

BENZIMIDAZOLE DERIVATIVES AND THEIR USES

The present invention relates generally to Transient Receptor Potential Canonical (TRPC) Channel proteins, and more particularly to inhibitors of Transient Receptor Potential Channel 6 (TRPC6) protein activity, pharmaceutical compositions comprising said inhibitors and to methods of using such inhibitors.

BACKGROUND OF THE INVENTION

The TRPC6 channel, a member of the Transient receptor potential (TRP) family, which is a non-selective cation-permeable channel, is activated by diacylglycerol and the like produced by activation of phospholipase C and exerts physiological and pathophysiological effects. TRPC6 has effects such as cardiac pathological hypertrophy and fibrosis, progression of myocardial damage in muscular dystrophy, acute pulmonary vasoconstriction, pathological progression in chronic hypoxia-induced pulmonary hypertension, allergic airway response, migration of cells such as neutrophils, increased permeability of endothelial cells on inflammation, pathological flattening of podocytes and progression of glomerular injury, and proliferation or infiltration of malignant tumors, and is diversely distributed in the brain, heart, lungs, kidneys, placenta, ovaries, spleen, and the like (see for example J. Clin. Invest. 116:3114-3126, 2006; Dev. Cell. 23:705-715, 2012; Circ. Res. 114:823-832, 2014; Proc. Natl. Acad. Sci. USA 103:19093-19098, 2006; J. Cardiovasc. Pharmacol. 57:140-147, 2011; Hypertension 63:173-80, 2014; Clin. Exp. Allergy 38:1548-1558, 2008; Acta. Physiol. 195:3-11, 2009; J. Exp. Med. 209:1953-1968, 2011; Arterioscler. Thromb. Vasc. Biol. 33:2121-2129, 2013; PLoS ONE 5: e12859, 2010; Expert. Opin. Ther. Targets. 14:513-27, 2010; and BMC Cancer 13:116, 2013). In familial focal segmental glomerulosclerosis (FSGS), gain-of-function mutants of TRPC6 have been identified, and in steroid resistant nephrotic syndrome or idiopathic pulmonary arterial hypertension patients, a single nucleotide polymorphism in the promoter region that increases mRNA expression of TRPC6 has been identified (see for example: Pediatr Res. 2013 Nov;74(5):511-6 and Circulation. 2009 May 5;119(17):2313-2322). Thus, it is considered that hyperfunction and increased expression of TRPC6 contribute to pathological progression of nephrotic syndrome, pulmonary hypertension and the like (see for example Science 308:1801-1804, 2005; Nat. Genet. 37:739-744, 2005; PLoS One 4: e7771, 2009; Clin. J. Am. Soc. Nephrol. 6:1139-1148, 2011; Mol. Biol. Cell. 22:1824-1835, 2011; BMC Nephrol. 14:104, 2013; Pediatr. Res. 74:511-516, 2013; and Nephrol. Dial. Transplant. 28:1830-1838, 2013). Furthermore, increased expression of TRPC6 has been reported in minimal change nephrotic syndrome, membranous nephropathy, and diabetic nephropathy (see, for example, Circulation 119:2313-2322, 2009; J. Am. Soc. Nephrol. 18:29-36, 2007; and Nephrol. Dial. Transplant. 27:921-929, 2012).

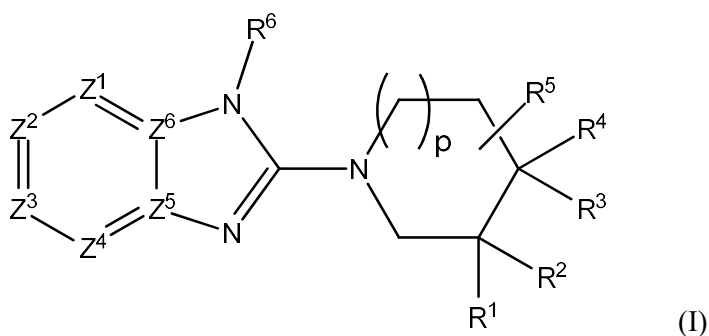
New approaches are needed to modulate TRPC6 activity and more particularly inhibit TRPC6 activity in the prevention and/or treatment of nephrotic syndrome, minimal change disease, focal segmental glomerulosclerosis, collapsing glomerulopathy, membranous nephropathy, membranoproliferative glomerulonephritis, IGA nephropathy, acute renal failure, chronic renal failure,

diabetic nephropathy, sepsis, pulmonary hypertension, acute lung disorder, acute respiratory distress syndrome (ARDS) heart failure, stroke, malignant tumor, and muscular dystrophy. There remains a need for agents that exploit different mechanisms of action and may have better outcomes in terms of relief of symptoms, safety, and patient mortality, both short-term and long-term.

SUMMARY

The present disclosure provides compounds which inhibit TRPC proteins, and more specifically inhibit TRPC6 proteins. The present disclosure provides, in one example, benzimidazole compounds which inhibit TRPC6 activity. Inhibition of TRPC6 activity may be particularly desirable in the treatment or prevention of a variety of diseases including nephrotic syndrome, focal segmental glomerulosclerosis, membranous nephropathy, diabetic nephropathy, heart failure, stroke, acute lung injury, acute respiratory distress syndrome (ARDS) and acute renal failure.

In one aspect, the present disclosure refers to a compound or pharmaceutically acceptable salt thereof, according to Formula I:



Wherein

p is 0 or 1;

when p is 0, then R¹ is hydrogen, C₁-C₆alkyl, halogen or hydroxy; R² is amino or aminoC₁-C₄alkyl; R³ is hydrogen; and R⁴ is C₁-C₆alkyl or phenyl; or

when p is 0, then R¹ and R³, taken in combination, form a fused C₃-C₆cycloalkyl ring or a fused 4 to 6 member heterocycle ring having 1 or 2 ring heteroatoms independently selected from N, O or S, which cycloalkyl or heterocycle is optionally substituted with amino; R² is hydrogen, C₁-C₆alkyl or aminoC₁-C₄alkyl; and R⁴ is hydrogen; or

when p is 1, then R¹ is NHR^{1a}; R^{1a} is hydrogen, C₁-C₄alkyl, C₃-C₇cycloalkyl, hydroxyC₁-C₄alkyl, or 4 to 6 member heterocycloalkyl having one ring heteroatom selected from N, O or S; R² is hydrogen, C₁-C₄alkyl, hydroxyC₁-C₄alkyl or C(O)NH₂; R³ is halogen, C₁-C₄alkyl, C₁-C₄alkoxy or hydroxy; and R⁴ is hydrogen, C₁-C₄alkyl or halogen; or

when p is 0 or 1, then CR¹R², taken in combination, form a spirocyclic 4 to 6 member heterocycloalkyl; R³ is hydrogen, halogen, C₁-C₄alkyl, C₁-C₄alkoxy, or hydroxy; and R⁴ is hydrogen or halogen; or

when p is 1, then R¹ and R³, taken in combination, form a fused 4 to 6 member heterocycle or a fused 3 to 7 member carbocycle, which heterocycle comprises a ring nitrogen atom and optionally 0 or 1 additional ring heteroatoms selected from N, O and S, and which carbocycle is substituted with amino; and R² is hydrogen; and R⁴ is hydrogen, halogen or hydroxy;

5 R⁵ represents 1 or 2 substituents independently selected from hydrogen, halogen, hydroxy, amino, C₁-C₆alkyl or C₁-C₆alkoxy;

R⁶ is -(CR⁷R⁸)-A; or

R⁶ is a 4 to 7 member lactam which is optionally substituted with one or two substituents independently selected from the group consisting of hydroxy, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, C₃-C₆cycloalkyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, hydroxyC₁-C₆alkyl, C₁-C₆alkoxyC₁-C₆alkyl, phenyl, 4 to 7 member heterocycle having 1 ring atoms selected from N, O or S and 0 or 1 additional ring N atoms or 5 or 6 member heteroaryl having one ring heteroatom selected from N, O or S and 0 or 1 additional ring nitrogen atom, wherein the heteroaryl, heterocycle or phenyl group is optionally substituted with 0, 1 or 2 C₁-C₆alkyl or halogen; or

15 R⁶ is a partially unsaturated 9 or 10 member bicyclic carbocycle, which is optionally substituted with 1 or 2 substituents independently selected from halogen, cyano, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, C(O)NH₂ and C(O)NHC₁-C₆alkyl;

A is 5 or 6 member heteroaryl, which heteroaryl comprises one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms, which heteroaryl is optionally substituted with 0, 1, 2, 3 or 4 groups independently selected from halogen, cyano, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, C₃-C₆cycloalkyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, C(O)N(R^A)₂, S(O)₂C₁-C₆alkyl, phenyl or 5 or 6 member heteroaryl having one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms, wherein the optional heteroaryl or phenyl substituent is further substituted with 0, 1 or 2 C₁-C₆alkyl; or

25 A is phenyl substituted with 1, 2 or 3 substituents independently selected from halogen, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, haloC₁-C₆alkyl, cyanoC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, cyanoC₁-C₆alkoxy, S(O)_qC₁-C₆alkyl, S(O)₂NH₂, S(O)₂NHC₁-C₆alkyl, S(O)₂N(C₁-C₆alkyl)₂, C(O)NH₂, C(O)NHC₁-C₆alkyl, C(O)N(C₁-C₆alkyl)₂, hydroxy, cyano, or 5 or 6 member heteroaryl having one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms which heteroaryl is further substituted with 0, 1 or 2 C₁-C₆alkyl; or

A is C(O)OR⁹ or C(O)NR⁹R¹⁰; or

A is optionally substituted 9 or 10 member aromatic or partially unsaturated bicyclic having 0, 1 or 2 ring nitrogen atoms and 0 or 1 additional ring heteroatoms selected from N, O or S, which bicyclic is substituted with 0, 1 or 2 substituents independently selected from the group consisting of halogen, cyano,

C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, C(O)NH₂, C(O)OH or C(O)NHC₁-C₆alkyl;

R^A is independently selected at each occurrence from hydrogen or C₁-C₄alkyl; or

N(R^A)₂, taken in combination, forms a 4 to 7 member azacycle which is optionally substituted

with 0, 1, or 2 C₁-C₄alkyl;

R⁷ is hydrogen, C₁-C₄alkyl or amino;

R⁸ is hydrogen or C₁-C₄alkyl; or

CR⁷R⁸, taken in combination form a 3 to 6 member cycloalkandiyl group;

R⁹ is hydrogen, C₁-C₆alkyl, C₃-C₆cycloalkyl, hydroxyC₁-C₆alkyl, C₁-C₄alkoxyC₁-C₆alkyl, haloC₁-C₆alkyl, cyano C₁-C₆alkyl or -(CH₂)_rR^{9A} wherein r is 0 or 1 and R^{9A} is phenyl, 4 to 7 member heterocycle having one ring heteroatoms selected from N, O or S, which ring sulfur may be optionally oxidized, and 0 or 1 additional ring N atoms or 5 or 6 member heteroaryl having one ring heteroatom selected from N, O or S and 0, 1, or 2 additional ring N atoms, which phenyl, heterocycle or heteroaryl is optionally substituted with 0, 1 or 2 halogen, C₁-C₄alkyl or C(O)C₁-C₄alkyl;

R¹⁰ is hydrogen, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, halo C₁-C₆alkyl, C₃-C₇cycloalkyl or saturated, partially unsaturated or aromatic 5 or 6 member heterocycle having 1 or 2 ring heteroatoms independently selected from N, O and S, which sulfur is optionally oxidized, and which heterocycle is optionally substituted with 1 or 2 substituents independently selected from C₁-C₆alkyl and halogen, which heterocycle has 1 or 2 ring hetero atoms selected from N, O or S, which sulfur may be optionally oxidized, and wherein each alkyl or cycloalkyl is optionally substituted with cyano, halogen, hydroxy, C₁-C₆alkoxy, S(O)_qC₁-C₆alkyl, 4 to 6 member heterocycle having 1 or 2 ring heteroatoms selected from N, O or S or 5 or 6 member heteroaryl having 1 ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms and where each heterocycle or heteroaryl is optionally substituted with 0, 1, or 2 C₁-C₄alkyl; or

NR⁹R¹⁰, taken in combination, form a monocyclic or bicyclic 4 to 10 member saturated or partially unsaturated heterocycle having one or two ring nitrogen atoms and 0 or 1 additional ring heteroatom selected from N, O or S, which ring sulfur may be optionally oxidized, which heterocycle is optionally substituted with 0, 1 or 2 substituents selected from halogen, oxo, hydroxy, cyano, C₁-C₆alkyl, C₃-C₆cycloalkyl, haloC₁-C₆alkyl, hydroxyC₁-C₆alkyl, cyanoC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, C₁-C₆alkoxyC₁-C₄alkyl, S(O)_qC₁-C₆alkyl, C₁-C₆alkylS(O)_qC₁-C₆alkyl CO₂H, C(O)C₁-C₆alkyl, C(O)OC₁-C₆alkyl, C(O)C₃-C₆cycloalkyl, N(R¹⁵)C(O)C₁-C₆alkyl or C(O)N(R¹⁵)₂, phenyl, 4 to 6 member heterocycle having 1 or 2 ring heteroatoms selected from N, O or S or a 5 or 6 member heteroaryl having 1 ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms and where each heterocycle or heteroaryl is optionally substituted with 0, 1, or 2 C₁-C₄alkyl;

q is 0, 1 or 2;

Z¹ is N or CR¹¹;

Z^2 is N or CR¹²;

Z^3 is N or CR¹³;

Z^4 is N or CR¹⁴,

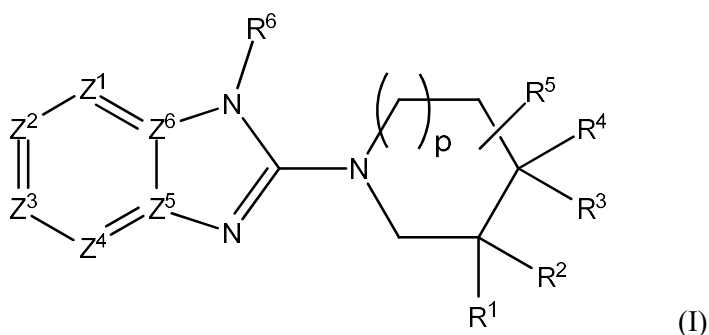
Z^5 and Z^6 are each independently N or C;

wherein 0, 1 or 2 of Z^1 , Z^2 , Z^3 , Z^4 , Z^5 and Z^6 are N;

each of R¹¹, R¹², R¹³ and R¹⁴ is independently selected from the group consisting of hydrogen, halogen, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, C₁-C₆alkoxy, haloC₁-C₆alkyl, haloC₁-C₆alkoxy, C₃-C₇cycloalkyl, cyano, SO₂C₁-C₆alkyl, phenyl, and saturated, partially unsaturated or aromatic 5 or 6 member heterocycle having 1 or 2 ring heteroatoms independently selected from N, O and S, which heterocycle is optionally substituted with 1 or 2 substituents independently selected from C₁-C₆alkyl and halogen; and

R¹⁵ is selected at each occurrence from hydrogen or C₁-C₄alkyl, or N(R¹⁵)₂, taken in combination, form a 4 to 7 member azacycle optionally substituted with 0, 1 or 2 C₁-C₄alkyl; with the proviso that compounds of Formula I do not include 1- [7-fluoro-6-methoxy-1-[[2-(trifluoromethyl)phenyl]methyl]-1*H*-benzimidazol-2-yl]-3-piperidinamine.

In another aspect, the present disclosure refers to a compound or pharmaceutically acceptable salt thereof, according to Formula I:



Wherein

p is 0 or 1;

when p is 0, then R¹ is hydrogen, C₁-C₆alkyl, halogen or hydroxy; R² is amino or aminoC₁-C₄alkyl; R³ is hydrogen; and R⁴ is C₁-C₆alkyl or phenyl; or

when p is 0, then R¹ and R³, taken in combination, form a fused C₃-C₆cycloalkyl ring or a fused 4 to 6 member heterocycle ring having 1 or 2 ring heteroatoms independently selected from N, O or S, which cycloalkyl or heterocycle is optionally substituted with amino; R² is hydrogen, C₁-C₆alkyl or aminoC₁-C₄alkyl; and R⁴ is hydrogen; or

when p is 1, then R¹ is NHR^{1a}; R^{1a} is hydrogen, C₁-C₄alkyl, C₃-C₇cycloalkyl, hydroxyC₁-C₄alkyl, or 4 to 6 member heterocycloalkyl having one ring heteroatom selected from N, O or S; R² is hydrogen, C₁-C₄alkyl, hydroxyC₁-C₄alkyl or C(O)NH₂; R³ is halogen, C₁-C₄alkyl, C₁-C₄alkoxy or hydroxy; and R⁴ is hydrogen, C₁-C₄alkyl or halogen; or

when p is 0 or 1, then C(NHR^{1a})R², taken in combination, form a spirocyclic 4 to 6 member heterocycloalkyl; R³ is hydrogen, halogen C₁-C₄alkyl, C₁-C₄alkoxy, or hydroxy; and R⁴ is hydrogen or halogen; or

when p is 1, then R¹ and R³, taken in combination, form a fused 4 to 6 member heterocycle or a fused 3 to 7 member carbocycle, which heterocycle comprises a ring nitrogen atom and optionally 0 or 1 additional ring heteroatoms selected from N, O and S, and which carbocycle is substituted with amino; and R² is hydrogen; and R⁴ is hydrogen, halogen or hydroxy;

R⁵ represents 1 or 2 substituents independently selected from hydrogen, halogen, hydroxy, amino, C₁-C₆alkyl or C₁-C₆alkoxy;

R⁶ is -(CR⁷R⁸)-A; or

R⁶ is a 4 to 7 member lactam which is optionally substituted with one or two substituents independently selected from the group consisting of hydroxy, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, hydroxyC₁-C₆alkyl, C₁-C₆alkoxyC₁-C₆alkyl, phenyl or 5 or 6 member heteroaryl having one ring heteroatom selected from N, O or S and 0 or 1 additional ring nitrogen atom, wherein the heteroaryl or phenyl group is optionally substituted with 0, 1 or 2 C₁-C₆alkyl or halogen; or

R⁶ is a partially unsaturated 9 or 10 member bicyclic carbocycle, which is optionally substituted with 1 or 2 substituents independently selected from halogen, cyano, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, C(O)NH₂ and C(O)NHC₁-C₆alkyl;

A is 5 or 6 member heteroaryl, which heteroaryl comprises one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms, which heteroaryl is optionally substituted with 0, 1, 2, 3 or 4 groups independently selected from halogen, cyano, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, C(O)NH₂, C(O)NHC₁-C₆alkyl, phenyl or 5 or 6 member heteroaryl having one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms, wherein the optional heteroaryl or phenyl substituent is further substituted with 0, 1 or 2 C₁-C₆alkyl; or

A is phenyl substituted with 1, 2 or 3 substituents independently selected from halogen, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, haloC₁-C₆alkyl, cyanoC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, cyanoC₁-C₆alkoxy, S(O)_qC₁-C₆alkyl, S(O)₂NH₂, S(O)₂NHC₁-C₆alkyl, S(O)₂N(C₁-C₆alkyl)₂, C(O)NH₂, C(O)NHC₁-C₆alkyl, C(O)N(C₁-C₆alkyl)₂, hydroxy, cyano, or 5 or 6 member heteroaryl having one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms which heteroaryl is further substituted with 0, 1 or 2 C₁-C₆alkyl; or

A is C(O)OR⁹ or C(O)NR⁹R¹⁰; or

A is optionally substituted 9 or 10 member aromatic or partially unsaturated bicyclicl having 0, 1 or 2 ring nitrogen atoms and 0 or 1 additional ring heteroatoms selected from N, O or S, which bicyclicl is substituted with 0, 1 or 2 substituents independently selected from the group consisting of halogen, cyano,

C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, C(O)NH₂, C(O)OH or C(O)NHC₁-C₆alkyl;

R⁷ is hydrogen, C₁-C₄alkyl or amino;

R⁸ is hydrogen or C₁-C₄alkyl; or

5 CR⁷R⁸, taken in combination form a 3 to 6 member cycloalkandiyl group;

R⁹ is hydrogen, C₁-C₆alkyl, hydroxyC₁-C₆alkyl, haloC₁-C₆alkyl or cyano C₁-C₆alkyl;

10 R¹⁰ is hydrogen, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, halo C₁-C₆alkyl, C₃-C₇cycloalkyl or 4 to 7 member heterocycle, which heterocycle has 1 or 2 ring hetero atoms selected from N, O or S, which sulfur may be optionally oxidized, and wherein each alkyl or cycloalkyl is optionally substituted with cyano, halogen, hydroxy, C₁-C₆alkoxy, S(O)_qC₁-C₆alkyl, 4 to 6 member heterocycle having 1 or 2 ring heteroatoms selected from N, O or S or 5 or 6 member heteroaryl having 1 ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms; or

15 NR⁹R¹⁰, taken in combination, form a monocyclic or bicyclic 4 to 9 member heterocycle having one ring nitrogen atom and 0 or 1 additional ring heteroatom selected from N, O or S, which ring sulfur may be optionally oxidized, which heterocycle is optionally substituted with 0, 1 or 2 substituents selected from halogen, oxo, hydroxy, cyano, C₁-C₆alkyl, halo C₁-C₆alkyl, hydroxyC₁-C₆alkyl, C₁-C₆alkoxy, S(O)_qC₁-C₆alkyl, CO₂H, C(O)C₁-C₆alkyl, or C(O)NH₂;

q is 0, 1 or 2;

Z¹ is N or CR¹¹;

20 Z² is N or CR¹²;

Z³ is N or CR¹³;

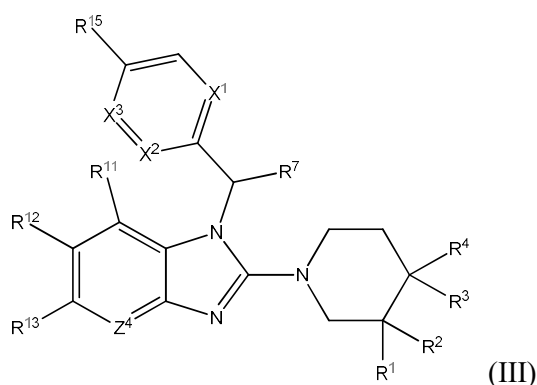
Z⁴ is N or CR¹⁴;

Z⁵ and Z⁶ are each independently N or C;

wherein 0, 1 or 2 of Z¹, Z², Z³, Z⁴, Z⁵ and Z⁶ are N;

25 each of R¹¹, R¹², R¹³ and R¹⁴ is independently selected from the group consisting of hydrogen, halogen, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, C₁-C₆alkoxy, haloC₁-C₆alkyl, haloC₁-C₆alkoxy, C₃-C₇cycloalkyl, cyano, SO₂C₁-C₆alkyl, phenyl, and saturated, partially unsaturated or aromatic 5 or 6 member heterocycle having 1 or 2 ring heteroatoms independently selected from N, O and S, which heterocycle is optionally substituted with 1 or 2 substituents independently selected from C₁-C₆alkyl and halogen; and with the proviso that compounds of Formula I do not include 1- [7-fluoro-6-methoxy-1-[[2-(trifluoromethyl)phenyl]methyl]-1*H*-benzimidazol-2-yl]-3-piperidinamine.

In another aspect, the present disclosure refers to a compound of Formula III:



Wherein

X¹ is CR¹⁶ or N;

X² is CR¹⁷ or N;

5 X³ is CR¹⁸ or N;

Z⁴ is N or CR¹⁴;

R¹ is NHR^{1a};

R^{1a} is hydrogen or C₁-C₄alkyl;

R² is hydrogen or C₁-C₄alkyl;

10 R³ is hydrogen or halogen;

R⁴ is hydrogen or halogen;

R⁷ is hydrogen, methyl or ethyl;

R¹¹ is hydrogen, halogen, cyano or C₁-C₄alkyl;

15 R¹² and R¹³ are each independently selected from the group consisting of hydrogen, halogen, cyano, C₁-C₄alkyl, haloC₁-C₄alkyl, C₁-C₄alkoxy, or haloC₁-C₄alkoxy;

R¹⁴ is hydrogen, halogen, cyano or C₁-C₄alkyl;

R¹⁵ is hydrogen, halogen, cyano, C₁-C₄alkyl, C₁-C₄alkoxy, haloC₁-C₄alkyl, haloC₁-C₄alkoxy, C(O)NH₂, C(O)NH(C₁-C₄alkyl) or 5 member heteroaryl having one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms;

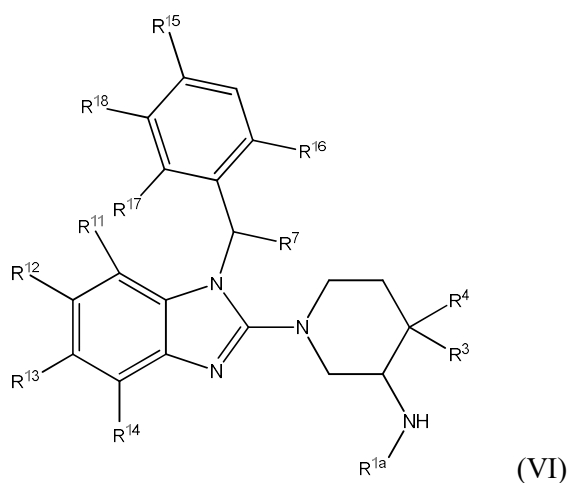
20 R¹⁶ is hydrogen, halogen, cyano, C₁-C₄alkyl, C₁-C₄alkoxy, haloC₁-C₄alkyl or haloC₁-C₄alkoxy;

R¹⁷ is hydrogen or halogen; and

R¹⁸ is hydrogen, halogen, cyano, C₁-C₄alkyl, C₁-C₄alkoxy, haloC₁-C₄alkyl or haloC₁-C₄alkoxy, wherein at least one of R¹⁵, R¹⁶, R¹⁷ or R¹⁸ is not hydrogen.

In another aspect, the present disclosure refers to a compound of Formula VI:

25



Wherein

R^{1a} is hydrogen or C₁-C₄alkyl;

R³ is hydrogen or halogen;

5 R⁴ is hydrogen or halogen;

R⁷ is hydrogen, methyl or ethyl;

R¹¹ is hydrogen, halogen, cyano or C₁-C₄alkyl;

R¹² and R¹³ are each independently selected from the group consisting of hydrogen, halogen, cyano, C₁-C₄alkyl, haloC₁-C₄alkyl, C₁-C₄alkoxy, or haloC₁-C₄alkoxy;

10 R¹⁴ is hydrogen, halogen, cyano or C₁-C₄alkyl;

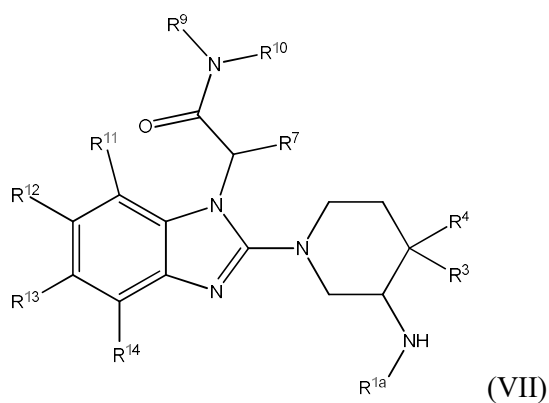
R¹⁵ is hydrogen, halogen, cyano, C₁-C₄alkyl, C₁-C₄alkoxy, haloC₁-C₄alkyl, haloC₁-C₄alkoxy, C(O)NH₂, C(O)NH(C₁-C₄alkyl) or 5 member heteroaryl having one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms;

R¹⁶ is hydrogen, halogen, cyano, C₁-C₄alkyl, C₁-C₄alkoxy, haloC₁-C₄alkyl or haloC₁-C₄alkoxy;

15 R¹⁷ is hydrogen or halogen; and

R¹⁸ is hydrogen, halogen, cyano, C₁-C₄alkyl, C₁-C₄alkoxy, haloC₁-C₄alkyl or haloC₁-C₄alkoxy, wherein at least one of R¹⁵, R¹⁶, R¹⁷ or R¹⁸ is not hydrogen.

In another aspect, the present disclosure refers to a compound of Formula VII:



Wherein

R^{1a} is hydrogen or C₁-C₄alkyl;

R³ is hydrogen or halogen;

R⁴ is hydrogen or halogen;

5 R⁷ is hydrogen, methyl or ethyl;

R⁹ is hydrogen, methyl or ethyl;

R¹⁰ is C₁-C₄alkyl or haloC₁-C₄alkyl wherein each alkyl is optionally substituted with cyano, halogen, hydroxy, C₁-C₆alkoxy or S(O)_qC₁-C₆alkyl; or

10 NR⁹R¹⁰, taken in combination, form a 4 to 6 member monocyclic azacycle or a 7 to 9 member bicyclic azacycle, each of which having one ring nitrogen atom and 0 or 1 additional ring heteroatom selected from N, O or S, which ring sulfur may be optionally oxidized, wherein each azacycle is optionally substituted with 0, 1 or 2 substituents selected from halogen, oxo, hydroxy, cyano, C₁-C₆alkyl, halo C₁-C₆alkyl, hydroxyC₁-C₆alkyl, C₁-C₆alkoxy, S(O)₂C₁-C₆alkyl, CO₂H, C(O)C₁-C₆alkyl, or C(O)NH₂;

R¹¹ is hydrogen, halogen, cyano or C₁-C₄alkyl;

15 R¹² and R¹³ are each independently selected from the group consisting of hydrogen, halogen, cyano, C₁-C₄alkyl, haloC₁-C₄alkyl, C₁-C₄alkoxy, or haloC₁-C₄alkoxy; and

R¹⁴ is hydrogen, halogen, cyano or C₁-C₄alkyl.

In another aspect, the present disclosure refers to a compound, selected from:

20 (S)-6-((2-(3-aminopiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;
(S)-6-((2-(3-aminopiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;
(S)-6-((2-(3-aminopiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;
6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

25 6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

30 6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

35 (R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-4-carbonitrile;

(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

5 (R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

10 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3S,4S)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(S)-6-((2-(5-amino-3,3-difluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazole-4-carbonitrile;

15 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-(trifluoromethoxy)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(trifluoromethoxy)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

20 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-5-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-6-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3aR,7aR)-hexahydro-1H-pyrrolo[2,3-c]pyridin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

25 6-((2-((3aR,7aS)-hexahydro-1H-pyrrolo[2,3-c]pyridin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3aS,7aS)-hexahydro-1H-pyrrolo[2,3-c]pyridin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

30 6-((2-((3aS,7aR)-hexahydro-1H-pyrrolo[2,3-c]pyridin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(R)-6-((2-(1,6-diazaspiro[3.5]nonan-6-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(S)-6-((2-(1,6-diazaspiro[3.5]nonan-6-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(3R,4R)-1-(1-((5-chloropyridin-2-yl)methyl)-6-(methylsulfonyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4R)-1-(1-((5-chloropyridin-2-yl)methyl)-5-(methylsulfonyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazole-4-carbonitrile;

5 (3R,4R)-1-(5,7-difluoro-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4R)-1-(4,6-difluoro-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

10 (3R,4R)-1-(5,7-difluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4R)-1-(4,6-difluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-4-carbonitrile;

15 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-4-carbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(3R,4S)-1-(1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

20 (3R,4S)-1-(1-((5-chloropyrimidin-2-yl)methyl)-5-fluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(R)-2-(3-amino-4,4-difluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

25 (R)-2-(3-amino-4,4-difluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

tert-butyl ((3R,4R)-1-(1-((5-cyanopyridin-2-yl)methyl)-5,6-dimethyl-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl)carbamate;

30 (S)-6-((2-(3-aminopiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

(S)-6-((2-(3-aminopiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

35 6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

5 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

(S)-2-(3-aminopiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

10 (S)-2-(3-aminopiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;

15 (R)-2-(3-amino-4,4-difluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

(R)-2-(3-amino-4,4-difluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;

(S)-6-((2-(3-aminopiperidin-1-yl)-4,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

20 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-4,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

25 (R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-4,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(S)-6-((2-(3-aminopiperidin-1-yl)-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(S)-6-((2-(3-aminopiperidin-1-yl)-5,7-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

30 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,7-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

35 6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5,7-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-5,7-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

5 2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;

(S)-6-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

10 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((1R,5S)-1-(aminomethyl)-3-azabicyclo[3.1.0]hexan-3-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

15 6-((2-((1S,5R)-1-(aminomethyl)-3-azabicyclo[3.1.0]hexan-3-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3aR,4R,6aS)-4-aminohexahydrocyclopenta[c]pyrrol-2(1H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3aS,4S,6aR)-4-aminohexahydrocyclopenta[c]pyrrol-2(1H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

20 6-((2-((3aR,4S,6aS)-4-aminohexahydrocyclopenta[c]pyrrol-2(1H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3aS,4R,6aR)-4-aminohexahydrocyclopenta[c]pyrrol-2(1H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

25 (R)-6-((2-(3-(aminomethyl)pyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

(S)-6-((2-(3-(aminomethyl)pyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

30 6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

(R)-1-(1-((5-chloropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4,4-difluoropiperidin-3-amine hydrochloride;

(3R,4S)-1-(1-((5-chloropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

5 (R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

10 (R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-4-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-4-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

15 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-3H-imidazo[4,5-b]pyridin-3-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)nicotinonitrile;

20 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)-N-(tert-butyl)nicotinamide;

6-((2-((3R,4R)-3-amino-4-hydroxypiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3S,4S)-3-amino-4-hydroxypiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

25 6-((2-(2,6-diazaspiro[3.4]octan-6-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((4aR,7aS)-hexahydropyrrolo[3,4-b][1,4]oxazin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((4aS,7aR)-hexahydropyrrolo[3,4-b][1,4]oxazin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

30 6-((2-((4aR,7aR)-hexahydropyrrolo[3,4-b][1,4]oxazin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((4aS,7aS)-hexahydropyrrolo[3,4-b][1,4]oxazin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

35 (S)-3-amino-1-(1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidine-3-carboxamide;

(R)-3-amino-1-(1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidine-3-carboxamide;

(S)-6-((2-(3-amino-3-(hydroxymethyl)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

5 (R)-6-((2-(3-amino-3-(hydroxymethyl)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4S)-3-amino-4-fluoro-1-piperidinyl)-6-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

10 6-((2-((3R,4S)-3-amino-4-fluoro-1-piperidinyl)-5-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R)-3-amino-4,4-difluoro-1-piperidinyl)-6-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R)-3-amino-4,4-difluoro-1-piperidinyl)-5-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

15 6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5-methyl-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-6-methyl-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

20 6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-6-chloro-5-methyl-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5-chloro-6-methyl-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-6-fluoro-5-methyl-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

25 6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5-fluoro-6-methyl-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3S)-3-(methylamino)-1-piperidinyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

30 6-((2-((3R)-3-(methylamino)-1-piperidinyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-6-(difluoromethoxy)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5-(difluoromethoxy)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-4-methoxy-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-4-methyl-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

5 5-((2-((3R,4S)-3-amino-4-fluoro-1-piperidiny)-6-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-2-pyrazinecarboxamide;

5-((2-((3R,4S)-3-amino-4-fluoro-1-piperidiny)-5-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-2-pyrazinecarboxamide;

10 6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-6-chloro-5-(trifluoromethoxy)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-5-chloro-6-(trifluoromethoxy)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-6-chloro-5-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

15 6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-5-chloro-6-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((5R)-1,7-diazaspiro[4.5]decan-7-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile,
6-((2-((5S)-1,7-diazaspiro[4.5]decan-7-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

20 6-((2-((6R)-1,8-diazaspiro[5.5]undecan-8-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((6S)-1,8-diazaspiro[5.5]undecan-8-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((4aR,8aR)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

25 6-((2-((4aS,8aS)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

5-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)-2-pyrazinecarboxamide;

30 5-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-6-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-2-pyrazinecarboxamide;

6-((2-((5R)-1,7-diazaspiro[4.5]decan-7-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((5S)-1,7-diazaspiro[4.5]decan-7-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R)-3-amino-4,4-difluoro-1-piperidiny)-5-methoxy-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R)-3-amino-4,4-difluoro-1-piperidinyl)-6-methoxy-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3S)-3-(methylamino)-1-piperidinyl)-6-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

5 6-((2-((3S)-3-(methylamino)-1-piperidinyl)-5-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3S)-3-amino-3-methyl-1-piperidinyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

(S)-6-((2-(3-aminopiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile
 10 2,2,2-trifluoroacetate;

(S)-6-((2-(3-aminopiperidin-1-yl)-5-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile
 2,2,2-trifluoroacetate;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4-chloro-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile 2,2,2-trifluoroacetate;

15 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

20 6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazole-4-carbonitrile;

25 (R)-2-(3-amino-4,4-difluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-5-fluoro-1H-benzo[d]imidazole-7-carbonitrile;

(R)-2-(3-amino-4,4-difluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazole-4-carbonitrile;

6-((2-((3R,4R)-3-amino-4-hydroxypiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

30 6-((2-((3R,4S)-3-amino-4-hydroxypiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(R)-4-((2-(3-amino-4,4-difluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

4-((2-((3R,4R)-3-amino-4-hydroxypiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile compound with 4-((2-((3S,4S)-3-amino-4-hydroxypiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile (1:1) dihydrochloride;

4-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-5,7-difluoro-1H-benzimidazol-1-yl)methyl)benzonitrile;

4-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-4,6-difluoro-1H-benzimidazol-1-yl)methyl)benzonitrile;

2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-1-(4-cyanobenzyl)-1H-benzimidazole-6-carbonitrile;

2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-1-(4-cyanobenzyl)-1H-benzimidazole-5-carbonitrile;

2-((3R)-3-amino-4,4-difluoro-1-piperidiny)-1-(4-cyanobenzyl)-1H-benzimidazole-6-carbonitrile;

2-((3R)-3-amino-4,4-difluoro-1-piperidiny)-1-(4-cyanobenzyl)-1H-benzimidazole-5-carbonitrile;

(R)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

4-((2-((3R,4R)-3-amino-4-methylpiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

4-((2-(3-(aminomethyl)-3-methylpyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

4-((2-((3S,4R)-3-amino-4-phenylpyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile & 4-((2-((3R,4S)-3-amino-4-phenylpyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

(S)-4-((2-(3-aminopyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

(S)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

4-((2-(6-amino-2-azaspiro[4.4]nonan-2-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

4-((2-(4-aminohexahydrocyclopenta[c]pyrrol-2(1H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

4-((2-((3S,4S)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

4-((2-((3S,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

4-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

(R)-4-((2-(3-(aminomethyl)-3-fluoropyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile 2,2,2-trifluoroacetate;

(S)-4-((2-(3-(aminomethyl)-3-fluoropyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile 2,2,2-trifluoroacetate;

(R)-4-((2-(3-(aminomethyl)-3-hydroxypyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile 2,2,2-trifluoroacetate;

(S)-4-((2-(3-(aminomethyl)-3-hydroxypyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile 2,2,2-trifluoroacetate;

(S)-4-((2-(3-(aminomethyl)pyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

(R)-4-((2-(3-(aminomethyl)pyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

4-((2-((3S,4S)-3-amino-4-methylpiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile
2,2,2-trifluoroacetate;

4-((2-((3S,4R)-3-amino-4-methylpiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile
2,2,2-trifluoroacetate;

5 4-((2-((3R,4S)-3-amino-4-methylpiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile
2,2,2-trifluoroacetate;

4-((2-((1S,5R)-1-(aminomethyl)-3-azabicyclo[3.1.0]hexan-3-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

10 4-((2-((1R,5S)-1-(aminomethyl)-3-azabicyclo[3.1.0]hexan-3-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

(R)-4-((2-(3-aminopiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

(R)-4-((2-(3-aminopiperidin-1-yl)-5-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

2-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

15 (3R,4R)-4-fluoro-1-(1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(3R,4R)-4-fluoro-1-(1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

20 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;

(3R,4R)-1-(1-((5-bromopyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

25 (3R,4R)-4-fluoro-1-(1-((5-(trifluoromethyl)pyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(3R,4R)-4-fluoro-1-(1-((5-methoxypyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

30 (3R,4R)-1-(1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-cyanopyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;
 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;
 5 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-bromopyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;
 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-bromopyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;
 10 5-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)pyrazine-2-carbonitrile;
 2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;
 2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;
 15 (3R,4R)-3-amino-1-(1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)piperidin-4-ol;
 (3R,4R)-3-amino-1-(1-((5-chloropyrimidin-2-yl)methyl)-5-fluoro-1H-benzo[d]imidazol-2-yl)piperidin-4-ol;
 20 6-((2-((3R,4R)-3-amino-4-hydroxypiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;
 6-((2-((3R,4R)-3-amino-4-hydroxypiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;
 (S)-1-(1-((5-chloropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
 (S)-5-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)picolinonitrile;
 25 (3R,4R)-1-(1-((5-chloropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;
 (R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;
 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyridin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile hydrochloride;
 30 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyridin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile hydrochloride;
 (3R,4R)-1-(1-((R)-1-(5-chloropyridin-2-yl)ethyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

(3R,4R)-1-(1-((S)-1-(5-chloropyridin-2-yl)ethyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

(3R,4R)-1-(1-((R)-1-(5-chloropyridin-2-yl)ethyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

5 (3R,4R)-1-(1-((S)-1-(5-chloropyridin-2-yl)ethyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

(3R,4R)-1-(5-chloro-1-((R)-1-(5-chloropyridin-2-yl)ethyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

10 (3R,4R)-1-(5-chloro-1-((S)-1-(5-chloropyridin-2-yl)ethyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

(3R,4R)-1-(6-chloro-1-((R)-1-(5-chloropyridin-2-yl)ethyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

(3R,4R)-1-(6-chloro-1-((S)-1-(5-chloropyridin-2-yl)ethyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

15 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((R)-1-(5-cyanopyridin-2-yl)ethyl)-1H-benzo[d]imidazole-6-carbonitrile hydrochloride;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((R)-1-(5-cyanopyridin-2-yl)ethyl)-1H-benzo[d]imidazole-5-carbonitrile hydrochloride;

20 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((S)-1-(5-cyanopyridin-2-yl)ethyl)-1H-benzo[d]imidazole-6-carbonitrile hydrochloride;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((S)-1-(5-cyanopyridin-2-yl)ethyl)-1H-benzo[d]imidazole-5-carbonitrile hydrochloride;

(3R,4R)-1-(1-((5-chloropyridin-2-yl)methyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

25 (3R,4R)-1-(5,6-difluoro-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

(R)-1-(1-((5-chloropyridin-2-yl)methyl)-5,7-difluoro-1H-benzo[d]imidazol-2-yl)-4,4-difluoropiperidin-3-amine hydrochloride;

30 (R)-1-(1-((5-chloropyridin-2-yl)methyl)-4,6-difluoro-1H-benzo[d]imidazol-2-yl)-4,4-difluoropiperidin-3-amine hydrochloride;

(R)-1-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)-2,3-dihydro-1H-indene-5-carbonitrile hydrochloride;

