted C_3-C_8 carbocyclyl or 3-8 membered heterocyclic ring with 1-3 heteroatoms selected from O, N and S, SO_2, C_1-C_6 straight or branched alkenyl, C_1-C_6 straight or branched alkynyl, , C_1-C_6 alkyloxy; C_1-C_6 alkylamino, C_1-C_6 alkylcarbonyl, C(O)-C_3-C_8-cycloalkyl, heteroalkyl, optionally substituted $CONH_2$, C_3–C_8 cycloalkyl, C_3–C_8cycloalkenyl, C_3–C_8heterocycloalkyl, C_3–C_8heterocycloalkenyl, carbocycyl, aryl, and heteroaryl, $-CH(CF_3)$-(CH)n-CO-N-R_3R_4, $-CH(CF_3)$-(CH)n-SO_2-NR_3R_4, $CH(CF_3)$-(CH)n-NR_3R_4,

$CH(CF_3)$-NR_3R_4, $CH(CF_3)$-(CH)n-SO_2-CHR_3R_4, wherein cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, carbocyclyl, aryl and heteroaryl groups are optionally substituted;

R_3 and R_4 are H, independently CH_3, C_3–C_8 cycloalkyl;

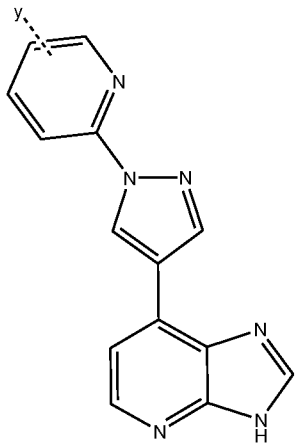
R_5 is unsubstituted or substituted 3-8 membered carbocylic ring or heterocyclic ring containing 1 to 3 heteroatoms selected from the group comprising O, N, S, SO_2;

R_6, is independently H, C_1-C_6 straight or branched alkyl, halogen;

X can be connected to Y at any atom so as to arrive at chemically viable bond;

n is 0 to 3.

4. The 1H-imidazo[4,5-b]pyridin-2(3H)-one compounds as claimed in claim 1, their pharmaceutically acceptable salts and isomers of formula III:



Wherein;

Y may be present at any position of the pyridine ring, preferably, at 4^{th} or 5^{th} position of pyridine;

Y is H, R_1, R_2, halo, CN, -CO-, COR_1, $(CH_2)n$, -$(CH_2)nCN$ -, CH_2CF_3, COOH, -$COOR_1$, -$CON(R_1)_2$,-$SO_2(CH_2)n$,-$SO_2N(R_1)_2$, -$OCOR_1$, -NR_1COR_1, -CONH, $CONR_1R_2$, -$CO(NH_2)n(CH_2)nSO_2$; -$CONH(CH_2)nOH$, $CONH(CH_2)nSO_2R_1R_2$, -CONH-$(CH_2)nCF_3$, -$CONH(CH_2)nCF_3$,-$NHCONH(CH_2)nCF_3$, , -$CH(CF_3)$-(CH)n-

CO-N-R_1R_2,$CH(CF_3)$-(CH)n-SO_2-(CH)n; $CH(OH)(CF_3)$(Heretocycle)R_1, $NHCONHR_1$, -$NHCOR_1R_2$, $NR_1CONR_1R_2$, (NH_2)n, -NH_2CH_2-, $NH_2CH_2CF_3$,

wherein the heterocycle is optionally substituted 3 to 8 membered saturated, mono-, fused- or bridged heterocyclic ring containing 1 to 3 heteroatoms, selected from the group comprising O, N, S;

wherein the substitution may independently be R_1 and R_2 at any position of the heterocyclic ring; $C_{1\text{-}6}$alk-aryl, Ar $C_{1\text{-}6}$ alkyl;

R_1 and R_2 are absent or independently selected from the group comprising H, halo, CN, CF_3, hydroxyl, Amino, SO_2, SO_2C_1-C_6 Alkyl, CH_2CF_3, C_1-C_6 straight or branched alkyl, C_1-C_6 straight or branched alkenyl, C_1-C_6 straight or branched alkynyl, halo-C_1-C_6 alkyl, C_1-C_6 alkyloxy; C_1-C_6 alkylamino,

n is 0 to 3.

5. The compounds of formula III, as claimed in claim 4, selected from the group comprising:

1133. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-methylpiperidin-4-yl)ethanol;

1134. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(tetrahydro-2H-pyran-4-yl)ethanol;

1176. 7-(1-(4-(1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1181. 7-(1-(5-((S)-1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

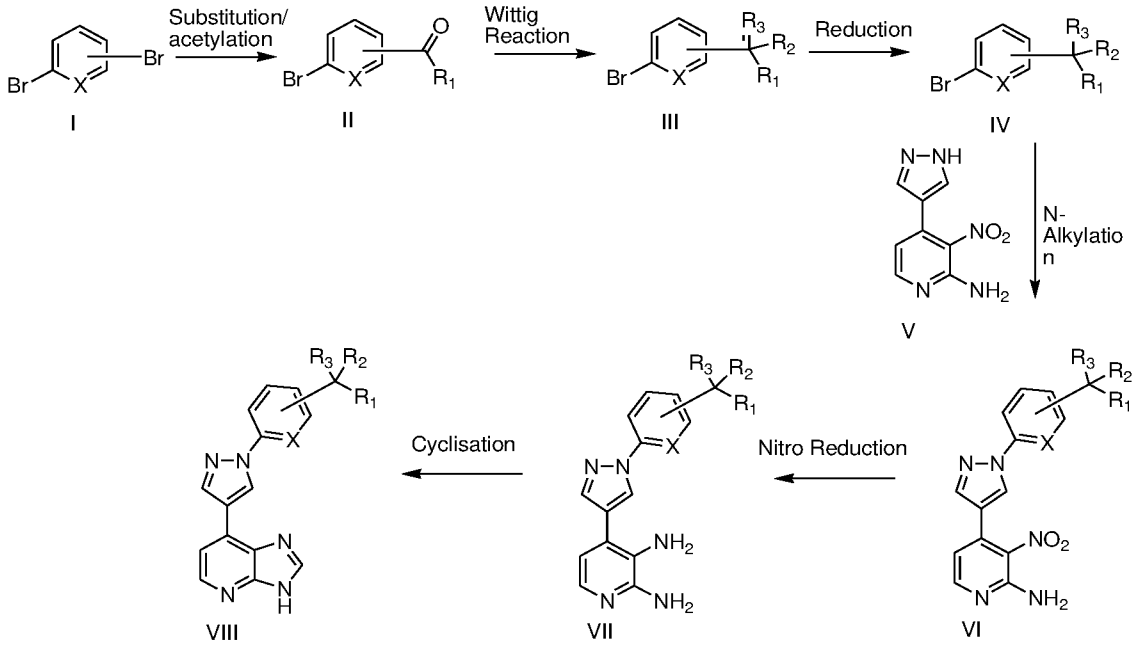
1182. 7-(1-(5-((R)-1,1,1-trifluoro-4-(methylsulfonyl)butan-2-yl)pyridin-2-yl)-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridine;

1225. (R)-1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-isopropylpyrrolidin-3-yl)ethanol;

1226. (S)-1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-isopropylpyrrolidin-3-yl)ethanol;

1231. 1-(6-(4-(3H-imidazo[4,5-b]pyridin-7-yl)-1H-pyrazol-1-yl)pyridin-3-yl)-2,2,2-trifluoro-1-(1-methylazetidin-3-yl)ethanol.

6. The process for preparing the compounds as claimed in claim 1, comprising the steps of:

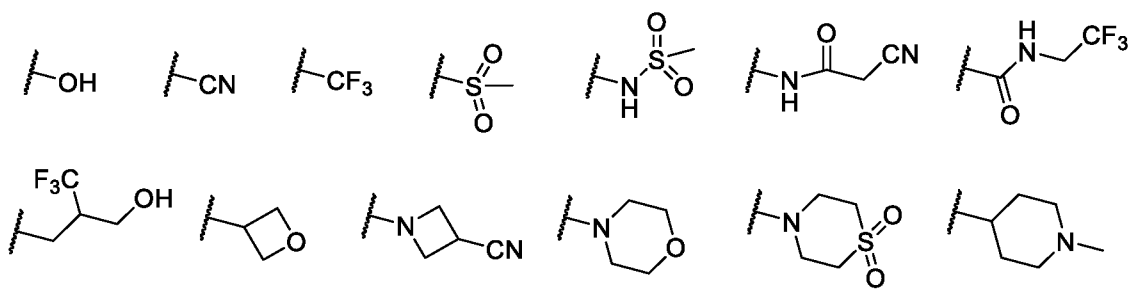


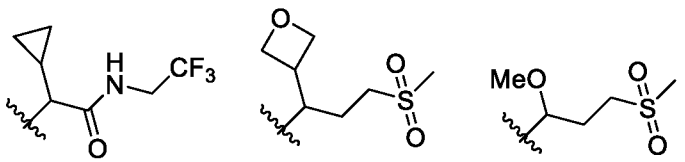
Wherein,

X is C, N,

R_2 and R_3 is H,

R_1:



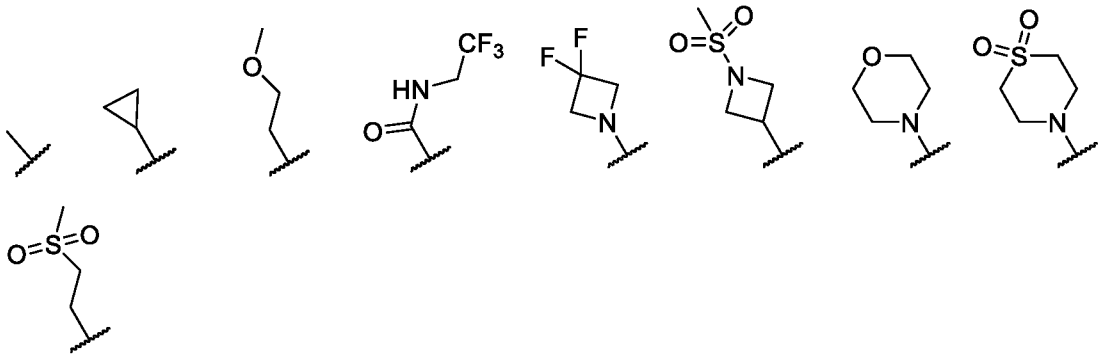


Wherein

X is C, N,

R_1 is CN and R_2 is H

R_3;

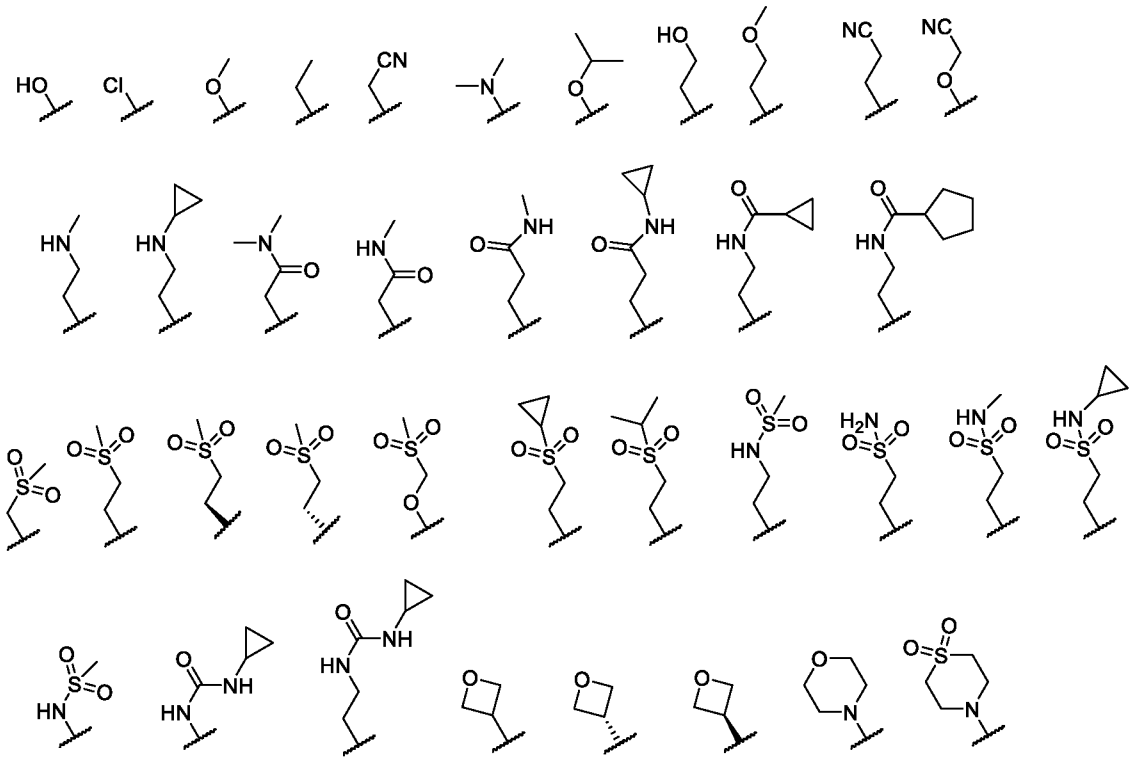


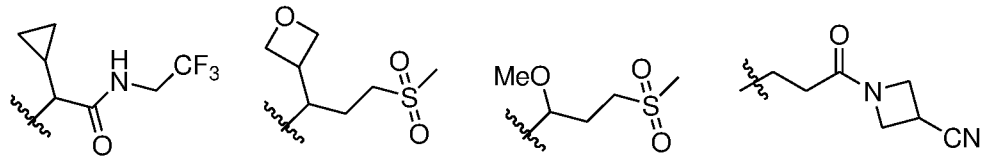
Wherein,

X is C, N,

R_1 CF_3 and R_2 is H,

R_3;