(S)-1-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)-2,3-dihydro-1H-indene-5-carbonitrile hydrochloride;

(R)-5-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)pyrazine-2-carbonitrile;

(R)-5-((2-(3-amino-4,4-difluoropiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)methyl)pyrazine-2-carbonitrile;

5 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-isopropylacetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(azetidin-1-yl)ethanone;

10 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(2-cyanopropyl)-N-ethylacetamide;

3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-methylpyrrolidin-2-one;

3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-phenylpiperidin-2-one;

15 3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-chlorophenyl)pyrrolidin-2-one;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-methoxypyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile hydrochloride;

20 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-methoxypyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile hydrochloride;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((6-(trifluoromethyl)pyridin-3-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile hydrochloride;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((6-(trifluoromethyl)pyridin-3-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile hydrochloride;

25 (S)-3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-methylpyrrolidin-2-one;

(R)-3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-methylpyrrolidin-2-one;

30 (S)-3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-chlorophenyl)pyrrolidin-2-one;

(R)-3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-chlorophenyl)pyrrolidin-2-one;

2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-1-((5-cyano-2-pyrazinyl)methyl)-1H-benzimidazole-6-carbonitrile;

2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-1-((5-cyano-2-pyrazinyl)methyl)-1H-benzimidazole-5-carbonitrile;

5-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-4,6-difluoro-1H-benzimidazol-1-yl)methyl)-2-pyrazinecarbonitrile;

5-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,7-difluoro-1H-benzimidazol-1-yl)methyl)-2-pyrazinecarbonitrile;

(3S)-1-(1-((5-fluoro-2-pyridinyl)methyl)-1H-benzimidazol-2-yl)-N-methyl-3-piperidinamine;

(3S)-1-(1-((5-chloro-2-pyridinyl)methyl)-1H-benzimidazol-2-yl)-N-methyl-3-piperidinamine;

6-((1R)-1-(2-((3S)-3-(methylamino)-1-piperidinyl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile;

6-((1S)-1-(2-((3S)-3-(methylamino)-1-piperidinyl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile;

(3R,4R)-1-(1-((5-chloro-2-pyrimidinyl)methyl)-5,7-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((5-chloro-2-pyrimidinyl)methyl)-4,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(5,6-difluoro-1-((1-methyl-1H-indazol-4-yl)methyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(5,6-difluoro-1-(5-quinolinylmethyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(5,6-difluoro-1-((1R)-1-(8-quinolinyl)ethyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(5,6-difluoro-1-((1S)-1-(8-quinolinyl)ethyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((3-(3-chlorophenyl)-1,2-oxazol-5-yl)methyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(5,6-difluoro-1-((1-methyl-1H-indazol-7-yl)methyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-(2,6-dichlorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

1-(1-azetidiny)-2-(2-((3S)-3-(methylamino)-1-piperidinyl)-1H-benzimidazol-1-yl)ethanone;

6-((1R)-1-(4,6-difluoro-2-((4aR,8aR)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile;

6-((1R)-1-(4,6-difluoro-2-((4aS,8aS)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile;

6-((1S)-1-(4,6-difluoro-2-((4aS,8aS)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile;

6-((1S)-1-(4,6-difluoro-2-((4aR,8aR)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile;

5 6-((1R)-1-(5,7-difluoro-2-((4aR,8aR)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile;

6-((1R)-1-(5,7-difluoro-2-((4aS,8aS)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile;

10 6-((1S)-1-(5,7-difluoro-2-((4aS,8aS)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile;

6-((1S)-1-(5,7-difluoro-2-((4aR,8aR)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile;

2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)-N-methylacetamide;

15 2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)-1-(4-morpholinyl)ethanone;

2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)-1-(1-pyrrolidinyl)ethanone;

20 2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)-N,N-dimethylacetamide;

(2R)-2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)-N,N-dimethylpropanamide;

(2S)-2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)-N,N-dimethylpropanamide;

25 2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)-1-(1-piperidinyl)ethanone;

2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)-N-ethylacetamide;

30 1-((5-chloro-2-pyrimidinyl)methyl)-2-((3R,4R)-4-fluoro-3-(methylamino)-1-piperidinyl)-1H-benzimidazole-6-carbonitrile;

1-((5-chloro-2-pyrimidinyl)methyl)-2-((3R,4R)-4-fluoro-3-(methylamino)-1-piperidinyl)-1H-benzimidazole-5-carbonitrile;

2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-6-chloro-1H-benzimidazol-1-yl)-1-(1-azetidiny)ethanone;

2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5-chloro-1H-benzimidazol-1-yl)-1-(1-azetidiny)ethanone;

2-((3R,4S)-3-amino-4-fluoro-1-piperidinyl)-1-(2-(1-azetidiny)-2-oxoethyl)-1H-benzimidazole-6-carbonitrile;

5 2-((3R,4S)-3-amino-4-fluoro-1-piperidinyl)-1-(2-(1-azetidiny)-2-oxoethyl)-1H-benzimidazole-5-carbonitrile;

(3R,4R)-1-(1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

10 (3R,4R)-1-(1-((5-chloropyrimidin-2-yl)methyl)-5-fluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(R)-6-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(R)-5-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)picolinonitrile 2,2,2-trifluoroacetate;

(R)-1-(1-(isoquinolin-7-ylmethyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

15 (R)-1-(1-((1-methyl-1H-indazol-7-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
6-((R)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile hydrochloride;

6-((S)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile hydrochloride;

20 6-((R)-1-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile hydrochloride;

6-((S)-1-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile hydrochloride;

25 6-((R)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)propyl)nicotinonitrile hydrochloride;

6-((S)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)propyl)nicotinonitrile hydrochloride;

(3R,4R)-1-(5,6-difluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

30 3-(1-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile;

(3R,4R)-1-(5,6-difluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

35 (3R,4S)-1-(5,6-difluoro-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4S)-4-fluoro-1-(1-((5-fluoropyrimidin-2-yl)methyl)-6-(trifluoromethyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(3R,4S)-4-fluoro-1-(1-((5-fluoropyrimidin-2-yl)methyl)-5-(trifluoromethyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

5 (R)-1-(5,6-difluoro-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4,4-difluoropiperidin-3-amine;

2-(2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)-1-(azetidin-1-yl)ethan-1-one;

10 2-(2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)-1-(azetidin-1-yl)ethan-1-one;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(2,2-dimethylpyrrolidin-1-yl)ethan-1-one;

6-((2-((3R,4S)-3-amino-4-hydroxypiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

15 6-((2-((3R,4S)-3-amino-4-hydroxypiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

4-((R)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile hydrochloride;

20 4-((S)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile hydrochloride;

(S)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-3-fluorobenzonitrile hydrochloride;

(S)-1-(1-(4-chlorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine hydrochloride;

25 4-((R)-1-(2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile hydrochloride;

4-((S)-1-(2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile hydrochloride;

4-((R)-1-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile hydrochloride;

30 4-((S)-1-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile hydrochloride;

(S)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-3-chlorobenzonitrile hydrochloride;

35 (3R,4R)-1-(1-((1R)-1-(2,4-dichlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((1S)-1-(2,4-dichlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((1R)-1-(2-chlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

5 (3R,4R)-1-(1-((1S)-1-(2-chlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((1R)-1-(3-chlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

10 (3R,4R)-1-(1-((1S)-1-(3-chlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((1R)-1-(2,5-dichlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((1S)-1-(2,5-dichlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

15 (3R,4R)-1-(1-((1R)-1-(2,4-difluorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((1S)-1-(2,4-difluorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

20 (3R,4R)-1-(1-((1R)-1-(3,4-dichlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((1S)-1-(3,4-dichlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((1R)-1-(2,5-difluorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

25 (3R,4R)-1-(1-((1S)-1-(2,5-difluorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(5,6-difluoro-1-((1R)-1-(4-(trifluoromethyl)phenyl)ethyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

30 (3R,4R)-1-(5,6-difluoro-1-((1R)-1-(4-(trifluoromethoxy)phenyl)ethyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-(5-chloro-2-(trifluoromethoxy)benzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(5,6-difluoro-1-(4-(1H-1,2,4-triazol-1-yl)benzyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

- 2-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)-5-chlorobenzonitrile;
- (3R,4R)-1-(1-(2,4-dichlorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;
- 5 4-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)-3-(difluoromethoxy)benzonitrile;
- (3R,4R)-1-(1-(2,5-dichlorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;
- (3R,4R)-1-(1-(4-(1,1-difluoroethyl)benzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;
- 10 4-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)-2-methylbenzonitrile;
- 4-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)-2-chlorobenzonitrile;
- 15 2-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)-4-chlorobenzonitrile;
- (3R,4R)-1-(1-(2-(difluoromethoxy)benzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;
- (3R,4R)-1-(1-(3-chloro-4-fluorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;
- 20 (3R,4R)-1-(1-(4-chloro-2-methoxybenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;
- (3R,4R)-1-(1-(2,4-difluorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;
- 25 (3R,4R)-1-(5,6-difluoro-1-(2-(trifluoromethyl)benzyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;
- 2-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)benzonitrile;
- (3R,4R)-1-(1-(2-chlorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;
- 30 (3R,4R)-1-(1-(2-chloro-4-fluorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;
- (3R,4R)-1-(5,6-difluoro-1-(4-fluoro-2-(trifluoromethyl)benzyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;
- (3R,4R)-1-(1-(3,4-difluorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;
- 35

(3R,4R)-1-(1-(4-chloro-2-fluorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-(3,4-dichlorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

5 (3R,4R)-1-(1-(4-chloro-3-fluorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(5,6-difluoro-1-(4-(trifluoromethyl)benzyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

10 (3R,4R)-1-(5,6-difluoro-1-(4-(trifluoromethoxy)benzyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-(4-(difluoromethyl)benzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(5,6-difluoro-1-(3-(trifluoromethoxy)benzyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

15 (3R,4R)-1-(5,6-difluoro-1-(3-(trifluoromethyl)benzyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

3-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)benzonitrile;

(3R,4R)-1-(1-(3-chlorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

20 (S)-1-(1-(4-fluorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(S)-1-(1-(4-(1,2,4-oxadiazol-3-yl)benzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(R)-1-(1-(4-(methylsulfonyl)benzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(R)-1-(1-(4-(1H-1,2,4-triazol-1-yl)benzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(R)-2-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

25 (R)-1-(1-(2,6-dichlorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(R)-1-(1-(2-chlorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(R)-1-(1-(4-(trifluoromethyl)benzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(R)-1-(1-(4-(trifluoromethoxy)benzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(R)-1-(1-(4-chlorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

30 (R)-1-(1-(3-chlorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(R)-1-(1-(4-(1,1-difluoroethyl)benzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(R)-2-(4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)phenyl)-2-methylpropanenitrile;

(R)-1-(1-(4-(difluoromethyl)benzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

35 (R)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-N-methylbenzamide;

(R)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-3-fluorobenzonitrile;
(R)-2-(4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)phenoxy)acetonitrile;
(R)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-N,N-dimethylbenzenesulfonamide;

5 (R)-1-(1-(4-methylbenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
(R)-1-(1-(4-fluorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
(R)-1-(1-((1-methyl-1H-indazol-7-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
(R)-1-(1-(2,4-difluorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
(R)-1-(1-(3,4-difluorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

10 (R)-1-(1-(4-chloro-3-fluorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
(R)-1-(1-((3-(3-chlorophenyl)isoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
(R)-1-(1-(3-chloro-4-methoxybenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
(R)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-3-chlorobenzonitrile;
(R)-1-(1-(2,4-dichlorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

15 (R)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-3-methoxybenzonitrile;
(R)-2-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-5-chlorobenzonitrile;
4-((R)-1-(2-((R)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile;
4-(1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile;
(R)-3-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

20 4-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile hydrochloride;
(S)-4-((2-(3-aminopiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile hydrochloride;
4-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

25 (S)-4-((2-(3-aminopiperidin-1-yl)-5-methoxy-3H-imidazo[4,5-b]pyridin-3-yl)methyl)benzonitrile hydrochloride;
(R)-4-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

30 (R)-4-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;
(R)-4-((2-(3-amino-4,4-difluoropiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

35 4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

4-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

(R)-4-((2-(3-amino-4,4-difluoropiperidin-1-yl)-4-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

5 4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-imidazo[4,5-c]pyridin-1-yl)methyl)benzonitrile;

10 4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-3H-imidazo[4,5-c]pyridin-3-yl)methyl)benzonitrile;

4-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-6-ethoxy-1H-benzimidazol-1-yl)methyl)benzonitrile;

4-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1H-imidazo[4,5-b]pyridin-1-yl)methyl)benzonitrile;

15 4-((2-((3R)-3-amino-4,4-difluoro-1-piperidiny)-6-fluoro-1H-benzimidazol-1-yl)methyl)benzonitrile;

4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-imidazo[4,5-b]pyridin-1-yl)methyl)benzonitrile;

20 (S)-4-((2-(3-aminopiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile 2,2,2-trifluoroacetate;

(S)-4-((2-(3-aminopiperidin-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)methyl)benzonitrile hydrochloride;

4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile hydrochloride;

25 (S)-4-((2-(3-aminopiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

(S)-4-((2-(3-aminopiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

(R)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)-2,3-dihydro-1H-indene-5-carbonitrile;

30 (S)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)-2,3-dihydro-1H-indene-5-carbonitrile;

(3R,4R)-4-fluoro-1-(1-((5-methoxypyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)azetidine-3-carbonitrile;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(3-(tert-butoxy)azetidin-1-yl)ethan-1-one;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(3,3-difluoroazetidin-1-yl)ethanone;

5 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(3-isopropylazetidin-1-yl)ethanone;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(6,6-difluoro-2-azaspiro[3.3]heptan-2-yl)ethanone;

10 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(7-oxa-2-azaspiro[3.5]nonan-2-yl)ethanone;

(R)-6-((2-(4,4-difluoro-3-(methylamino)piperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(R)-6-((2-(4,4-difluoro-3-((2-hydroxyethyl)amino)piperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

15 (S)-6-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinic acid;

(S)-6-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinamide;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetic acid;

20 6-((R)-1-(4,6-difluoro-2-((3R,4R)-4-fluoro-3-(methylamino)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile;

6-((S)-1-(4,6-difluoro-2-((3R,4R)-4-fluoro-3-(methylamino)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile;

25 6-((R)-1-(5,7-difluoro-2-((3R,4R)-4-fluoro-3-(methylamino)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile; and

6-((S)-1-(5,7-difluoro-2-((3R,4R)-4-fluoro-3-(methylamino)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile.

In another aspect, the present disclosure refers to a compound, selected from:

30 6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazole-4-carbonitrile;

(3R,4R)-1-(4,6-difluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

5 (R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-4-methoxy-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

10 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

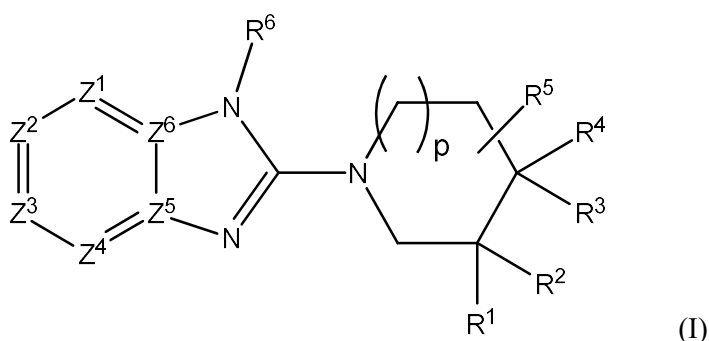
(3R,4R)-4-fluoro-1-(1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine; and

(3R,4R)-1-(1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine.

15 In another aspect, the present disclosure refers to a pharmaceutical composition comprising a pharmaceutically acceptable excipient, carrier or adjuvant and at least one compound as described herein. In yet another aspect, the present disclosure refers to the use of at least one compound as described herein, or a pharmaceutical salt thereof or a pharmaceutical composition thereof in the manufacture of a medicament for treating a disease or disorder mediated by TRPC6 in a mammal, wherein the disease or
20 disorder mediated by TRPC6 is selected from the group consisting of nephrotic syndrome, minimal change disease, focal segmental glomerulosclerosis, collapsing glomerulopathy, membranous nephropathy, membranoproliferative glomerulonephritis, IGA nephropathy, acute renal failure, chronic renal failure, diabetic nephropathy, sepsis, pulmonary hypertension, acute lung disorder, acute respiratory distress syndrome (ARDS), heart failure, stroke, malignant tumor, and muscular dystrophy. In yet another
25 aspect, the present disclosure refers to a a compound as described herein for use as a medicament.

The disclosure provides, in one example, substituted benzimidazole compounds which modulate the activity of TRPC6. Preferably, the substituted benzimidazole compounds of the disclosure are TRPC6 inhibitors.

30 The substituted benzimidazole compounds of the disclosure are compounds and salts according to Formula (I):



Also provided is a pharmaceutical composition comprising a pharmaceutically acceptable excipient, carrier or adjuvant and at least one compound of Formula (I) or subformulae thereof.

Pharmaceutical compositions provided by the disclosure are suitable for use in the treatment of disease modulated by TRPC6 activity. In certain examples the pharmaceutical compositions of the disclosure are suitable for use in the treatment of, e.g., treatment of nephrotic syndrome, minimal change disease, focal segmental glomerulosclerosis, collapsing glomerulopathy, membranous nephropathy, membranoproliferative glomerulonephritis, IGA nephropathy, acute renal failure, chronic renal failure, diabetic nephropathy, sepsis, pulmonary hypertension, acute lung disorder, heart failure, stroke, malignant tumor or muscular dystrophy.

Also provided is a packaged pharmaceutical composition, comprising a pharmaceutical composition comprising a pharmaceutically acceptable excipient, carrier or adjuvant and at least one compound of formula (I) or subformulae thereof, and instructions for using the composition to treat a patient suffering from a disease mediated by TRPC6 activity or more particularly to treat a patient suffering from nephrotic syndrome, minimal change disease, focal segmental glomerulosclerosis, collapsing glomerulopathy, membranous nephropathy, membranoproliferative glomerulonephritis, IGA nephropathy, acute renal failure, chronic renal failure, diabetic nephropathy, sepsis, pulmonary hypertension, acute lung disorder, acute respiratory distress syndrome (ARDS) heart failure, stroke, malignant tumor or muscular dystrophy. In certain instances, the patient is suffering from nephrotic syndrome, membranous nephropathy, and acute renal failure.

Also provided is a method of treating or preventing disease in a mammal which method comprises administering to a mammal in need thereof a therapeutically effective amount of at least one compound of formula (I) or subformulae thereof or a pharmaceutical composition comprising a pharmaceutically acceptable excipient, carrier or adjuvant and at least one compound of formula (I) or subformulae thereof.

Also provided is a method for modulating TRPC6 activity in a mammal, which method comprises administering to the mammal in need thereof a therapeutically effective amount of at least one compound of formula (I) or subformulae thereof or a pharmaceutical composition comprising a pharmaceutically acceptable excipient, carrier or adjuvant and at least one compound of formula (I) or subformulae thereof. Another example of the disclosure relates to a method of treating a TRPC6-mediated disease or disorder,

the method comprising administering a TRPC6 inhibitor of the disclosure to a patient in need of therapy. In certain examples, the TRPC6 mediated disease or disorder is selected from nephrotic syndrome, minimal change disease, focal segmental glomerulosclerosis, collapsing glomerulopathy, membranous nephropathy, membranoproliferative glomerulonephritis, IGA nephropathy, acute renal failure, chronic renal failure, diabetic nephropathy, sepsis, pulmonary hypertension, acute lung disorder, acute respiratory distress syndrome (ARDS), heart failure, stroke, malignant tumor or muscular dystrophy. In certain instances, the patient is suffering from nephrotic syndrome, membranous nephropathy, and acute renal failure .

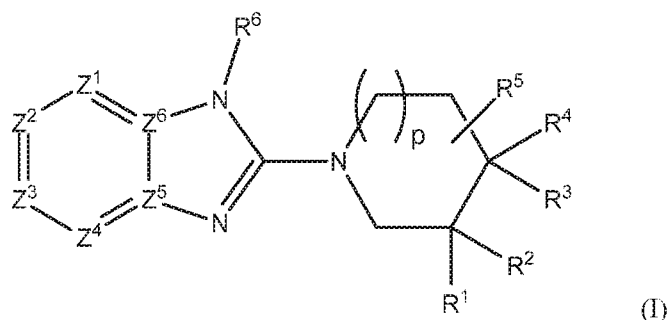
Also provided is the use, in the manufacture of a medicament for treating or preventing disease mediated by TRPC6 activity, of at least one compound of formula I or subformulae thereof.

Other examples will be apparent to those skilled in the art from the following detailed description.

DETAILED DESCRIPTION OF THE INVENTION

The invention related generally to compounds of Formula I and salts and tautomers thereof which inhibit TRPC protein activity and more particularly inhibit TRPC6 protein activity. In particular, the invention relates to compounds which selectively inhibit TRPC6 protein activity.

In a first embodiment, the invention provides a compound or pharmaceutically acceptable salt thereof, according to Formula I:



Wherein

p is 0 or 1;

when p is 0, then R¹ is hydrogen, C₁-C₆alkyl, halogen or hydroxy; R² is amino or aminoC₁-

5 C₄alkyl; R³ is hydrogen; and R⁴ is hydrogen, C₁-C₆alkyl or phenyl; or

when p is 0, then R¹ and R³, taken in combination, form a fused C₃-C₆cycloalkyl ring or a fused 4 to 6 member heterocycle ring having 1 or 2 ring heteroatoms independently selected from N, O or S, which cycloalkyl or heterocycle is optionally substituted with amino; R² is hydrogen, C₁-C₆alkyl or aminoC₁-C₄alkyl; and R⁴ is hydrogen; or

10 when p is 1, then R¹ is NHR^{1a}; R^{1a} is hydrogen, C₁-C₄alkyl, C₃-C₇cycloalkyl, hydroxyC₁-C₄alkyl, or 4 to 6 member heterocycloalkyl having one ring heteroatom selected from N, O or S; R² is hydrogen, C₁-C₄alkyl, hydroxyC₁-C₄alkyl or C(O)NH₂; R³ is hydrogen, halogen, C₁-C₄alkyl, C₁-C₄alkoxy or hydroxy; and R⁴ is hydrogen, C₁-C₄alkyl or halogen; or

15 when p is 0 or 1, then CR¹R², taken in combination, form a spirocyclic 4 to 6 member heterocycloalkyl; R³ is hydrogen, halogen, C₁-C₄alkyl, C₁-C₄alkoxy, or hydroxy; and R⁴ is hydrogen or halogen; or

20 when p is 1, then R¹ and R³, taken in combination, form a fused 4 to 6 member heterocycle or a fused 3 to 7 member carbocycle, which heterocycle comprises a ring nitrogen atom and optionally 0 or 1 additional ring heteroatoms selected from N, O and S, and which carbocycle is substituted with amino; and R² is hydrogen; and R⁴ is hydrogen, halogen or hydroxy;

R⁵ represents 1 or 2 substituents independently selected from hydrogen, halogen, hydroxy, amino, C₁-C₆alkyl or C₁-C₆alkoxy;

R⁶ is -(CR⁷R⁸)-A; or

25 R⁶ is a 4 to 7 member lactam which is optionally substituted with one or two substituents independently selected from the group consisting of hydroxy, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, C₃-C₆cycloalkyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, hydroxyC₁-C₆alkyl, C₁-C₆alkoxyC₁-C₆alkyl, phenyl, 4 to 7 member heterocycle having 1 ring atoms selected from N, O or S and 0 or 1 additional ring N atoms or 5 or 6 member heteroaryl having one ring heteroatom selected from N, O or S and 0 or 1 additional ring nitrogen atom, wherein the heteroaryl, heterocycle or phenyl group is optionally

30 substituted with 0, 1 or 2 C₁-C₆alkyl or halogen; or

R⁶ is a partially unsaturated 9 or 10 member bicyclic carbocycle, which is optionally substituted with 1 or 2 substituents independently selected from halogen, cyano, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, C(O)NH₂ and C(O)NHC₁-C₆alkyl;

A is 5 or 6 member heteroaryl, which heteroaryl comprises one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms, which heteroaryl is optionally substituted with 0, 1, 2, 3 or 4 groups independently selected from halogen, cyano, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, C₃-C₆cycloalkyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, C(O)N(R^A)₂, S(O)₂C₁-C₆alkyl, phenyl or 5 or 6 member heteroaryl having one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms, wherein the optional heteroaryl or phenyl substituent is further substituted with 0, 1 or 2 C₁-C₆alkyl; or

A is phenyl substituted with 1, 2 or 3 substituents independently selected from halogen, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, haloC₁-C₆alkyl, cyanoC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, cyanoC₁-C₆alkoxy, S(O)₂C₁-C₆alkyl, S(O)₂NH₂, S(O)₂NHC₁-C₆alkyl, S(O)₂N(C₁-C₆alkyl)₂, C(O)NH₂, C(O)NHC₁-C₆alkyl, C(O)N(C₁-C₆alkyl)₂, hydroxy, cyano, or 5 or 6 member heteroaryl having one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms which heteroaryl is further substituted with 0, 1 or 2 C₁-C₆alkyl; or

A is C(O)OR⁹ or C(O)NR⁹R¹⁰; or

A is optionally substituted 9 or 10 member aromatic or partially unsaturated bicycle having 0, 1 or 2 ring nitrogen atoms and 0 or 1 additional ring heteroatoms selected from N, O or S, which bicycle is substituted with 0, 1 or 2 substituents independently selected from the group consisting of halogen, cyano, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, C(O)NH₂, C(O)OH or C(O)NHC₁-C₆alkyl;

R^A is independently selected at each occurrence from hydrogen or C₁-C₄alkyl; or

N(R^A)₂, taken in combination, forms a 4 to 7 member azacycle which is optionally substituted with 0, 1, or 2 C₁-C₄alkyl;

R⁷ is hydrogen, C₁-C₄alkyl or amino;

R⁸ is hydrogen or C₁-C₄alkyl; or

CR⁷R⁸, taken in combination form a 3 to 6 member cycloalkandiyl group;

R⁹ is hydrogen, C₁-C₆alkyl, C₃-C₆cycloalkyl, hydroxyC₁-C₆alkyl, C₁-C₄alkoxyC₁-C₆alkyl, haloC₁-C₆alkyl, cyano C₁-C₆alkyl or -(CH₂)_rR^{9A} wherein r is 0 or 1 and R^{9A} is phenyl, 4 to 7 member heterocycle having one ring heteroatoms selected from N, O or S, which ring sulfur may be optionally oxidized, and 0 or 1 additional ring N atoms or 5 or 6 member heteroaryl having one ring heteroatom selected from N, O or S and 0, 1, or 2 additional ring N atoms, which phenyl, heterocycle or heteroaryl is optionally substituted with 0, 1 or 2 halogen, C₁-C₄alkyl or C(O)C₁-C₄alkyl;

R^{10} is hydrogen, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, halo C_1 - C_6 alkyl, C_3 - C_7 cycloalkyl or saturated, partially unsaturated or aromatic 5 or 6 member heterocycle having 1 or 2 ring heteroatoms independently selected from N, O and S, which sulfur is optionally oxidized, and which heterocycle is optionally substituted with 1 or 2 substituents independently selected from C_1 - C_6 alkyl and halogen, which heterocycle has 1 or 2 ring hetero atoms selected from N, O or S, which sulfur may be optionally oxidized, and wherein each alkyl or cycloalkyl is optionally substituted with cyano, halogen, hydroxy, C_1 - C_6 alkoxy, $S(O)_qC_1$ - C_6 alkyl, 4 to 6 member heterocycle having 1 or 2 ring heteroatoms selected from N, O or S or 5 or 6 member heteroaryl having 1 ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms and where each heterocycle or heteroaryl is optionally substituted with 0, 1, or 2 C_1 - C_4 alkyl; or

NR^9R^{10} , taken in combination, form a monocyclic or bicyclic 4 to 10 member saturated or partially unsaturated heterocycle having one or two ring nitrogen atoms and 0 or 1 additional ring heteroatom selected from N, O or S, which ring sulfur may be optionally oxidized, which heterocycle is optionally substituted with 0, 1 or 2 substituents selected from halogen, oxo, hydroxy, cyano, C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, halo C_1 - C_6 alkyl, hydroxy C_1 - C_6 alkyl, cyano C_1 - C_6 alkyl, C_1 - C_6 alkoxy, halo C_1 - C_6 alkoxy, C_1 - C_6 alkoxy C_1 - C_4 alkyl, $S(O)_qC_1$ - C_6 alkyl, C_1 - C_6 alkyl $S(O)_qC_1$ - C_6 alkyl CO_2H , $C(O)C_1$ - C_6 alkyl, $C(O)OC_1$ - C_6 alkyl, $C(O)C_3$ - C_6 cycloalkyl, $N(R^{15})C(O)C_1$ - C_6 alkyl or $C(O)N(R^{15})_2$, phenyl, 4 to 6 member heterocycle having 1 or 2 ring heteroatoms selected from N, O or S or a 5 or 6 member heteroaryl having 1 ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms and where each heterocycle or heteroaryl is optionally substituted with 0, 1, or 2 C_1 - C_4 alkyl;

q is 0, 1 or 2;

Z^1 is N or CR^{11} ;

Z^2 is N or CR^{12} ;

Z^3 is N or CR^{13} ;

Z^4 is N or CR^{14} ;

Z^5 and Z^6 are each independently N or C;

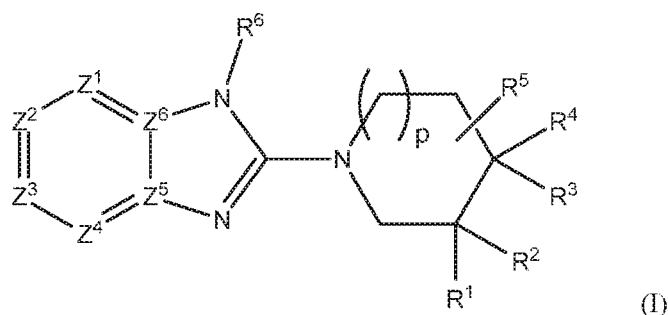
wherein 0, 1 or 2 of Z^1 , Z^2 , Z^3 , Z^4 , Z^5 and Z^6 are N;

each of R^{11} , R^{12} , R^{13} and R^{14} is independently selected from the group consisting of hydrogen, halogen, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_1 - C_6 alkoxy, halo C_1 - C_6 alkyl, halo C_1 - C_6 alkoxy, C_3 - C_7 cycloalkyl, cyano, SO_2C_1 - C_6 alkyl, phenyl, and saturated, partially unsaturated or aromatic 5 or 6 member heterocycle having 1 or 2 ring heteroatoms independently selected from N, O and S, which heterocycle is optionally substituted with 1 or 2 substituents independently selected from C_1 - C_6 alkyl and halogen; and

R^{15} is selected at each occurrence from hydrogen or C_1 - C_4 alkyl or $N(R^{15})_2$ taken in combination form a 4 to 7 member azacycle optionally substituted with 0, 1 or 2 C_1 - C_4 alkyl; with the proviso that

compounds of Formula I do not include 1- [7-fluoro-6-methoxy-1-[[2-(trifluoromethyl)phenyl]methyl]-1*H*-benzimidazol-2-yl]-3-piperidinamine.

In a second embodiment of the invention, compounds and salts according to Formula I are provided which are generally represented by the structure:



Wherein

p is 0 or 1;

when p is 0, then R¹ is hydrogen, C₁-C₆alkyl, halogen or hydroxy; R² is amino or aminoC₁-C₄alkyl; R³ is hydrogen; and R⁴ is hydrogen, C₁-C₆alkyl or phenyl; or

when p is 0, then R¹ and R³, taken in combination, form a fused C₃-C₆cycloalkyl ring or a fused 4 to 6 member heterocycle ring having 1 or 2 ring heteroatoms independently selected from N, O or S, which cycloalkyl or heterocycle is optionally substituted with amino; R² is hydrogen, C₁-C₆alkyl or aminoC₁-C₄alkyl; and R⁴ is hydrogen; or

when p is 1, then R¹ is NHR^{1a}; R^{1a} is hydrogen, C₁-C₄alkyl, C₃-C₇cycloalkyl, hydroxyC₁-C₄alkyl, or 4 to 6 member heterocycloalkyl having one ring heteroatom selected from N, O or S; R² is hydrogen, C₁-C₄alkyl, hydroxyC₁-C₄alkyl or C(O)NH₂; R³ is hydrogen, halogen, C₁-C₄alkyl, C₁-C₄alkoxy or hydroxy; and R⁴ is hydrogen, C₁-C₄alkyl or halogen; or

when p is 0 or 1, then C(NHR^{1a})R², taken in combination, form a spirocyclic 4 to 6 member heterocycloalkyl; R³ is hydrogen, halogen C₁-C₄alkyl, C₁-C₄alkoxy, or hydroxy; and R⁴ is hydrogen or halogen; or

when p is 1, then R¹ and R³, taken in combination, form a fused 4 to 6 member heterocycle or a fused 3 to 7 member carbocycle, which heterocycle comprises a ring nitrogen atom and optionally 0 or 1 additional ring heteroatoms selected from N, O and S, and which carbocycle is substituted with amino; and R² is hydrogen; and R⁴ is hydrogen, halogen or hydroxy;

R⁵ represents 1 or 2 substituents independently selected from hydrogen, halogen, hydroxy, amino, C₁-C₆alkyl or C₁-C₆alkoxy;

R⁶ is -(CR⁷R⁸)-A; or

R⁶ is a 4 to 7 member lactam which is optionally substituted with one or two substituents independently selected from the group consisting of hydroxy, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl,

haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, hydroxyC₁-C₆alkyl, C₁-C₆alkoxyC₁-C₆alkyl, phenyl or 5 or 6 member heteroaryl having one ring heteroatom selected from N, O or S and 0 or 1 additional ring nitrogen atom, wherein the heteroaryl or phenyl group is optionally substituted with 0, 1 or 2 C₁-C₆alkyl or halogen; or

5 R⁶ is a partially unsaturated 9 or 10 member bicyclic carbocycle, which is optionally substituted with 1 or 2 substituents independently selected from halogen, cyano, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, C(O)NH₂ and C(O)NHC₁-C₆alkyl;

A is 5 or 6 member heteroaryl, which heteroaryl comprises one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms, which heteroaryl is optionally substituted with 0, 1, 2,
10 3 or 4 groups independently selected from halogen, cyano, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, C(O)NH₂, C(O)NHC₁-C₆alkyl, phenyl or 5 or 6 member heteroaryl having one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms, wherein the optional heteroaryl or phenyl substituent is further substituted with 0, 1 or 2 C₁-C₆alkyl; or

15 A is phenyl substituted with 1, 2 or 3 substituents independently selected from halogen, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, haloC₁-C₆alkyl, cyanoC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, cyanoC₁-C₆alkoxy, S(O)_qC₁-C₆alkyl, S(O)₂NH₂, S(O)₂NHC₁-C₆alkyl, S(O)₂N(C₁-C₆alkyl)₂, C(O)NH₂, C(O)NHC₁-C₆alkyl, C(O)N(C₁-C₆alkyl)₂, hydroxy, cyano, or 5 or 6 member heteroaryl having one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms which heteroaryl is
20 further substituted with 0, 1 or 2 C₁-C₆alkyl; or

A is C(O)OR⁹ or C(O)NR⁹R¹⁰; or

A is optionally substituted 9 or 10 member aromatic or partially unsaturated bicycle having 0, 1 or 2 ring nitrogen atoms and 0 or 1 additional ring heteroatoms selected from N, O or S, which bicycle is substituted with 0, 1 or 2 substituents independently selected from the group consisting of halogen, cyano,
25 C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, C(O)NH₂, C(O)OH or C(O)NHC₁-C₆alkyl;

R⁷ is hydrogen, C₁-C₄alkyl or amino;

R⁸ is hydrogen or C₁-C₄alkyl; or

CR⁷R⁸, taken in combination form a 3 to 6 member cycloalkandiyl group;

30 R⁹ is hydrogen, C₁-C₆alkyl, hydroxyC₁-C₆alkyl, haloC₁-C₆alkyl or cyano C₁-C₆alkyl;

R¹⁰ is hydrogen, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, halo C₁-C₆alkyl, C₃-C₇cycloalkyl or 4 to 7 member heterocycle, which heterocycle has 1 or 2 ring hetero atoms selected from N, O or S, which sulfur may be optionally oxidized, and wherein each alkyl or cycloalkyl is optionally substituted with cyano, halogen, hydroxy, C₁-C₆alkoxy, S(O)_qC₁-C₆alkyl, 4 to 6 member heterocycle having 1 or 2 ring

heteroatoms selected from N, O or S or 5 or 6 member heteroaryl having 1 ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms; or

NR^9R^{10} , taken in combination, form a monocyclic or bicyclic 4 to 9 member heterocycle having one ring nitrogen atom and 0 or 1 additional ring heteroatom selected from N, O or S, which ring sulfur may be optionally oxidized, which heterocycle is optionally substituted with 0, 1 or 2 substituents selected from halogen, oxo, hydroxy, cyano, $\text{C}_1\text{-C}_6$ alkyl, halo $\text{C}_1\text{-C}_6$ alkyl, hydroxy $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ alkoxy, $\text{S(O)}_q\text{C}_1\text{-C}_6$ alkyl, CO_2H , $\text{C(O)C}_1\text{-C}_6$ alkyl, or C(O)NH_2 ;

q is 0, 1 or 2;

Z^1 is N or CR^{11} ;

Z^2 is N or CR^{12} ;

Z^3 is N or CR^{13} ;

Z^4 is N or CR^{14} ;

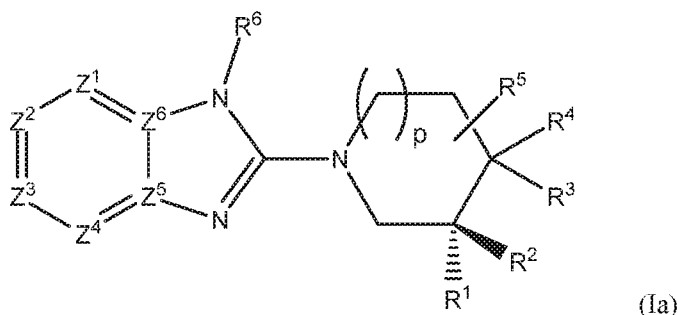
Z^5 and Z^6 are each independently N or C;

wherein 0, 1 or 2 of Z^1 , Z^2 , Z^3 , Z^4 , Z^5 and Z^6 are N;

each of R^{11} , R^{12} , R^{13} and R^{14} is independently selected from the group consisting of hydrogen, halogen, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_2\text{-C}_6$ alkenyl, $\text{C}_2\text{-C}_6$ alkynyl, $\text{C}_1\text{-C}_6$ alkoxy, halo $\text{C}_1\text{-C}_6$ alkyl, halo $\text{C}_1\text{-C}_6$ alkoxy, $\text{C}_3\text{-C}_7$ cycloalkyl, cyano, $\text{SO}_2\text{C}_1\text{-C}_6$ alkyl, phenyl, and saturated, partially unsaturated or aromatic 5 or 6 member heterocycle having 1 or 2 ring heteroatoms independently selected from N, O and S, which heterocycle is optionally substituted with 1 or 2 substituents independently selected from $\text{C}_1\text{-C}_6$ alkyl and halogen; and with the proviso that compounds of Formula I do not include 1- [7-fluoro-6-methoxy-1-[[2-(trifluoromethyl)phenyl]methyl]-1*H*-benzimidazol-2-yl]-3-piperidinamine.

The proviso is presented in the first embodiment to specifically exclude and disclaim the identified compound which is indexed as CAS Number 1014407-24-9.

In certain aspects of the first or second embodiment, compounds of Formula I include compounds of Formula Ia:



Where variables p, R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , Z^1 , Z^2 , Z^3 , Z^4 , Z^5 and Z^6 are as defined in the first or second embodiment.

In a third embodiment, the invention provides compounds of the first or second embodiment in which p is 0; R¹ is hydrogen, C₁-C₆alkyl, halogen or hydroxy; R² is aminoC₁-C₄alkyl; and R³ and R⁴ are hydrogen.

5 In a fourth embodiment, the invention provides compounds of the first or second embodiment in which p is 0; R¹ and R³, taken in combination, form a fused C₃-C₆cycloalkyl ring or a fused 4 to 6 member azacycle ring, which cycloalkyl or azacycle is optionally substituted with amino; and R² and R⁴ are hydrogen.

In a fifth embodiment, the invention provides compounds of the fourth embodiment in which R¹ and R³ taken in combination, form a fused pyrrolidine; and R² and R⁴ are hydrogen.

10 In a sixth embodiment, the invention provides compounds of the first or second embodiment in which p is 1, R¹ is NHR^{1a}; R^{1a} is hydrogen, C₁-C₄alkyl, C₃-C₇cycloalkyl or 4 to 6 member heterocycloalkyl having one ring heteroatom selected from N, O or S; R² is hydrogen or C₁-C₄alkyl; R³ is hydrogen, halogen, C₁-C₄alkyl, C₁-C₄alkoxy, or hydroxy; and R⁴ is hydrogen, halogen or C₁-C₄alkyl.

15 In a seventh embodiment, the invention provides compounds of the sixth embodiment in which R¹ is NHR^{1a}; R^{1a} is hydrogen, methyl, ethyl, propyl, isopropyl or cyclopropyl; R² is hydrogen or methyl; R³ is hydrogen, halogen, methyl, ethyl, methoxy, ethoxy, or hydroxy; and R⁴ is hydrogen, halogen, methyl or ethyl. In certain aspects of the seventh embodiment, compounds are provided in which R^{1a} is hydrogen or methyl; R² is hydrogen, R³ is hydrogen, fluorine, methyl or hydroxy; and R⁴ is hydrogen, halogen, methyl or ethyl.

20 In an eighth embodiment, the invention provides compounds of the sixth or seventh embodiment in which R¹ is NH₂; R² is hydrogen; R³ is hydrogen, fluorine, methyl, or hydroxy; and R⁴ is hydrogen, fluorine or methyl.

In a ninth embodiment, the invention provides compounds of the first or second embodiment in which p is 1; CR¹R², taken in combination, form a spirocyclic 4 to 6 member heterocycloalkyl; R³ is 25 hydrogen, halogen or C₁-C₄alkyl, C₁-C₄alkoxy, hydroxy; and R⁴ is hydrogen or halogen.

In a tenth embodiment, the invention provides compounds of the first or second embodiment in which p is 1; R¹ and R³, taken in combination, form a fused 4 or 5 member carbocycle substituted with amino; and R² and R⁴ are hydrogen.

30 In an eleventh embodiment, the invention provides compounds of any one of the first to tenth embodiment in which R⁵ represents 1 or 2 substituents independently selected from hydrogen, halogen, hydroxy, C₁-C₄alkyl.

In a twelfth embodiment, the invention provides compounds of the eleventh embodiment in which R⁵ represent hydrogen.