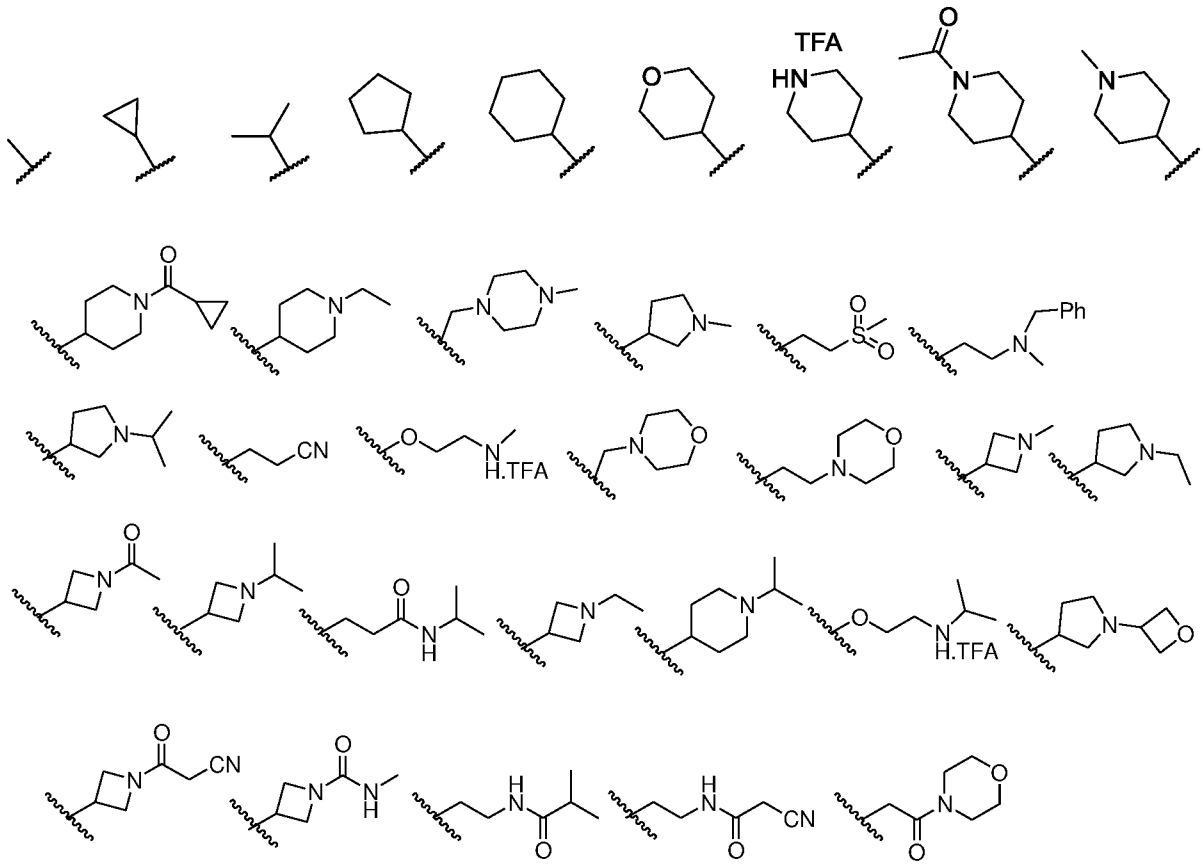


Wherein,

X is C, N,

R_1 is CF_3 and R_2 is OH

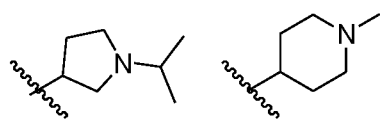
R_3



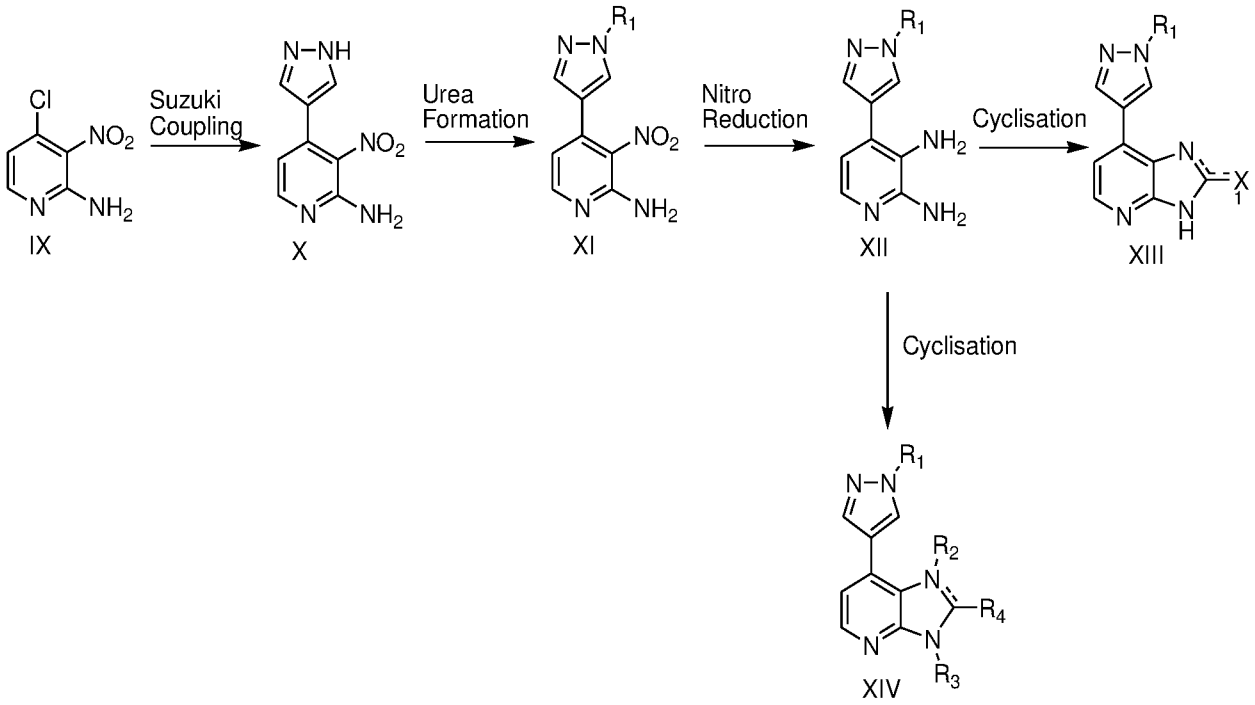
X is C, N,

R_1 is CF_3 and R_2 is OCH_3

R_3