35 In a thirteenth embodiment, the invention provides compounds of any one of the first to twelfth embodiment in which wherein R⁶ is -(CR⁷R⁸)-A.

In a fourteenth embodiment, the invention provides compounds of the thirteenth embodiment in which R^7 is hydrogen, methyl or ethyl; R^8 is hydrogen; or CR^7R^8 , taken in combination form a cyclopropandiyl group.

5 In a fifteenth embodiment, the invention provides compounds of the thirteenth or fourteenth embodiment in which R^7 is hydrogen or methyl; and R^8 is hydrogen.

10 In a sixteenth embodiment, the invention provides compounds of any one of the thirteenth to fifteenth embodiment in which A is 5 or 6 member heteroaryl, which heteroaryl comprises one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms, which heteroaryl is optionally substituted with 0, 1, or 2 groups independently selected from halogen, cyano, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, halo C_1 - C_6 alkyl, C_1 - C_6 alkoxy, halo C_1 - C_6 alkoxy, $C(O)NH_2$, $C(O)NHC_1$ - C_6 alkyl, phenyl or 5 or 6 member heteroaryl having one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms, wherein the optional heteroaryl or phenyl substituent is further substituted with 0, 1 or 2 C_1 - C_6 alkyl.

15 In a seventeenth embodiment, the invention provides compounds of the sixteenth embodiment in which A is pyridin-2-yl, pyridin-3-yl, pyrimidin-2-yl, or pyrazin-2-yl, each of which is substituted with 1 to 3 groups independently selected from the group consisting of halogen, cyano, C_1 - C_4 alkyl, halo C_1 - C_4 alkyl, C_1 - C_4 alkoxy, halo C_1 - C_4 alkoxy, $C(O)NH_2$, $C(O)NHC_1$ - C_4 alkyl, phenyl or 5 member heteroaryl having one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms, wherein the optional heteroaryl or phenyl substituent is further substituted with 0, 1 or 2 C_1 - C_6 alkyl.

20 In an eighteenth embodiment, the invention provides compounds of any one of the thirteenth to fifteenth embodiment in which A is phenyl substituted with 1, 2 or 3 substituents independently selected from halogen, C_1 - C_6 alkyl, halo C_1 - C_6 alkyl, C_1 - C_6 alkoxy, halo C_1 - C_6 alkoxy, hydroxy, cyano, or 5 or 6 member heteroaryl having one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms which heteroaryl is further substituted with 0, 1 or 2 C_1 - C_6 alkyl.

25 In a nineteenth embodiment, the invention provides compounds of the eighteenth embodiment in which A is phenyl substituted with one substituent selected from the group consisting of halogen, C_1 - C_4 alkyl, halo C_1 - C_4 alkyl, C_1 - C_4 alkoxy, halo C_1 - C_4 alkoxy, hydroxy, cyano, or 5 member heteroaryl having one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms, and wherein the phenyl group is further optionally substituted with halogen, C_1 - C_4 alkyl, C_1 - C_4 alkoxy, halo C_1 - C_4 alkyl or halo C_1 - C_4 alkoxy.

In a twentieth embodiment, the invention provides compounds of the eighteenth or nineteenth embodiment in which A is phenyl substituted with 1 or 2 substituents independently selected from halogen, C_1 - C_3 alkyl, halo C_1 - C_4 alkyl, C_1 - C_4 alkoxy, halo C_1 - C_4 alkoxy, hydroxy or cyano.

35 In a twenty-first embodiment, the invention provides compounds of any one of the thirteenth to fifteenth embodiment in which A is $C(O)NR^9R^{10}$;

R^9 is hydrogen, or C_1 - C_4 alkyl;

R^{10} is C_1 - C_4 alkyl, halo C_1 - C_4 alkyl, C_3 - C_7 cycloalkyl or 4 to 7 member heterocycle, which heterocycle has 1 or 2 ring hetero atoms selected from N, O or S, which sulfur may be optionally oxidized, and wherein each alkyl or cycloalkyl is optionally substituted with cyano, halogen, hydroxy, C_1 - C_6 alkoxy, $S(O)_qC_1$ - C_6 alkyl; or

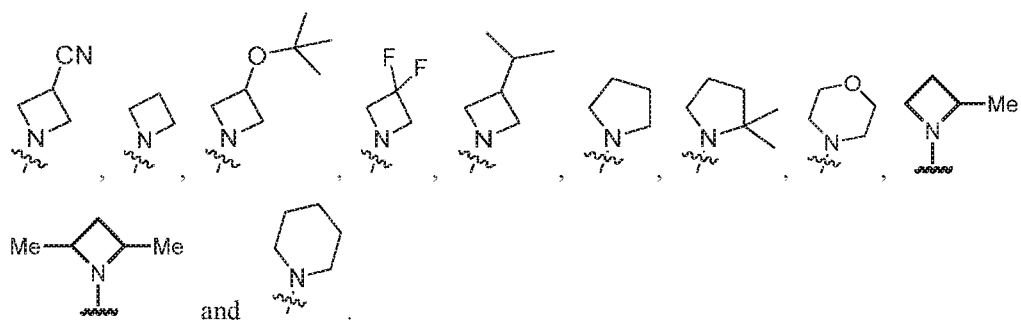
NR^9R^{10} , taken in combination, form a monocyclic or bicyclic 4 to 9 member azacycle having one ring nitrogen atom and 0 or 1 additional ring heteroatom selected from N, O or S, which ring sulfur may be optionally oxidized, which azacycle is optionally substituted with 0, 1 or 2 substituents selected from halogen, oxo, hydroxy, cyano, C_1 - C_6 alkyl, halo C_1 - C_6 alkyl, hydroxy C_1 - C_6 alkyl, C_1 - C_6 alkoxy, $S(O)_2C_1$ - C_6 alkyl, CO_2H , $C(O)C_1$ - C_6 alkyl, or $C(O)NH_2$.

In a twenty second embodiment, the invention provides compounds of the twenty first embodiment in which R^9 is hydrogen, methyl or ethyl; and

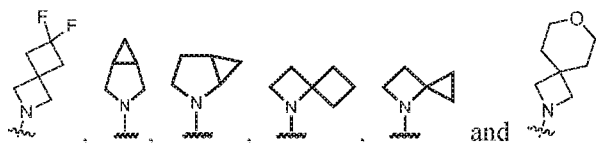
R^{10} is C_1 - C_4 alkyl or halo C_1 - C_4 alkyl wherein each alkyl is optionally substituted with cyano, halogen, hydroxy, C_1 - C_6 alkoxy or $S(O)_qC_1$ - C_6 alkyl.

In a twenty third embodiment, the invention provides compounds of the twenty first embodiment in which NR^9R^{10} , taken in combination, form a 4 to 6 member monocyclic azacycle or a 7 to 9 member bicyclic azacycle, each of which having one ring nitrogen atom and 0 or 1 additional ring heteroatom selected from N, O or S, which ring sulfur may be optionally oxidized, wherein each azacycle is optionally substituted with 0, 1 or 2 substituents selected from halogen, oxo, hydroxy, cyano, C_1 - C_6 alkyl, halo C_1 - C_6 alkyl, hydroxy C_1 - C_6 alkyl, C_1 - C_6 alkoxy, $S(O)_2C_1$ - C_6 alkyl, CO_2H , $C(O)C_1$ - C_6 alkyl, or $C(O)NH_2$.

In a twenty fourth embodiment, the invention provides compounds of the twenty third embodiment in which the 4 to 6 member monocyclic azacycle is selected from the group consisting of:

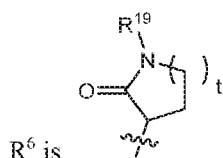


In a twenty fifth embodiment, the invention provides compounds of the twenty third embodiment in which the 7 to 9 member bicyclic azacycle is selected from the group consisting of:



In a twenty sixth embodiment, the invention provides compounds of any one of the first to twelfth embodiment in which R^6 is a 2-oxo-pyrrolidin-3-yl or 2-oxo-piperidin-3-yl each of which is substituted at nitrogen with C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, halo C_1 - C_6 alkyl, C_1 - C_6 alkoxy, halo C_1 - C_6 alkoxy, hydroxy C_1 - C_6 alkyl, C_1 - C_6 alkoxy C_1 - C_6 alkyl, phenyl or 5 or 6 member heteroaryl having one ring heteroatom selected from N, O or S and 0 or 1 additional ring nitrogen atom, wherein the heteroaryl or phenyl group is optionally substituted with 0, 1 or 2 C_1 - C_6 alkyl or halogen.

In a twenty seventh embodiment, the invention provides compounds of the twenty sixth embodiment in which



Wherein t is 1 or 2; and

R^{19} is C_1 - C_6 alkyl, phenyl substituted with 0, 1 or 2 halogen.

In a twenty eighth embodiment, the invention provides compounds of any one of the first to twenty seventh embodiment in which Z^1 is CR^{11} ;

Z^2 is CR^{12} ;

Z^3 is CR^{13} ;

Z^4 is N or CR^{14} ;

Z^5 and Z^6 are each C;

R^{11} is hydrogen, halogen, cyano or C_1 - C_4 alkyl;

R^{12} and R^{13} are each independently selected from the group consisting of hydrogen, halogen, cyano, C_1 - C_4 alkyl, halo C_1 - C_4 alkyl, C_1 - C_4 alkoxy, halo C_1 - C_4 alkoxy, C_3 - C_6 cycloalkyl or 5 member saturated, partially unsaturated or aromatic 5 or 6 member heterocycle having 1 or 2 ring heteroatoms independently selected from N, O and S; and

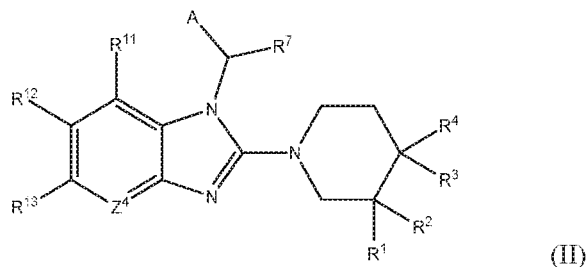
R^{14} is hydrogen, halogen, cyano or C_1 - C_4 alkyl.

In certain aspects of the twenty eighth embodiment, compounds are provided in which R^{11} is hydrogen.

In certain other aspects of the twenty eighth embodiment, compounds are provided in which R^{14} is hydrogen, fluorine, chlorine, methyl or cyano. In certain aspects of the twenty eighth embodiment, compounds are provided in which R^{12} and R^{13} are each independently selected from the group consisting of hydrogen, fluorine, chlorine, cyano, C_1 - C_4 alkyl, halo C_1 - C_4 alkyl, C_1 - C_4 alkoxy, and halo C_1 - C_4 alkoxy.

In yet other aspects of the twenty eighth embodiment, compounds are provided in which R^{11} is hydrogen; R^{14} is hydrogen, fluorine, chlorine, methyl or cyano; and R^{12} and R^{13} are each independently selected from the group consisting of hydrogen, fluorine, chlorine, cyano, methyl, ethyl, methoxy, ethoxy, fluoromethyl, difluoromethyl, trifluoromethyl, fluoromethoxy, difluoromethoxy, and trifluoromethoxy.

In a twenty ninth embodiment, the invention provides compounds of the first or second embodiment which include compounds of Formula II:



Wherein

R¹ is NHR^{1a},

R^{1a} is hydrogen, C₁-C₄alkyl, C₃-C₇cycloalkyl or 4 to 6 member heterocycloalkyl having one ring heteroatom selected from N, O or S;

R² is hydrogen or C₁-C₄alkyl;

R³ is hydrogen, halogen, C₁-C₄alkyl, C₁-C₄alkoxy, or hydroxy;

R⁴ is hydrogen or halogen;

R⁷ is hydrogen, methyl or ethyl;

A is C(O)NR⁹R¹⁰, or

A is 5 or 6 member heteroaryl, which heteroaryl comprises one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms, which heteroaryl is optionally substituted with 0, 1, or 2 groups independently selected from halogen, cyano, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, C(O)NH₂, C(O)NHC₁-C₆alkyl, phenyl or 5 or 6 member heteroaryl having one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms, wherein the optional heteroaryl or phenyl substituent is further substituted with 0, 1 or 2 C₁-C₆alkyl; or

A is phenyl substituted with one substituent selected from the group consisting of halogen, C₁-C₄alkyl, haloC₁-C₄alkyl, C₁-C₄alkoxy, haloC₁-C₄alkoxy, hydroxy, cyano, or 5 member heteroaryl having one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms, and wherein the phenyl group is further optionally substituted with halogen, C₁-C₄alkyl, C₁-C₄alkoxy, haloC₁-C₄alkyl or haloC₁-C₄alkoxy.

R⁹ is hydrogen, or C₁-C₄alkyl;

R¹⁰ is C₁-C₄alkyl, haloC₁-C₄alkyl, C₃-C₇cycloalkyl or 4 to 7 member heterocycle, which heterocycle has 1 or 2 ring hetero atoms selected from N, O or S, which sulfur may be optionally oxidized, and wherein each alkyl or cycloalkyl is optionally substituted with cyano, halogen, hydroxy, C₁-C₆alkoxy, S(O)_qC₁-C₆alkyl; or

NR⁹R¹⁰, taken in combination, form a monocyclic or bicyclic 4 to 9 member azacycle having one ring nitrogen atom and 0 or 1 additional ring heteroatom selected from N, O or S, which ring sulfur may

be optionally oxidized, which azacycle is optionally substituted with 0, 1 or 2 substituents selected from halogen, oxo, hydroxy, cyano, C₁-C₆alkyl, halo C₁-C₆alkyl, hydroxyC₁-C₆alkyl, C₁-C₆alkoxy, S(O)₂C₁-C₆alkyl, CO₂H, C(O)C₁-C₆alkyl, or C(O)NH₂;

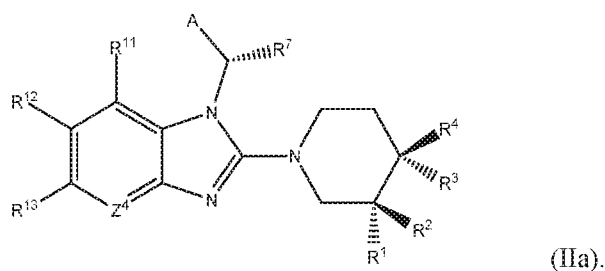
Z⁴ is CR¹⁴ or N;

5 R¹¹ is hydrogen, halogen, cyano or C₁-C₄alkyl;

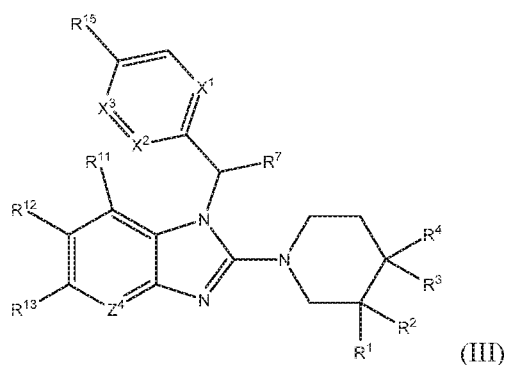
R¹² and R¹³ are each independently selected from the group consisting of hydrogen, halogen, cyano, C₁-C₄alkyl, haloC₁-C₄alkyl, C₁-C₄alkoxy, haloC₁-C₄alkoxy, C₃-C₆cycloalkyl or 5 member saturated, partially unsaturated or aromatic 5 or 6 member heterocycle having 1 or 2 ring heteroatoms independently selected from N, O and S; and

10 R¹⁴ is hydrogen, halogen, cyano or C₁-C₄alkyl.

In certain aspects of the twenty ninth embodiment, compounds of Formula (II) include compounds of Formula (IIa):



In a thirtieth embodiment, the invention provides compounds of the twenty ninth embodiment which include compounds of Formula III:



Wherein

X¹ is CR¹⁶ or N;

X² is CR¹⁷ or N;

20 X³ is CR¹⁸ or N;

Z⁴ is N or CR¹⁴;

R¹ is NHR^{1a};

R^{1a} is hydrogen or C₁-C₄alkyl;

R² is hydrogen or C₁-C₄alkyl;

R^3 is hydrogen or halogen;

R^4 is hydrogen or halogen;

R^7 is hydrogen, methyl or ethyl;

R^{11} is hydrogen, halogen, cyano or C_1 - C_4 alkyl;

R^{12} and R^{13} are each independently selected from the group consisting of hydrogen, halogen, cyano, C_1 - C_4 alkyl, halo C_1 - C_4 alkyl, C_1 - C_4 alkoxy, or halo C_1 - C_4 alkoxy;

R^{14} is hydrogen, halogen, cyano or C_1 - C_4 alkyl;

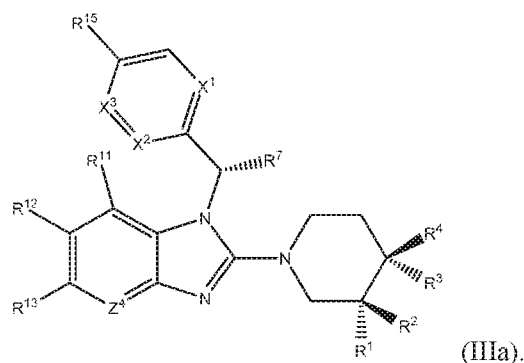
R^{15} is hydrogen, halogen, cyano, C_1 - C_4 alkyl, C_1 - C_4 alkoxy, halo C_1 - C_4 alkyl, halo C_1 - C_4 alkoxy, $C(O)NH_2$, $C(O)NH(C_1-C_4alkyl)$ or 5 member heteroaryl having one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms;

R^{16} is hydrogen, halogen, cyano, C_1 - C_4 alkyl, C_1 - C_4 alkoxy, halo C_1 - C_4 alkyl or halo C_1 - C_4 alkoxy;

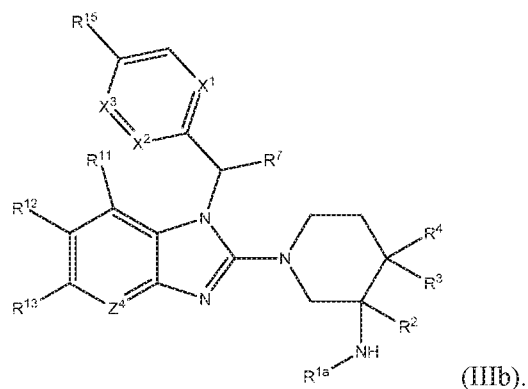
R^{17} is hydrogen or halogen; and

R^{18} is hydrogen, halogen, cyano, C_1 - C_4 alkyl, C_1 - C_4 alkoxy, halo C_1 - C_4 alkyl or halo C_1 - C_4 alkoxy, wherein at least one of R^{15} , R^{16} , R^{17} or R^{18} is not hydrogen.

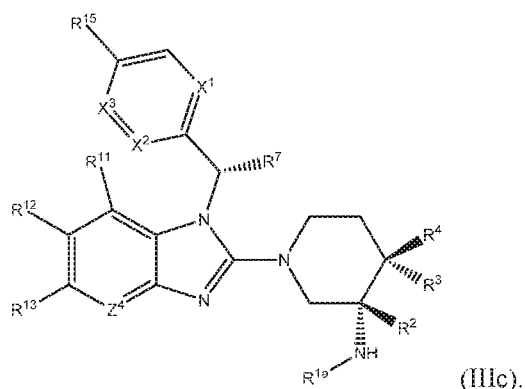
In certain aspects of the thirtieth embodiment, compounds of Formula (III) include compounds of Formula (IIIa):



In certain other aspects of the thirtieth embodiment, compounds of Formula (III) include compounds of Formula (IIIb):

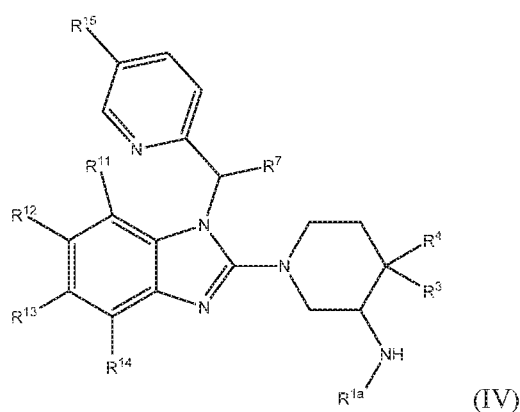


In certain other aspects of the thirtieth embodiment, compounds of Formula (IIIb) include compounds of Formula (IIIc):



In a thirty first embodiment, the invention provides compounds of the twenty ninth or thirtieth embodiment in which R^2 is hydrogen, R^7 is hydrogen or methyl; and Z^4 is CR^{14} .

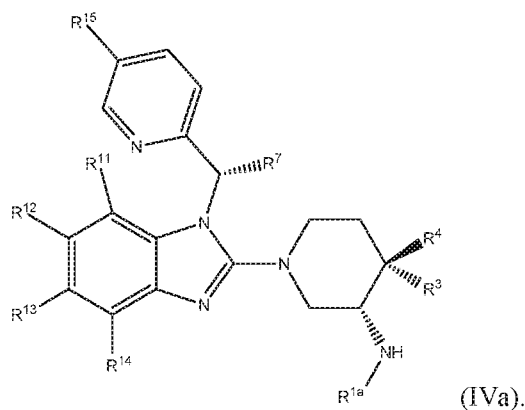
In a thirty second embodiment, the invention provides compounds of the twenty ninth embodiment which include compounds of Formula (IV):



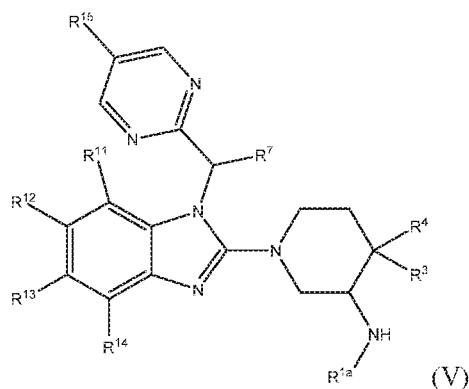
Wherein:

- R^{1a} is hydrogen or C_1 - C_4 alkyl;
- R^3 is hydrogen or halogen;
- R^4 is hydrogen or halogen;
- R^7 is hydrogen, methyl or ethyl;
- R^{11} is hydrogen, halogen, cyano or C_1 - C_4 alkyl;
- R^{12} and R^{13} are each independently selected from the group consisting of hydrogen, halogen, cyano, C_1 - C_4 alkyl, halo C_1 - C_4 alkyl, C_1 - C_4 alkoxy, or halo C_1 - C_4 alkoxy;
- R^{14} is hydrogen, halogen, cyano or C_1 - C_4 alkyl; and
- R^{15} is hydrogen, halogen, cyano, C_1 - C_4 alkyl, C_1 - C_4 alkoxy, halo C_1 - C_4 alkyl, halo C_1 - C_4 alkoxy, $C(O)NH_2$, or $C(O)NH(C_1$ - C_4 alkyl).

In certain aspects of the thirty second embodiment, compounds of Formula (IV) include compounds of Formula (IVa):



In a thirty third embodiment, the invention provides compounds of the twenty ninth embodiment which include compounds of Formula (V):



Wherein:

R^{1a} is hydrogen or C₁-C₄alkyl;

R³ is hydrogen or halogen;

R⁴ is hydrogen or halogen;

R⁷ is hydrogen, methyl or ethyl;

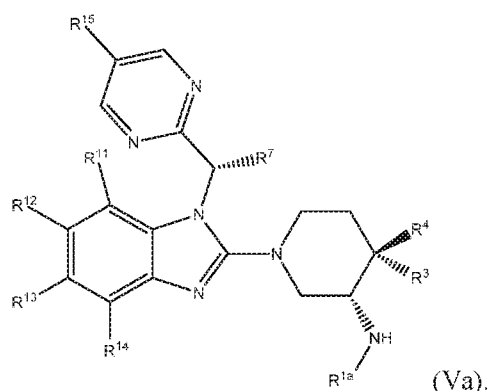
R¹¹ is hydrogen, halogen, cyano or C₁-C₄alkyl;

R¹² and R¹³ are each independently selected from the group consisting of hydrogen, halogen, cyano, C₁-C₄alkyl, haloC₁-C₄alkyl, C₁-C₄alkoxy, or haloC₁-C₄alkoxy;

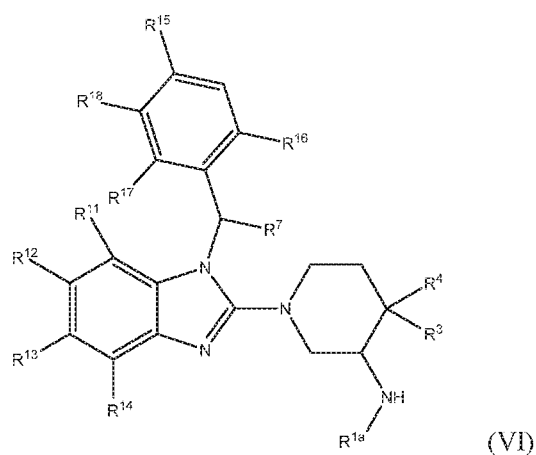
R¹⁴ is hydrogen, halogen, cyano or C₁-C₄alkyl; and

R¹⁵ is hydrogen, halogen, cyano, C₁-C₄alkyl, C₁-C₄alkoxy, haloC₁-C₄alkyl, haloC₁-C₄alkoxy, C(O)NH₂, or C(O)NH(C₁-C₄alkyl).

In certain aspects of the thirty third embodiment, compounds of Formula (V) include compounds of Formula (Va):



In a thirty fourth embodiment, the invention provides compounds of the twenty ninth embodiment which include compounds of Formula (VI):



Wherein

R^{1a} is hydrogen or C_1 - C_4 alkyl;

R^3 is hydrogen or halogen;

R^4 is hydrogen or halogen;

R^7 is hydrogen, methyl or ethyl;

R^{11} is hydrogen, halogen, cyano or C_1 - C_4 alkyl;

R^{12} and R^{13} are each independently selected from the group consisting of hydrogen, halogen, cyano, C_1 - C_4 alkyl, halo C_1 - C_4 alkyl, C_1 - C_4 alkoxy, or halo C_1 - C_4 alkoxy;

R^{14} is hydrogen, halogen, cyano or C_1 - C_4 alkyl;

R^{15} is hydrogen, halogen, cyano, C_1 - C_4 alkyl, C_1 - C_4 alkoxy, halo C_1 - C_4 alkyl, halo C_1 - C_4 alkoxy,

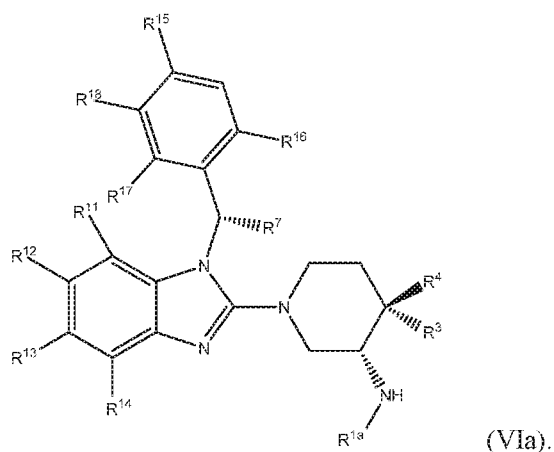
$C(O)NH_2$, $C(O)NH(C_1-C_4alkyl)$ or 5 member heteroaryl having one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms;

R^{16} is hydrogen, halogen, cyano, C_1 - C_4 alkyl, C_1 - C_4 alkoxy, halo C_1 - C_4 alkyl or halo C_1 - C_4 alkoxy;

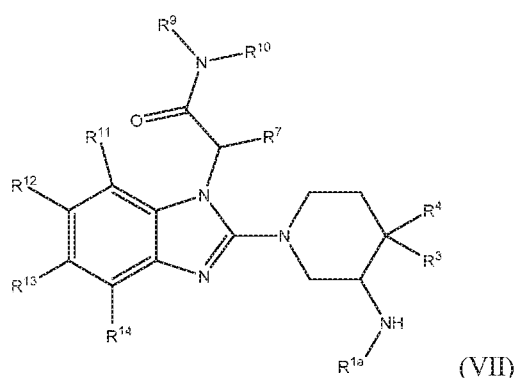
R^{17} is hydrogen or halogen; and

R^{18} is hydrogen, halogen, cyano, C_1 - C_4 alkyl, C_1 - C_4 alkoxy, halo C_1 - C_4 alkyl or halo C_1 - C_4 alkoxy, wherein at least one of R^{15} , R^{16} , R^{17} or R^{18} is not hydrogen.

In certain aspects of the thirty fourth embodiment, compounds of Formula (VI) include compounds of Formula (VIa):



In a thirty fifth embodiment, the invention provides compounds of the twenty ninth embodiment which include compounds of Formula (VII):



Wherein

R^{1a} is hydrogen or C_1 - C_4 alkyl;

R^3 is hydrogen or halogen;

R^4 is hydrogen or halogen;

R^7 is hydrogen, methyl or ethyl;

R^9 is hydrogen, methyl or ethyl;

R^{10} is C_1 - C_4 alkyl or halo C_1 - C_4 alkyl wherein each alkyl is optionally substituted with cyano, halogen, hydroxy, C_1 - C_6 alkoxy or $S(O)_qC_1$ - C_6 alkyl; or

NR^9R^{10} , taken in combination, form a 4 to 6 member monocyclic azacycle or a 7 to 9 member bicyclic azacycle, each of which having one ring nitrogen atom and 0 or 1 additional ring heteroatom selected from N, O or S, which ring sulfur may be optionally oxidized, wherein each azacycle is

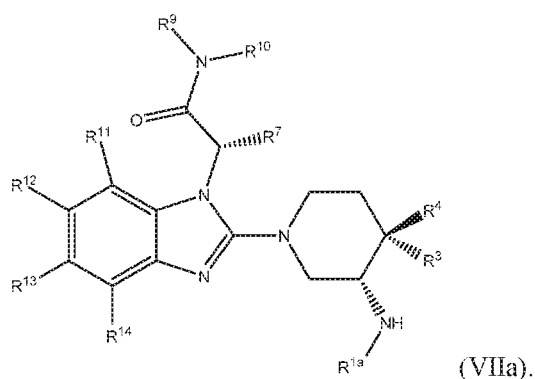
optionally substituted with 0, 1 or 2 substituents selected from halogen, oxo, hydroxy, cyano, C₁-C₆alkyl, halo C₁-C₆alkyl, hydroxyC₁-C₆alkyl, C₁-C₆alkoxy, S(O)₂C₁-C₆alkyl, CO₂H, C(O)C₁-C₆alkyl, or C(O)NH₂;

R¹¹ is hydrogen, halogen, cyano or C₁-C₄alkyl;

R¹² and R¹³ are each independently selected from the group consisting of hydrogen, halogen, cyano, C₁-C₄alkyl, haloC₁-C₄alkyl, C₁-C₄alkoxy, or haloC₁-C₄alkoxy; and

R¹⁴ is hydrogen, halogen, cyano or C₁-C₄alkyl.

In certain aspects of the thirty fifth embodiment, compounds of Formula (VII) include compounds of Formula (VIIa):



In a thirty sixth embodiment, the invention provides compounds of any one of the twenty ninth to thirty fifth embodiment in which R¹¹ is hydrogen.

In a thirty seventh embodiment, the invention provides compounds of any one of the thirty first to thirty fifth embodiment in which R^{1a} is hydrogen or methyl; R³ is hydrogen or fluorine; and R⁴ is hydrogen or fluorine.

In a thirty eighth embodiment, the invention provides compounds of the first or second embodiment in which the compound is recited in the below Table A.

TABLE A

(S)-6-((2-(3-aminopiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;
 (S)-6-((2-(3-aminopiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;
 (S)-6-((2-(3-aminopiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;
 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

5 (R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-4-carbonitrile;

(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

10 (R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

15 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3S,4S)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(S)-6-((2-(5-amino-3,3-difluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazole-4-carbonitrile;

20 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-(trifluoromethoxy)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(trifluoromethoxy)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

25 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-5-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-6-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3aR,7aR)-hexahydro-1H-pyrrolo[2,3-c]pyridin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

30 6-((2-((3aR,7aS)-hexahydro-1H-pyrrolo[2,3-c]pyridin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3aS,7aS)-hexahydro-1H-pyrrolo[2,3-c]pyridin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3aS,7aR)-hexahydro-1H-pyrrolo[2,3-c]pyridin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(R)-6-((2-(1,6-diazaspiro[3.5]nonan-6-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(S)-6-((2-(1,6-diazaspiro[3.5]nonan-6-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

5 (3R,4R)-1-(1-((5-chloropyridin-2-yl)methyl)-6-(methylsulfonyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4R)-1-(1-((5-chloropyridin-2-yl)methyl)-5-(methylsulfonyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

10 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazole-4-carbonitrile;

(3R,4R)-1-(5,7-difluoro-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4R)-1-(4,6-difluoro-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

15 (3R,4R)-1-(5,7-difluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4R)-1-(4,6-difluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

20 2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-4-carbonitrile;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-4-carbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

25 (3R,4S)-1-(1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4S)-1-(1-((5-chloropyrimidin-2-yl)methyl)-5-fluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(R)-2-(3-amino-4,4-difluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

30 (R)-2-(3-amino-4,4-difluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

35 tert-butyl ((3R,4R)-1-(1-((5-cyanopyridin-2-yl)methyl)-5,6-dimethyl-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl)carbamate;

(S)-6-((2-(3-aminopiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

(S)-6-((2-(3-aminopiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

5 6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

10 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

(S)-2-(3-aminopiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

15 (S)-2-(3-aminopiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

20 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;

(R)-2-(3-amino-4,4-difluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

(R)-2-(3-amino-4,4-difluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;

25 (S)-6-((2-(3-aminopiperidin-1-yl)-4,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-4,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

30 (R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-4,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(S)-6-((2-(3-aminopiperidin-1-yl)-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(S)-6-((2-(3-aminopiperidin-1-yl)-5,7-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

35 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,7-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

5 6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5,7-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-5,7-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

10 2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;

(S)-6-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

15 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((1R,5S)-1-(aminomethyl)-3-azabicyclo[3.1.0]hexan-3-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

20 6-((2-((1S,5R)-1-(aminomethyl)-3-azabicyclo[3.1.0]hexan-3-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3aR,4R,6aS)-4-aminohexahydrocyclopenta[c]pyrrol-2(1H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

25 6-((2-((3aS,4S,6aR)-4-aminohexahydrocyclopenta[c]pyrrol-2(1H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3aR,4S,6aS)-4-aminohexahydrocyclopenta[c]pyrrol-2(1H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3aS,4R,6aR)-4-aminohexahydrocyclopenta[c]pyrrol-2(1H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

30 (R)-6-((2-(3-(aminomethyl)pyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

(S)-6-((2-(3-(aminomethyl)pyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

5 (R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

(R)-1-(1-((5-chloropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4,4-difluoropiperidin-3-amine hydrochloride;

10 (3R,4S)-1-(1-((5-chloropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

15 (R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-4-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

20 6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-4-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-3H-imidazo[4,5-b]pyridin-3-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)nicotinonitrile;

25 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)-N-(tert-butyl)nicotinamide;

6-((2-((3R,4R)-3-amino-4-hydroxypiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

30 6-((2-((3S,4S)-3-amino-4-hydroxypiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-(2,6-diazaspiro[3.4]octan-6-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((4aR,7aS)-hexahydropyrrolo[3,4-b][1,4]oxazin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

35 6-((2-((4aS,7aR)-hexahydropyrrolo[3,4-b][1,4]oxazin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((4aR,7aR)-hexahydropyrrolo[3,4-b][1,4]oxazin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((4aS,7aS)-hexahydropyrrolo[3,4-b][1,4]oxazin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

5 (S)-3-amino-1-(1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidine-3-carboxamide;

(R)-3-amino-1-(1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidine-3-carboxamide;

10 (S)-6-((2-(3-amino-3-(hydroxymethyl)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(R)-6-((2-(3-amino-3-(hydroxymethyl)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4S)-3-amino-4-fluoro-1-piperidiny)-6-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

15 6-((2-((3R,4S)-3-amino-4-fluoro-1-piperidiny)-5-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R)-3-amino-4,4-difluoro-1-piperidiny)-6-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

20 6-((2-((3R)-3-amino-4,4-difluoro-1-piperidiny)-5-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-5-methyl-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-6-methyl-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

25 6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-6-chloro-5-methyl-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-5-chloro-6-methyl-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

30 6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-6-fluoro-5-methyl-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-5-fluoro-6-methyl-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3S)-3-(methylanino)-1-piperidiny)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R)-3-(methy lamino)-1-piperidiny l)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny l)-6-(difluoromethoxy)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

5 6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny l)-5-(difluoromethoxy)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny l)-4-methoxy-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

10 6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny l)-4-methyl-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

5-((2-((3R,4S)-3-amino-4-fluoro-1-piperidiny l)-6-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-2-pyrazinecarboxamide;

5-((2-((3R,4S)-3-amino-4-fluoro-1-piperidiny l)-5-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-2-pyrazinecarboxamide;

15 6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny l)-6-chloro-5-(trifluoromethoxy)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny l)-5-chloro-6-(trifluoromethoxy)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

20 6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny l)-6-chloro-5-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny l)-5-chloro-6-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((5R)-1,7-diazaspiro[4.5]decan-7-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile, 6-((2-((5S)-1,7-diazaspiro[4.5]decan-7-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

25 6-((2-((6R)-1,8-diazaspiro[5.5]undecan-8-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((6S)-1,8-diazaspiro[5.5]undecan-8-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

30 6-((2-((4aR,8aR)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((4aS,8aS)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

5-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny l)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)-2-pyrazinecarboxamide;

5-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-6-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-2-pyrazinecarboxamide;
6-((2-((5R)-1,7-diazaspiro[4.5]decan-7-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;
6-((2-((5S)-1,7-diazaspiro[4.5]decan-7-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;
5 6-((2-((3R)-3-amino-4,4-difluoro-1-piperidiny)-5-methoxy-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;
6-((2-((3R)-3-amino-4,4-difluoro-1-piperidiny)-6-methoxy-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;
6-((2-((3S)-3-(methylamino)-1-piperidiny)-6-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;
10 6-((2-((3S)-3-(methylamino)-1-piperidiny)-5-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;
6-((2-((3S)-3-amino-3-methyl-1-piperidiny)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;
(S)-6-((2-(3-aminopiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile
15 2,2,2-trifluoroacetate;
(S)-6-((2-(3-aminopiperidin-1-yl)-5-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile
2,2,2-trifluoroacetate;
6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4-chloro-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile 2,2,2-trifluoroacetate;
20 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;
6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;
25 6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;
6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;
2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazole-4-carbonitrile;
30 (R)-2-(3-amino-4,4-difluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-5-fluoro-1H-benzo[d]imidazole-7-carbonitrile;
(R)-2-(3-amino-4,4-difluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazole-4-carbonitrile;

6-((2-((3R,4R)-3-amino-4-hydroxypiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4S)-3-amino-4-hydroxypiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

5 (R)-4-((2-(3-amino-4,4-difluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

4-((2-((3R,4R)-3-amino-4-hydroxypiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile compound with 4-((2-((3S,4S)-3-amino-4-hydroxypiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile (1:1) dihydrochloride;

4-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,7-difluoro-1H-benzimidazol-1-yl)methyl)benzonitrile;

10 4-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-4,6-difluoro-1H-benzimidazol-1-yl)methyl)benzonitrile;

2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-1-(4-cyanobenzyl)-1H-benzimidazole-6-carbonitrile;

2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-1-(4-cyanobenzyl)-1H-benzimidazole-5-carbonitrile;

15 2-((3R)-3-amino-4,4-difluoro-1-piperidinyl)-1-(4-cyanobenzyl)-1H-benzimidazole-6-carbonitrile;

2-((3R)-3-amino-4,4-difluoro-1-piperidinyl)-1-(4-cyanobenzyl)-1H-benzimidazole-5-carbonitrile;

(R)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

4-((2-((3R,4R)-3-amino-4-methylpiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

4-((2-(3-(aminomethyl)-3-methylpyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

20 4-((2-((3S,4R)-3-amino-4-phenylpyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile & 4-((2-((3R,4S)-3-amino-4-phenylpyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

(S)-4-((2-(3-aminopyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

(S)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

4-((2-(6-amino-2-azaspiro[4.4]nonan-2-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

25 4-((2-(4-aminohexahydrocyclopenta[c]pyrrol-2(1H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

4-((2-((3S,4S)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

4-((2-((3S,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

4-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

30 4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

(R)-4-((2-(3-(aminomethyl)-3-fluoropyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile 2,2,2-trifluoroacetate;

(S)-4-((2-(3-(aminomethyl)-3-fluoropyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile 2,2,2-trifluoroacetate;

(R)-4-((2-(3-(aminomethyl)-3-hydroxypyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile 2,2,2-trifluoroacetate;

(S)-4-((2-(3-(aminomethyl)-3-hydroxypyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile 2,2,2-trifluoroacetate;

5 (S)-4-((2-(3-(aminomethyl)pyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

(R)-4-((2-(3-(aminomethyl)pyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

4-((2-((3S,4S)-3-amino-4-methylpiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile 2,2,2-trifluoroacetate;

4-((2-((3S,4R)-3-amino-4-methylpiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile

10 2,2,2-trifluoroacetate;

4-((2-((3R,4S)-3-amino-4-methylpiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile 2,2,2-trifluoroacetate;

4-((2-((1S,5R)-1-(aminomethyl)-3-azabicyclo[3.1.0]hexan-3-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

15 4-((2-((1R,5S)-1-(aminomethyl)-3-azabicyclo[3.1.0]hexan-3-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

(R)-4-((2-(3-aminopiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

(R)-4-((2-(3-aminopiperidin-1-yl)-5-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

2-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

20 (3R,4R)-4-fluoro-1-(1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(3R,4R)-4-fluoro-1-(1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

25 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;

(3R,4R)-1-(1-((5-bromopyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-

30 amine;

(3R,4R)-4-fluoro-1-(1-((5-(trifluoromethyl)pyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(3R,4R)-4-fluoro-1-(1-((5-methoxypyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(3R,4R)-1-(1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

5 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;

10 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-cyanopyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-bromopyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

15 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-bromopyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;

5-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)pyrazine-2-carbonitrile;

20 2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;

(3R,4R)-3-amino-1-(1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)piperidin-4-ol;

25 (3R,4R)-3-amino-1-(1-((5-chloropyrimidin-2-yl)methyl)-5-fluoro-1H-benzo[d]imidazol-2-yl)piperidin-4-ol;

6-((2-((3R,4R)-3-amino-4-hydroxypiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

30 6-((2-((3R,4R)-3-amino-4-hydroxypiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(S)-1-(1-((5-chloropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(S)-5-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)picolinonitrile;

(3R,4R)-1-(1-((5-chloropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyridin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile hydrochloride;

5 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyridin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile hydrochloride;

(3R,4R)-1-(1-((R)-1-(5-chloropyridin-2-yl)ethyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