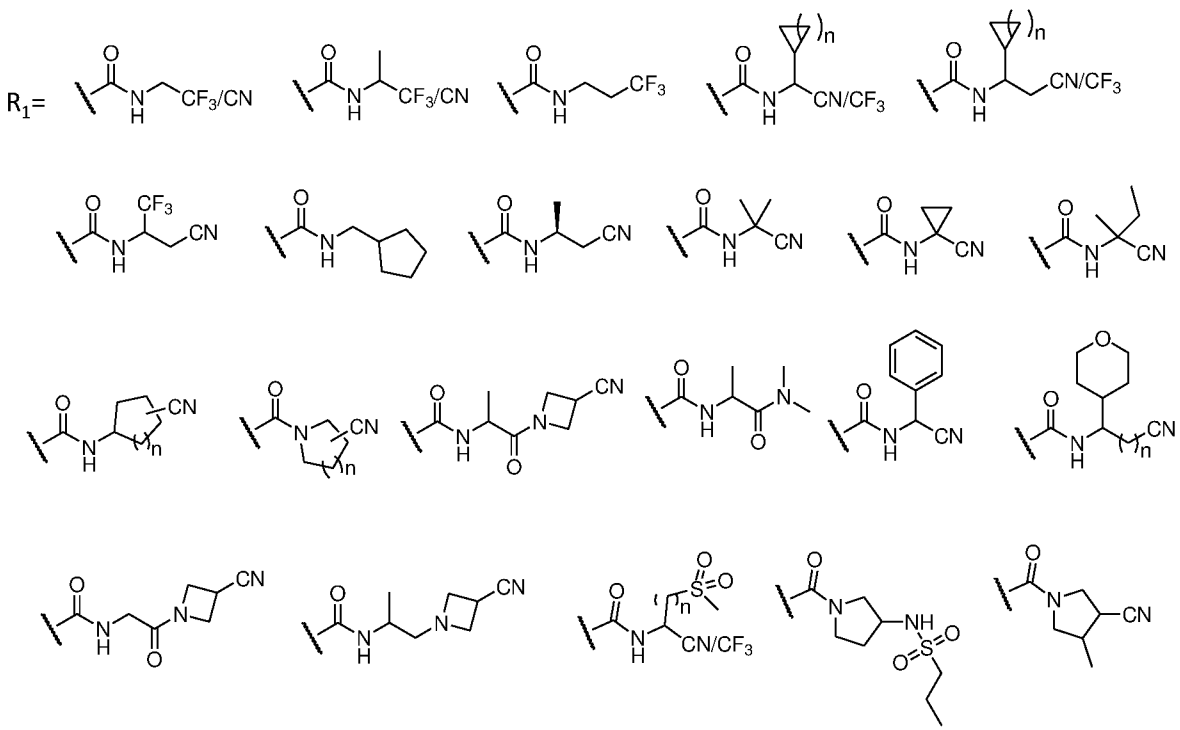


7. The process for preparing the compounds as claimed in claim 1, comprising the steps of:

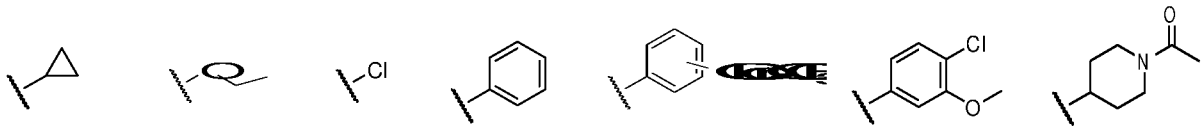


X_1= O or H R_2= H or –CH3 R_3= H or –CH3

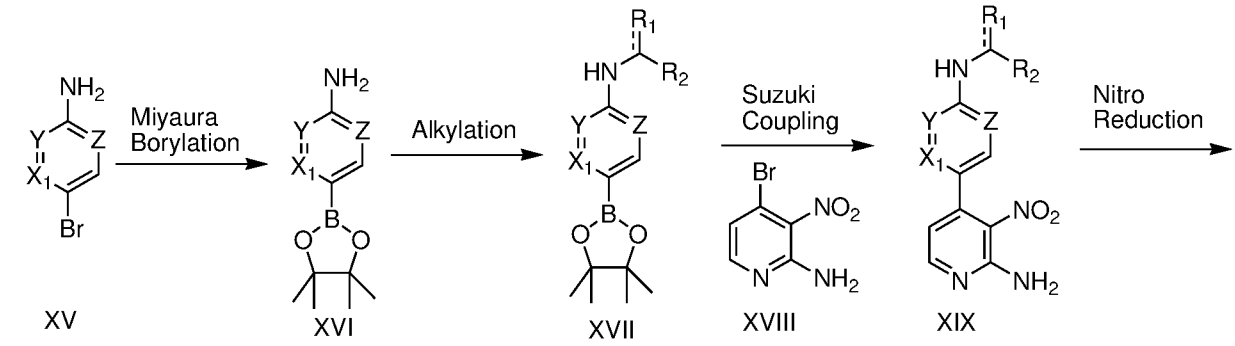
R_1;