10 (3R,4R)-1-(1-((S)-1-(5-chloropyridin-2-yl)ethyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

(3R,4R)-1-(1-((R)-1-(5-chloropyridin-2-yl)ethyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

(3R,4R)-1-(1-((S)-1-(5-chloropyridin-2-yl)ethyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

15 (3R,4R)-1-(5-chloro-1-((R)-1-(5-chloropyridin-2-yl)ethyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

(3R,4R)-1-(5-chloro-1-((S)-1-(5-chloropyridin-2-yl)ethyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

20 (3R,4R)-1-(6-chloro-1-((R)-1-(5-chloropyridin-2-yl)ethyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

(3R,4R)-1-(6-chloro-1-((S)-1-(5-chloropyridin-2-yl)ethyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((R)-1-(5-cyanopyridin-2-yl)ethyl)-1H-benzo[d]imidazole-6-carbonitrile hydrochloride;

25 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((R)-1-(5-cyanopyridin-2-yl)ethyl)-1H-benzo[d]imidazole-5-carbonitrile hydrochloride;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((S)-1-(5-cyanopyridin-2-yl)ethyl)-1H-benzo[d]imidazole-6-carbonitrile hydrochloride;

30 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((S)-1-(5-cyanopyridin-2-yl)ethyl)-1H-benzo[d]imidazole-5-carbonitrile hydrochloride;

(3R,4R)-1-(1-((5-chloropyridin-2-yl)methyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

(3R,4R)-1-(5,6-difluoro-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

(R)-1-(1-((5-chloropyridin-2-yl)methyl)-5,7-difluoro-1H-benzo[d]imidazol-2-yl)-4,4-difluoropiperidin-3-amine hydrochloride;

(R)-1-(1-((5-chloropyridin-2-yl)methyl)-4,6-difluoro-1H-benzo[d]imidazol-2-yl)-4,4-difluoropiperidin-3-amine hydrochloride;

5 (R)-1-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)-2,3-dihydro-1H-indene-5-carbonitrile hydrochloride;

(S)-1-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)-2,3-dihydro-1H-indene-5-carbonitrile hydrochloride;

10 (R)-5-((2-((3-amino-4,4-difluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)pyrazine-2-carbonitrile;

(R)-5-((2-((3-amino-4,4-difluoropiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)methyl)pyrazine-2-carbonitrile;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-isopropylacetamide;

15 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(azetidin-1-yl)ethanone;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(2-cyanopropyl)-N-ethylacetamide;

20 3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-methylpyrrolidin-2-one;

3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-phenylpiperidin-2-one;

3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-chlorophenyl)pyrrolidin-2-one;

25 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-methoxypyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile hydrochloride;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-methoxypyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile hydrochloride;

30 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((6-(trifluoromethyl)pyridin-3-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile hydrochloride;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((6-(trifluoromethyl)pyridin-3-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile hydrochloride;

(S)-3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-methylpyrrolidin-2-one;

(R)-3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-methylpyrrolidin-2-one;

(S)-3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-chlorophenyl)pyrrolidin-2-one;

5 (R)-3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-chlorophenyl)pyrrolidin-2-one;

2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-1-((5-cyano-2-pyrazinyl)methyl)-1H-benzimidazole-6-carbonitrile;

10 2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-1-((5-cyano-2-pyrazinyl)methyl)-1H-benzimidazole-5-carbonitrile;

5-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-4,6-difluoro-1H-benzimidazol-1-yl)methyl)-2-pyrazinecarbonitrile;

5-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-5,7-difluoro-1H-benzimidazol-1-yl)methyl)-2-pyrazinecarbonitrile;

15 (3S)-1-(1-((5-fluoro-2-pyridinyl)methyl)-1H-benzimidazol-2-yl)-N-methyl-3-piperidinamine;

(3S)-1-(1-((5-chloro-2-pyridinyl)methyl)-1H-benzimidazol-2-yl)-N-methyl-3-piperidinamine;

6-((1R)-1-(2-((3S)-3-(methylamino)-1-piperidiny)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile;

20 6-((1S)-1-(2-((3S)-3-(methylamino)-1-piperidiny)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile;

(3R,4R)-1-(1-((5-chloro-2-pyrimidinyl)methyl)-5,7-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((5-chloro-2-pyrimidinyl)methyl)-4,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

25 (3R,4R)-1-(5,6-difluoro-1-((1-methyl-1H-indazol-4-yl)methyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(5,6-difluoro-1-(5-quinolinylmethyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

30 (3R,4R)-1-(5,6-difluoro-1-((1R)-1-(8-quinolinyl)ethyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(5,6-difluoro-1-((1S)-1-(8-quinolinyl)ethyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((3-(3-chlorophenyl)-1,2-oxazol-5-yl)methyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(5,6-difluoro-1-((1-methyl-1H-indazol-7-yl)methyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-(2,6-dichlorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

5 1-(1-azetidiny)-2-(2-((3S)-3-(methylamino)-1-piperidiny)-1H-benzimidazol-1-yl)ethanone;

6-((1R)-1-(4,6-difluoro-2-((4aR,8aR)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile;

6-((1R)-1-(4,6-difluoro-2-((4aS,8aS)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile;

10 6-((1S)-1-(4,6-difluoro-2-((4aS,8aS)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile;

6-((1S)-1-(4,6-difluoro-2-((4aR,8aR)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile;

15 6-((1R)-1-(5,7-difluoro-2-((4aR,8aR)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile;

6-((1R)-1-(5,7-difluoro-2-((4aS,8aS)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile;

6-((1S)-1-(5,7-difluoro-2-((4aS,8aS)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile;

20 6-((1S)-1-(5,7-difluoro-2-((4aR,8aR)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile;

2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-5,6-difluoro-1H-benzimidazol-1-yl)-N-methylacetamide;

25 2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-5,6-difluoro-1H-benzimidazol-1-yl)-1-(4-morpholinyl)ethanone;

2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-5,6-difluoro-1H-benzimidazol-1-yl)-1-(1-pyrrolidinyl)ethanone;

2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-5,6-difluoro-1H-benzimidazol-1-yl)-N,N-dimethylacetamide;

30 (2R)-2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-5,6-difluoro-1H-benzimidazol-1-yl)-N,N-dimethylpropanamide;

(2S)-2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-5,6-difluoro-1H-benzimidazol-1-yl)-N,N-dimethylpropanamide;

35 2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-5,6-difluoro-1H-benzimidazol-1-yl)-1-(1-piperidiny)ethanone;

2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-5,6-difluoro-1H-benzimidazol-1-yl)-N-ethylacetamide;

1-((5-chloro-2-pyrimidinyl)methyl)-2-((3R,4R)-4-fluoro-3-(methylamino)-1-piperidiny)-1H-benzimidazole-6-carbonitrile;

5 1-((5-chloro-2-pyrimidinyl)methyl)-2-((3R,4R)-4-fluoro-3-(methylamino)-1-piperidiny)-1H-benzimidazole-5-carbonitrile;

2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-6-chloro-1H-benzimidazol-1-yl)-1-(1-azetidiny)ethanone;

10 2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-5-chloro-1H-benzimidazol-1-yl)-1-(1-azetidiny)ethanone;

2-((3R,4S)-3-amino-4-fluoro-1-piperidiny)-1-(2-(1-azetidiny)-2-oxoethyl)-1H-benzimidazole-6-carbonitrile;

2-((3R,4S)-3-amino-4-fluoro-1-piperidiny)-1-(2-(1-azetidiny)-2-oxoethyl)-1H-benzimidazole-5-carbonitrile;

15 (3R,4R)-1-(1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4R)-1-(1-((5-chloropyrimidin-2-yl)methyl)-5-fluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(R)-6-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

20 (R)-5-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)picolinonitrile 2,2,2-trifluoroacetate;

(R)-1-(1-(isoquinolin-7-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(R)-1-(1-(1-methyl-1H-indazol-7-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

6-((R)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile

25 hydrochloride;

6-((S)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile hydrochloride;

6-((R)-1-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile hydrochloride;

30 6-((S)-1-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile hydrochloride;

6-((R)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)propyl)nicotinonitrile hydrochloride;

35 6-((S)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)propyl)nicotinonitrile hydrochloride;

(3R,4R)-1-(5,6-difluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

3-(1-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile;

5 (3R,4R)-1-(5,6-difluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4S)-1-(5,6-difluoro-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

10 (3R,4S)-4-fluoro-1-(1-((5-fluoropyrimidin-2-yl)methyl)-6-(trifluoromethyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(3R,4S)-4-fluoro-1-(1-((5-fluoropyrimidin-2-yl)methyl)-5-(trifluoromethyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(R)-1-(5,6-difluoro-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4,4-difluoropiperidin-3-amine;

15 2-(2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)-1-(azetidin-1-yl)ethan-1-one;

2-(2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)-1-(azetidin-1-yl)ethan-1-one;

20 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(2,2-dimethylpyrrolidin-1-yl)ethan-1-one;

6-((2-((3R,4S)-3-amino-4-hydroxypiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4S)-3-amino-4-hydroxypiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

25 4-((R)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile hydrochloride;

4-((S)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile hydrochloride;

30 (S)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-3-fluorobenzonitrile hydrochloride;

(S)-1-(1-(4-chlorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine hydrochloride;

4-((R)-1-(2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile hydrochloride;

35 4-((S)-1-(2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile hydrochloride;

4-((R)-1-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile hydrochloride;

4-((S)-1-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile hydrochloride;

5 (S)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-3-chlorobenzonitrile hydrochloride;

(3R,4R)-1-(1-((1R)-1-(2,4-dichlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

10 (3R,4R)-1-(1-((1S)-1-(2,4-dichlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((1R)-1-(2-chlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((1S)-1-(2-chlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

15 (3R,4R)-1-(1-((1R)-1-(3-chlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((1S)-1-(3-chlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

20 (3R,4R)-1-(1-((1R)-1-(2,5-dichlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((1S)-1-(2,5-dichlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((1R)-1-(2,4-difluorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

25 (3R,4R)-1-(1-((1S)-1-(2,4-difluorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((1R)-1-(3,4-dichlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

30 (3R,4R)-1-(1-((1S)-1-(3,4-dichlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((1R)-1-(2,5-difluorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((1S)-1-(2,5-difluorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(5,6-difluoro-1-((1R)-1-(4-(trifluoromethyl)phenyl)ethyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(5,6-difluoro-1-((1R)-1-(4-(trifluoromethoxy)phenyl)ethyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

5 (3R,4R)-1-(1-(5-chloro-2-(trifluoromethoxy)benzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(5,6-difluoro-1-(4-(1H-1,2,4-triazol-1-yl)benzyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

10 2-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)-5-chlorobenzonitrile;

(3R,4R)-1-(1-(2,4-dichlorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

4-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)-3-(difluoromethoxy)benzonitrile;

15 (3R,4R)-1-(1-(2,5-dichlorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-(4-(1,1-difluoroethyl)benzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

20 4-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)-2-methylbenzonitrile;

4-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)-2-chlorobenzonitrile;

2-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)-4-chlorobenzonitrile;

25 (3R,4R)-1-(1-(2-(difluoromethoxy)benzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-(3-chloro-4-fluorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

30 (3R,4R)-1-(1-(4-chloro-2-methoxybenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-(2,4-difluorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(5,6-difluoro-1-(2-(trifluoromethyl)benzyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

- 2-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)benzonitrile;
- (3R,4R)-1-(1-(2-chlorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;
- (3R,4R)-1-(1-(2-chloro-4-fluorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-
- 5 piperidinamine;
- (3R,4R)-1-(5,6-difluoro-1-(4-fluoro-2-(trifluoromethyl)benzyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;
- (3R,4R)-1-(1-(3,4-difluorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-
- piperidinamine;
- 10 (3R,4R)-1-(1-(4-chloro-2-fluorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;
- (3R,4R)-1-(1-(3,4-dichlorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-
- piperidinamine;
- (3R,4R)-1-(1-(4-chloro-3-fluorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-
- 15 piperidinamine;
- (3R,4R)-1-(5,6-difluoro-1-(4-(trifluoromethyl)benzyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;
- (3R,4R)-1-(5,6-difluoro-1-(4-(trifluoromethoxy)benzyl)-1H-benzimidazol-2-yl)-4-fluoro-3-
- piperidinamine;
- 20 (3R,4R)-1-(1-(4-(difluoromethyl)benzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;
- (3R,4R)-1-(5,6-difluoro-1-(3-(trifluoromethoxy)benzyl)-1H-benzimidazol-2-yl)-4-fluoro-3-
- piperidinamine;
- (3R,4R)-1-(5,6-difluoro-1-(3-(trifluoromethyl)benzyl)-1H-benzimidazol-2-yl)-4-fluoro-3-
- 25 piperidinamine;
- 3-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)benzonitrile;
- (3R,4R)-1-(1-(3-chlorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;
- (S)-1-(1-(4-fluorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
- 30 (S)-1-(1-(4-(1,2,4-oxadiazol-3-yl)benzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
- (R)-1-(1-(4-(methylsulfonyl)benzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
- (R)-1-(1-(4-(1H-1,2,4-triazol-1-yl)benzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
- (R)-2-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;
- (R)-1-(1-(2,6-dichlorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
- 35 (R)-1-(1-(2-chlorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(R)-1-(1-(4-(trifluoromethyl)benzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
 (R)-1-(1-(4-(trifluoromethoxy)benzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
 (R)-1-(1-(4-chlorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
 (R)-1-(1-(3-chlorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
 5 (R)-1-(1-(4-(1,1-difluoroethyl)benzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
 (R)-2-(4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)phenyl)-2-methylpropanenitrile;
 (R)-1-(1-(4-(difluoromethyl)benzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
 (R)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-N-methylbenzamide;
 10 (R)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-3-fluorobenzonitrile;
 (R)-2-(4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)phenoxy)acetonitrile;
 (R)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-N,N-dimethylbenzenesulfonamide;
 (R)-1-(1-(4-methylbenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
 15 (R)-1-(1-(4-fluorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
 (R)-1-(1-((1-methyl-1H-indazol-7-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
 (R)-1-(1-(2,4-difluorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
 (R)-1-(1-(3,4-difluorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
 (R)-1-(1-(4-chloro-3-fluorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
 20 (R)-1-(1-(3-(3-chlorophenyl)isoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
 (R)-1-(1-(3-chloro-4-methoxybenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
 (R)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-3-chlorobenzonitrile;
 (R)-1-(1-(2,4-dichlorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
 (R)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-3-methoxybenzonitrile;
 25 (R)-2-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-5-chlorobenzonitrile;
 4-((R)-1-(2-((R)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile;
 4-(1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile;
 (R)-3-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;
 4-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile hydrochloride;
 30 (S)-4-((2-(3-aminopiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile hydrochloride;
 4-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

(S)-4-((2-(3-aminopiperidin-1-yl)-5-methoxy-3H-imidazo[4,5-b]pyridin-3-yl)methyl)benzonitrile hydrochloride;

(R)-4-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

5 (R)-4-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

(R)-4-((2-(3-amino-4,4-difluoropiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

10 4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

4-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

(R)-4-((2-(3-amino-4,4-difluoropiperidin-1-yl)-4-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

15 4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-imidazo[4,5-c]pyridin-1-yl)methyl)benzonitrile;

20 4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-3H-imidazo[4,5-c]pyridin-3-yl)methyl)benzonitrile;

4-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny1)-6-ethoxy-1H-benzimidazol-1-yl)methyl)benzonitrile;

4-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1H-imidazo[4,5-b]pyridin-1-yl)methyl)benzonitrile;

25 4-((2-((3R)-3-amino-4,4-difluoro-1-piperidiny1)-6-fluoro-1H-benzimidazol-1-yl)methyl)benzonitrile;

4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-imidazo[4,5-b]pyridin-1-yl)methyl)benzonitrile;

30 (S)-4-((2-(3-aminopiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile 2,2,2-trifluoroacetate;

(S)-4-((2-(3-aminopiperidin-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)methyl)benzonitrile hydrochloride;

4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile hydrochloride;

35 (S)-4-((2-(3-aminopiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

(S)-4-((2-(3-aminopiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;
 (R)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)-2,3-dihydro-1H-indene-5-carbonitrile;
 (S)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)-2,3-dihydro-1H-indene-5-carbonitrile;
 5 (3R,4R)-4-fluoro-1-(1-((5-methoxypyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
 1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)azetidine-3-carbonitrile;
 10 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(3-(tert-butoxy)azetidin-1-yl)ethan-1-one;
 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(3,3-difluoroazetidin-1-yl)ethanone;
 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(3-isopropylazetidin-1-yl)ethanone;
 15 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(6,6-difluoro-2-azaspiro[3.3]heptan-2-yl)ethanone;
 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(7-oxa-2-azaspiro[3.5]nonan-2-yl)ethanone;
 20 (R)-6-((2-(4,4-difluoro-3-(methylamino)piperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;
 (R)-6-((2-(4,4-difluoro-3-((2-hydroxyethyl)amino)piperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;
 (S)-6-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinic acid;
 25 (S)-6-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinamide;
 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinamide;
 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetic acid;
 6-((R)-1-(4,6-difluoro-2-((3R,4R)-4-fluoro-3-(methylamino)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile;
 30 6-((S)-1-(4,6-difluoro-2-((3R,4R)-4-fluoro-3-(methylamino)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile;
 6-((R)-1-(5,7-difluoro-2-((3R,4R)-4-fluoro-3-(methylamino)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile; and

6-((S)-1-(5,7-difluoro-2-((3R,4R)-4-fluoro-3-(methylamino)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile.

In another aspect of the thirty eighth embodiment, the invention provides compounds of the first embodiment in which the compound is recited in the below Table A-1:

TABLE A-1

2-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)pyrimidine-5-carbonitrile;
 2-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)pyrimidine-5-carbonitrile;
 (3R,4R)-4-fluoro-1-(6-fluoro-1-((5-methoxypyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;
 (3R,4R)-4-fluoro-1-(5-fluoro-1-((5-methoxypyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4-cyano-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;
 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide;
 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-methoxy-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;
 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-methoxy-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide;
 6-((2-((3R,4R)-3-amino-4-methoxypiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;
 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-4-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;
 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(trifluoromethyl)-3H-imidazo[4,5-b]pyridin-3-yl)methyl)nicotinonitrile;
 (3R,4R)-1-(1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)-4-methoxypiperidin-3-amine;
 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-bromo-1H-benzo[d]imidazol-1-yl)-1-(azetidin-1-yl)ethan-1-one;
 (3R,4R)-1-(1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)-4-methoxypiperidin-3-amine;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(trifluoromethyl)-1H-imidazo[4,5-b]pyridin-1-yl)methyl)nicotinonitrile;

5 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)-1-morpholinoethan-1-one;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

10 2-(2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide;

2-(2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

6-((2-((3R,4S)-3-amino-4-methoxypiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

15 2-(2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)-1-morpholinoethan-1-one;

(R)-2-(2-(3-amino-4,4-difluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

20 2-(2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

(3R,4S)-1-(1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)-4-methoxypiperidin-3-amine;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-(trifluoromethoxy)-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide;

25 2-(6-fluoro-2-((3R,4R)-4-fluoro-3-(methylamino)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-bromo-1H-benzo[d]imidazol-1-yl)-1-(azetidin-1-yl)ethan-1-one;

30 2-(2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide;

2-(6-fluoro-2-(1,7-diazaspiro[4.5]decan-7-yl)-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)-1-morpholinoethan-1-one;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(trifluoromethoxy)-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(trifluoromethoxy)-1H-benzo[d]imidazol-1-yl)-1-morpholinoethan-1-one;

5 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-7-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(3R,4S)-1-(1-((5-chloropyrimidin-2-yl)methyl)-5-fluoro-1H-benzo[d]imidazol-2-yl)-4-methoxypiperidin-3-amine;

10 2-(2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)-1-morpholinoethan-1-one;

2-(5-fluoro-2-((3R,4R)-4-fluoro-3-(methylamino)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

2-(2-(3-amino-4-methylpyrrolidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

15 2-(2-((3R,4R)-3-amino-4-hydroxypiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

(R)-2-(2-(3-amino-4,4-difluoropiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

20 2-(2-((3R,4R)-3-amino-4-methoxypiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

2-(2-((3R)-3-amino-4-hydroxypiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

2-(2-((3R,4R)-3-amino-4-methoxypiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

25 2-(2-(3-(aminomethyl)-3-fluoropyrrolidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

2-(2-(3-(aminomethyl)-3-fluoropyrrolidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

30 2-(6-fluoro-2-((4aR,8aR)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

(S)-2-(2-(3-aminopyrrolidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

(R)-2-(2-(3-aminopyrrolidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

(S)-2-(2-(3-(aminomethyl)pyrrolidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

2-(6-fluoro-2-((4aR,8aR)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

5 2-(5-fluoro-2-((4aS,8aS)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

(3R,4R)-3-amino-1-(1-((5-chloropyrimidin-2-yl)methyl)-5-fluoro-1H-benzo[d]imidazol-2-yl)piperidin-4-ol;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)-1-morpholinoethanone;

10 (3R,4R)-3-amino-1-(1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)piperidin-4-ol;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)-1-morpholinoethanone;

15 (3R,4R)-1-(1-((R)-1-(5-chloropyrimidin-2-yl)ethyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-(trifluoromethyl)-1H-imidazo[4,5-b]pyridin-1-yl)methyl)nicotinonitrile;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

20 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(thiazol-2-yl)acetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide;

25 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-1-(azetidin-1-yl)ethan-1-one;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(3-(trifluoromethyl)piperidin-1-yl)ethan-1-one;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)ethan-1-one;

30 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(2-methylmorpholino)ethan-1-one;

(3R,4R)-1-(1-((R)-1-(5-chloropyrimidin-2-yl)ethyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-7-methoxy-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

5 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(azocan-1-yl)ethan-1-one;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-(pyrazin-2-yl)piperazin-1-yl)ethan-1-one;

10 methyl 1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)piperidine-4-carboxylate;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(2-ethylmorpholino)ethan-1-one;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)-1-(azetidin-1-yl)ethan-1-one;

15 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(1,1-dioxido-2,3-dihydrothiophen-3-yl)-N-phenylacetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-methylpiperidin-1-yl)ethan-1-one;

20 (3R,4R)-4-fluoro-1-(6-fluoro-1-((4-methoxypyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(2-ethylmorpholino)ethan-1-one;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-(trifluoromethyl)-3H-imidazo[4,5-b]pyridin-3-yl)methyl)nicotinonitrile;

25 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)-1-(azetidin-1-yl)ethan-1-one;

1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)piperidine-2-carboxamide;

30 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(1,1-dioxidotetrahydrothiophen-3-yl)-N-(thiophen-2-ylmethyl)acetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(octahydroisoquinolin-2(1H)-yl)ethan-1-one;

(3R,4R)-4-fluoro-1-(5-fluoro-1-((4-methoxypyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(1,1-dioxidotetrahydrothiophen-3-yl)-N-methylacetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-cyclopropyl-N-(1,1-dioxidotetrahydrothiophen-3-yl)acetamide;

5 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(1,1-dioxidotetrahydrothiophen-3-yl)-N-ethylacetamide;

4-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)piperazin-2-one;

10 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-(pyrrolidine-1-carbonyl)piperidin-1-yl)ethan-1-one;

1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)piperidine-3-carboxamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-(cyclopropanecarbonyl)piperazin-1-yl)ethan-1-one;

15 1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)piperidine-4-carboxamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(2-cyanopropan-2-yl)-N-methylacetamide;

20 1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)-N-methylpiperidine-4-carboxamide;

N-(1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)piperidin-3-yl)acetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-(piperidine-1-carbonyl)piperidin-1-yl)ethan-1-one;

25 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-(azepane-1-carbonyl)piperidin-1-yl)ethan-1-one;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(1,1-dioxidotetrahydrothiophen-3-yl)-N-(2-methoxyethyl)acetamide;

30 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-(3-methylpiperidine-1-carbonyl)piperidin-1-yl)ethan-1-one;

1-(4-acetylpiperazin-1-yl)-2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)ethan-1-one;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(1,1-dioxidotetrahydrothiophen-3-yl)-N-((tetrahydrofuran-2-yl)methyl)acetamide;

1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)-N-isopropyl-N-methylpiperidine-4-carboxamide;

2-(2-((3R,4R)-3-amino-4-methoxypiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

5 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-7-methoxy-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-4-methoxy-1H-benzo[d]imidazol-1-yl)-1-morpholinoethan-1-one;

10 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-7-methoxy-1H-benzo[d]imidazol-1-yl)-1-morpholinoethan-1-one;

(R)-3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-cyclopropylpyrrolidin-2-one;

(S)-3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(tetrahydro-2H-pyran-4-yl)pyrrolidin-2-one;

15 (S)-3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-cyclopropylpyrrolidin-2-one;

(R)-3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(tetrahydro-2H-pyran-4-yl)pyrrolidin-2-one;

20 (3R,4R)-1-(5,6-difluoro-1-((5-methylthiazol-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4R)-1-(4,6-difluoro-1-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4R)-1-(5,6-difluoro-1-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

25 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

(3R,4R)-1-(1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-imidazo[4,5-b]pyridin-2-yl)-4-fluoropiperidin-3-amine;

30 (3R,4R)-1-(4,6-difluoro-1-((5-(methylsulfonyl)pyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4R)-1-(1-((5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)methyl)-4,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

(3R,4R)-1-(1-((5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)methyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

5 (3R,4R)-4-fluoro-1-(6-fluoro-1-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(3R,4R)-1-(5,6-difluoro-1-((5-(methylsulfonyl)pyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

10 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide;

(3R,4R)-1-(5,6-difluoro-1-((5-methylisoxazol-3-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4,6-difluoro-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide;

15 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide;

(3R,4R)-1-(5,6-difluoro-1-((5-methylloxazol-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

20 (3R,4R)-1-(5,6-difluoro-1-((4-methylthiazol-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4R)-4-fluoro-1-(6-fluoro-1-((3-(trifluoromethyl)-1,2,4-oxadiazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

25 (3R,4R)-1-(5,6-difluoro-1-((5-methyl-1,3,4-oxadiazol-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4R)-1-(5,6-difluoro-1-((5-methyl-1,2,4-oxadiazol-3-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

30 (3R,4R)-1-(1-((5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4R)-4-fluoro-1-(6-fluoro-1-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)-1H-imidazo[4,5-b]pyridin-2-yl)piperidin-3-amine;

(3R,4R)-1-(1-((4,5-dimethylloxazol-2-yl)methyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide;

(3R,4R)-1-(1-((5-ethyl-1,2,4-oxadiazol-3-yl)methyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

5 (3R,4R)-1-(1-((5-cyclopropyl-1,2,4-oxadiazol-3-yl)methyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4R)-1-(5,6-difluoro-1-((3-methylisoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

10 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

(3R,4R)-1-(1-((5-cyclopropyl-1,3,4-oxadiazol-2-yl)methyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4R)-4-fluoro-1-(5-fluoro-1-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

15 (3R,4R)-1-(3-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-3H-imidazo[4,5-b]pyridin-2-yl)-4-fluoropiperidin-3-amine;

(3R,4R)-4-fluoro-1-(5-fluoro-1-((3-(trifluoromethyl)-1,2,4-oxadiazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

20 (3R,4R)-4-fluoro-1-(6-fluoro-1-((4-methyl-2-phenylthiazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(3R,4R)-1-(1-((4,5-dimethyl-4H-1,2,4-triazol-3-yl)methyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4R)-1-(1-((5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)methyl)-5-fluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

25 (R)-4,4-difluoro-1-(6-fluoro-1-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(3R,4R)-1-(1-((2,4-dimethylthiazol-5-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

30 (3R,4R)-4-fluoro-1-(6-fluoro-3-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)-3H-imidazo[4,5-b]pyridin-2-yl)piperidin-3-amine;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,7-difluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide;

(3R,4R)-4-fluoro-1-(5-fluoro-1-((4-methyl-2-phenylthiazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,7-difluoro-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide;

5 (3R,4R)-1-(5,7-difluoro-1-((5-(methylsulfonyl)pyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4R)-1-(1-((2,4-dimethylthiazol-5-yl)methyl)-5-fluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

10 (R)-4,4-difluoro-1-(5-fluoro-1-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(3R,4R)-1-(1-((5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)methyl)-5,7-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4R)-1-(5,7-difluoro-1-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

15 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(2-methylazetidin-1-yl)ethanone;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(2,2-difluoroethyl)-N-methylacetamide;

20 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-cyclopropyl-N-methylacetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-((R)-1-cyanoethyl)-N-methylacetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-((R)-1-(pyridin-2-yl)ethyl)acetamide;

25 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-ethyl-N-methylacetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(2-fluoroethyl)-N-methylacetamide;

30 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-((1R,5S)-3-azabicyclo[3.1.0]hexan-3-yl)ethanone;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(1-(pyridin-2-yl)ethyl)acetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(2-azabicyclo[3.1.0]hexan-2-yl)ethanone;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-((S)-1-cyanoethyl)-N-methylacetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(tetrahydrofuran-3-yl)acetamide;

5 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(1-cyanopropan-2-yl)-N-methylacetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(1-(pyridin-4-yl)ethyl)acetamide;

10 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(1,1,1-trifluoropropan-2-yl)acetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(cyanomethyl)-N-methylacetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-propylacetamide;

15 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-cyclopropyl-N-(2-hydroxyethyl)acetamide;

1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)-3-fluoropyrrolidine-3-carbonitrile;

20 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)ethanone;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(hexahydropyrano[4,3-b][1,4]oxazin-4(7H)-yl)ethanone;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(2-cyanopropyl)-N-methylacetamide;

25 -(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(3,3,3-trifluoropropyl)acetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-((1R,5S)-6,6-difluoro-3-azabicyclo[3.1.0]hexan-3-yl)ethanone;

30 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-(pyrimidin-2-yl)piperazin-1-yl)ethanone;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(2-isopropylazetidin-1-yl)ethanone;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(3-(difluoromethoxy)pyrrolidin-1-yl)ethanone;

4-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)morpholine-2-carbonitrile;

2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(3-hydroxypiperidin-1-yl)ethanone;

5 1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)-4-methylpiperidine-4-carbonitrile;

2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(3,4-dihydro-1,8-naphthyridin-1(2H)-yl)ethanone;

10 2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-cyclopropyl-N-(2,2-difluoroethyl)acetamide;

2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(5H-pyrrolo[3,4-b]pyridin-6(7H)-yl)ethanone;

2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-((tetrahydrofuran-3-yl)methyl)acetamide;

15 2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(2,2-difluoroethyl)-N-methylacetamide;

2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide;

20 (R)-1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)pyrrolidine-2-carbonitrile;

2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-((1r,4R)-4-hydroxycyclohexyl)-N-methylacetamide;

2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-((S)-1-(pyridin-2-yl)ethyl)acetamide;

25 2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(octahydro-1H-pyrano[4,3-b]pyridin-1-yl)ethanone;

2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-hydroxypiperidin-1-yl)ethanone;

30 1-(3-(1H-1,2,4-triazol-1-yl)azetidin-1-yl)-2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)ethanone;

7-(2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)hexahydroimidazo[1,5-a]pyrazin-3(2H)-one;

2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(2-cyanoethyl)-N-((tetrahydrofuran-3-yl)methyl)acetamide;

4-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)-N-methylmorpholine-2-carboxamide;

2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(3-((methylsulfonyl)methyl)pyrrolidin-1-yl)ethanone;

5 2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(5,6-dihydro-[1,2,4]triazolo[1,5-a]pyrazin-7(8H)-yl)ethanone;

2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(2-(methoxymethyl)morpholino)ethanone;

10 2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(3-hydroxy-3-methylpyrrolidin-1-yl)ethanone;

2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-(methylsulfonyl)piperazin-1-yl)ethanone;

N-((1-acetylpyrrolidin-3-yl)methyl)-2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-ethylacetamide;

15 2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(1,1-dioxidotetrahydro-2H-thiopyran-4-yl)-N-methylacetamide;

2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-((1,1-dioxidotetrahydrothiophen-3-yl)methyl)-N-methylacetamide;

20 2-(1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)piperidin-4-yl)-2-methylpropanenitrile;

1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)-N-methylpiperidine-3-carboxamide;

2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(2-hydroxyethyl)-N-(pyridin-3-ylmethyl)acetamide;

25 2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(2-cyanoethyl)-N-(tetrahydro-2H-pyran-4-yl)acetamide;

1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)-N,N-dimethylpiperidine-3-carboxamide;

30 1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)-4-(methoxymethyl)piperidine-4-carbonitrile;

7-(2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)tetrahydro-1H-oxazolo[3,4-a]pyrazin-3(5H)-one;

2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-(thiazol-2-yl)acetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-(2,2,2-trifluoroethyl)acetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-cyclopropyl-N-(2,2,2-trifluoroethyl)acetamide;

5 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-(2-methoxyethyl)-N-methylacetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-((S)-tetrahydrofuran-3-yl)acetamide;

10 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-((R)-tetrahydrofuran-3-yl)acetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-((S)-1-(pyridin-2-yl)ethyl)acetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-((S)-tetrahydrofuran-3-yl)-N-(2,2,2-trifluoroethyl)acetamide;

15 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-cyclobutylacetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-((S)-1-cyanopropan-2-yl)acetamide;

20 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-((R)-1-cyanopropan-2-yl)acetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-ethyl-N-(2-methoxyethyl)acetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-((R)-tetrahydrofuran-3-yl)-N-(2,2,2-trifluoroethyl)acetamide;

25 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-(3,3,3-trifluoropropyl)acetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-((R)-1-(pyridin-2-yl)ethyl)acetamide;

30 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-((S)-tetrahydrofuran-3-yl)acetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-((R)-tetrahydrofuran-3-yl)acetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-1-(2-methylazetidin-1-yl)ethan-1-one;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-1-((S)-3-methylmorpholino)ethan-1-one;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-1-((R)-2-methylpyrrolidin-1-yl)ethan-1-one;

5 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-1-((R)-3-(methoxymethyl)morpholino)ethan-1-one;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-1-((R)-3-methylmorpholino)ethan-1-one;

10 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-1-((S)-2-methylpyrrolidin-1-yl)ethan-1-one;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-1-(3,5-dimethylmorpholino)ethan-1-one;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-1-(3-ethylmorpholino)ethan-1-one;

15 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-1-((S)-3-cyclopropylmorpholino)ethan-1-one;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-1-((R)-3-(hydroxymethyl)morpholino)ethan-1-one; and

20 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-1-(3,3-dimethylmorpholino)ethan-1-one.

In a thirty ninth embodiment, the invention provides compounds of the first or second embodiment in which the compound is recited in the below Table B:

25 TABLE B

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-4-carbonitrile;

30 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-(trifluoromethoxy)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

35 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazole-4-carbonitrile;

(3R,4R)-1-(4,6-difluoro-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4R)-1-(4,6-difluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

5 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-4-carbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

10 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

15 (R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)nicotinonitrile;

20 6-((2-((3R)-3-amino-4,4-difluoro-1-piperidinyl)-6-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5-(difluoromethoxy)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

25 6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-4-methoxy-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R)-3-amino-4,4-difluoro-1-piperidinyl)-6-methoxy-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

30 2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazole-4-carbonitrile;

(R)-2-(3-amino-4,4-difluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazole-4-carbonitrile;

35 4-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-4,6-difluoro-1H-benzimidazol-1-yl)methyl)benzonitrile;

4-((2-((3S,4S)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;
 4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;
 (R)-4-((2-(3-aminopiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;
 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-
 5 benzo[d]imidazole-6-carbonitrile;
 (3R,4R)-4-fluoro-1-(1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-
 amine;
 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-fluoropyrimidin-2-yl)methyl)-1H-
 benzo[d]imidazole-6-carbonitrile;
 10 2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-
 benzo[d]imidazole-6-carbonitrile;
 (3R,4R)-3-amino-1-(1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-
 yl)piperidin-4-ol;
 (R)-1-(1-((5-chloropyridin-2-yl)methyl)-4,6-difluoro-1H-benzo[d]imidazol-2-yl)-4,4-
 15 difluoropiperidin-3-amine hydrochloride;
 (3R,4R)-1-(1-((5-chloro-2-pyrimidinyl)methyl)-4,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-
 piperidinamine;
 2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)-1-(1-
 piperidinyl)ethanone;
 20 2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-6-chloro-1H-benzimidazol-1-yl)-1-(1-
 azetidiny)ethanone;
 (3R,4R)-1-(1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)-4-
 fluoropiperidin-3-amine;
 (3R,4R)-1-(1-((5-chloropyrimidin-2-yl)methyl)-5-fluoro-1H-benzo[d]imidazol-2-yl)-4-
 25 fluoropiperidin-3-amine;
 (3R,4R)-1-(5,6-difluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-
 fluoropiperidin-3-amine;
 (3R,4S)-4-fluoro-1-(1-((5-fluoropyrimidin-2-yl)methyl)-6-(trifluoromethyl)-1H-
 benzo[d]imidazol-2-yl)piperidin-3-amine; and
 30 4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-
 yl)methyl)benzonitrile hydrochloride.

In a fortieth embodiment, the invention provides compounds of the first or second embodiment in which the compound is recited in the below Table C:

35 TABLE C

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-(trifluoromethoxy)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

5 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazole-4-carbonitrile;

(3R,4R)-1-(4,6-difluoro-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4R)-1-(4,6-difluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

10 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

15 (R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

20 6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-4-methoxy-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R)-3-amino-4,4-difluoro-1-piperidinyl)-6-methoxy-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazole-4-carbonitrile;

25 (R)-2-(3-amino-4,4-difluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazole-4-carbonitrile;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

30 (3R,4R)-4-fluoro-1-(1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

(R)-1-(1-((5-chloropyridin-2-yl)methyl)-4,6-difluoro-1H-benzo[d]imidazol-2-yl)-4,4-difluoropiperidin-3-amine hydrochloride;

35

(3R,4R)-1-(1-((5-chloro-2-pyrimidinyl)methyl)-4,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine; and

(3R,4R)-1-(1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine.

5 In a forty first embodiment, the invention provides compounds of the first or second embodiment in which the compound is recited in the below Table D:

TABLE D

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

10 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazole-4-carbonitrile;

(3R,4R)-1-(4,6-difluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

15 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;
(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

20 6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-4-methoxy-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

2-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

(3R,4R)-4-fluoro-1-(1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine; and

25 (3R,4R)-1-(1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine.

In a further embodiment, each of the compounds disclosed herein are provided in the form of a pharmaceutically acceptable salt.

30 In a forty second embodiment, the invention provides 6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile. In certain aspects of the forty second embodiment, the invention provides a pharmaceutically acceptable salt of 6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile.

35 In a forty third embodiment, the invention provides 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazole-4-carbonitrile. In certain aspects of

the forty third embodiment, the invention provides a pharmaceutically acceptable salt of 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazole-4-carbonitrile.

In a forty fourth embodiment, the invention provides (3R,4R)-1-(4,6-difluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine. In certain aspects of the forty fourth embodiment, the invention provides a pharmaceutically acceptable salt of (3R,4R)-1-(4,6-difluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine.

In a forty fifth embodiment, the invention provides 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile. In certain aspects of the forty fifth embodiment, the invention provides a pharmaceutically acceptable salt of 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile.

In a forty sixth embodiment, the invention provides (R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile. In certain aspects of the forty sixth embodiment, the invention provides a pharmaceutically acceptable salt of (R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile. The hydrochloride salt is a particularly preferred aspect of the forty sixth embodiment, e.g., (R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride.

In a forty seventh embodiment, the invention provides (R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile. In certain aspects of the forty seventh embodiment, the invention provides a pharmaceutically acceptable salt of (R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile.

In a forty eighth embodiment, the invention provides 6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-4-methoxy-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile. In certain aspects of the forty eighth embodiment, the invention provides a pharmaceutically acceptable salt of 6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-4-methoxy-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile.

In a forty ninth embodiment, the invention provides 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile. In certain aspects of the forty ninth embodiment, the invention provides a pharmaceutically acceptable salt of (2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile.

In a fiftieth embodiment, the invention provides (3R,4R)-4-fluoro-1-(1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine. In certain aspects of the fiftieth embodiment, the invention provides a pharmaceutically acceptable salt of (3R,4R)-4-fluoro-1-(1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine.

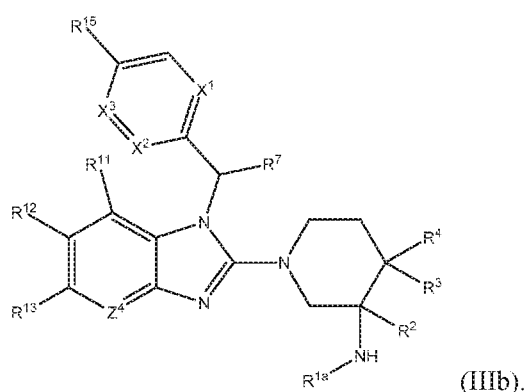
In a fifty first embodiment, the invention provides (3R,4R)-1-(1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine. In certain aspects of the fifty

first embodiment, the invention provides a pharmaceutically acceptable salt of (3R,4R)-1-(1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine.

In a further aspect of each of the forty second to fifty first embodiment, each of the the compounds and pharmaceutically acceptable salts provided therein may be used in the preparation of a medicament for use in treating a disease mediated by TRPC6 activity. In certain aspects, the compounds provided in the forty second to fifty first embodiment, or pharmaceutically acceptable salt thereof, may be used in the manufacture of a medicament for the treatment of a disease or disorder selected from nephrotic syndrome, minimal change disease, focal segmental glomerulosclerosis, collapsing glomerulopathy, membranous nephropathy, membranoproliferative glomerulonephritis, IGA nephropathy, acute renal failure, chronic renal failure, diabetic nephropathy, sepsis, pulmonary hypertension, acute lung disorder, acute respiratory distress syndrome (ARDS), heart failure, stroke, malignant tumor or muscular dystrophy. In still other aspects, the compounds of the forty second to fifty first embodiment, or pharmaceutically acceptable salt thereof may be used in the preparation of a medicament for the treatment of nephrotic syndrome, membranous nephropathy and acute renal failure.

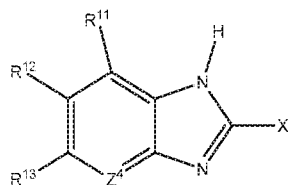
In a fifty second embodiment, a method of treating disease or disorder in a patient in need of therapy is provided, the method comprises the step of administering a pharmaceutically acceptable composition comprising a compound of any one of the forty second to fifty first embodiments, or a pharmaceutically acceptable salt thereof, wherein the disease or disorder is selected from nephrotic syndrome, minimal change disease, focal segmental glomerulosclerosis, collapsing glomerulopathy, membranous nephropathy, membranoproliferative glomerulonephritis, IGA nephropathy, acute renal failure, chronic renal failure, diabetic nephropathy, sepsis, pulmonary hypertension, acute lung disorder, acute respiratory distress syndrome (ARDS), heart failure, stroke, malignant tumor or muscular dystrophy. In certain aspects of the fifty first embodiment the disease or disorder is selected from nephrotic syndrome, membranous nephropathy and acute renal failure.