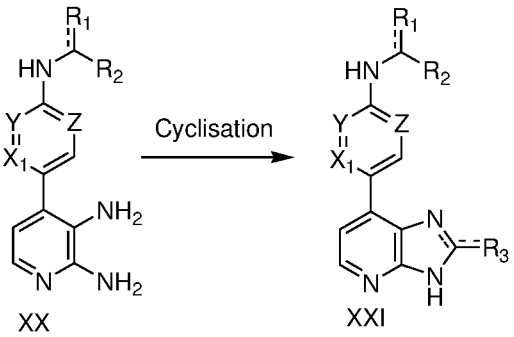


R_4;



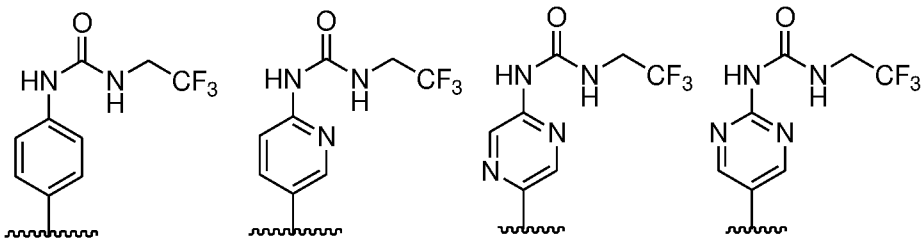
8. A process for preparing the compounds as claimed in claim 1, comprising the steps of:



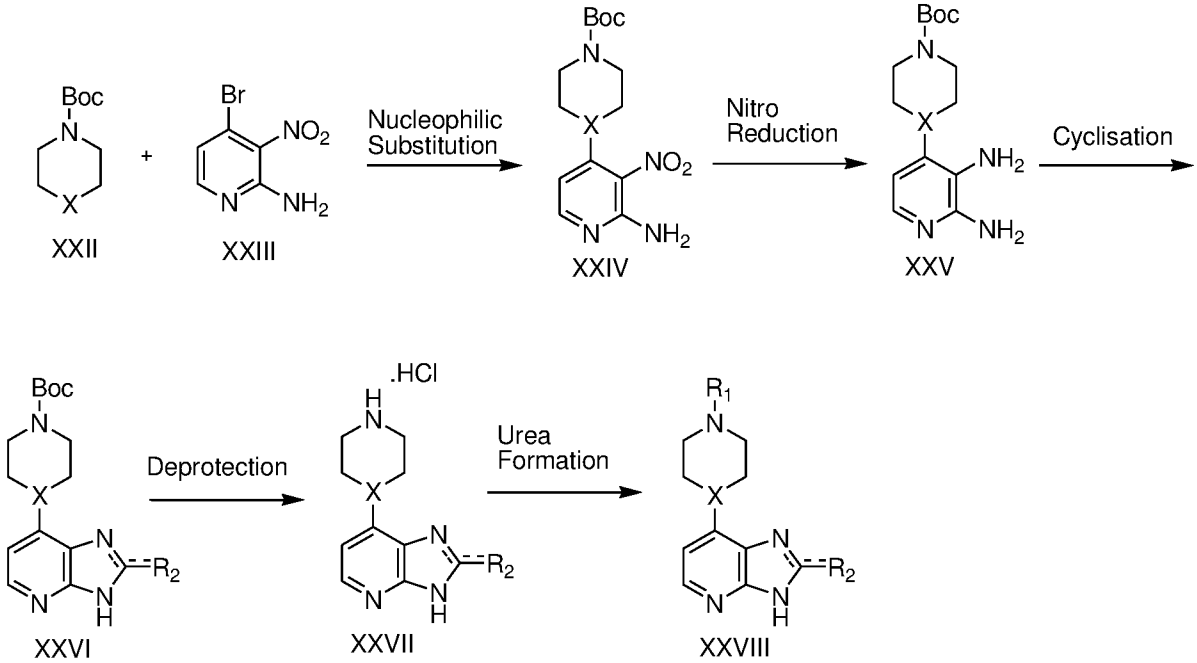


X1, Y, Z is C, N.