In a further embodiment, the invention provides methods of making a compound of formula IIIb or a subformulae thereof.

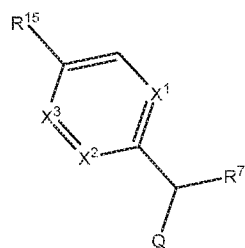


The method comprising the synthetic steps of

(a) Alkylating a halogenated benzimidazole having the formula:

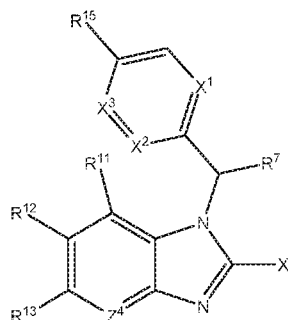


with an electrophilic moiety having the formula:



under basic conditions to provide an alkylated halogenated benzimidazole

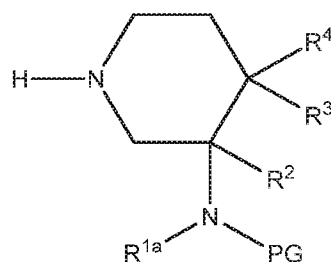
5 compound having the formula:



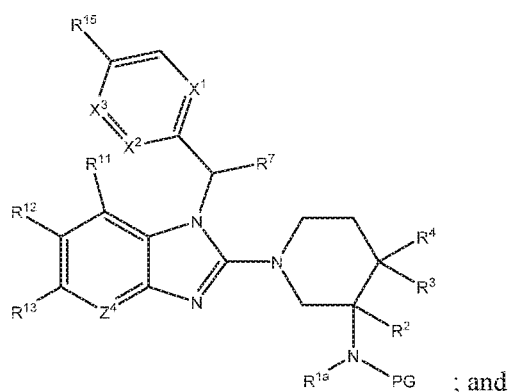
wherein X is chlorine, bromine or iodine and Q is chlorine, bromine, iodine, C₁-C₆alkylsulfonate or optionally substituted phenylsulfonate;

(b) Coupling the alkylated halogenated benzimidazole generated in step (a) with a protected

10 piperidine having the formula:



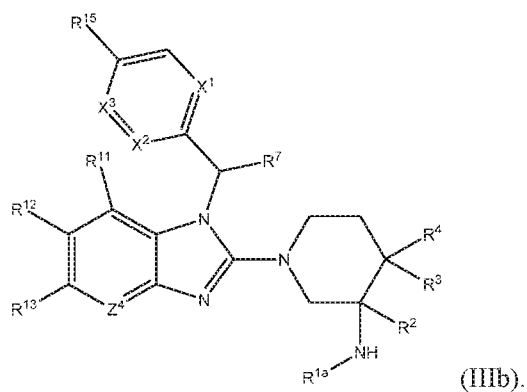
wherein PG is an amide protecting group stable to nucleophilic aromatic substitution (such as an alkoxycarbonyl protecting group) under conditions conducive to nucleophilic aromatic substitution to generate an alkylated 2-(piperidin-1-yl)benzimidazole compound having the formula:



(c) removing PG from the alkylated 2-(piperidin-1-yl)benzimidazole compound formed in step (b) to generate the compound of Formula (IIIb), wherein variables X^1 , X^2 , X^3 , Z^4 , R^{1a} , R^2 , R^3 , R^4 , R^7 , R^{11} , R^{12} , R^{13} and R^{15} have the definitions provided in the thirtieth embodiment

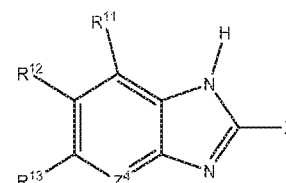
5 In preferred aspects of the synthetic method, the basic conditions of step (a) comprise contacting the halogenated benzimidazole with the electrophilic moiety in the presence of a carbonate base, such as potassium carbonate or more preferably cesium carbonate.

10 In a further embodiment, the invention provides methods of making compounds of formula IIIb or a subformulae thereof.

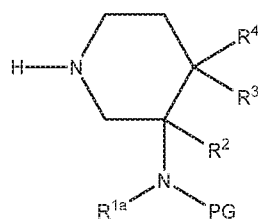


The method comprising the synthetic steps of

(a) Coupling a halogenated benzimidazole having the formula:

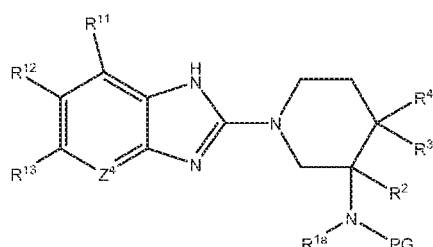


with a protected piperidine having the formula:



under conditions conducive to

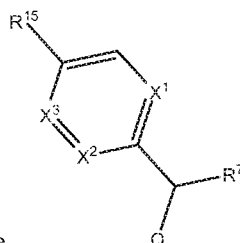
nucleophilic aromatic substitution to generate a 2-(piperidin-1-yl)benzimidazole compound having the



formula:

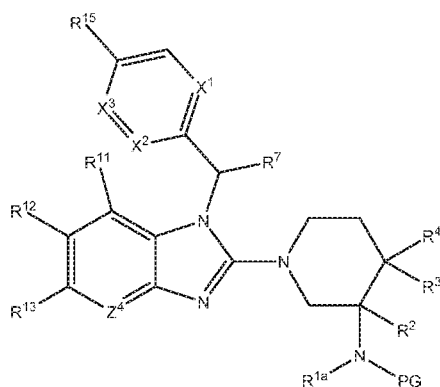
5 wherein X is chlorine, bromine or iodine and PG is an amide protecting group stable to nucleophilic aromatic substitution such as an alkoxycarbonyl protecting group;

(b) Alkylating the 2-(piperidin-1-yl)benzimidazole compound generated in step (a) with an



electrophilic moiety having the structure

under basic conditions to provide an alkylated 2-(piperidin-1-yl)benzimidazole compound having the

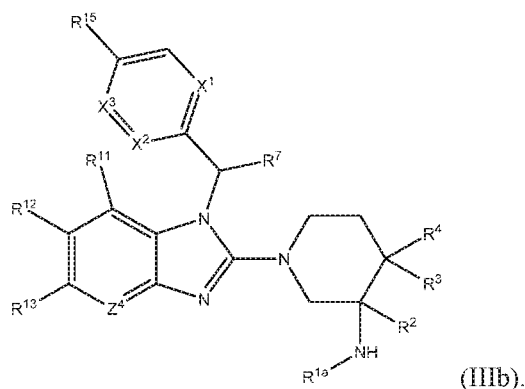


10 formula :

wherein Q is chlorine, bromine, iodine, C₁-C₆alkylsulfonate or optionally substituted phenylsulfonate;

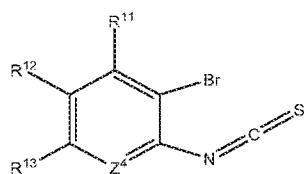
(c) removing PG from the alkylated 2-(piperidin-1-yl)benzimidazole compound generated in step (b) to generate the compound of Formula (IIIb), wherein variables X^1 , X^2 , X^3 , Z^4 , R^{1a} , R^2 , R^3 , R^4 , R^7 , R^{11} , R^{12} , R^{13} and R^{15} have the definitions provided in the thirtieth embodiment.

In a further embodiment, the invention provides methods of making compounds of formula IIIb or a subformulae thereof.

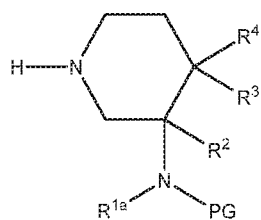


The method comprising the synthetic steps of

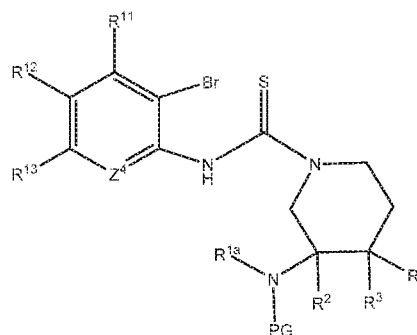
(a) Coupling a brominated isothiocyanate compound having the formula



with a protected piperidine compound having the formula:



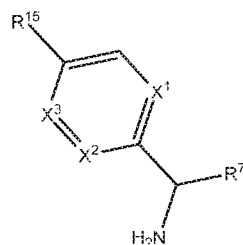
under conditions conducive to thiourea formation to generate a N,N' -



disubstituted thiourea compound having the formula

wherein PG is an amide protecting group such as an alkoxycarbonyl protecting group;

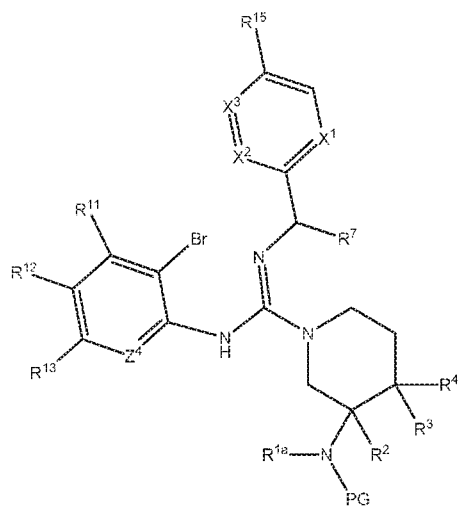
(b) Condensing the N,N'-disubstituted thiourea compound generated in step (a) with



an amine compound having the formula

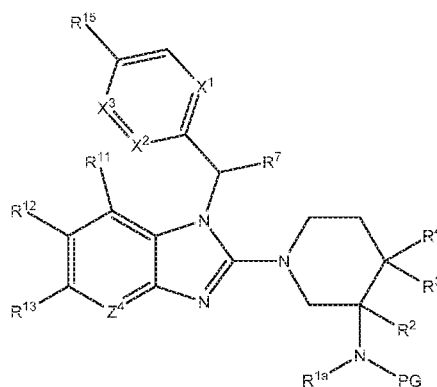
under conditions suitable to

guanidine formation to provide a N,N',N''-trisubstituted guanidine compound having the



formula:

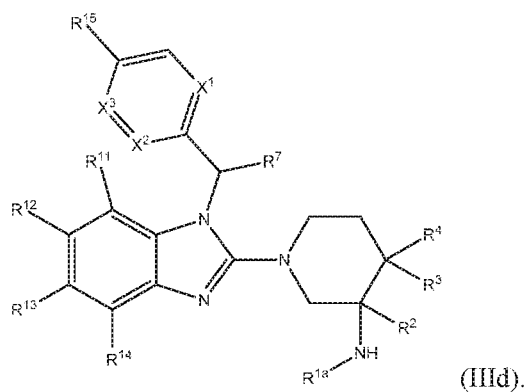
5 (c) Intramolecular cyclization of the N,N',N''-trisubstituted guanidine compound generated in step (b) in presence of a transition metal catalyst to form an alkylated 2-(piperidin-1-yl)benzimidazole



compound having the formula:

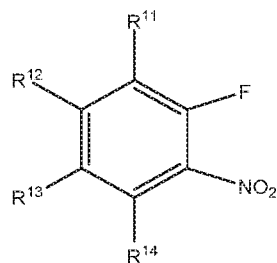
(d) removing PG from the alkylated 2-(piperidin-1-yl)benzimidazole compound generated in step (c) to provide a compound of Formula (IIIb), wherein variables X¹, X², X³, Z⁴, R^{1a}, R², R³, R⁴, R⁷,
10 R¹¹, R¹², R¹³ and R¹⁵ have the definitions provided in the thirtieth embodiment.

In a further embodiment, the invention provides methods of making compounds of formula IIIId or a subformulae thereof.

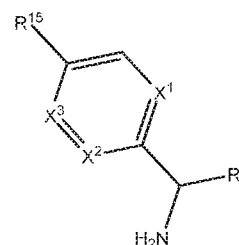


The method comprising the synthetic steps of

- a) coupling an optionally substituted ortho-fluoro nitrobenzene compound having the formula:

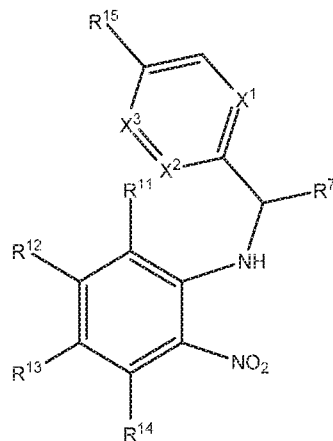


with a primary amine having the formula:



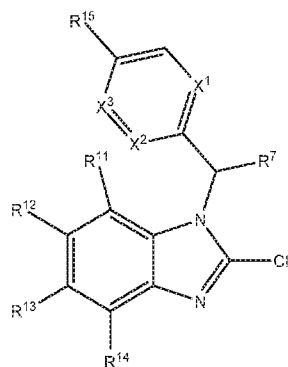
5

under conditions suitable for nucleophilic aromatic substitution to provide a secondary amine



amine having the formula:

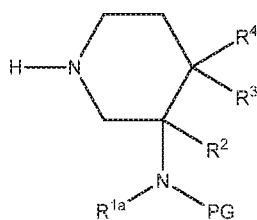
- b) generating an alkylated-2-chlorobenzimidazole compound having the formula:



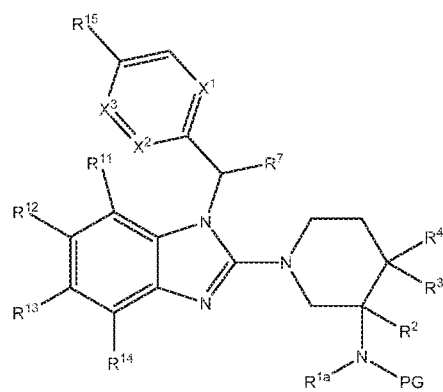
by reduction of the nitro substituent in the secondary amine

compounds generated in step (a) to form *in situ* a dianiline compound, cyclizing said dianiline with a carbonyl source and chlorination (with a chlorine source such as e.g., P(O)Cl₃) to generate the alkylated-2-chlorobenzimidazole compound;

- c) coupling the alkylated-2-chlorobenzimidazole compound generated in step (b) with a protected



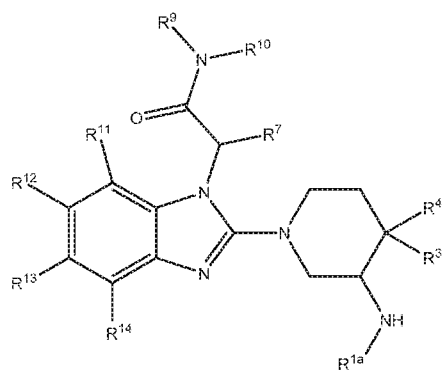
piperidine having the formula: under conditions suitable for nucleophilic aromatic substitution to generate an alkylated 2-(piperidin-1-yl)benzimidazole compound having



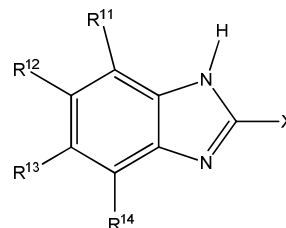
the formula:

- d) removing the PG from the alkylated 2-(piperidin-1-yl)benzimidazole compound generated in step (c), to generate the compound of Formula (VII), wherein variables X¹, X², X³, R^{1a}, R², R³, R⁴, R⁷, R¹¹, R¹², R¹³, R¹⁴ and R¹⁵ have the definitions provided in the thirtieth embodiment.

In a further embodiment, the invention provides methods of making compounds of formula VII or a subformulae thereof.

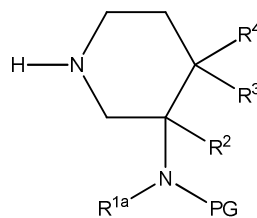


(VII)



(a) Coupling a halogenated benzimidazole having the formula:

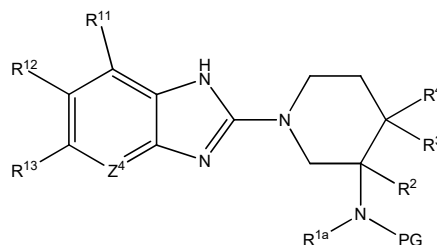
with a



protected piperidine having the formula

under conditions conducive

to nucleophilic aromatic substitution to generate a 2-(piperidin-1-yl)benzimidazole compound

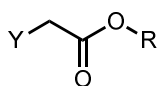


having the formula

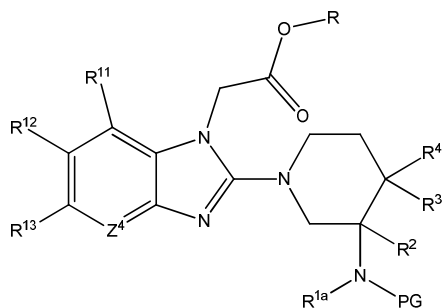
wherein X is chlorine, bromine

or iodine and PG is an amide protecting group stable to nucleophilic aromatic substitution such as an alkoxycarbonyl protecting group;

(b) Alkylating the 2-(piperidin-1-yl)benzimidazole compound generated in step (a) with a



halo ester, , wherein Y is chlorine, bromine or iodine and R is C₁-C₆alkyl, to generate an substituted 1-acetyl-2-(piperidin-1-yl)benzimidazole compound having the formula:



(c) Saponification of the substituted 1-acetyl-2-(piperidin-1-yl)benzimidazole compound generated in step (b) to provide a free acid followed by amination with an amine, HNR⁹R¹⁰, under conditions conducive to amide bond formation to provide a 1-[(2-piperidin-1-yl)benzimidazole]acetamide compound;

(d) removing PG from the 1-[(2-piperidin-1-yl)benzimidazole]]acetamide compound generated in step (c) to generate the compound of Formula (VII), wherein variables X^1 , X^2 , X^3 , Z^4 , R^{1a} , R^2 , R^3 , R^4 , R^7 , R^{11} , R^{12} , R^{13} and R^{15} have the definitions provided in the thirty fourth embodiment.

5 In another embodiment, pharmaceutical compositions are provided which comprise one or more pharmaceutically acceptable carriers and a therapeutically effective amount of a compound of any one of formulae I or a subformulae thereof. In some aspects, the composition is formulated in a form selected from the group consisting of an injectable fluid, an aerosol, a tablet, a pill, a capsule, a syrup, a cream, a gel and a transdermal patch.

10 In another embodiment, combinations, in particular pharmaceutical combinations, are provided which comprise a therapeutically effective amount of the compound any one of formulae I or a subformulae thereof.

In another embodiment, methods of modulating TRPC protein activity in a subject are provided which methods comprise administering to the subject a therapeutically effective amount of Formula I or a subformulae thereof. In preferred aspects of the embodiment, methods of inhibiting TRPC6 activity in a subject are provided, which methods comprise administering to the subject a therapeutically effective amount of a compound of Formula I or subformulae thereof. In certain aspects of the embodiment, method of inhibiting TRPC6 activity in a subject are provided, which methods comprise administering to the subject a therapeutically effective amount of a compound of Formula I or subformulae thereof.

20 In yet other embodiments, methods of treating a disorder or a disease in a subject mediated by TRPC protein activity are provided, in particular methods of treating a disease or disorder mediated by TRPC6 protein activity are provided. The methods comprise administering to the subject a therapeutically effective amount of the compound of Formula I or a subformulae thereof.

25 In another embodiment, methods of treating or preventing a disease or disorder are provided where the disease or disorder is selected from nephrotic syndrome, minimal change disease, focal segmental glomerulosclerosis, collapsing glomerulopathy, membranous nephropathy, membranoproliferative glomerulonephritis, IGA nephropathy, acute renal failure, chronic renal failure, diabetic nephropathy, sepsis, pulmonary hypertension, acute lung disorder, acute respiratory distress syndrome (ARDS), heart failure, stroke, malignant tumor or muscular dystrophy which method comprises the step of administering to a subject in need of therapy a therapeutically effective amount of a compound or salt of Formula I or a subformulae thereof. In certain aspects of this embodiment, the method comprises treating a disease or disorder selected from nephrotic syndrome, minimal change disease, focal segmental glomerulosclerosis, collapsing glomerulopathy, membranous nephropathy, membranoproliferative glomerulonephritis, IGA nephropathy, acute renal failure, chronic renal failure, diabetic nephropathy, sepsis, pulmonary hypertension, acute lung disorder, acute respiratory distress syndrome (ARDS), heart failure, stroke,

malignant tumor or muscular dystrophy. In certain instances, the treatment methods and/or the prevention methods are suitable for the treatment and or prevention nephrotic syndrome, membranous nephropathy, and acute renal failure.

In another aspect, the invention provides for the use of compounds of Formula I or a subformulae thereof for use in the preparation of a medicament or for use in the manufacture of a medicament for the treatment of a disorder or disease in a subject mediated by TRPC protein activity. In certain other aspects, the invention provides for the use of a compound according to formula I or a subformulae thereof in the treatment of nephrotic syndrome, minimal change disease, focal segmental glomerulosclerosis, collapsing glomerulopathy, membranous nephropathy, membranoproliferative glomerulonephritis, IGA nephropathy, acute renal failure, chronic renal failure, diabetic nephropathy, sepsis, pulmonary hypertension, acute lung disorder, acute respiratory distress syndrome (ARDS), heart failure, stroke, malignant tumor or muscular dystrophy. In certain instances, the invention provides for the use of compounds of Formula I or a subformulae thereof for use in the preparation of a medicament or for use in the manufacture of a medicament or the treatment of a disease or disorder in a subject selected from nephrotic syndrome, membranous nephropathy, and acute renal failure.

For purposes of interpreting this specification, the following definitions will apply and whenever appropriate, terms used in the singular will also include the plural and vice versa.

As used herein, the term "alkyl" refers to a fully saturated branched or unbranched hydrocarbon moiety having up to 20 carbon atoms. Unless otherwise provided, alkyl refers to hydrocarbon moieties having 1 to 20 carbon atoms, 1 to 16 carbon atoms, 1 to 10 carbon atoms, 1 to 7 carbon atoms, or 1 to 4 carbon atoms. Representative examples of alkyl include, but are not limited to, methyl, ethyl, n-propyl, iso-propyl, n-butyl, sec-butyl, iso-butyl, tert-butyl, n-pentyl, isopentyl, neopentyl, n-hexyl, 3-methylhexyl, 2,2-dimethylpentyl, 2,3-dimethylpentyl, n-heptyl, n-octyl, n-nonyl, n-decyl and the like.

As used herein, the term "alkylene" refers to divalent alkyl group as defined herein above having 1 to 20 carbon atoms. Unless otherwise provided, alkylene refers to moieties having 1 to 20 carbon atoms, 1 to 16 carbon atoms, 1 to 10 carbon atoms, 1 to 7 carbon atoms, or 1 to 4 carbon atoms. Representative examples of alkylene include, but are not limited to, methylene, ethylene, n-propylene, iso-propylene, n-butylene, sec-butylene, iso-butylene, tert-butylene, n-pentylene, isopentylene, neopentylene, n-hexylene, 3-methylhexylene, 2,2-dimethylpentylene, 2,3-dimethylpentylene, n-heptylene, n-octylene, n-nonylene, n-decylene and the like.

As used herein, the term "haloalkyl" refers to an alkyl as defined herein, which is substituted with one or more halo groups as defined herein. The haloalkyl can be monohaloalkyl, dihaloalkyl or polyhaloalkyl including perhaloalkyl. A monohaloalkyl can have one iodo, bromo, chloro or fluoro within the alkyl group. Dihaloalkyl and polyhaloalkyl groups can have two or more of the same halo atoms or a

combination of different halo groups within the alkyl. Typically the polyhaloalkyl contains up to 12, or 10, or 8, or 6, or 4, or 3, or 2 halo groups. Non-limiting examples of haloalkyl include fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, pentafluoroethyl, heptafluoropropyl, difluorochloromethyl, dichlorofluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl and dichloropropyl. A perhaloalkyl refers to an alkyl having all hydrogen atoms replaced with halo atoms.

As used herein, the term "hydroxy alkyl" refers to an alkyl as defined herein which is substituted with one or more hydroxy groups. The term "hydroxy cycloalkyl-alkyl" refers to an alkyl group that is substituted with a cycloalkyl group, as defined herein, and further substituted with a hydroxy group. The hydroxy group can be on the alkyl group, the cycloalkyl group, or on each of the alkyl and cycloalkyl groups.

The term "aryl" refers to an aromatic hydrocarbon group having 6-20 carbon atoms in the ring portion. Typically, aryl is monocyclic, bicyclic or tricyclic aryl having 6-20 carbon atoms. Furthermore, the term "aryl" as used herein, refers to an aromatic substituent which can be a single aromatic ring, or multiple aromatic rings that are fused together. Non-limiting examples include phenyl, naphthyl or tetrahydronaphthyl, each of which may optionally be substituted with 1-4 substituents, such as alkyl, trifluoromethyl, cycloalkyl, halogen, hydroxy, alkoxy, acyl, alkyl-C(O)-O-, aryl-O-, heteroaryl-O-, amino, thiol, alkyl-S-, aryl-S-, nitro, cyano, carboxy, alkyl-O-C(O)-, carbamoyl, alkyl-S(O)-, sulfonyl, sulfonamido, phenyl, and heterocyclyl.

As used herein, the term "heterocycle," "heterocyclyl," "heterocycloalkyl" or "heterocyclo" refers to a saturated or unsaturated non-aromatic ring or ring system, e.g., which is a 4-, 5-, 6-, or 7-membered monocyclic, 7-, 8-, 9-, 10-, 11-, or 12-membered bicyclic or 10-, 11-, 12-, 13-, 14- or 15-membered tricyclic ring system and contains at least one heteroatom selected from O, S and N, where the N and S can also optionally be oxidized to various oxidation states. The heterocyclic group can be attached at a heteroatom or a carbon atom. The heterocyclyl can include fused or bridged rings as well as spirocyclic rings. Examples of heterocycles include tetrahydrofuran, dihydrofuran, 1, 4-dioxane, morpholine, 1,4-dithiane, piperazine, piperidine, 1,3-dioxolane, imidazolidine, imidazoline, pyrroline, pyrrolidine, tetrahydropyran, dihydropyran, oxathiolane, dithiolane, 1,3-dioxane, 1,3-dithiane, oxathiane, thiomorpholine, azetidine, thiazolidine, morpholine, and the like.

As used herein, the term "azacycle" refers to a heterocycle which comprises at least one ring nitrogen atoms and which may optionally comprise 0, 1 or 2 additional ring heteroatoms selected from N, O or S.

As used herein, the term "cycloalkyl" refers to saturated or partially unsaturated monocyclic, bicyclic or tricyclic hydrocarbon groups of 3-12 carbon atoms. For the avoidance of doubt, cycloalkyl is

not intended to include aromatic groups such as naphthylene or phenyl. Unless otherwise provided, cycloalkyl refers to cyclic hydrocarbon groups having between 3 and 9 ring carbon atoms or between 3 and 7 ring carbon atoms, each of which can be optionally substituted with one, or two, or three, or more substituents independently selected from the group consisting of alkyl, halo, oxo, hydroxy, alkoxy, alkyl-C(O)-, acylamino, carbamoyl, alkyl-NH-, (alkyl)₂N-, thiol, alkyl-S-, nitro, cyano, carboxy, alkyl-O-C(O)-, sulfonyl, sulfonamido, sulfamoyl, and heterocyclyl. Exemplary monocyclic hydrocarbon groups include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclopentenyl, cyclohexyl and cyclohexenyl and the like. Exemplary bicyclic hydrocarbon groups include bornyl, indyl, hexahydroindyl, tetrahydronaphthyl, decahydronaphthyl, bicyclo[2.1.1]hexyl, bicyclo[2.2.1]heptyl, bicyclo[2.2.1]heptenyl, 6,6-dimethylbicyclo[3.1.1]heptyl, 2,6,6-trimethylbicyclo[3.1.1]heptyl, bicyclo[2.2.2]octyl and the like. Exemplary tricyclic hydrocarbon groups include adamantyl and the like. The term "hydroxy cycloalkyl" refers specifically to a cycloalkyl group substituted with one or more hydroxy groups.

As used herein, the term "alkoxy" refers to alkyl-O-, wherein alkyl is defined herein above. Representative examples of alkoxy include, but are not limited to, methoxy, ethoxy, propoxy, 2-propoxy, butoxy, tert-butoxy, pentyloxy, hexyloxy, cyclopropyloxy-, cyclohexyloxy- and the like. Typically, alkoxy groups have about 1-7, more preferably about 1-4 carbons.

As used herein, the term "cycloalkoxy" refers to cycloalkyl-O- and cycloalkyl-alkyl-O, wherein cycloalkyl and alkyl are defined herein above. Representative examples of cycloalkoxy include, but are not limited to, cyclopropyloxy, cyclobutyloxy, cyclopentyloxy, 1-methylcyclopropyloxy, cyclopropylmethoxy, 1-methylcyclobutyloxy and the like. Typically, cycloalkoxy groups have about 3-7, more preferably about 3-6 carbon atoms.

Divalent substituents are represented with a "diyl" suffix. Thus a divalent alkyl linker is referred to as an alkandiyl group and a divalent cycloalkane group is referred to as a cycloalkandiyl (e.g., cyclopropandiyl).

As used herein, the term "heteroaryl" refers to a 5-14 membered monocyclic- or bicyclic- or tricyclic-aromatic ring system, having 1 to 8 heteroatoms selected from N, O and S. In certain preferred aspects, the heteroaryl is a 5-10 membered ring system (e.g., 5-7 membered monocycle or an 8-10 membered bicycle) or a 5-7 membered ring system. Exemplary monocyclic heteroaryl groups include 2- or 3-thienyl, 2- or 3-furyl, 2- or 3-pyrrolyl, 2-, 4-, or 5-imidazolyl, 3-, 4-, or 5-pyrazolyl, 2-, 4-, or 5-thiazolyl, 3-, 4-, or 5-isothiazolyl, 2-, 4-, or 5-oxazolyl, 3-, 4-, or 5-isoxazolyl, 3- or 5-1,2,4-triazolyl, 4- or 5-1,2,3-triazolyl, tetrazolyl, 2-, 3-, or 4-pyridyl, 3- or 4-pyridazinyl, 3-, 4-, or 5-pyrazinyl, 2-pyrazinyl, and 2-, 4-, and 5-pyrimidinyl. Exemplary bicyclic heteroaryl groups include 1-, 3-, 4-, 5-, 6-, 7-, or 8-isoquinolinyl, 2-, 3-, 4-, 5-, 6-, 7-, or 8-quinolinyl, 1-, 3-, 4-, 5-, 6-, 7-, or 8-isoquinolinyl, 1-, 2-, 4-, 5-, 6-, 7-, or 8-benzimidazolyl and 1-, 2-, 3-, 4-, 5-, 6-, 7-, or 8-indolyl.

The term "heteroaryl" also refers to a group in which a heteroaromatic ring is fused to one or more aryl, cycloaliphatic, or heterocyclyl rings, where the radical or point of attachment is on the heteroaromatic ring.

The terms "bicycle" and "bicycyl" refers to a ring sytem having two fused rings each of which
5 rings may be carbocyclic or heterocyclic and each of which rings may be saturated, unsaturated or aromatic.

As used herein, the term "halogen" or "halo" refers to fluoro, chloro, bromo, and iodo.

As used herein, the term "optionally substituted" unless otherwise specified refers to a group that is unsubstituted or is substituted with one or more, typically 1, 2, 3 or 4, suitable non-hydrogen
10 substituents. If the identity of the "optional substituent" is not clearly defined in context of the optionally substituted group, then each optional substituent is independently selected from the group consisting of: alkyl, hydroxy, halogen, oxo, amino, alkylamino, dialkylamino, alkoxy, cycloalkyl, CO₂H, heterocycloalkyloxy (which denotes a heterocyclic group bonded through an oxygen bridge), -CO₂alkyl, mercapto, nitro, cyano, sulfamoyl, sulfonamide, aryl, -OC(O)alkyl, -OC(O)aryl, aryl-S-, aryloxy; alkylthio,
15 formyl (i.e., HC(O)-), -C(O)NH₂, aralkyl (alkyl substituted with aryl), aryl and aryl substituted with alkyl, cycloalkyl, alkoxy, hydroxy, amino, alkyl-C(O)-NH-, alkylamino, dialkylamino or halogen. It is understood that where a group is indicated to be optionally substituted, the disclosure includes embodiments in which the group is unsubstituted as well as embodiments in which the group is substituted.

As used herein, the term "isomers" refers to different compounds that have the same molecular
20 formula but differ in arrangement and configuration of the atoms. Also as used herein, the term "an optical isomer" or "a stereoisomer" refers to any of the various stereo isomeric configurations which may exist for a given compound of the present invention and includes geometric isomers. It is understood that a substituent may be attached at a chiral center of a carbon atom. Therefore, the invention includes
25 enantiomers, diastereomers or racemates of the compound. "Enantiomers" are a pair of stereoisomers that are non-superimposable mirror images of each other. A 1:1 mixture of a pair of enantiomers is a "racemic" mixture. The term is used to designate a racemic mixture where appropriate. The use of "rel" indicates that the diastereomeric orientation is known but the absolute stereochemistry is not. In cases where the absolute stereochemistry has not been determined the optical rotation and/or chiral chromatography conditions will
30 indicate which isomer is present.

"Diastereoisomers" are stereoisomers that have at least two asymmetric atoms, but which are not mirror-images of each other. The absolute stereochemistry is specified according to the Cahn-Ingold-Prelog R-S system. When a compound is a pure enantiomer the stereochemistry at each chiral carbon may be specified by either R or S. Resolved compounds whose absolute configuration is unknown can be

designated (+) or (-) depending on the direction (dextro- or levorotatory) which they rotate plane polarized light at the wavelength of the sodium D line or retention time on chiral chromatography separation. Certain of the compounds described herein contain one or more asymmetric centers or axes and may thus give rise to enantiomers, diastereomers, and other stereoisomeric forms that may be defined, in terms of absolute stereochemistry, as (R)- or (S)-, or with the (+) or (-) sign. The present invention is meant to include all such possible isomers, including racemic mixtures, optically pure forms and intermediate mixtures. Optically active (R)- and (S)-isomers may be prepared using chiral synthons or chiral reagents, or resolved using conventional techniques. If the compound contains a double bond, the substituent may be E or Z configuration. If the compound contains a disubstituted cycloalkyl, the cycloalkyl substituent may have a cis- or trans-configuration.

It is understood that for any compound provided herein, including any compound of Formula (I), or any embodiment thereof, or any compound of Table A, B, or C, or a salt of any of the foregoing, the compound may exist in any stereochemical form, such as a single enantiomer, diastereomer, or tautomer or a mixture of one or more enantiomers, diastereomers, and tautomers in any ratio.

As used herein, the terms "salt" or "salts" refers to an acid addition or base addition salt of a compound of the invention. "Salts" include in particular "pharmaceutical acceptable salts". The term "pharmaceutically acceptable salts" refers to salts that retain the biological effectiveness and properties of the compounds of this invention and, which typically are not biologically or otherwise undesirable. In many cases, the compounds of the present invention are capable of forming acid and/or base salts by virtue of the presence of amino and/or carboxyl groups or groups similar thereto.

Pharmaceutically acceptable acid addition salts can be formed with inorganic acids and organic acids.

Inorganic acids from which salts can be derived include, for example, hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid, and the like.

Organic acids from which salts can be derived include, for example, acetic acid, propionic acid, glycolic acid, oxalic acid, maleic acid, malonic acid, succinic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, benzenesulfonic acid, toluenesulfonic acid, sulfosalicylic acid, and the like.

Pharmaceutically acceptable base addition salts can be formed with inorganic and organic bases.

Inorganic bases from which salts can be derived include, for example, ammonium salts and metals from columns I to XII of the periodic table. In certain embodiments, the salts are derived from sodium, potassium, ammonium, calcium, magnesium, iron, silver, zinc, and copper. In certain other embodiments, the salts are selected from ammonium, potassium, sodium, calcium and magnesium salts.

Organic bases from which salts can be derived include, for example, primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines, basic ion exchange resins, and the like. Certain organic amines include isopropylamine, benzathine, choline, diethanolamine, diethylamine, lysine, meglumine, piperazine and tromethamine.

5 In another aspect, the present invention provides compounds as disclosed herein in acetate, ascorbate, adipate, aspartate, benzoate, besylate, bromide/hydrobromide, bicarbonate/carbonate, bisulfate/sulfate, camphorsulfonate, caprate, chloride/hydrochloride, chlorthalidone, citrate, ethandisulfonate, fumarate, gluceptate, gluconate, glucuronate, glutamate, glutarate, glycolate, hippurate, hydroiodide/iodide, isethionate, lactate, lactobionate, laurylsulfate, malate, maleate, malonate, mandelate, mesylate, methylsulphate, mucate, naphthoate, napsylate, nicotinate, nitrate, octadecanoate, oleate, oxalate, palmitate, pamoate, phosphate/hydrogen phosphate/dihydrogen phosphate, polygalacturonate, propionate, sebacate, stearate, succinate, sulfosalicylate, sulfate, tartrate, tosylate trifenatate, trifluoroacetate or xinafoate salt form. In yet another aspect, the present invention provides compounds as disclosed herein in C₁-C₄alkyl sulfonic acid, benzenesulfonic acid or mono-, di- or tri-C₁-C₄alkyl substituted benzene sulfonic acid addition salt form.

Any formula given herein is also intended to represent unlabeled forms as well as isotopically labeled forms of the compounds. Isotopically labeled compounds have structures depicted by the formulas given herein except that one or more atoms are replaced by an atom having a selected atomic mass or mass number. Examples of isotopes that can be incorporated into compounds of the invention include isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorous, fluorine, and chlorine, such as ²H, ³H, ¹¹C, ¹³C, ¹⁴C, ¹⁵N, ¹⁸F, ³¹P, ³²P, ³⁵S, ³⁶Cl, ¹²⁴I, ¹²⁵I respectively. The invention includes various isotopically labeled compounds as defined herein, for example those into which radioactive isotopes, such as ³H, ¹³C, and ¹⁴C, are present. Such isotopically labelled compounds are useful in metabolic studies (with ¹⁴C), reaction kinetic studies (with, for example ²H or ³H), detection or imaging techniques, such as positron emission tomography (PET) or single-photon emission computed tomography (SPECT) including drug or substrate tissue distribution assays, or in radioactive treatment of patients. In particular, an ¹⁸F or labeled compound may be particularly desirable for PET or SPECT studies. Isotopically labeled compounds of this invention and salts thereof can generally be prepared by carrying out the procedures disclosed in the schemes or in the examples and preparations described below by substituting a readily available isotopically labeled reagent for a non-isotopically labeled reagent.

Further, substitution with heavier isotopes, particularly deuterium (i.e., ²H or D) may afford certain therapeutic advantages resulting from greater metabolic stability, for example increased in vivo half-life or reduced dosage requirements or an improvement in therapeutic index. It is understood that deuterium in this context is regarded as a substituent of a compound of the formula (I). The concentration

of such a heavier isotope, specifically deuterium, may be defined by the isotopic enrichment factor. The term "isotopic enrichment factor" as used herein means the ratio between the isotopic abundance and the natural abundance of a specified isotope. If a substituent in a compound of this invention is denoted deuterium, such compound has at least 50% deuterium incorporation at each designated deuterium atom, 60% deuterium incorporation, at least 75% deuterium incorporation, at least 90% deuterium incorporation, at least 95% deuterium incorporation, at least 99% deuterium incorporation, or at least 99.5% deuterium incorporation.

The compounds of the present invention may inherently or by design form solvates with solvents (including water). Therefore, it is intended that the invention embrace both solvated and unsolvated forms. The term "solvate" refers to a molecular complex of a compound of the present invention (including salts thereof) with one or more solvent molecules. Such solvent molecules are those commonly used in the pharmaceutical art, which are known to be innocuous to a recipient, e.g., water, ethanol, dimethylsulfoxide, acetone and other common organic solvents. The term "hydrate" refers to a molecular complex comprising a compound of the invention and water. Pharmaceutically acceptable solvates in accordance with the invention include those wherein the solvent of crystallization may be isotopically substituted, e.g. D₂O, d₆-acetone, d₆-DMSO.

The term "a therapeutically effective amount" of a compound of the present invention refers to an amount of the compound of the present invention that will elicit the biological or medical response of a subject, for example, reduction or inhibition of an enzyme or a protein activity, or ameliorate symptoms, alleviate conditions, slow or delay disease progression, or prevent a disease, etc. In one non-limiting embodiment, the term "a therapeutically effective amount" refers to the amount of the compound of the present invention that, when administered to a subject, is effective to (1) at least partially alleviating, inhibiting, preventing and/or ameliorating a condition, or a disorder, or a disease or biological process (i) mediated by TRPC6 activity, or (ii) associated with TRPC6 activity; or (2) inhibiting the activity of TRPC6. In another non-limiting embodiment, the term "a therapeutically effective amount" refers to the amount of the compound of the present invention that, when administered to a cell, or a tissue, or a non-cellular biological material, or a medium, is effective to at least partially inhibit TRPC6 activity.

As used herein, the term "subject" refers to an animal. Typically the animal is a mammal. A subject also refers to for example, primates (e.g., humans), cows, sheep, goats, horses, dogs, cats, rabbits, rats, mice, fish, birds and the like. In certain embodiments, the subject is a primate. In yet other embodiments, the subject is a human.

As used herein, the term "inhibit", "inhibition" or "inhibiting" refers to the reduction or suppression of a given condition, symptom, or disorder, or disease, or a significant decrease in the baseline activity of a biological activity or process.

As used herein, the term "treat", "treating" or "treatment" of any disease or disorder refers in one embodiment, to ameliorating the disease or disorder (i.e., slowing or arresting or reducing the development of the disease or at least one of the clinical symptoms thereof). In another embodiment "treat", "treating" or "treatment" refers to alleviating or ameliorating at least one physical parameter including those which may not be discernible by the patient. In yet another embodiment, "treat", "treating" or "treatment" refers to modulating the disease or disorder, either physically, (e.g., stabilization of a discernible symptom), physiologically, (e.g., stabilization of a physical parameter), or both.

As used herein, the term "prevent," "preventing" or "prevention" of any disease or disorder refers in one embodiment, to delay or avoidance of onset of the disease or disorder (i.e., slowing or preventing the onset of the disease or disorder in a patient susceptible to development of the disease or disorder).

As used herein, a subject is "in need of" a treatment if such subject would benefit biologically, medically or in quality of life from such treatment.

As used herein, the term "a," "an," "the" and similar terms used in the context of the present invention (especially in the context of the claims) are to be construed to cover both the singular and plural unless otherwise indicated herein or clearly contradicted by the context.

Any asymmetric atom (e.g., carbon or the like) of the compound(s) of the present invention can be present in racemic or enantiomerically enriched, for example the (R)-, (S)- or (R,S)-configuration. In certain embodiments, each asymmetric atom has at least 50% enantiomeric excess, at least 60% enantiomeric excess, at least 70% enantiomeric excess, at least 80% enantiomeric excess, at least 90% enantiomeric excess, at least 95% enantiomeric excess, or at least 99% enantiomeric excess in the (R)- or (S)-configuration. Substituents at atoms with unsaturated bonds may, if possible, be present in cis-(Z)- or trans-(E)-form.

Accordingly, as used herein a compound of the present invention can be in the form of one of the possible isomers, rotamers, atropisomers, tautomers or mixtures thereof, for example, as substantially pure geometric (cis or trans) isomers, diastereomers, optical isomers (antipodes), racemates or mixtures thereof.

Any resulting mixtures of isomers can be separated on the basis of the physicochemical differences of the constituents, into the pure or substantially pure geometric or optical isomers, diastereomers, racemates, for example, by chromatography and/or fractional crystallization.

Any resulting racemates of final products or intermediates can be resolved into the optical antipodes by known methods, e.g., by separation of the diastereomeric salts thereof, obtained with an optically active acid or base, and liberating the optically active acidic or basic compound. In particular, a basic moiety may thus be employed to resolve the compounds of the present invention into their optical antipodes, e.g., by fractional crystallization of a salt formed with an optically active acid, e.g., tartaric acid, dibenzoyl tartaric acid, diacetyl tartaric acid, di-O,O'-p-toluoyl tartaric acid, mandelic acid, malic acid or camphor-10-sulfonic acid. Racemic products can also be resolved by chiral chromatography, e.g., high

performance liquid chromatography (HPLC) or supercritical fluid chromatography (SFC) using a chiral adsorbent.

Mixtures of isomers obtainable according to the invention can be separated in a manner known to those skilled in the art into the individual isomers; diastereoisomers can be separated, for example, by partitioning between polyphasic solvent mixtures, recrystallization and/or chromatographic separation, for example over silica gel or by e.g. medium pressure liquid chromatography over a reversed phase column, and racemates can be separated, for example, by the formation of salts with optically pure salt-forming reagents and separation of the mixture of diastereoisomers so obtainable, for example by means of fractional crystallization, or by chromatography over optically active column materials.

Within the scope of this text, only a readily removable group that is not a constituent of the particular desired end product of the compounds of the present invention is designated a "protecting group", unless the context indicates otherwise. The protection of functional groups by such protecting groups, the protecting groups themselves, and their cleavage reactions are described for example in standard reference works, such as J. F. W. McOmie, "Protective Groups in Organic Chemistry", Plenum Press, London and New York 1973, in T. W. Greene and P. G. M. Wuts, "Protective Groups in Organic Synthesis", Third edition, Wiley, New York 1999, in "The Peptides"; Volume 3 (editors: E. Gross and J. Meienhofer), Academic Press, London and New York 1981, in "Methoden der organischen Chemie" (Methods of Organic Chemistry), Houben Weyl, 4th edition, Volume 15/I, Georg Thieme Verlag, Stuttgart 1974, in H.-D. Jakubke and H. Jeschkeit, "Aminosäuren, Peptide, Proteine" (Amino acids, Peptides, Proteins), Verlag Chemie, Weinheim, Deerfield Beach, and Basel 1982, and in Jochen Lehmann, "Chemie der Kohlenhydrate: Monosaccharide and Derivate" (Chemistry of Carbohydrates: Monosaccharides and Derivatives), Georg Thieme Verlag, Stuttgart 1974. A characteristic of protecting groups is that they can be removed readily (i.e. without the occurrence of undesired secondary reactions) for example by solvolysis, reduction, photolysis or alternatively under physiological conditions (e.g. by enzymatic cleavage).

Intermediates and final products can be worked up and/or purified according to standard methods, e.g. using chromatographic methods, distribution methods, (re-) crystallization, and the like.

All methods described herein can be performed in any suitable order unless otherwise indicated herein or otherwise clearly contradicted by context. The use of any and all examples, or exemplary language (e.g. "such as") provided herein is intended merely to better illuminate the invention and does not pose a limitation on the scope of the invention otherwise claimed.

Any process steps disclosed herein can be carried out under reaction conditions that are known to those skilled in the art, including those mentioned specifically, in the absence or, customarily, in the presence of solvents or diluents, including, for example, solvents or diluents that are inert towards the reagents used and dissolve them, in the absence or presence of catalysts, condensation or neutralizing

agents, for example ion exchangers, such as cation exchangers, e.g. in the H^+ form, depending on the nature of the reaction and/or of the reactants at reduced, normal or elevated temperature, for example in a temperature range of from about $-100^\circ C$. to about $250^\circ C$, including, for example, from approximately $-80^\circ C$. to approximately $250^\circ C$, for example at from -80 to $-60^\circ C$, at room temperature, at from -20 to $40^\circ C$. or at reflux temperature, under atmospheric pressure or in a closed vessel, where appropriate under pressure, and/or in an inert atmosphere, for example under an argon or nitrogen atmosphere.

The solvents from which those solvents that are suitable for any particular reaction may be selected include those mentioned specifically or, for example, water, esters, such as lower alkyl-lower alkanates, for example ethyl acetate, ethers, such as aliphatic ethers, for example diethyl ether, or cyclic ethers, for example tetrahydrofuran or dioxane, liquid aromatic hydrocarbons, such as benzene or toluene, alcohols, such as methanol, ethanol or 1- or 2-propanol, nitriles, such as acetonitrile, halogenated hydrocarbons, such as methylene chloride or chloroform, acid amides, such as dimethylformamide or dimethyl acetamide, bases, such as heterocyclic nitrogen bases, for example pyridine or N-methylpyrrolidin-2-one, carboxylic acid anhydrides, such as lower alkanic acid anhydrides, for example acetic anhydride, cyclic, linear or branched hydrocarbons, such as cyclohexane, hexane or isopentane, methycyclohexane, or mixtures of those solvents, for example aqueous solutions, unless otherwise indicated in the description of the processes. Such solvent mixtures may also be used in working up, for example by chromatography or partitioning.

In another aspect, the present invention provides a pharmaceutical composition comprising a compound of the present invention, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier. In a further embodiment, the composition comprises at least two pharmaceutically acceptable carriers, such as those described herein. For purposes of the present invention, unless designated otherwise, solvates and hydrates are generally considered compositions. Preferably, pharmaceutically acceptable carriers are sterile. The pharmaceutical composition can be formulated for particular routes of administration such as oral administration, parenteral administration, and rectal administration, etc. In addition, the pharmaceutical compositions of the present invention can be made up in a solid form (including without limitation capsules, tablets, pills, granules, powders or suppositories), or in a liquid form (including without limitation solutions, suspensions or emulsions). The pharmaceutical compositions can be subjected to conventional pharmaceutical operations such as sterilization and/or can contain conventional inert diluents, lubricating agents, or buffering agents, as well as adjuvants, such as preservatives, stabilizers, wetting agents, emulsifiers and buffers, etc.

As used herein, the term "pharmaceutically acceptable carrier" includes any and all solvents, dispersion media, coatings, surfactants, antioxidants, preservatives (e.g., antibacterial agents, antifungal agents), isotonic agents, absorption delaying agents, salts, preservatives, drugs, drug stabilizers, binders, excipients, disintegration agents, lubricants, sweetening agents, flavoring agents, dyes, and the like and

combinations thereof, as would be known to those skilled in the art (see, for example, Remington's Pharmaceutical Sciences, 18th Ed. Mack Printing Company, 1990, pp. 1289-1329). Except insofar as any conventional carrier is incompatible with the active ingredient, its use in the therapeutic or pharmaceutical compositions is contemplated.

5 Typically, the pharmaceutical compositions are tablets or gelatin capsules comprising the active ingredient together with one or more of: a) diluents, e.g., lactose, dextrose, sucrose, mannitol, sorbitol, cellulose and/or glycine; b) lubricants, e.g., silica, talcum, stearic acid, its magnesium or calcium salt and/or polyethyleneglycol; for tablets also c) binders, e.g., magnesium aluminum silicate, starch paste, gelatin, tragacanth, methylcellulose, sodium carboxymethylcellulose and/or polyvinylpyrrolidone; if
10 desired d) disintegrants, e.g., starches, agar, alginic acid or its sodium salt, or effervescent mixtures; and e) absorbents, colorants, flavors and sweeteners. Tablets may be either film coated or enteric coated according to methods known in the art. Suitable compositions for oral administration include an effective amount of a compound of the invention in the form of tablets, lozenges, aqueous or oily suspensions, dispersible powders or granules, emulsion, hard or soft capsules, or syrups or elixirs. Compositions
15 intended for oral use are prepared according to any method known in the art for the manufacture of pharmaceutical compositions and such compositions can contain one or more agents selected from the group consisting of sweetening agents, flavoring agents, coloring agents and preserving agents in order to provide pharmaceutically elegant and palatable preparations. Tablets may contain the active ingredient in admixture with nontoxic pharmaceutically acceptable excipients which are suitable for the manufacture of
20 tablets. These excipients are, for example, inert diluents, such as calcium carbonate, sodium carbonate, lactose, calcium phosphate or sodium phosphate; granulating and disintegrating agents, for example, corn starch, or alginic acid; binding agents, for example, starch, gelatin or acacia; and lubricating agents, for example magnesium stearate, stearic acid or talc. The tablets are uncoated or coated by known techniques to delay disintegration and absorption in the gastrointestinal tract and thereby provide a sustained action
25 over a longer period. For example, a time delay material such as glyceryl monostearate or glyceryl distearate can be employed. Formulations for oral use can be presented as hard gelatin capsules wherein the active ingredient is mixed with an inert solid diluent, for example, calcium carbonate, calcium phosphate or kaolin, or as soft gelatin capsules wherein the active ingredient is mixed with water or an oil medium, for example, peanut oil, liquid paraffin or olive oil. Certain injectable compositions are aqueous
30 isotonic solutions or suspensions, and suppositories are advantageously prepared from fatty emulsions or suspensions. Said compositions may be sterilized and/or contain adjuvants, such as preserving, stabilizing, wetting or emulsifying agents, solution promoters, salts for regulating the osmotic pressure and/or buffers. In addition, they may also contain other therapeutically valuable substances. Said compositions are prepared according to conventional mixing, granulating or coating methods, respectively, and contain
35 about 0.1-75%, or contain about 1-50%, of the active ingredient. Suitable compositions for transdermal

application include an effective amount of a compound of the invention with a suitable carrier. Carriers suitable for transdermal delivery include absorbable pharmacologically acceptable solvents to assist passage through the skin of the host. For example, transdermal devices are in the form of a bandage comprising a backing member, a reservoir containing the compound optionally with carriers, optionally a rate controlling barrier to deliver the compound of the skin of the host at a controlled and predetermined rate over a prolonged period of time, and means to secure the device to the skin. Suitable compositions for topical application, e.g., to the skin and eyes, include aqueous solutions, suspensions, ointments, creams, gels or sprayable formulations, e.g., for delivery by aerosol or the like. Such topical delivery systems will in particular be appropriate for dermal application, e.g., for the treatment of skin cancer, e.g., for prophylactic use in sun creams, lotions, sprays and the like. They are thus particularly suited for use in topical, including cosmetic, formulations well-known in the art. Such may contain solubilizers, stabilizers, tonicity enhancing agents, buffers and preservatives. As used herein a topical application may also pertain to an inhalation or to an intranasal application. They may be conveniently delivered in the form of a dry powder (either alone, as a mixture, for example a dry blend with lactose, or a mixed component particle, for example with phospholipids) from a dry powder inhaler or an aerosol spray presentation from a pressurized container, pump, spray, atomizer or nebulizer, with or without the use of a suitable propellant.

The present invention further provides anhydrous pharmaceutical compositions and dosage forms comprising the compounds of the present invention as active ingredients, since water may facilitate the degradation of certain compounds.

Anhydrous pharmaceutical compositions and dosage forms of the invention can be prepared using anhydrous or low moisture containing ingredients and low moisture or low humidity conditions. An anhydrous pharmaceutical composition may be prepared and stored such that its anhydrous nature is maintained. Accordingly, anhydrous compositions are packaged using materials known to prevent exposure to water such that they can be included in suitable formulary kits. Examples of suitable packaging include, but are not limited to, hermetically sealed foils, plastics, unit dose containers (e.g., vials), blister packs, and strip packs.

The invention further provides pharmaceutical compositions and dosage forms that comprise one or more agents that reduce the rate by which the compound of the present invention as an active ingredient will decompose. Such agents, which are referred to herein as "stabilizers," include, but are not limited to, antioxidants such as ascorbic acid, pH buffers, or salt buffers, etc.

Prophylactic and Therapeutic Uses

The compounds disclosed herein in free form or in pharmaceutically acceptable salt form, exhibit valuable pharmacological properties, e.g. TRPC protein modulating properties and more particularly

inhibition of TRPC6 protein activity, e.g. as indicated in in vitro and in vivo tests as provided in the next sections and are therefore indicated for therapy.

The present invention provides methods of treating a disease or disorder associated with TRPC6 protein activity by administering to a subject in need thereof an effective amount of a compound disclosed herein. In certain aspects, the disease or disorder suitable for therapy by administration of the compound of the invention include, but are not limited to, nephrotic syndrome, minimal change disease, focal segmental glomerulosclerosis, collapsing glomerulopathy, membranous nephropathy, membranoproliferative glomerulonephritis, IGA nephropathy, acute renal failure, chronic renal failure, diabetic nephropathy, sepsis, pulmonary hypertension, acute lung disorder, acute respiratory distress syndrome (ARDS), heart failure, stroke, malignant tumor or muscular dystrophy. In certain instances, the patient is suffering from nephrotic syndrome, membranous nephropathy, and acute renal failure.

In a specific embodiment, the present invention provides a method of treating or preventing renal disease by administering to a subject in need thereof an effective amount of a compound disclosed herein. In certain embodiments, patients who are currently asymptomatic but are at risk of developing renal disease are suitable for administration with a compound of the invention. The methods of treating or preventing renal disease include, but are not limited to, methods of treating or preventing nephrotic syndrome, membranous nephropathy, acute renal failure, sepsis, chronic renal failure and diabetic nephropathy.

The pharmaceutical composition or combination of the present invention can be in unit dosage of about 1-1000 mg of active ingredient(s) for a subject of about 50-70 kg, or about 1-500 mg or about 1-250 mg or about 1-150 mg or about 0.5-100 mg, or about 1-50 mg of active ingredients. The therapeutically effective dosage of a compound, the pharmaceutical composition, or the combinations thereof, is dependent on the species of the subject, the body weight, age and individual condition, the disorder or disease or the severity thereof being treated. A physician, clinician or veterinarian of ordinary skill can readily determine the effective amount of each of the active ingredients necessary to prevent, treat or inhibit the progress of the disorder or disease.

The above-cited dosage properties are demonstrable in vitro and in vivo tests using advantageously mammals, e.g., mice, rats, dogs, monkeys or isolated organs, tissues and preparations thereof. The compounds of the present invention can be applied in vitro in the form of solutions, e.g., aqueous solutions, and in vivo either enterally, parenterally, advantageously intravenously, e.g., as a suspension or in aqueous solution. The dosage in vitro may range between about 10^{-3} molar and 10^{-9} molar concentrations. A therapeutically effective amount in vivo may range depending on the route of administration, between about 0.1-500 mg/kg, or between about 1-100 mg/kg.

The activity of a compound according to the present invention can be assessed by in vitro & in vivo methods, such as those described in the examples below.

The compound of the present invention may be administered either simultaneously with, or before or after, one or more other therapeutic agent. The compound of the present invention may be administered
5 separately, by the same or different route of administration, or together in the same pharmaceutical composition as the other agents.

In one embodiment, the invention provides a product comprising a compound disclosed herein and at least one other therapeutic agent as a combined preparation for simultaneous, separate or sequential use in therapy. In one embodiment, the therapy is the treatment of a disease or condition mediated by
10 TRPC protein activity. In preferred aspects, the therapy is a treatment for nephrotic syndrome, minimal change disease, focal segmental glomerulosclerosis, collapsing glomerulopathy, membranous nephropathy, membranoproliferative glomerulonephritis, IGA nephropathy, acute renal failure, chronic renal failure, diabetic nephropathy, sepsis, pulmonary hypertension, acute lung disorder, acute respiratory distress syndrome (ARDS), heart failure, stroke, malignant tumor, or muscular dystrophy.

Products provided as a combined preparation include a composition comprising the compound disclosed herein and the other therapeutic agent(s) together in the same pharmaceutical composition, or the compound disclosed herein and the other therapeutic agent(s) in separate form, e.g. in the form of a kit.
15

In one embodiment, the invention provides a pharmaceutical composition comprising a compound as disclosed herein and another therapeutic agent(s). Optionally, the pharmaceutical composition may
20 comprise a pharmaceutically acceptable carrier, as described above.

In one embodiment, the invention provides a kit comprising two or more separate pharmaceutical compositions, at least one of which contains a compound disclosed herein. In one embodiment, the kit comprises means for separately retaining said compositions, such as a container, divided bottle, or divided foil packet. An example of such a kit is a blister pack, as typically used for the packaging of tablets,
25 capsules and the like.

The kit of the invention may be used for administering different dosage forms, for example, oral and parenteral, for administering the separate compositions at different dosage intervals, or for titrating the separate compositions against one another. To assist compliance, the kit of the invention typically comprises directions for administration.

In the combination therapies of the invention, the compound of the invention and the other therapeutic agent may be manufactured and/or formulated by the same or different manufacturers. Moreover, the compound of the invention and the other therapeutic may be brought together into a combination therapy: (i) prior to release of the combination product to physicians (e.g. in the case of a kit
30

comprising the compound of the invention and the other therapeutic agent); (ii) by the physician themselves (or under the guidance of the physician) shortly before administration; (iii) in the patient themselves, e.g. during sequential administration of the compound of the invention and the other therapeutic agent.

5 Accordingly, the invention provides the use of a compound as disclosed herein for treating a disease or condition mediated by TRPC protein activity wherein the medicament is prepared for administration with another therapeutic agent. The invention also provides the use of another therapeutic agent for treating a disease or condition mediated by the TRPC protein activity, wherein the medicament is administered with a compound as disclosed herein. In another aspect, the invention provides the use of a
10 compound as disclosed herein for treating a disease or disorder selected from nephrotic syndrome, minimal change disease, focal segmental glomerulosclerosis, collapsing glomerulopathy, membranous nephropathy, membranoproliferative glomerulonephritis, IGA nephropathy, acute renal failure, chronic renal failure, diabetic nephropathy, sepsis, pulmonary hypertension, acute lung disorder, acute respiratory distress syndrome (ARDS), heart failure, stroke, malignant tumor, or muscular dystrophy wherein the
15 medicament is prepared for administration with another therapeutic agent. The invention also provides the use of another therapeutic agent for treating a disease or disorder selected from nephrotic syndrome, minimal change disease, focal segmental glomerulosclerosis, collapsing glomerulopathy, membranous nephropathy, membranoproliferative glomerulonephritis, IGA nephropathy, acute renal failure, chronic renal failure, diabetic nephropathy, sepsis, pulmonary hypertension, acute lung disorder, acute respiratory
20 distress syndrome (ARDS), heart failure, stroke, malignant tumor, or muscular dystrophy, wherein the medicament is administered with a compound as disclosed herein.

 The invention also provides a compound as disclosed herein for use in a method of treating a disease or condition mediated by TRPC protein activity wherein the compound is prepared for administration with another therapeutic agent. The invention also provides another therapeutic agent for
25 use in a method of treating a disease or condition mediated by TRPC protein activity, wherein the other therapeutic agent is prepared for administration with a compound as disclosed herein. The invention also provides a compound as disclosed herein for use in a method of treating a disease or condition mediated by TRPC protein activity, wherein the compound is administered with another therapeutic agent. The invention also provides another therapeutic agent for use in a method of treating a disease or condition
30 mediated by TRPC protein activity, wherein the other therapeutic agent is administered with a compound as disclosed herein.

 The invention also provides the use of a compound as disclosed herein for treating a disease or condition mediated by TRPC protein activity wherein the patient has previously (e.g. within 24 hours) been treated with another therapeutic agent. The invention also provides the use of another therapeutic

agent for treating a disease or condition mediated by TRPC protein activity wherein the patient has previously (e.g. within 24 hours) been treated with a compound as disclosed herein.

The pharmaceutical compositions can be administered alone or in combination with other molecules known to have a beneficial effect in treatment of kidney disease or more particularly in the treatment of FSGS, nephrotic syndrome, minimal change diseases or diabetic kidney disease. A combination therapy regimen may be additive, or it may produce synergistic results (e.g., improvement in kidney function which is more than expected for the combined use of the two agents). In some embodiments, the present invention provide a combination therapy for preventing and/or treating kidney disease or more particularly FSGS, nephrotic syndrome or minimal change diseases with a compound of the invention and a second therapeutic agent selected from the group consisting of ACE/ARB (such as captopril, lisinopril or losartan), steroid therapy (such as prednisone), immunomodulators (such as mycophenolate mofetil, tacrolimus or cyclosporine A), adrenocorticotrophic hormone analogs (such as acthar gel), anti-CD20 antibodies (such as rituximab), calcium channel blockers (such as amlodipine), diuretics (such as hydrochlorothiazide), antiplatelet agents (such as dipyridamole), anticoagulants (such as heparin), DPP-4 inhibitors (such as sitagliptin), SGLT2 inhibitors (such as dapagliflozin), anti-hyperlipidemia (such as rosuvastatin), anemia therapy (darbepoetin alfa), or anti-hyperuricemia (febuxostat).

In one embodiment, the invention provides a method of inhibiting the activity of a TRPC protein, or more preferably inhibiting the activity of TRPC6 protein, in a subject, wherein the method comprises administering to the subject a therapeutically effective amount of the compound according to the definition of Formula (I). The invention further provides methods of inhibiting the activity of a TRPC protein, or more preferably inhibiting the activity of TRPC6 protein in a subject by administering a compound as disclosed herein, wherein the method comprises administering to the subject a therapeutically effective amount of the compound as disclosed herein.

In one embodiment, the invention provides a compound as disclosed herein, for use as a medicament.

In one embodiment, the invention provides the use of a compound as disclosed herein for the treatment of a disorder or disease in a subject characterized by the activity of a TRPC protein, or more preferably the activity of TRPC6 protein. In particular, the invention provides the use of a compound as disclosed herein for the treatment of a disorder or disease mediated by the activity of a TRPC protein, or more preferably the activity of TRPC6 protein, e.g., nephrotic syndrome, minimal change disease, focal segmental glomerulosclerosis, collapsing glomerulopathy, membranous nephropathy, membranoproliferative glomerulonephritis, IGA nephropathy, acute renal failure, chronic renal failure, diabetic nephropathy, sepsis, pulmonary hypertension, acute lung disorder, acute respiratory distress syndrome (ARDS), heart failure, stroke, malignant tumor, or muscular dystrophy. In certain preferred

aspects, the invention provides for the use of a compound as disclosed herein for the treatment of a disorder or disease mediated by the activity of TRPC6 protein selected from nephrotic syndrome, membranous nephropathy and acute renal failure.

In one embodiment, the invention provides the use of a compound as disclosed herein in the manufacture of a medicament for the treatment of a disorder or disease in a subject characterized by activity of a TRPC protein, or more preferably the activity of TRPC6 protein. More particularly in the manufacture of a medicament for the treatment of a disease or disorder in a subject characterized by activity of a TRPC protein, or more preferably the activity of TRPC6 protein, e.g., nephrotic syndrome, minimal change disease, focal segmental glomerulosclerosis, collapsing glomerulopathy, membranous nephropathy, membranoproliferative glomerulonephritis, IGA nephropathy, acute renal failure, chronic renal failure, diabetic nephropathy, sepsis, pulmonary hypertension, acute lung disorder, acute respiratory distress syndrome (ARDS), heart failure, stroke, malignant tumor, or muscular dystrophy. In certain preferred aspects, the invention provides the use of a compound as disclosed herein in the manufacture of a medicament for the treatment of nephrotic syndrome, membranous nephropathy and acute renal failure.

In one embodiment, the invention provides the use of a compound as disclosed herein for the treatment of a disorder or disease in a subject characterized by activity of a TRPC protein, or more preferably the activity of TRPC6 protein. More particularly, the invention provides uses of the compounds provided herein in the treatment of a disease or disorder characterized by activity of a TRPC protein, or more preferably the activity of TRPC6 protein, e.g., nephrotic syndrome, minimal change disease, focal segmental glomerulosclerosis, collapsing glomerulopathy, membranous nephropathy, membranoproliferative glomerulonephritis, IGA nephropathy, acute renal failure, chronic renal failure, diabetic nephropathy, sepsis, pulmonary hypertension, acute lung disorder, acute respiratory distress syndrome (ARDS), heart failure, stroke, malignant tumor, or muscular dystrophy. In certain embodiments, the uses of the compounds provided herein is for the treatment of a disease or disorder is selected from nephrotic syndrome, membranous nephropathy and acute renal failure.

In a specific embodiment, the present invention provides use of the compounds of the invention for treating or preventing nephrotic syndrome, membranous nephropathy, acute renal failure, sepsis, chronic renal failure, diabetic nephropathy, pulmonary hypertension, acute lung disorder, acute respiratory distress syndrome (ARDS), heart failure, stroke, malignant tumor or muscular dystrophy. In certain embodiments, patients who are currently asymptomatic but are at risk of developing a symptomatic nephrotic syndrome, membranous nephropathy, acute renal failure, sepsis, chronic renal failure, diabetic nephropathy, pulmonary hypertension, acute lung disorder, acute respiratory distress syndrome (ARDS), heart failure, stroke, malignant tumor or muscular dystrophy are suitable for administration with a compound of the invention. The use in treating or preventing nephrotic syndrome, membranous nephropathy, acute renal failure, sepsis, chronic renal failure, diabetic nephropathy, pulmonary

hypertension, acute lung disorder, acute respiratory distress syndrome (ARDS), heart failure, stroke, malignant tumor or muscular dystrophy include, but are not limited to, uses in treating or preventing one or more symptoms or aspects of nephrotic syndrome, membranous nephropathy, acute renal failure, sepsis, chronic renal failure, diabetic nephropathy, pulmonary hypertension, acute lung disorder, acute respiratory distress syndrome (ARDS), heart failure, stroke, malignant tumor or muscular dystrophy.

The invention further includes any variant of the present processes, in which an intermediate product obtainable at any stage thereof is used as starting material and the remaining steps are carried out, or in which the starting materials are formed in situ under the reaction conditions, or in which the reaction components are used in the form of their salts or optically pure materials.

The following examples are intended to illustrate the invention and are not to be construed as being limitations thereon. Temperatures are given in degrees centigrade ($^{\circ}$ C.). If not mentioned otherwise, all evaporations are performed under reduced pressure, typically between about 15 mm Hg and 100 mm Hg (=20-133 mbar). The structure of final products, intermediates and starting materials is confirmed by standard analytical methods, e.g., microanalysis and spectroscopic characteristics, e.g., MS, IR, NMR.

Abbreviations used are those conventional in the art.

The invention relates also to those forms of the process in which a compound obtainable as an intermediate at any stage of the process is used as starting material and the remaining process steps are carried out, or in which a starting material is formed under the reaction conditions or is used in the form of a derivative, for example in a protected form or in the form of a salt, or a compound obtainable by the process according to the invention is produced under the process conditions and processed further in situ.

All starting materials, building blocks, reagents, acids, bases, dehydrating agents, solvents and catalysts utilized to synthesize the compounds of the present invention are either commercially available or can be produced by organic synthesis methods known to one of ordinary skill in the art.

Experimental

Unless otherwise noted, all materials were obtained from commercial suppliers and used without further purification. All parts are by weight and temperatures are in degrees centigrade unless otherwise indicated. All microwave assisted reactions were conducted with a Smith Synthesizer from Biotage. Mass spectral data was determined by electrospray ionization technique. All examples were purified to >95% purity as determined by high-performance liquid chromatography. Unless otherwise stated, reactions were run at room temperature.

Commercially available materials were purchased from Sigma Aldrich, HDH Pharma, Pharmablock, Alfa Aesar, Enovation Chemicals, and Combi-Blocks.

Compound names, i.e., IUPAC names, for compounds described in the instant application were generated using ChemDraw compound naming software.

The following abbreviations are used:

	CDI -	1,1'-carbonyldiimidazole
	DCM -	dichloromethane
	DMSO -	dimethyl sulfoxide
5	DMF -	<i>N,N</i> -dimethylformamide
	THF -	tetrahydrofuran
	Et ₂ O -	diethyl ether
	EtOAc -	ethyl acetate
	EtOH -	ethyl alcohol
10	Ms -	mesylate
	MeCN -	acetonitrile
	MeOH -	methyl alcohol
	SFC -	supercritical fluid chromatography
	TFA -	trifluoroacetic acid

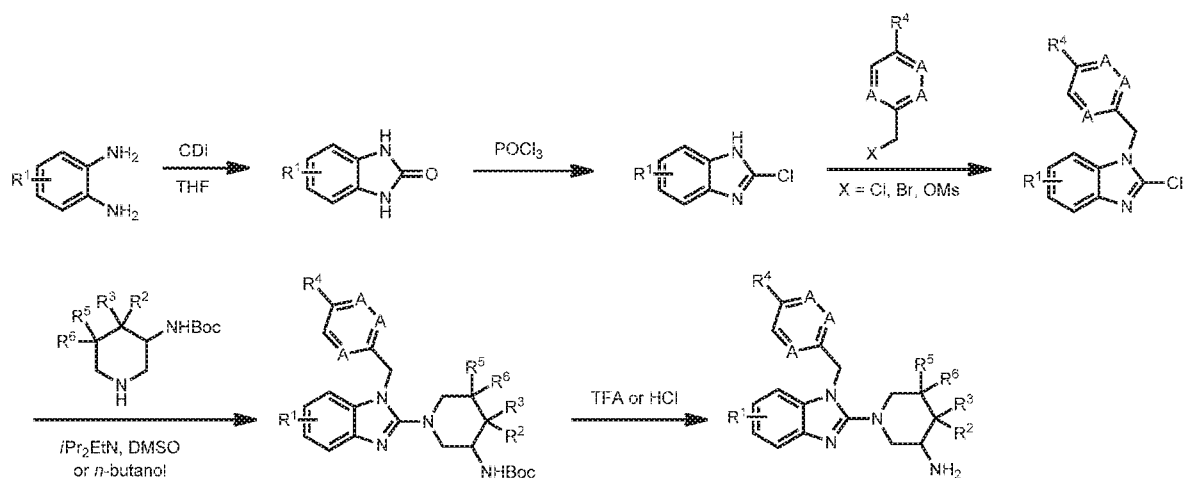
	tmp -	2,2,6,6-tetramethylpiperidine
	h -	hour
	min -	min
	rt -	room temperature (22-25 °C)
5	mL	milliliters
	μL	microliters
	g	grams
	μg	micrograms
	mg	milligrams
10	μmol	micromolar

General Method of Preparation

The compounds described herein are prepared using techniques known to one skilled in the art through the reaction sequences depicted in schemes 1-6 as well as by other methods. Furthermore, in the following schemes, where specific acids, bases, reagents, coupling agents, solvents, etc. are mentioned, it is understood that other suitable acids, bases, reagents, coupling agents, solvents, etc. may be used and are included within the scope of the present invention.

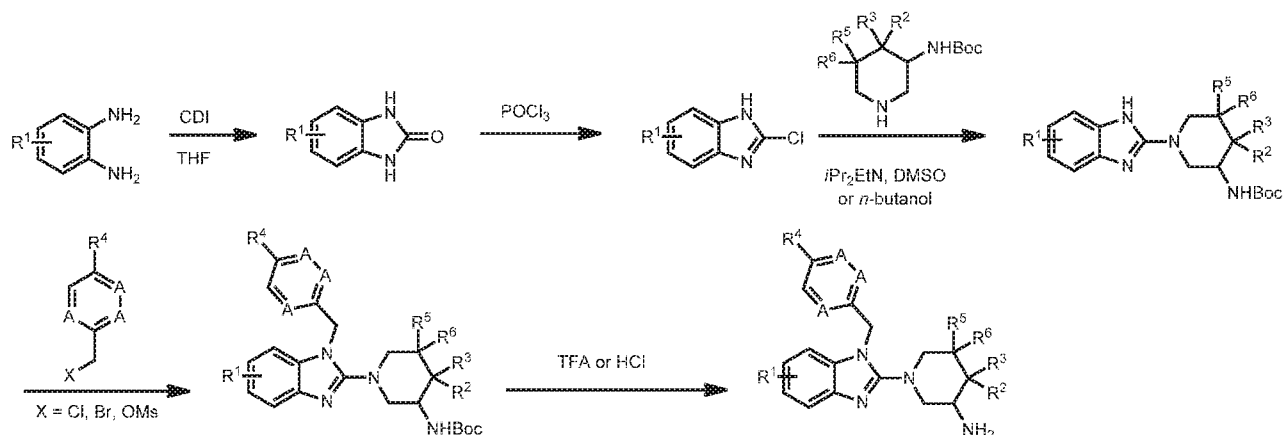
Synthesis of selected compounds of the present invention were prepared as described in Scheme 1. CDI coupling of the desired bis-aniline provided the corresponding benzimidazolone. Subjection to refluxing POCl₃ delivered the chlorobenzimidazole. These intermediates could be alkylated with a variety of electrophiles, then subjected to SnAr conditions to provide the Boc protected penultimate intermediates. Exposure to a variety of acids effected Boc deprotection to furnish the final products.

Scheme 1



An alternative approach to benzimidazole intermediates which was used to synthesize additional compounds in the present invention is shown in Scheme 2. CDI coupling of the desired bis-aniline provided the corresponding benzimidazolone. Subjection to refluxing POCl₃ delivered the chlorobenzimidazole. These intermediates were heated with base and nucleophile to provide the S_NAr products. Alkylation with a variety of electrophiles followed by acidic Boc deprotection furnished the final compounds.

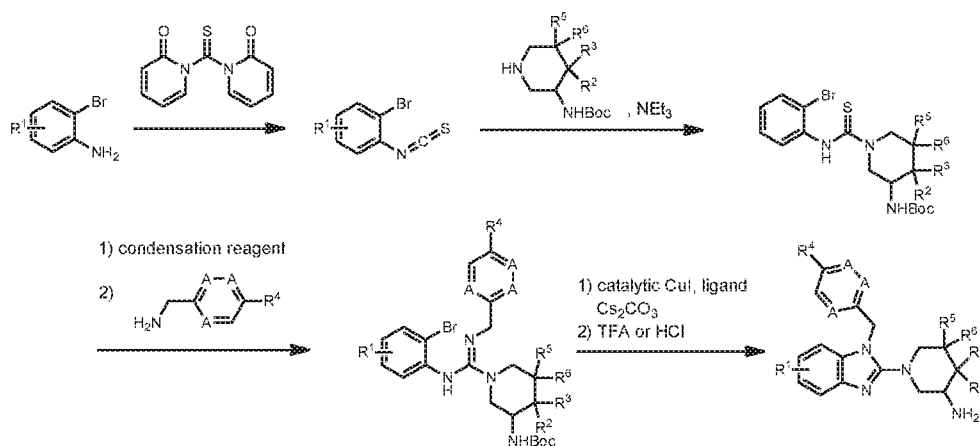
Scheme 2



Additionally, examples in this invention could be synthesized by the methods shown in Scheme 3-6.

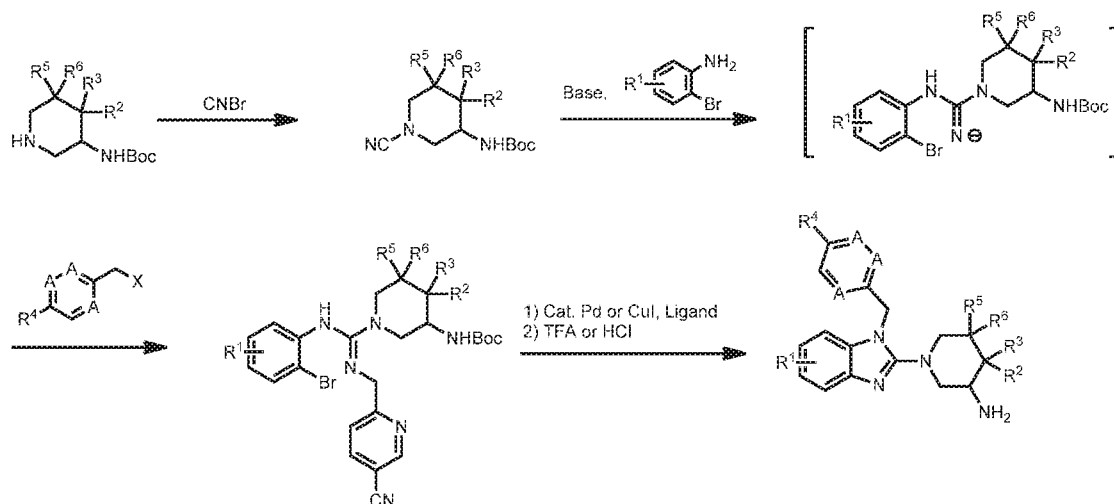
Scheme 3

Isothiocyanate formation was accomplished using a variety of reagents. Addition of secondary amines followed by condensation with primary amines provided the corresponding substituted guanidine. Intramolecular cyclizations were accomplished using copper catalysis. Final acidic Boc deprotection furnished the desired compounds.



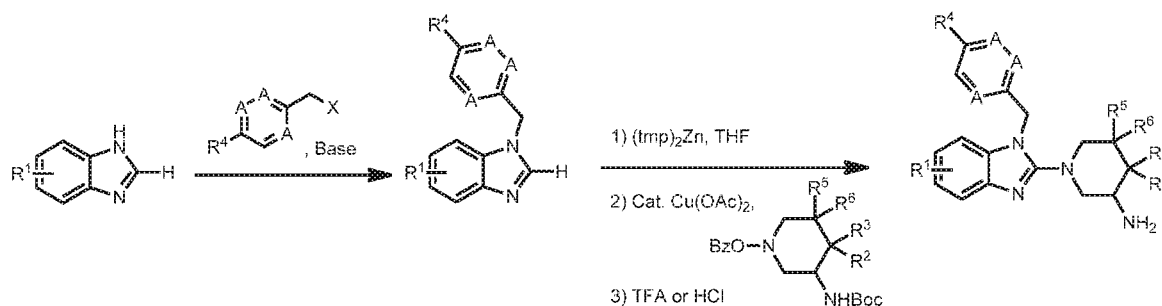
Scheme 4

Subjection of substituted piperidines to cyanogen bromide provided the corresponding piperidine-1-carbonitriles. These were susceptible to nucleophile attack by a variety of aniline nucleophiles, which were then trapped with benzyl electrophiles. The corresponding guanidine underwent intramolecular crosscoupling under palladium and copper catalysis. Final Boc deprotection under acidic conditions furnished the desired compounds.



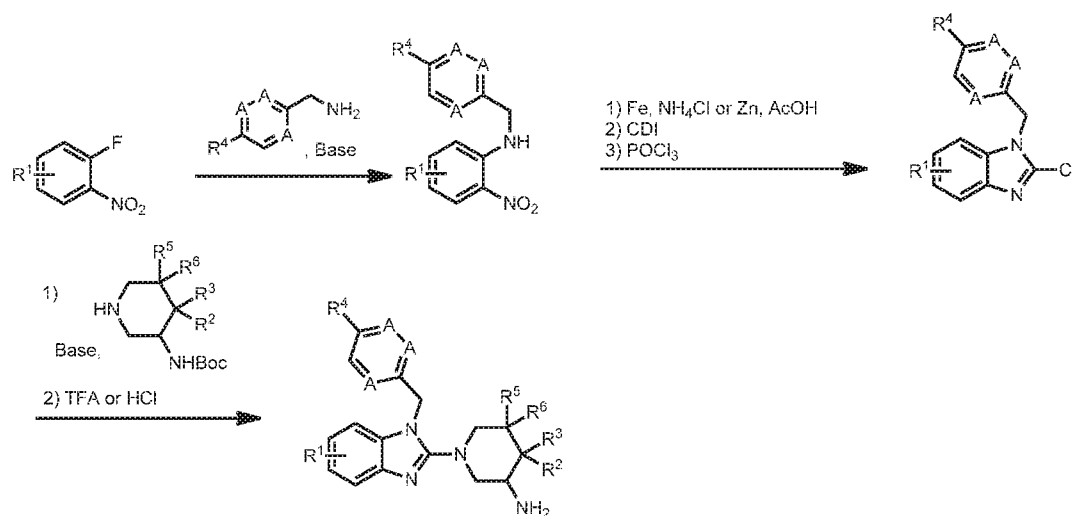
Scheme 5

Benzimidazoles were alkylated with a variety of electrophiles and base. These intermediates were subjected to $\text{Zn}(\text{tmp})_2$, copper catalysis, and benzoylhydroxylamines to furnish the aminated products. Final subjection to acidic Boc deprotection conditions yielded the desired products.

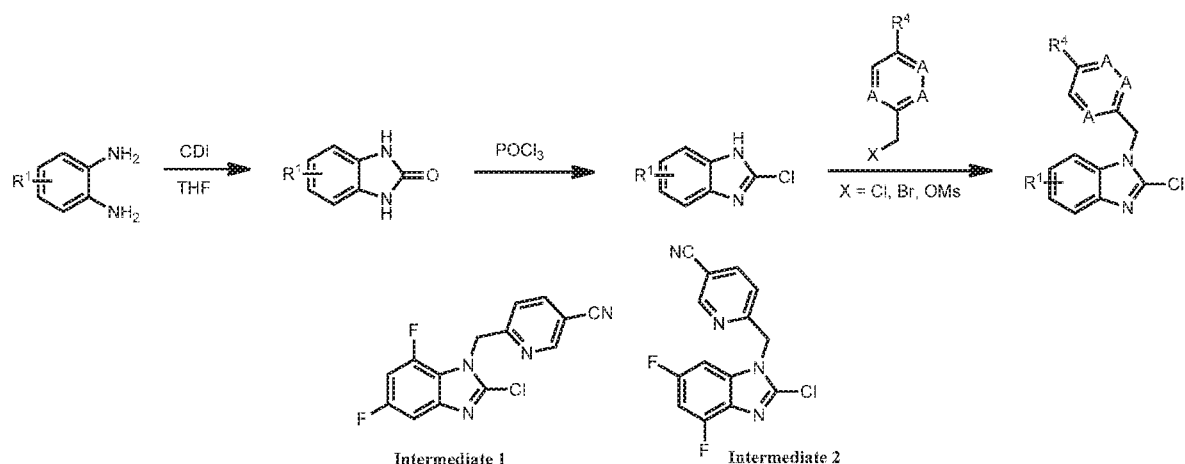


Scheme 6

SnAr transformations were accomplished on substituted fluoro-nitrobenzenes using primary benzyl amines and base. The corresponding nitro intermediates were reduced with iron or zinc, then subjected to CDI couplings and POCl_3 chlorination reactions. These intermediates were resubjected to SnAr conditions then Boc deprotected under acidic conditions to furnish the final compounds.