R_3 is H, O, carbocycle,



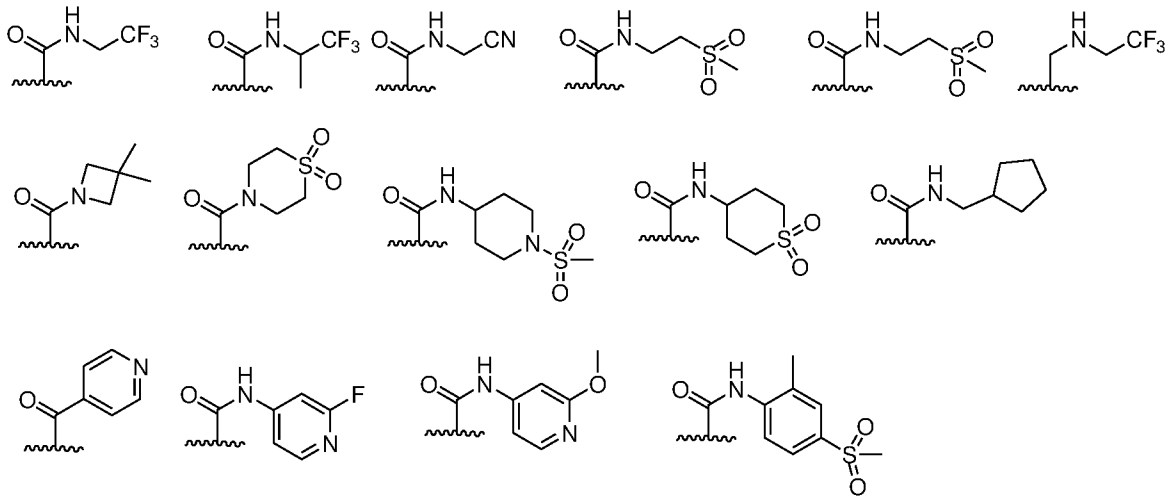
9. A process for preparing the compounds as claimed in claim 1, comprising the steps of:



X is C, N.

R_2 is H, O, carbocycle,

R_1 =



10. A Pharmaceutical composition comprising the compounds as claimed in claim 1 along with pharmaceutically acceptable excipients.

11. The Pharmaceutical composition as claimed in claim 10, when administered as orally, nasally, parenterally (intravenous, intramuscular, or subcutaneous), topically, transdermally, intravaginally, intravesically, intracistemally, or rectally, in the form of solid, semi-solid, lyophilized powder, or liquid dosage forms.

12. Compounds as claimed in claim 1, as selective JAK 1 inhibitor.

13. Compounds as claimed in claim 1 for their use in treating cancer, including, but not limited to, carcinomas, sarcomas, lymphomas, leukemias, myelomas, germ cell tumors, blastomas, tumors of the central and peripheral nervous system and other tumors including melanomas, seminoma and Kaposi's sarcoma and the like, acquired immunodeficiency syndrome (AIDS), Addison's disease, adult respiratory distress syndrome, allergies, ankylosing spondylitis, amyloidosis, asthma, autoimmune hemolytic anemia, autoimmune thyroiditis, Crohn's disease, episodic lymphopenia with lymphocytotoxins, erythroblastosis fetalis, Goodpasture's syndrome, Graves' disease, Hashimoto's thyroiditis, hypereosinophilia, irritable bowel syndrome and other interbowel diseases, Lupus, myasthenia gravis, myocardial or pericardial inflammation, pancreatitis, polymyositis, psoriasis, Reiter's syndrome, scleroderma, systemic analphylaxis, ulcerative colitis, nephritis (including glomerulonephritis), gout, arthritis (such as rheumatoid arthritis and osteoarthritis), erythema, dermatitis, dermatomyositis, bronchitis, cholecystitis, sepis and gastritis.