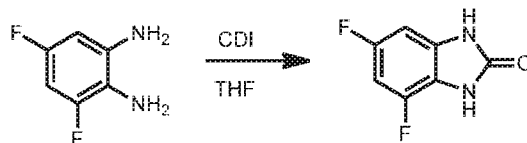


Scheme 7. General Synthesis of Alkylated Intermediates



Intermediate 1: 6-((2-chloro-5,7-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile and

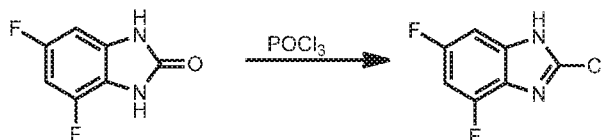
Intermediate 2: 6-((2-chloro-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile



Step 1. 4,6-difluoro-1H-benzo[d]imidazol-2(3H)-one

- 3,5-difluorobenzene-1,2-diamine (210.0 g, 1.457 mol, 1.0 equiv) and CDI (236.0 g, 1.457 mol, 1.0 equiv) were dissolved in anhydrous THF (2.5 L, 11.9 mL/g) and stirred for 12h at room temperature. LCMS indicated completion of the reaction. Reaction mixture was diluted with water (6.0 L) and extracted with ethyl acetate (2 x 6.0 L). The combined organic layer was dried over sodium sulphate, filtered and concentrated under reduced pressure to provide crude 4,6-difluoro-1H-benzo[d]imidazol-2(3H)-one as black solid which was used for next step without further purification. ¹H NMR (400 MHz, DMSO-*d*₆): δ

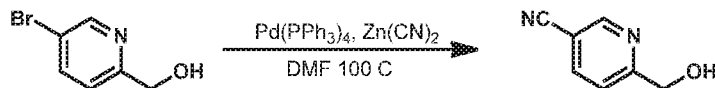
11.20 (s, 1H), 11.05 (s, 1H), 6.85 (td, $J = 10.7, 2.2$ Hz, 1H), 6.69 (dd, $J = 8.6, 2.2$ Hz, 1H). MS (ESI, pos. ion) m/z : 171.0 [M+1]



5 Step 2. 2-chloro-4,6-difluoro-1H-benzo[d]imidazole

4,6-difluoro-1H-benzo[d]imidazol-2(3H)-one (180.0 g, 1.058 mol, 1.0 equiv) was suspended in POCl₃ (2.0 L) and heated under stirring at 110 °C for 2h, at which time LCMS indicated completion of the reaction. Excess POCl₃ was removed via vacuum distillation and the remaining residue was diluted with acetonitrile (1.0 L) and sat. aq. sodium bicarbonate solution (1.0 L), then extracted with ethyl acetate (2 x 4.0 L). The combined organic layer was dried over sodium sulfate, filtered and concentrated under reduced pressure to provide 2-chloro-4,6-difluoro-1H-benzo[d]imidazole as brown solid which was used for next reaction without further purification. ¹H NMR (400 MHz, DMSO-*d*₆): 13.40 (bs, 1H), 7.31 – 7.03 (m, 2H). MS (ESI, pos. ion) m/z : 189.0 [M+1].

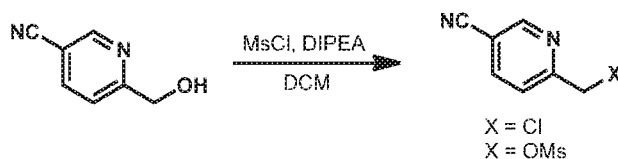
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15 Step 3. 6-(hydroxymethyl)nicotinonitrile

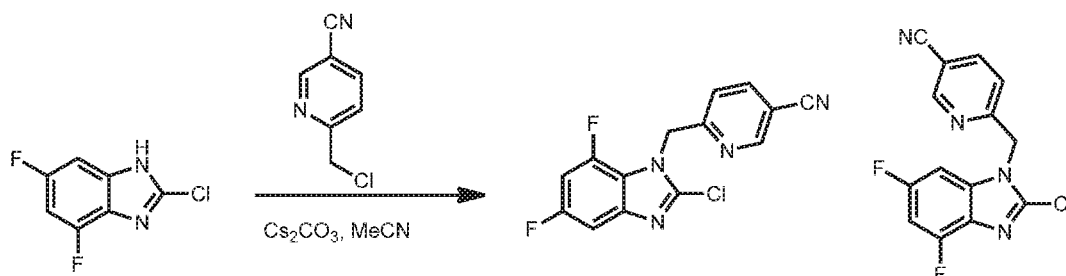
(5-bromopyridin-2-yl)methanol (75.0 g, 399.0 mmol, 1.0 equiv), zinc cyanide (141.0 g, 1.197 mol, 3.0 equiv) and tetrakis(triphenylphosphine)palladium(0) (46.1 g, 39.9 mmol, 0.1 equiv) were dissolved in N,N-dimethylformamide (750.0 mL, 10.0 mL/g) and degassed with nitrogen for 30 minutes. The reaction mixture was heated at 110 °C for 2 h. LCMS indicated formation of the product. After completion of the reaction, the mixture was allowed to cool to room temperature, diluted with water (700 mL) and extracted with ethyl acetate (3 x 700 mL). The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The crude material was adsorbed onto a plug of silica gel (230-400 mesh) and purified through a Biotage Isolera-one pre-packed silica gel column, eluting with a gradient of 40% ethyl acetate in hexane to provide 6-(hydroxymethyl)nicotinonitrile as white solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.93 (dt, $J = 1.8, 0.8$ Hz, 1H), 8.32 – 8.28 (m, 1H), 7.66 (dt, $J = 8.3, 0.9$ Hz, 1H), 5.68 (td, $J = 5.9, 0.8$ Hz, 1H), 4.64 (d, $J = 5.8$ Hz, 2H). MS (ESI, pos. ion) m/z : 135.0 [M+1]

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Step 4. 6-(chloromethyl)nicotinonitrile and (5-cyanopyridin-2-yl)methyl methanesulfonate

6-(hydroxymethyl)nicotinonitrile (25.0 g, 186.0 mmol, 1.0 equiv) was dissolved in dichloromethane (360.0 mL, 14.4 mL/g) and cooled to 0 °C. N,N-diisopropylethylamine (48.8 mL, 280.0 mmol, 1.5 equiv) was added, followed by dropwise addition of methanesulfonyl chloride (16.0 g, 205.0 mmol, 1.1 equiv) over 15 minutes. The reaction mixture was allowed to warm to room temperature and stirred for 45 min. LCMS indicated formation of the product. The reaction mixture was diluted with water (500 mL) and extracted with DCM (2 x 250 mL). The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure to get crude material which was adsorbed into a plug of silica gel (230-400 mesh) and purified by chromatography through a Biotage Isolera-one pre-packed silica gel column, eluting with a gradient of 15% ethyl acetate in hexane to afford 6-(chloromethyl)nicotinonitrile (VI) as yellowish solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.03 (dd, J = 2.2, 1.0 Hz, 1H), 8.38 (dd, J = 8.1, 2.2 Hz, 1H), 7.77 (dd, J = 8.1, 0.9 Hz, 1H), 4.88 (s, 2H). Further elution of the column with a gradient of 50% ethyl acetate in hexane provided (5-cyanopyridin-2-yl)methyl methanesulfonate as brown solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.06 (dt, J = 2.1, 1.0 Hz, 1H), 8.41 (dt, J = 8.2, 1.7 Hz, 1H), 7.73 (dd, J = 8.2, 1.0 Hz, 1H), 5.42 (d, J = 1.1 Hz, 2H), 3.34 (s, 3H). MS (ESI, pos. ion) *m/z*: 213.2 [M+1]. Both compounds were competent electrophiles in the alkylation (step 5).

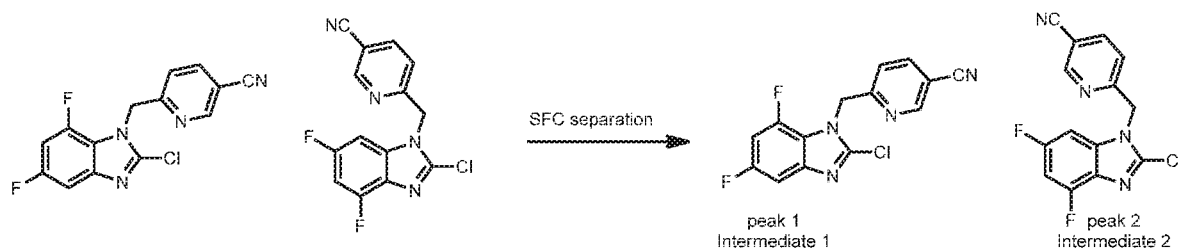


Step 5. 6-((2-chloro-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile and 6-((2-chloro-5,7-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile

2-chloro-4,6-difluoro-1H-benzo[d]imidazole (50.0 g, 265.0 mmol, 1.0 equiv) and 6-(chloromethyl)nicotinonitrile (40.5 g, 265.0 mmol, 1.0 equiv) was dissolved in acetonitrile (500.0 mL, 10.0 mL/g) at room temperature. Cesium carbonate (138.0 g, 427.0 mmol, 1.6 equiv) was added and the mixture was stirred at room temperature for 12h. The reaction mixture was diluted with water (200 mL) and extracted with ethyl acetate (2 x 200 mL). The combined organic layers were dried over sodium sulfate, filtered and concentrate under reduced pressure. The crude material was adsorbed onto a plug of silica gel (60-120 mesh) and purified by column chromatography, eluting with a gradient of 25% ethyl acetate in hexane to provide 6-((2-chloro-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile and 6-((2-chloro-5,7-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile as a mixture of isomers (light yellow

solid). In some instances, the mixture of isomers was carried forward without separation and in others the isomers were separated at this stage.

Step 6. Separation of 6-((2-chloro-5,7-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile (Intermediate 1) and 6-((2-chloro-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile (Intermediate 2)



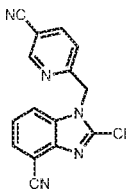
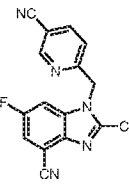
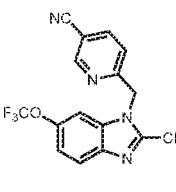
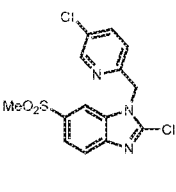
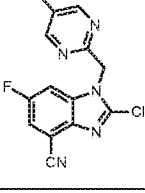
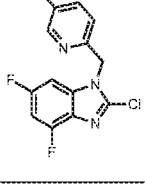
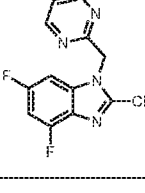
1.0 g sample was dissolved in 20 mL Methanol, Column Lux C4 (250 × 50 mm, 5 μ m), Mobile phase: 70:30 (A : B), A: Liquid CO₂, B: Methanol, Flow Rate: 120 mL/min, Wave length: 220nm, Sample load: 100mg/injection, Inlet pressure: 200-210 bar, Cycle time: 3.5, Run time: 10. In total, (51.0 g mixture of isomers) was separated by SFC to get 6-((2-chloro-5,7-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile (Intermediate 1, peak 1) and 6-((2-chloro-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile (Intermediate 2, peak 2) as yellow solids. *Peak 1*: ¹H NMR (400 MHz, DMSO-*d*₆): δ 8.90 (d, *J* = 2.0 Hz, 1H), 8.37 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.70 (d, *J* = 8.2 Hz, 1H), 7.42 (dd, *J* = 9.0, 2.2 Hz, 1H), 7.22 (ddd, *J* = 11.9, 10.3, 2.2 Hz, 1H), 5.79 (s, 2H). MS (ESI, pos. ion) *m/z*: 304.0 [M+1]. *Peak 2*: ¹H NMR (400 MHz, DMSO-*d*₆): δ 8.91 (t, *J* = 3.0 Hz, 1H), 8.37 (ddd, *J* = 8.2, 4.4, 2.1 Hz, 1H), 7.67 (dd, *J* = 8.4, 4.2 Hz, 1H), 7.49 (dt, *J* = 8.7, 3.0 Hz, 1H), 7.20 (tdd, *J* = 10.7, 4.5, 2.1 Hz, 1H), 5.79 (d, *J* = 3.8 Hz, 2H). MS (ESI, pos. ion) *m/z*: 304.0 [M+1].

The following intermediates were synthesized using a sequence analogous to that used to synthesize Intermediates 1 and 2 and general Scheme 7 above:

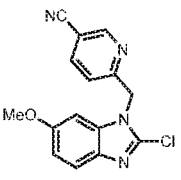
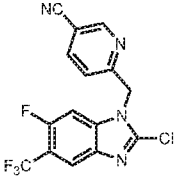
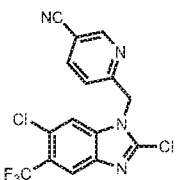
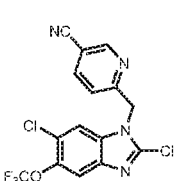
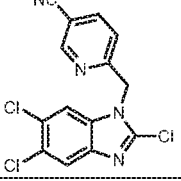
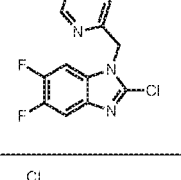
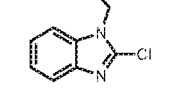
Table 1. Alkylated Intermediates

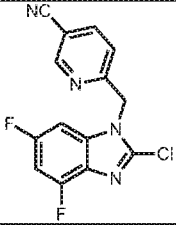
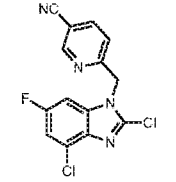
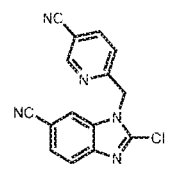
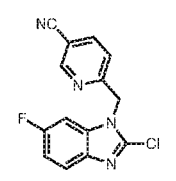
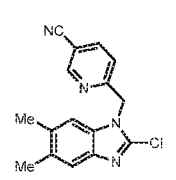
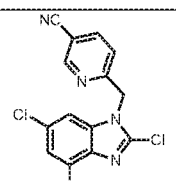
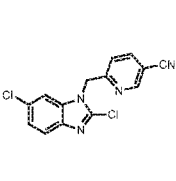
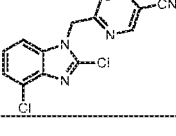
Int #	Structure	Compound Name	¹ H NMR	MS MH+	Separation Conditions
1		6-((2-chloro-5,7-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	¹ H NMR (400 MHz, DMSO- <i>d</i> ₆): δ 8.90 (d, <i>J</i> = 2.0 Hz, 1H), 8.37 (dd, <i>J</i> = 8.2, 2.1 Hz, 1H), 7.70 (d, <i>J</i> = 8.2 Hz, 1H), 7.42 (dd, <i>J</i> = 9.0, 2.2 Hz, 1H), 7.22 (ddd, <i>J</i> = 11.9, 10.3, 2.2 Hz, 1H), 5.79 (s, 2H)	304.0	Column Lux C4, 30% MeOH, peak 1

Int #	Structure	Compound Name	¹ H NMR	MS MH+	Separation Conditions
2		6-((2-chloro-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	¹ H NMR (400 MHz, DMSO-d ₆): δ 8.91 (t, J = 3.0 Hz, 1H), 8.37 (ddd, J = 8.2, 4.4, 2.1 Hz, 1H), 7.67 (dd, J = 8.4, 4.2 Hz, 1H), 7.49 (dt, J = 8.7, 3.0 Hz, 1H), 7.20 (tdd, J = 10.7, 4.5, 2.1 Hz, 1H), 5.79 (d, J = 3.8 Hz, 2H)	304.0	Column Lux C4, 30% MeOH, peak 2
3		6-((2,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	¹ H NMR (400 MHz, DMSO-d ₆): δ 8.90 (dd, J = 2.1, 0.9 Hz, 1H), 8.36 (dd, J = 8.2, 2.2 Hz, 1H), 7.80 (d, J = 2.1 Hz, 1H), 7.68 – 7.60 (m, 2H), 7.29 (dd, J = 8.6, 2.1 Hz, 1H), 5.79 (s, 2H)	303.0	YMC Amyose SA, Methanol THF (70:30) 40 %; peak 1
4		6-((2,5-dichloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	¹ H NMR (400 MHz, DMSO-d ₆): δ 8.90 (d, J = 2.1 Hz, 1H), 8.35 (dd, J = 8.2, 2.1 Hz, 1H), 7.74 (d, J = 2.0 Hz, 1H), 7.66 – 7.55 (m, 2H), 7.33 (dd, J = 8.7, 2.1 Hz, 1H), 5.79 (s, 2H)	303.0	YMC Amyose SA, Methanol THF (70:30) 40 %; peak 2
5		6-((2-chloro-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	¹ H NMR (400 MHz, DMSO-d ₆): δ 8.93 – 8.86 (m, 1H), 8.34 (dd, J = 8.2, 2.1 Hz, 1H), 7.67 – 7.58 (m, 2H), 7.54 (dd, J = 9.2, 2.6 Hz, 1H), 7.17 – 7.06 (m, 1H), 5.75 (s, 2H)	287.0	YMC Amyose SA, Methanol THF (70:30) 40 %; peak 1
6		6-((2-chloro-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	¹ H NMR (400 MHz, DMSO-d ₆): δ 8.90 (d, J = 2.3 Hz, 1H), 8.34 (dt, J = 8.0, 2.3 Hz, 1H), 7.59 (tq, J = 7.5, 2.2 Hz, 2H), 7.48 (dq, J = 9.5, 2.4 Hz, 1H), 7.24 – 7.05 (m, 1H), 5.77 (s, 2H)	287.0	YMC Amyose SA, Methanol THF (70:30) 40 %; peak 2
7		6-((2-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	¹ H NMR (400 MHz, DMSO-d ₆): δ 8.92 (d, J = 2.1 Hz, 1H), 8.34 (dd, J = 8.1, 2.1 Hz, 1H), 7.67 – 7.54 (m, 3H), 7.30 – 7.245 (m, 2H), 5.76 (s, 2H)	269.2	--
8		6-((2-chloro-4-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	--	337.2	--
9 ^a		6-((2,6-dichloro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)nicotinonitrile	--	304.0	Separated at final product

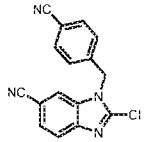
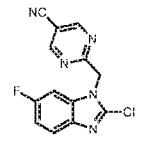
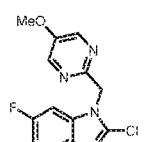
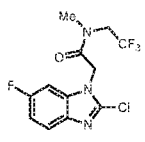
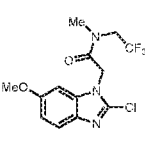
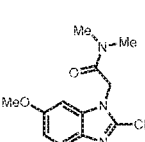
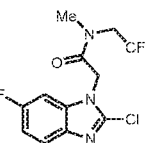
Int #	Structure	Compound Name	¹ H NMR	MS MH+	Separation Conditions
10		2-chloro-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-4-carbonitrile	--	294.0	--
11		2-chloro-1-((5-cyanopyridin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazole-4-carbonitrile	--	312.2	--
12 ^a		6-((2-chloro-6-(trifluoromethoxy)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	--	353.2	Separated at final product
13 ^a		2-chloro-1-((5-chloropyridin-2-yl)methyl)-6-(methylsulfonyl)-1H-benzo[d]imidazole	--	357.8	Separated at final product
14		2-chloro-1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazole-4-carbonitrile	--	323.8	--
15 ^a		2-chloro-4,6-difluoro-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazole	--	298.0	Separated at final product
16 ^a		2-chloro-4,6-difluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole	--	299.0	Separated at final product

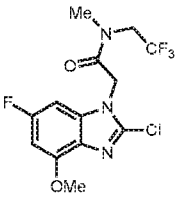
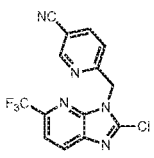
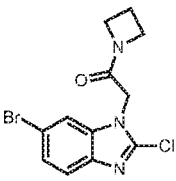
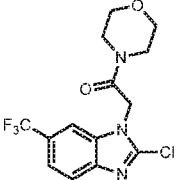
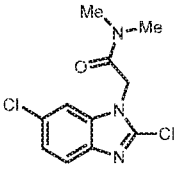
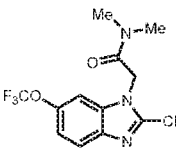
Int #	Structure	Compound Name	¹ H NMR	MS MH+	Separation Conditions
17 ^a		2-chloro-1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazole	--	297.0	Separated at final product
18		2-chloro-6-fluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-4-carbonitrile	--	306.2	--
19 ^a		6-((2-chloro-6-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	--	337.0	Separated at final product
20 ^a		6-((2,5-dichloro-6-methyl-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	--	317.0	Separated at final product
21 ^a		6-((2-chloro-6-(difluoromethoxy)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	--	335.0	Separated at final product
22		6-((2-chloro-4-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	--	299.2	Separated at final product
23		6-((2-chloro-4-methyl-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	--	283.2	--

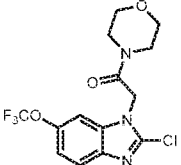
Int #	Structure	Compound Name	¹ H NMR	MS MH+	Separation Conditions
24 ^a		6-((2-chloro-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	--	299.2	Separated at final product
25 ^a		6-((2-chloro-6-fluoro-5-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	--	355.0	Separated at final product
26 ^a		6-((2,6-dichloro-5-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	--	371.0	Separated at final product
27 ^a		6-((2,6-dichloro-5-(trifluoromethoxy)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	--	387.0	Separated at final product
28		6-((2,5,6-trichloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	--	337.0	--
29		6-((2-chloro-5,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	--	305.1	--
30		2-chloro-1-((5-chloropyridin-2-yl)methyl)-1H-benzimidazole	--	278.2	--

Int #	Structure	Compound Name	¹ H NMR	MS MH+	Separation Conditions
31 ^a		6-((2-chloro-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	--	305.2	Separated at final product
32		6-((2,4-dichloro-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	--	321.0	--
33 ^a		2-chloro-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile	--	294.0	Separated at final product
34 ^a		6-((2-chloro-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	--	287.0	Separated at final product
35		6-((2-chloro-5,6-dimethyl-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	--	297.0	--
36		6-((2,4,6-trichloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	--	336.8	--
37 ^a		6-((2,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	--	304.0	Separated at final product
38		6-((2,4-dichloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	--	304.2	--

Int #	Structure	Compound Name	¹ H NMR	MS MH+	Separation Conditions
		yl)methyl)nicotinonitrile			
39 ^a		2-chloro-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile	--	294.2	Separated at final product
40 ^a		6-((2-chloro-6-methyl-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	--	283.2	Separated at final product
41 ^a		6-((2-chloro-5-fluoro-6-methyl-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	--	301.2	Separated at final product
42 ^a		5-((2-chloro-6-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)pyrazine-2-carbonitrile	--	338.2	Separated at final product
43		5-((2-chloro-5,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)pyrazine-2-carbonitrile	--	306.2	--
44 ^a		4-((2-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	--	268.2	--
45 ^a		4-((2-chloro-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	--	304.2	Separated at final product

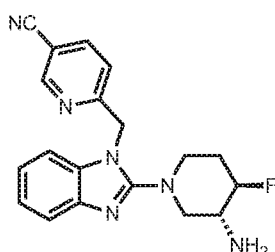
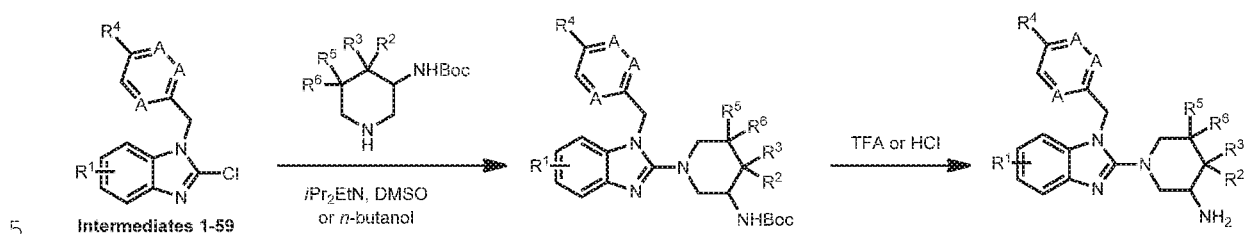
Int #	Structure	Compound Name	¹ H NMR	MS MH+	Separation Conditions
		yl)methyl)benz onitrile			
46 ^a		2-chloro-1-(4-cyanobenzyl)-1H-benzo[d]imidazole-6-carbonitrile	--	293.2	Separated at final product
47 ^a		2-((2-chloro-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)pyrimidine-5-carbonitrile	--	288.2	Separated at final product
48 ^a		2-chloro-6-fluoro-1-((5-methoxypyrimidin-2-yl)methyl)-1H-benzo[d]imidazole	--	293.2	Separated at final product
49 ^a		2-(2-chloro-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	--	324.2	Separated at final product
50 ^a		2-(2-chloro-6-methoxy-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	--	336.0	Separated at final product
51 ^a		2-(2-chloro-6-methoxy-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide	--	268.2	Separated at final product
52		2-(2-chloro-4-cyano-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	--	349.2	--

Int #	Structure	Compound Name	¹ H NMR	MS MH+	Separation Conditions
		(2,2,2-trifluoroethyl)acetamide			
53 ^a		2-(2-chloro-6-fluoro-4-methoxy-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	--	354.2	Separated at final product
54 ^a		6-((2-chloro-5-(trifluoromethyl)-3H-imidazo[4,5-b]pyridin-3-yl)methyl)nicotinonitrile	--	338.2	Separated at final product
55 ^a		1-(azetidin-1-yl)-2-(6-bromo-2-chloro-1H-benzo[d]imidazol-1-yl)ethanone	--	329.2	Separated at final product
56 ^a		2-(2-chloro-6-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)-1-morpholinoethanone	--	348.2	Separated at final product
57 ^a		2-(2,6-dichloro-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide	--	273.0	Separated at final product
58 ^a		2-(2-chloro-6-(trifluoromethoxy)-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide	--	322.2	Separated at final product

Int #	Structure	Compound Name	¹ H NMR	MS MH+	Separation Conditions
59 ^a		2-(2-chloro-6-(trifluoromethoxy)-1H-benzo[d]imidazol-1-yl)-1-morpholinoethanone	---	264.2	Separated at final product

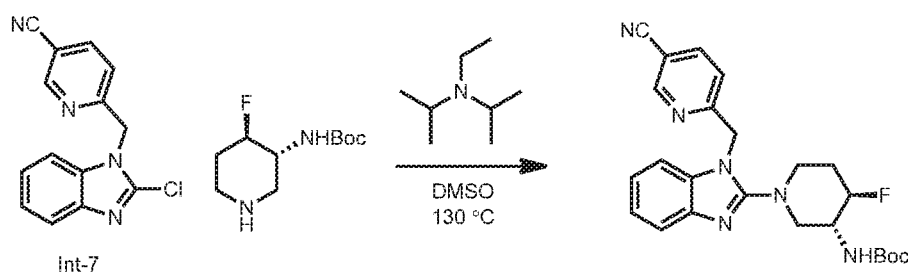
[a] Mixture of isomers formed through non-selective benzylation that were separated at final product or penultimate intermediate

Scheme 8. Advancement of alkylated intermediates to final products



Example 38: 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile

10



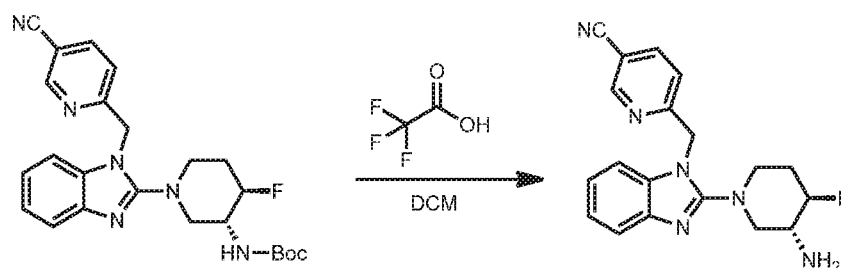
Step 1. tert-butyl ((3R,4R)-1-(1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl)carbamate

15 1,1'-dimethyltriethylamine (1.300 ml, 7.44 mmol), tert-butyl ((3R,4R)-4-fluoropiperidin-3-yl)carbamate (0.975 g, 4.47 mmol), 6-(2-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile (**Intermediate 7**, 1 g,

3.72 mmol), and dimethyl sulfoxide (7.44 ml) were combined in a flask and heated to 130 °C for 36 hours. The mixture was cooled, poured into water, then extracted with EtOAc (3X). The organics were combined, dried over Na₂SO₄, filtered, and concentrated. The crude material was loaded onto an 80g RediSep ISCO cartridge, eluting with 10-50% EtOAc in heptanes to provide tert-butyl ((3R,4R)-1-(1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl)carbamate as a light orange foam. MS (ESI, pos. ion) m/z: 451.2 [M+1]

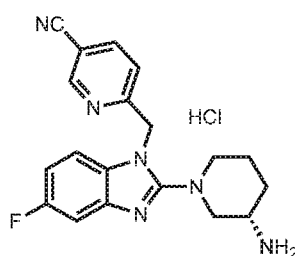
Note: n-butanol is a competent substitute for DMSO. Difluorinated piperidines required heating to 150 C.

10 Boc Deprotection Procedure with TFA (Procedure B)

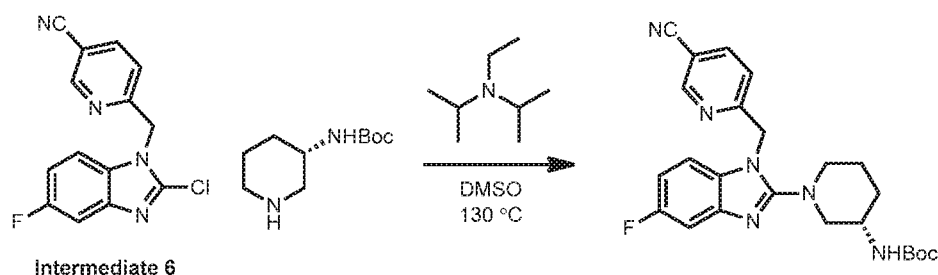


Step 2. 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile (Example 43)

Tert-butyl ((3R,4R)-1-(1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl)carbamate (1.31 g, 2.91 mmol, 1 equiv) was dissolved in DCM (10 mL) and slowly dripped into a flask of cooled (0 °C) TFA (~10 mL). After 1 hour, deprotection was complete. The mixture was poured onto an SCX column (pre-wetted with MeOH), flushed with MeOH, then eluted with methanolic ammonia. The methanolic ammonia was concentrated, and the light orange oil redissolved in MeCN/water, frozen, and lyophilized to provide the title compound as a light yellow solid. ¹H NMR (500 MHz, MeOD) δ 8.81-8.92 (m, 1 H), 8.23 (dd, J=8.30, 2.08 Hz, 1 H), 7.49-7.66 (m, 2H), 7.17-7.39 (m, 3H), 5.64 (s, 2H), 4.69-4.86 (m, 1H), 3.92-4.06 (m, 1H), 3.61-3.79 (m, 2H), 3.20-3.32 (m, 2H), 2.24-2.41 (m, 1H), 1.92-2.14 (m, 1H). (ESI, pos. ion) m/z: 351.2 [M+1]



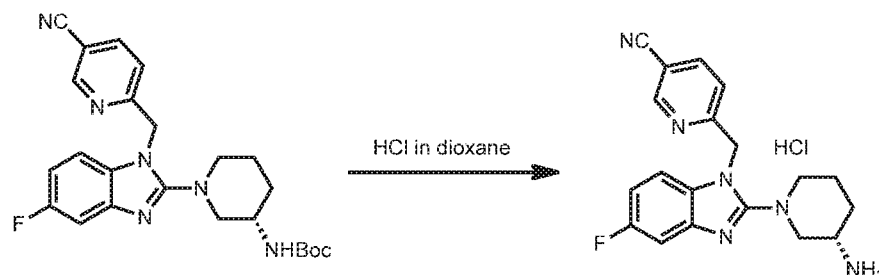
Example 45: 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride



Step 1. (S)-tert-butyl (1-((5-cyanopyridin-2-yl)methyl)-5-fluoro-1H-benzo[d]imidazol-2-yl)piperidin-3-ylcarbamate

To a suspension of 6-((2-chloro-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile (150 mg, 0.523 mmol) and hunig's base (137 μ l, 0.785 mmol) in 1-butanol (2093 μ l) was added (S)-tert-butyl piperidin-3-ylcarbamate (115 mg, 0.576 mmol). The reaction was stirred at 130 °C overnight. After 24 hours, the reaction mixture was concentrated and purified by column chromatography, eluting with 20-100% ethyl acetate in heptane, to provide the title compound as an off white solid. (ESI, pos. ion) m/z: 451.2 [M+1]

Boc Deprotection with HCl (Procedure A)

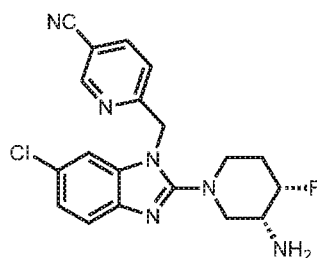


(S)-6-((2-(3-aminopiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride (Example 51)

Step 2. (S)-tert-butyl (1-((5-cyanopyridin-2-yl)methyl)-5-fluoro-1H-benzo[d]imidazol-2-yl)piperidin-3-ylcarbamate (77 mg) was dissolved in dioxane (2 mL), and 4 N HCl in dioxane (585 μ L, 2.340 mmol) was added. The reaction was stirred at ambient temperature. After 16 hours, LC/MS analysis showed the reaction was complete. The reaction mixture was concentrated in vacuo to provide the title compound as an off white solid. ^1H NMR (400 MHz, d_6 -DMSO) δ 8.94 (s, 1H), 8.48 (br s, 2H), 8.40 (dd, J =2.18, 8.19 Hz, 1H), 7.77 (d, J =8.19 Hz, 1H), 7.40 (dd, J =2.85, 8.66 Hz, 2H), 7.14 (dt, J =2.38, 9.33 Hz, 1H), 5.65-5.84 (m, 2H), 3.89 (br d, J =10.57 Hz, 1H), 3.28-3.52 (m, 3H), 3.18 (br t, J =9.80 Hz, 1H), 1.94-2.02 (m, 1H), 1.81-1.93 (m, 1H), 1.47-1.72 (m, 2H). (ESI, pos. ion) m/z: 351.0 [M+1].

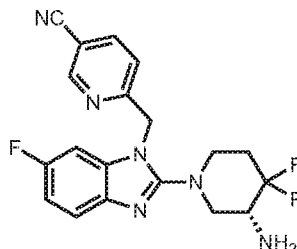
Note: The HCl salt was sometimes converted to a free base form using an aqueous work up or using ion exchange chromatography. Isolation of salt or free base is specified in table.

The following compounds were made in a manner analogous to that outlined above:



Example 8: 6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile was synthesized on a 1 mmol scale following a procedure analogous to sequence outlined above using the TFA Boc deprotection (procedure B). It was separated at the Boc intermediate: Chiralcel OD-H, 25% IPA, peak 1. ¹H NMR (500 MHz, MeOD) δ 8.86 (d, J=1.30 Hz, 1H), 8.14-8.20 (m, 1H), 7.47 (d, J=8.56 Hz, 1H), 7.44 (d, J=8.30 Hz, 1H), 7.23 (d, J=2.08 Hz, 1H), 7.19 (dd, J=1.95, 8.43 Hz, 1H), 5.53 (s, 2H), 4.33-4.50 (m, 1H), 3.53-3.61 (m, 1H), 3.43-3.50 (m, 1H), 3.02-3.20 (m, 2H), 2.95 (dd, J=8.69, 12.33 Hz, 1H), 2.12-2.24 (m, 1H), 1.82-1.94 (m, 1H). (ESI, pos. ion) m/z: 387.2 [M+1].



Example 93: (R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile

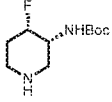
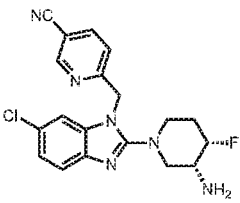
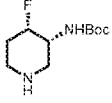
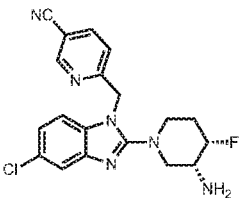
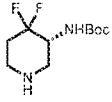
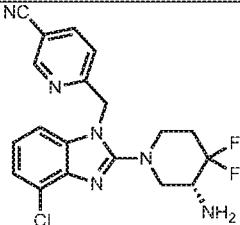
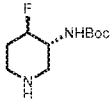
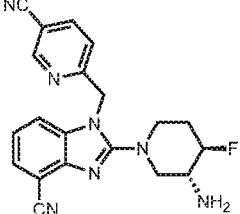
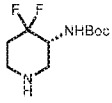
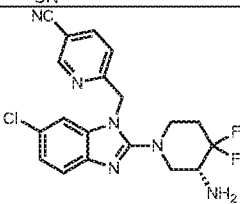
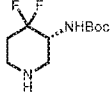
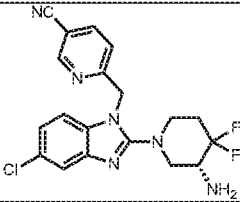
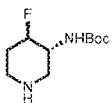
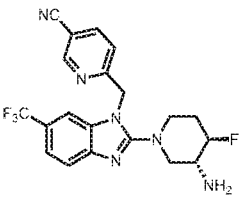
(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile was synthesized on a 1.9 mmol scale following a procedure analogous to the sequence outlines above, using the TFA Boc deprotection (procedure B). It was separated at the chlorobenzimidazole intermediate (YMC Amyose SA, Methanol THF (70:30) 40 %; peak 1). ¹H NMR (500 MHz, MeOD) δ 8.84 (d, J=1.82 Hz, 1H), 8.15 (dd, J=2.08, 8.30 Hz, 1H), 7.40-7.52 (m, 2H), 6.91-7.00 (m, 2H), 5.47-5.62 (m, 2H), 3.34-3.54 (m, 2H), 3.08-3.28 (m, 3H), 2.21-2.36 (m, 1H), 2.00-2.21 (m, 1H). (ESI, pos. ion) m/z: 351.0 [M+1].