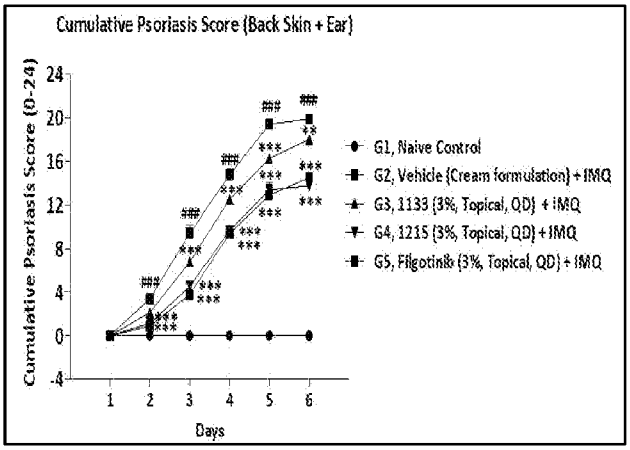


Figure 1a

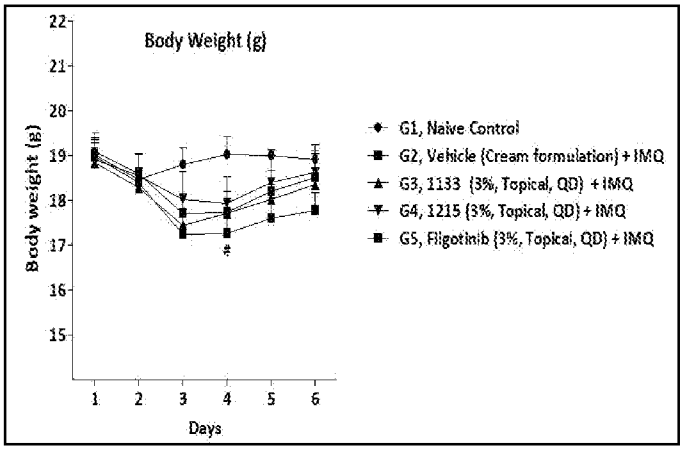


Figure 1b

Figure 1

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IN2020/050471

A. CLASSIFICATION OF SUBJECT MATTER
C07D471/04,A61K31/437,A61P35/00 Version=2020.01

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07D, A61K, A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

STNext, TotalPatent One, IPO Internal Database

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 20180289680 A1 (SICHUAN KELUN-BIOTECH BIOPHARMACEUTICAL CO. LTD., [CN]) 11 October 2018 (11.10.2018) Abstract, paragraphs [0003], [0004], example 4 and claims 4, 18-26;	1,3,10-13
Y	Abstract, paragraphs [0003], [0004], example 4 and claims 4, 18-26;	2,4-9
X	CAS REGISTRY Database (RN: 2177263-65-7), Entered STN: 20 February 2018 (20.02.2018) Compound CAS RN:2177263-65-7;	1,3
Y	VASBINDER MM et al, "Identification of azabenzimidazoles as potent JAK1 selective inhibitors", BIOORGANIC & MEDICINAL CHEMISTRY LETTERS (2016), Vol. 26, Pages: 60-67, Published online on 12 November 2015 (12.11.2015), DOI: 10.1016/j.bmcl.2015.11.031; Abstract, compounds in tables I-IV, and reaction scheme-1;	2,4-9
Y	WO 2013116291 A1 (CEPHALON, INC. [US]) 8 August 2013 (08.08.2013) Compounds in examples, and	

☒ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"D" document cited by the applicant in the international application
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
28-08-2020	28-08-2020
Name and mailing address of the ISA/ Indian Patent Office Plot No.32, Sector 14,Dwarka,New Delhi-110075 Facsimile No.	Authorized officer Veera Raghavulu Kattula Telephone No. +91-1125300200

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	claim 1;	2,4-9
Y	WO 2019076716 A1 (GALAPAGOS NV [BE]) 25 April 2019 (25.04.2019) Paragraphs [0002]-[0004], [0008]-[0010], compounds in table III, and claims 1, 15;	2,4-9;
A	WO 2009099594 A1 (CYTOKINETICS, INCORPORATED [US]) 13 August 2009 (13.08.2009) compounds in paragraph [100]	1-5

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IN2020/050471

Citation	Pub.Date	Family	Pub.Date
US 20180289680 A1	11-10-2018	CN 108137603 A	08-06-2018
		WO 2017097224 A1	15-06-2017
		JP 2018536634 A	13-12-2018
		EP 3360878 A1	15-08-2018
WO 2013116291 A1	08-08-2013	ES 2567552 T3	25-04-2016
		EP 2809671 A1	10-12-2014
		US 20140350011 A1	27-11-2014
WO 2019076716 A1	25-04-2019	GB 201717260 D0	06-12-2017
		CN 111225916 A	02-06-2020
		CA 3079449 A1	25-04-2019
		AU 2018350592 A1	04-06-2020
		TW 201918483 A	16-05-2019
		IL 273943 D0	31-05-2020
WO 2009099594 A1	13-08-2009	KR 20100119773 A	10-11-2010
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		EP 2244711 A1	03-11-2010
		AU 2009210787 A1	13-08-2009
		CA 2713864 A1	13-08-2009
		JP 2011510985 A	07-04-2011
		IL 207367 D0	30-12-2010