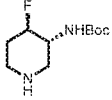
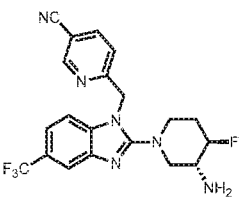
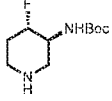
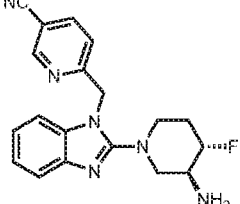
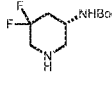
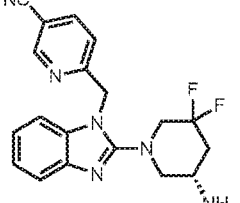
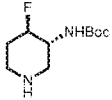
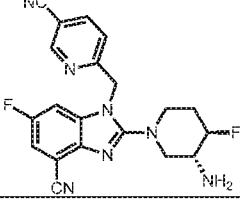
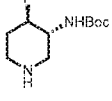
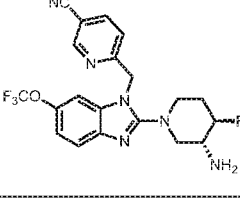
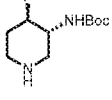
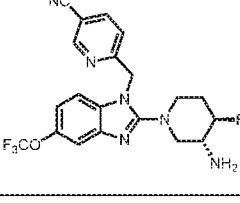
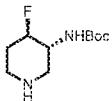
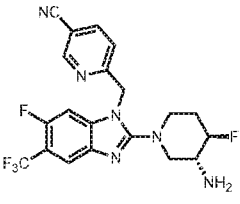
The examples in Table 2 were synthesized using a sequence analogous to that used to synthesize **Examples 38, 45, 8, and 88** and general Scheme 8 above:

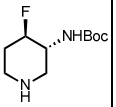
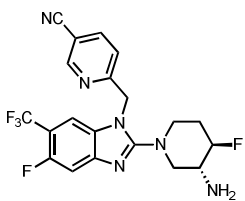
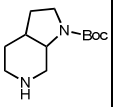
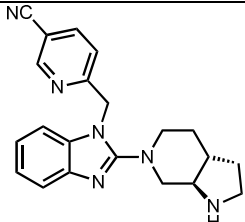
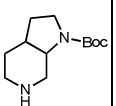
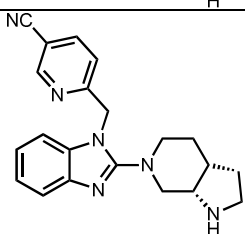
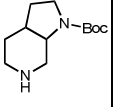
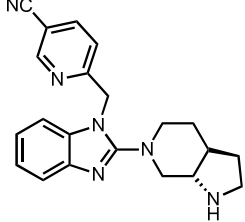
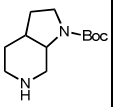
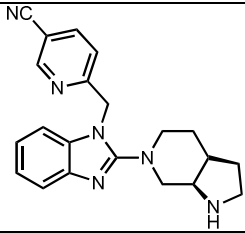
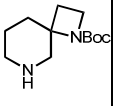
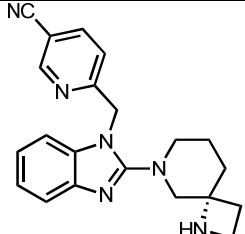
Table 2. Compounds made following Scheme 8

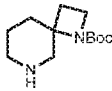
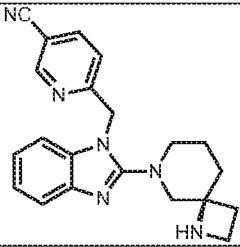
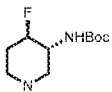
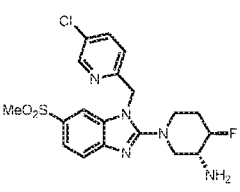
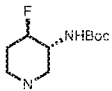
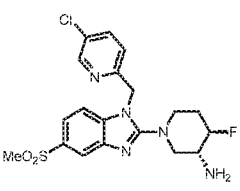
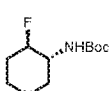
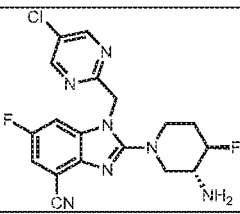
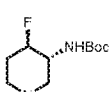
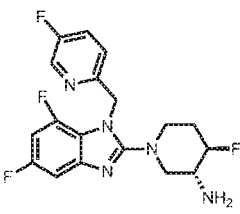
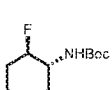
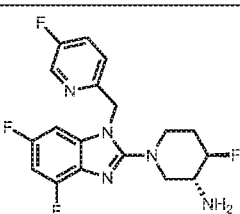
Boc Deprotection procedure: A = HCl procedure, B = TFA procedure

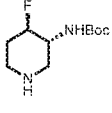
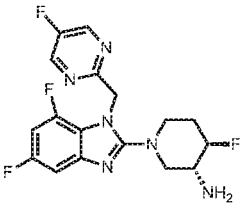
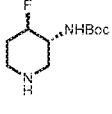
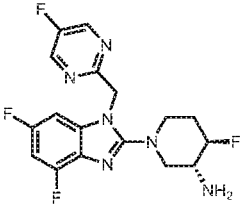
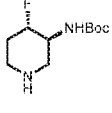
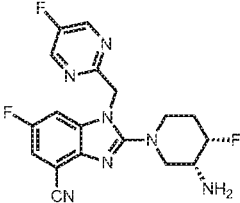
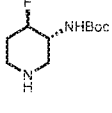
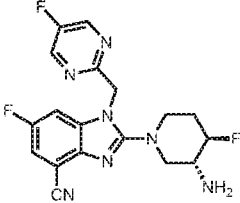
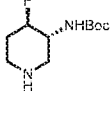
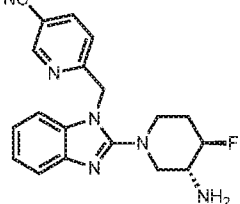
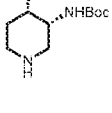
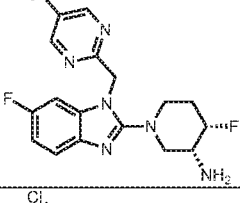
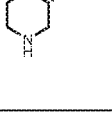
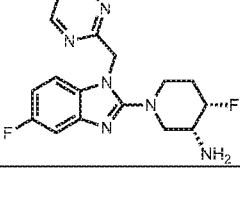
Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
1	37		B		(S)-6-((2-(3-aminopiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	367.0
2	37		B		(S)-6-((2-(3-aminopiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	367.0
3	38		B		(S)-6-((2-(3-aminopiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	367.0
4	38		B		6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	385.0
5	38		B		6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	385.0
6	37		B		6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	385.0
7	37		B		6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	385.0

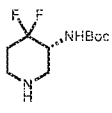
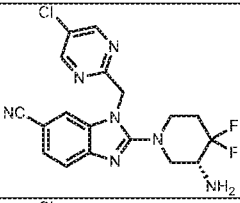
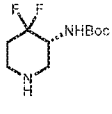
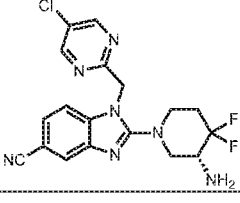
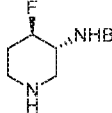
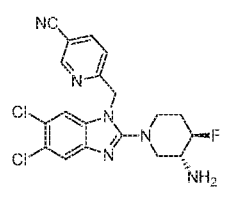
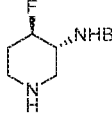
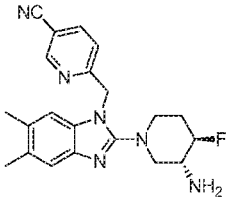
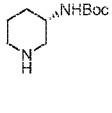
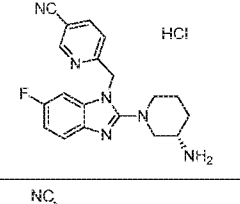
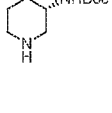
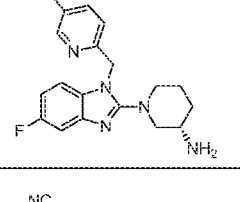
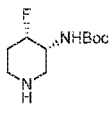
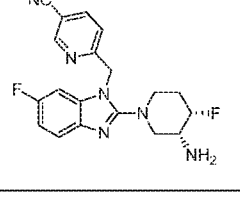
Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
8	37		B		6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	385.0
9	37		B		6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	385.0
10	38		B		(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	403.0
11	10		B		2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-4-carbonitrile	376.0
12	37		B		(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	403.0
13	37		B		(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	403.0
14	19		B		6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	419.0

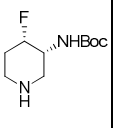
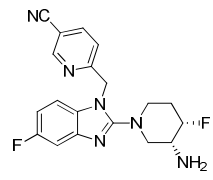
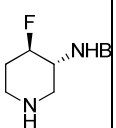
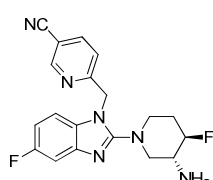
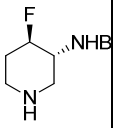
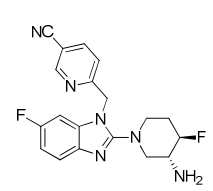
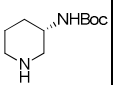
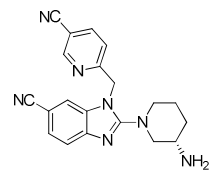
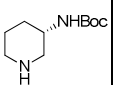
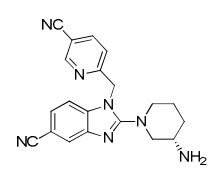
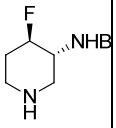
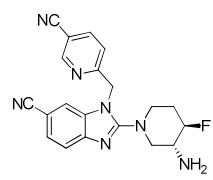
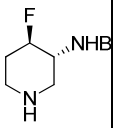
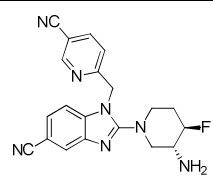
Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
15	19		B		6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	419.0
16	7		B		6-((2-((3S,4S)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	351.2
17	7		B		(S)-6-((2-(5-amino-3,3-difluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	369.2
18	11		B		2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazole-4-carbonitrile	394.4
19	12		B		6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-(trifluoromethoxy)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	435.4
20	12		B		6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(trifluoromethoxy)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	435.4
21	25		B		6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-5-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	437.0

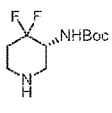
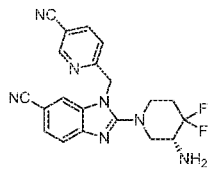
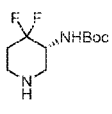
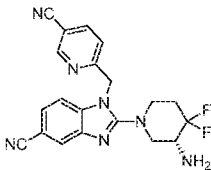
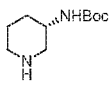
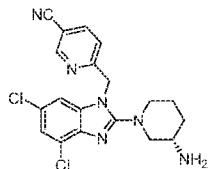
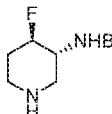
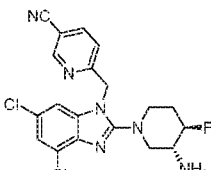
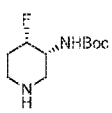
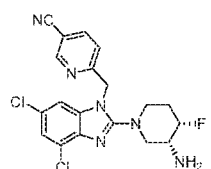
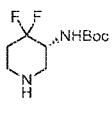
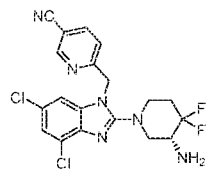
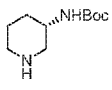
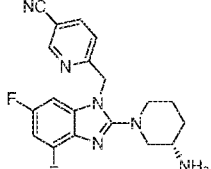
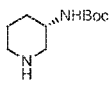
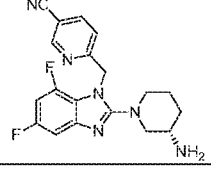
Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
22	25		B		6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-6-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	437.0
23	7		B		6-((2-((3aR,7aR)-hexahydro-1H-pyrrolo[2,3-c]pyridin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	359.2
24	7		B		6-((2-((3aR,7aS)-hexahydro-1H-pyrrolo[2,3-c]pyridin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	359.2
25	7		B		6-((2-((3aS,7aS)-hexahydro-1H-pyrrolo[2,3-c]pyridin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	359.2
26	7		B		6-((2-((3aS,7aR)-hexahydro-1H-pyrrolo[2,3-c]pyridin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	359.2
27	7		B		(R)-6-((2-(1,6-diazaspiro[3.5]nonan-6-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	359.2

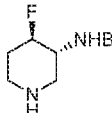
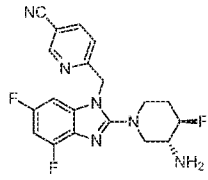
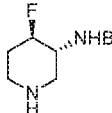
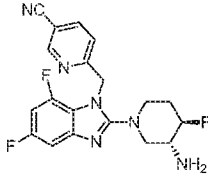
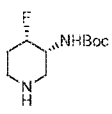
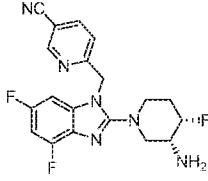
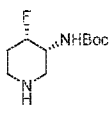
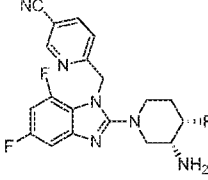
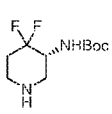
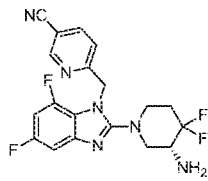
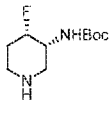
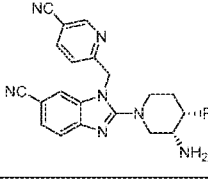
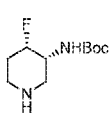
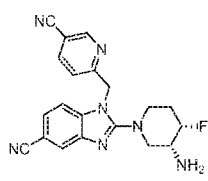
Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
28	7		B		(S)-6-((2-(1,6-diazaspiro[3.5]nonan-6-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	359.2
29	13		B		(3R,4R)-1-(1-((5-chloropyridin-2-yl)methyl)-6-(methylsulfonyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	438.0
30	13		B		(3R,4R)-1-(1-((5-chloropyridin-2-yl)methyl)-5-(methylsulfonyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	438.0
31	14		B		2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazole-4-carbonitrile	404.0
32	15		B		(3R,4R)-1-(5,7-difluoro-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	380.0
33	15		B		(3R,4R)-1-(4,6-difluoro-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	380.0

Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
34	16		B		(3R,4R)-1-((5,7-difluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	381.2
35	16		B		(3R,4R)-1-((4,6-difluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	381.2
36	18		B		2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-4-carbonitrile	338.0
37	18		B		2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-4-carbonitrile	338.0
38	7		B		6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	351.2
39	17		B		(3R,4S)-1-((1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	379.2
40	17		B		(3R,4S)-1-((1-((5-chloropyrimidin-2-yl)methyl)-5-fluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	379.2

Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
41	39		B		(R)-2-(3-amino-4,4-difluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile	404.2
42	39		B		(R)-2-(3-amino-4,4-difluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile	404.2
43	28		B		6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	419.0
44	35		B		tert-butyl ((3R,4R)-1-(1-((5-cyanopyridin-2-yl)methyl)-5,6-dimethyl-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl)carbamate	379.2
45	34		A		(S)-6-((2-(3-aminopiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride	351.0
46	34		A		(S)-6-((2-(3-aminopiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride	351.0
47	34		A		6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride	369.0

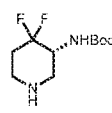
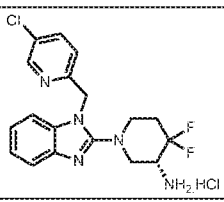
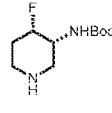
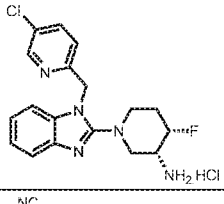
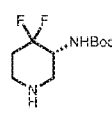
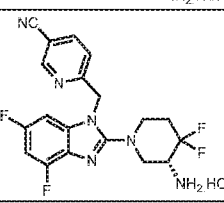
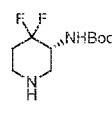
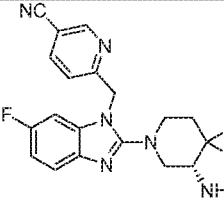
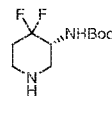
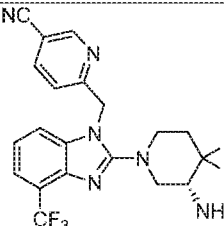
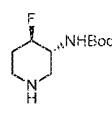
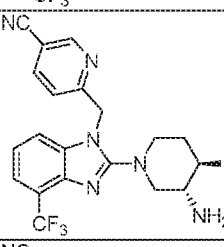
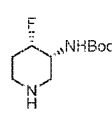
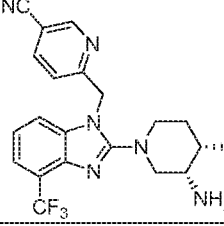
Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
48	34		A		6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride	369.0
49	34		A		6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride	369.0
50	5		A		6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride	369.0
51	33		B		(S)-2-(3-aminopiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile	358.0
52	33		B		(S)-2-(3-aminopiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile	358.0
53	33		B		2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile	376.0
54	33		B		2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile	376.0

Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
55	33		B		(R)-2-(3-amino-4,4-difluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile	394.0
56	33		B		(R)-2-(3-amino-4,4-difluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile	394.0
57	36		B		(S)-6-((2-(3-aminopiperidin-1-yl)-4,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	401.0
58	36		B		6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	419.0
59	36		B		6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-4,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	419.0
60	36		B		(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-4,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	437.0
61	31		B		(S)-6-((2-(3-aminopiperidin-1-yl)-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	369.0
62	31		B		(S)-6-((2-(3-aminopiperidin-1-yl)-5,7-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	369.0

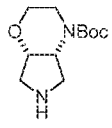
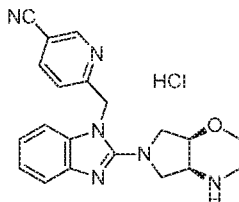
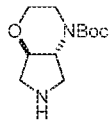
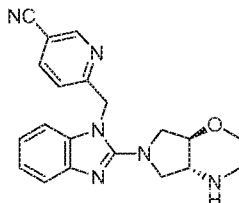
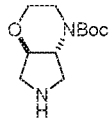
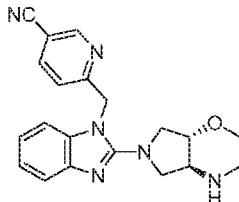
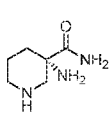
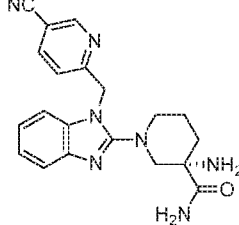
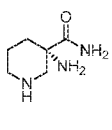
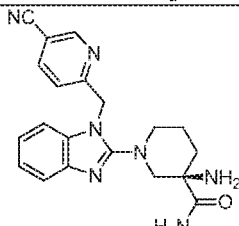
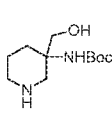
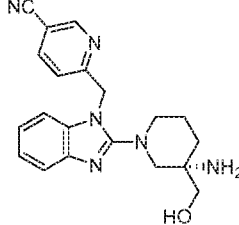
Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
					yl)methyl)nicotinonitrile	
63	31		B		6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	387.0
64	31		B		6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,7-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	387.0
65	31		B		6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	387.0
66	31		B		6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5,7-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	387.0
67	31		B		(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-5,7-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	405.0
68	33		B		2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile	376.0
69	33		B		2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile	376.0

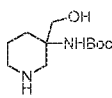
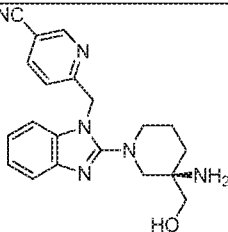
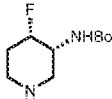
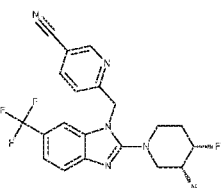
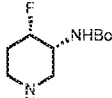
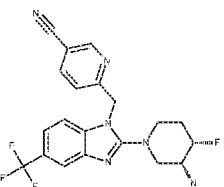
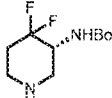
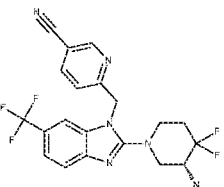
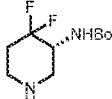
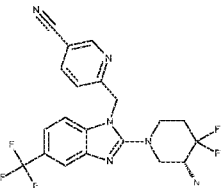
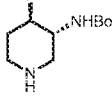
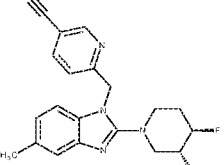
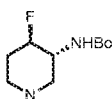
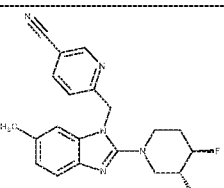
Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
70	7		A		(S)-6-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	333.0
71	34		A		(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride	387.0
72	29		B		6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	387.0
73	7		A		6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	351.0
74	7		A		6-((2-((1R,5S)-1-(aminomethyl)-3-azabicyclo[3.1.0]hexan-3-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride	345.2
75	7		A		6-((2-((1S,5R)-1-(aminomethyl)-3-azabicyclo[3.1.0]hexan-3-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride	345.2
76	7		A		6-((2-((3aR,4R,6aS)-4-amino-1,2,3,4,5,6-hexahydrocyclopenta[c]pyrrol-2(1H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride	359.0

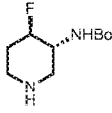
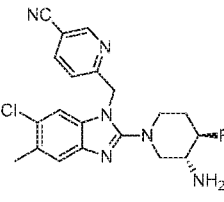
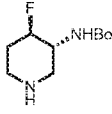
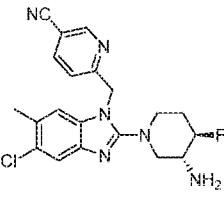
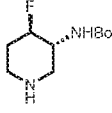
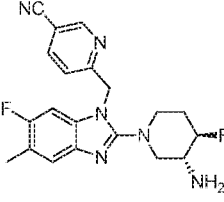
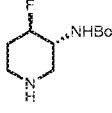
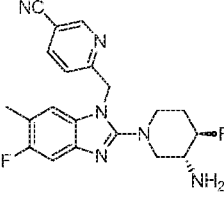
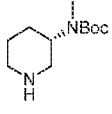
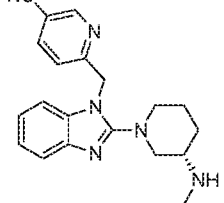
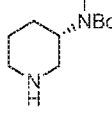
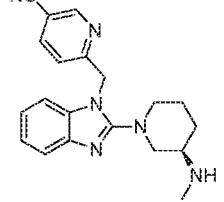
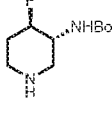
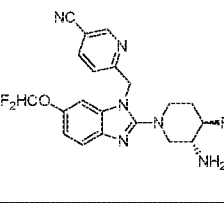
Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
77	7		A		6-((2-((3aS,4S,6aR)-4-aminohexahydrocyclopenta[c]pyrrol-2(1H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride	359.0
78	7		A		6-((2-((3aR,4S,6aS)-4-aminohexahydrocyclopenta[c]pyrrol-2(1H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride	359.2
79	7		A		6-((2-((3aS,4R,6aR)-4-aminohexahydrocyclopenta[c]pyrrol-2(1H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride	359.2
80	7		A		(R)-6-((2-(3-(aminomethyl)pyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride	333.2
81	7		A		(S)-6-((2-(3-(aminomethyl)pyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride	333.2
82	28		B		6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride	419.2
83	29		B		6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride	387.2
84	29		B		(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride	405.2

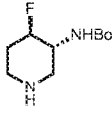
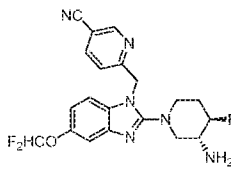
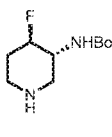
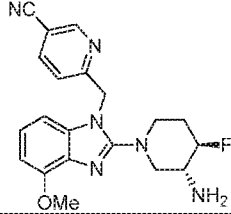
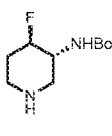
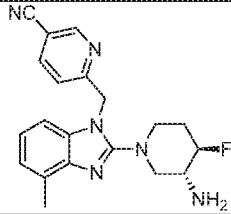
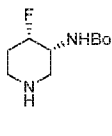
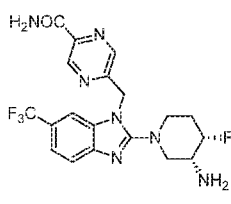
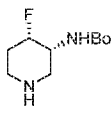
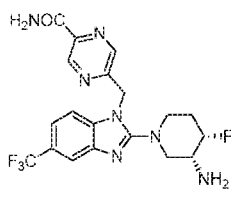
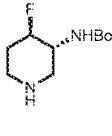
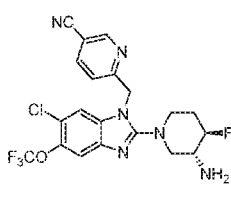
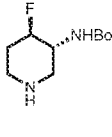
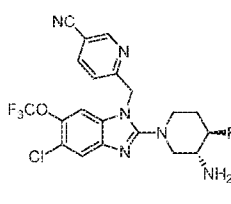
Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
					yl)methyl)nicotinonitrile hydrochloride	
85	30		B		(R)-1-(1-((5-chloropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4,4-difluoropiperidin-3-amine hydrochloride	378.2
86	30		B		(3R,4S)-1-(1-((5-chloropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride	360.2
87	31		B		(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride	405.2
88	5		B		(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	387.2
89	8		A		(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-4-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	437.2
90	8		A		6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	419.2
91	8		A		6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-4-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	419.2

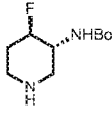
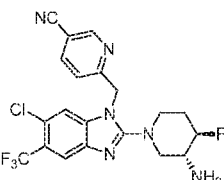
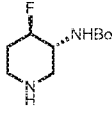
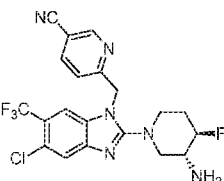
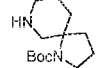
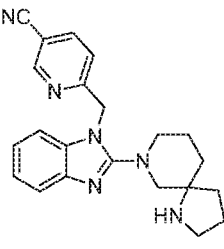
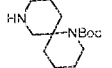
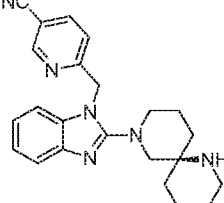
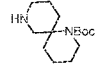
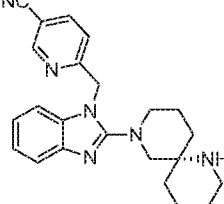
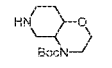
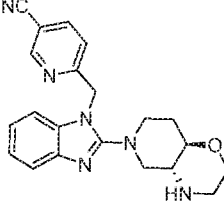
Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
92	9		A		6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-3H-imidazo[4,5-b]pyridin-3-yl)methyl)nicotinonitrile	386.2
93	9		A		6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)nicotinonitrile	386.0
94	9		A ^b		6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)-N-(tert-butyl)nicotinamide	460.2
95	7		A		6-((2-((3R,4R)-3-amino-4-hydroxypiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	349.2
96	7		A		6-((2-((3S,4S)-3-amino-4-hydroxypiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	349.2
97	7		A		6-((2-(2,6-diazaspiro[3.4]octan-6-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	345.2
98	7		A		6-((2-((4aR,7aS)-hexahydropyrrolo[3,4-b][1,4]oxazin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride	361.2

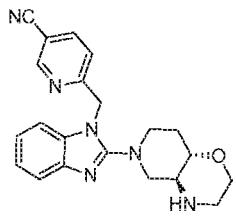
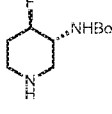
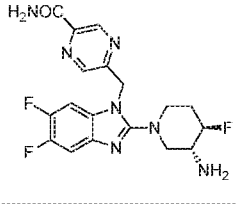
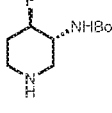
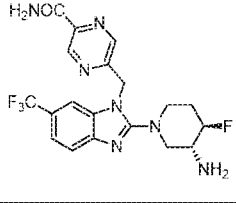
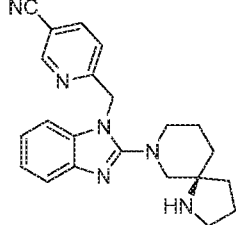
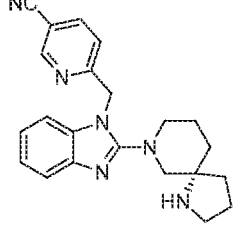
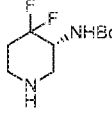
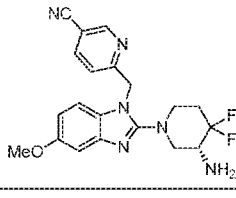
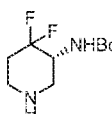
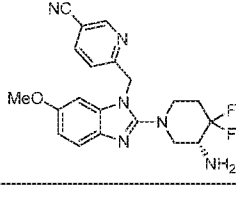
Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
99	7		A		6-((2-((4aS,7aR)-hexahydropyrrolo[3,4-b][1,4]oxazin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride	361.2
100	7		A		6-((2-((4aR,7aR)-hexahydropyrrolo[3,4-b][1,4]oxazin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	361.2
101	7		A		6-((2-((4aS,7aS)-hexahydropyrrolo[3,4-b][1,4]oxazin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	361.2
102	7		--		(S)-3-amino-1-(1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidine-3-carboxamide	376.2
103	7		--		(R)-3-amino-1-(1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidine-3-carboxamide	376.2
104	7		A		(S)-6-((2-(3-amino-3-(hydroxymethyl)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	363.2

Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
105	7		A		(R)-6-((2-(3-amino-3-(hydroxymethyl)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	363.2
106	19		B		6-((2-((3R,4S)-3-amino-4-fluoro-1-piperidinyl)-6-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	419.2
107	19		B		6-((2-((3R,4S)-3-amino-4-fluoro-1-piperidinyl)-5-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	419.2
108	19		B		6-((2-((3R)-3-amino-4,4-difluoro-1-piperidinyl)-6-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	437.2
109	19		B		6-((2-((3R)-3-amino-4,4-difluoro-1-piperidinyl)-5-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	437.2
110	40		B		6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5-methyl-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	365.2
111	40		B		6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-6-methyl-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	365.2

Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
112	20		B		6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-6-chloro-5-methyl-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	399.1
113	20		B		6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5-chloro-6-methyl-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	399.1
114	41		B		6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-6-fluoro-5-methyl-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	383.1
115	41		B		6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5-fluoro-6-methyl-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	383.1
116	7		B		6-((2-((3S)-3-(methylamino)-1-piperidinyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	347.2
117	7		B		6-((2-((3R)-3-(methylamino)-1-piperidinyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	347.2
118	21		B		6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-6-(difluoromethoxy)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	417.2

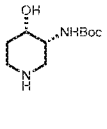
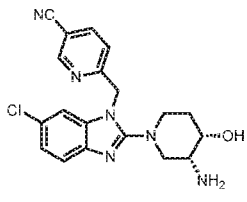
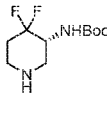
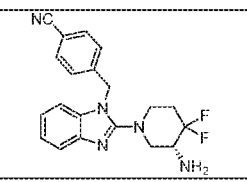
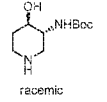
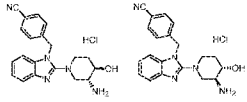
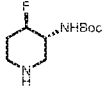
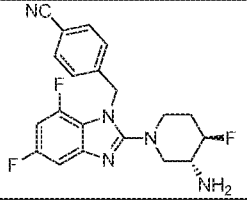
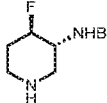
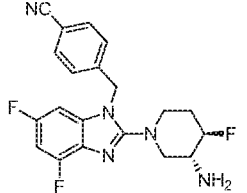
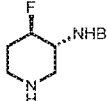
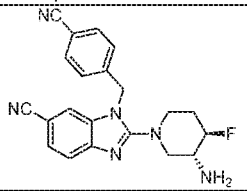
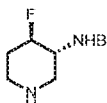
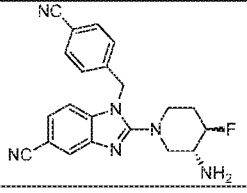
Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
119	21		B		6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5-(difluoromethoxy)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	417.2
120	22		B		6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-4-methoxy-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	381.2
121	23		B		6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-4-methyl-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	365.2
122 a	42		B		5-((2-((3R,4S)-3-amino-4-fluoro-1-piperidinyl)-6-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-2-pyrazinecarboxamide	438.2
123 a	42		B		5-((2-((3R,4S)-3-amino-4-fluoro-1-piperidinyl)-5-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-2-pyrazinecarboxamide	438.2
124	27		B		6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-6-chloro-5-(trifluoromethoxy)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	469.2
125	27		B		6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5-chloro-6-(trifluoromethoxy)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	469.2

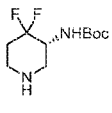
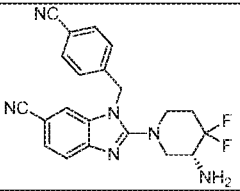
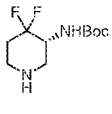
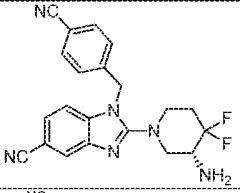
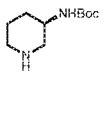
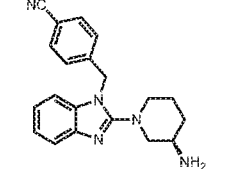
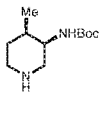
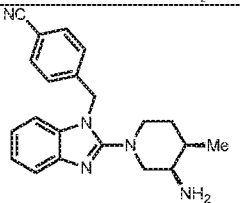
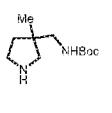
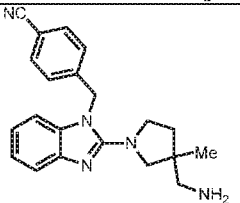
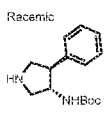
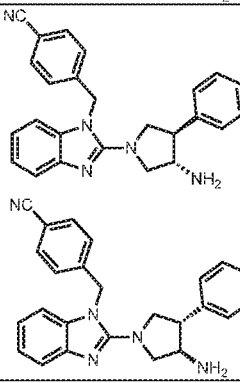
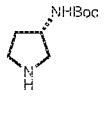
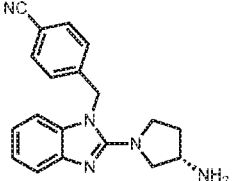
Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
126	26		B		6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-6-chloro-5-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	453.2
127	26		B		6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5-chloro-6-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	453.2
128	7		B		6-((2-((5R)-1,7-diazaspiro[4.5]decan-7-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	373.2
129	7		B		6-((2-((6R)-1,8-diazaspiro[5.5]undecan-8-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	387.2
130	7		B		6-((2-((6S)-1,8-diazaspiro[5.5]undecan-8-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	387.2
131	7		B		6-((2-((4aR,8aR)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	375.2

Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
132	7		B		6-((2-((4aS,8aS)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	375.2
133 a	43		B		5-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)-2-pyrazinecarboxamide	406.2
134 a	42		B		5-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-6-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-2-pyrazinecarboxamide	438.2
135	7		B		6-((2-((5R)-1,7-diazaspiro[4.5]decan-7-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	373.2
136	7		B		6-((2-((5S)-1,7-diazaspiro[4.5]decan-7-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	373.2
137	24		B		6-((2-((3R)-3-amino-4,4-difluoro-1-piperidinyl)-5-methoxy-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	399.2
138	24		B		6-((2-((3R)-3-amino-4,4-difluoro-1-piperidinyl)-6-methoxy-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	399.2

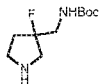
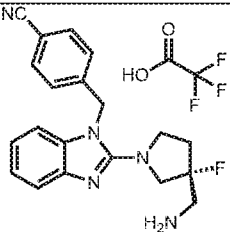
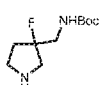
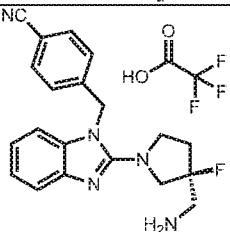
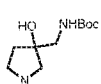
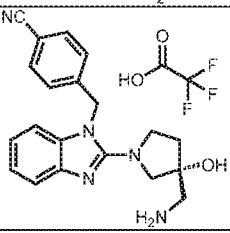
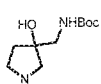
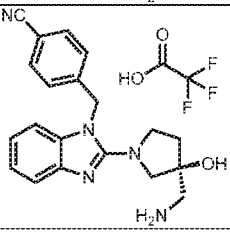
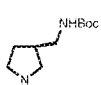
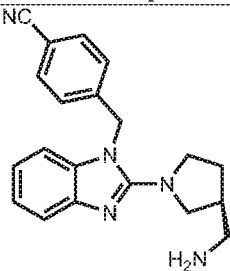
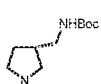
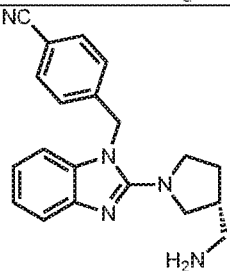
Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
139	19		B		6-((2-((3S)-3-(methylamino)-1-piperidinyl)-6-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	415.2
140	19		B		6-((2-((3S)-3-(methylamino)-1-piperidinyl)-5-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	415.2
141	7		B		6-((2-((3S)-3-amino-3-methyl-1-piperidinyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile	347.2
142	24		B		(S)-6-((2-(3-aminopiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile 2,2,2-trifluoroacetate	363.2
143	24		B		(S)-6-((2-(3-aminopiperidin-1-yl)-5-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile 2,2,2-trifluoroacetate	363.2
144	32		B		6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4-chloro-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile 2,2,2-trifluoroacetate	403.0
145	24		A		6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride	381.0

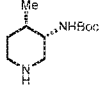
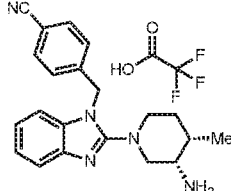
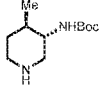
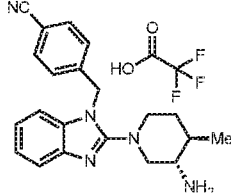
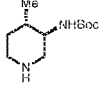
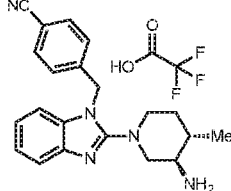
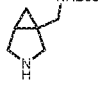
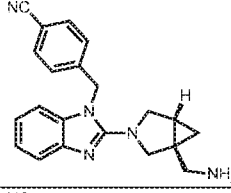
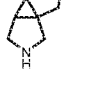
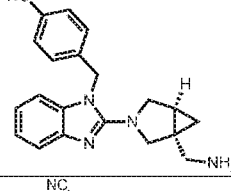
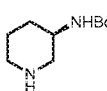
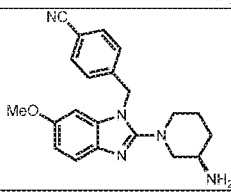
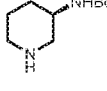
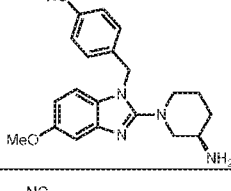
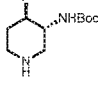
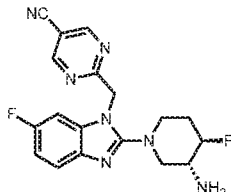
Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
146	24		A		6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride	381.0
147	24		A		6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride	381.0
148	24		A		6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride	381.0
149	14		B		2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazole-4-carbonitrile	404.0
150	14		B		(R)-2-(3-amino-4,4-difluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-5-fluoro-1H-benzo[d]imidazole-7-carbonitrile	422.0
151	14		B		(R)-2-(3-amino-4,4-difluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazole-4-carbonitrile	422.0
152	3		B		6-((2-((3R,4R)-3-amino-4-hydroxypiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	383.2

Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
153	3		B		6-((2-((3R,4S)-3-amino-4-hydroxypiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	383.2
154	44		B		(R)-4-((2-(3-amino-4,4-difluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	368.2
155	44		A		4-((2-((3R,4R)-3-amino-4-hydroxypiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile compound with 4-((2-((3S,4S)-3-amino-4-hydroxypiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile (1:1) dihydrochloride	346.2
156	45		B		4-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,7-difluoro-1H-benzimidazol-1-yl)methyl)benzonitrile	386.2
157	45		B		4-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-4,6-difluoro-1H-benzimidazol-1-yl)methyl)benzonitrile	386.2
158	46		B		2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-1-(4-cyanobenzyl)-1H-benzimidazole-6-carbonitrile	375.2
159	46		B		2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-1-(4-cyanobenzyl)-1H-benzimidazole-5-carbonitrile	375.2

Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
160	46		B		2-((3R)-3-amino-4,4-difluoro-1-piperidinyl)-1-(4-cyanobenzyl)-1H-benzimidazole-6-carbonitrile	393.3
161	46		B		2-((3R)-3-amino-4,4-difluoro-1-piperidinyl)-1-(4-cyanobenzyl)-1H-benzimidazole-5-carbonitrile	393.3
162	44		A		(R)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	332.2
163	44		A		4-((2-((3R,4R)-3-amino-4-methylpiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	346.0
164 c	44		A		4-((2-(3-(aminomethyl)-3-methylpyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	346.2
165	44		A		4-((2-((3S,4R)-3-amino-4-phenylpyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile & 4-((2-((3R,4S)-3-amino-4-phenylpyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	394.2
166	44		A		(S)-4-((2-(3-aminopyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	318.2

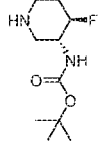
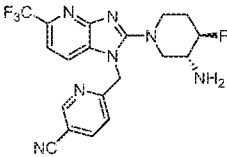
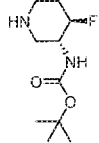
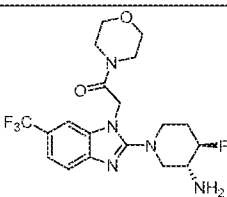
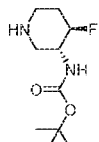
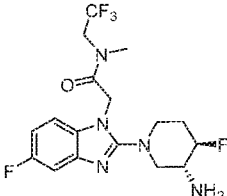
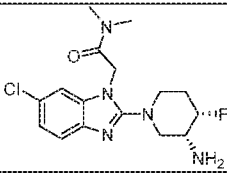
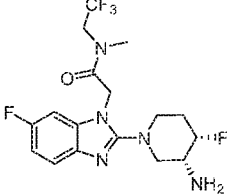
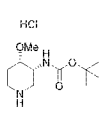
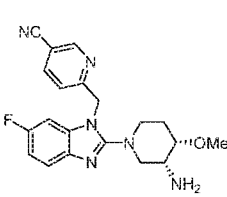
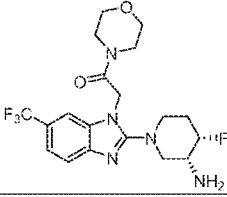
Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
167	44		A		(S)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	332.2
168	44		A		4-((2-(6-amino-2-azaspiro[4.4]nonan-2-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	32.0
169	44		A		4-((2-(4-aminohexahydrocyclopenta[c]pyrrol-2(1H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	358.2
170	44		A		4-((2-((3S,4S)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	350.2
171	44		A		4-((2-((3S,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	350.2
172	44		A		4-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	350.2
173	44		A		4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	350.2

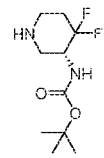
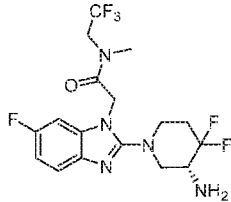
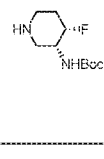
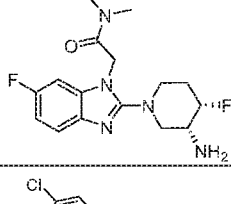
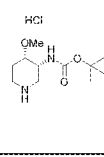
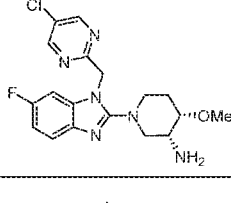
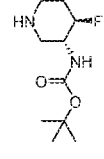
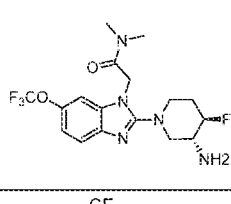
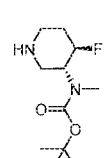
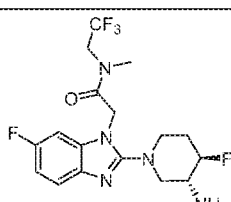
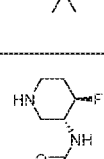
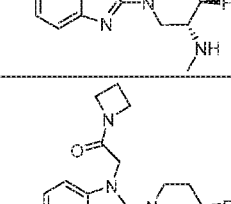
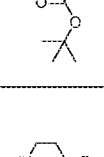
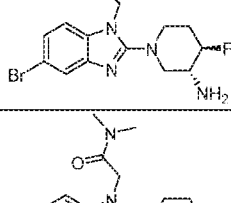
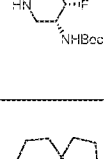
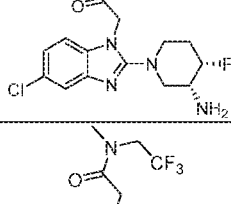
Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
174	44		B		(R)-4-((2-(3-(4-cyanophenyl)-1H-benzotriazol-1-yl)methyl)-2,2,2-trifluoroacetyl)pyrrolidine-1-yl)-1H-benzotriazole	350.0
175	44		B		(S)-4-((2-(3-(4-cyanophenyl)-1H-benzotriazol-1-yl)methyl)-2,2,2-trifluoroacetyl)pyrrolidine-1-yl)-1H-benzotriazole	350.0
176	44		B		(R)-4-((2-(3-(4-cyanophenyl)-1H-benzotriazol-1-yl)methyl)-2,2,2-trifluoroacetyl)pyrrolidine-1-yl)-1H-benzotriazole	348.2
177	44		B		(S)-4-((2-(3-(4-cyanophenyl)-1H-benzotriazol-1-yl)methyl)-2,2,2-trifluoroacetyl)pyrrolidine-1-yl)-1H-benzotriazole	348.2
178	44		A		(S)-4-((2-(3-(4-cyanophenyl)-1H-benzotriazol-1-yl)methyl)pyrrolidin-1-yl)-1H-benzotriazole Molecular Weight: 331.41	332.2
179	44		A		(R)-4-((2-(3-(4-cyanophenyl)-1H-benzotriazol-1-yl)methyl)pyrrolidin-1-yl)-1H-benzotriazole Molecular Weight: 331.41	332.2

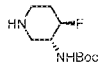
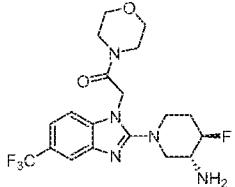
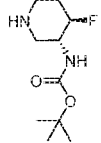
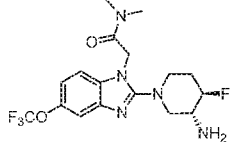
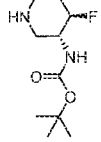
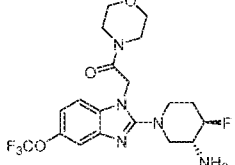
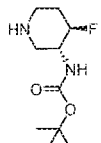
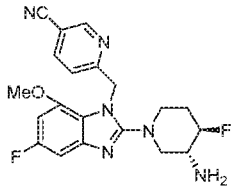
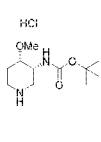
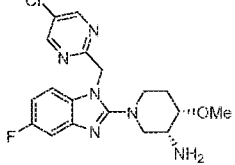
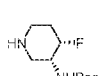
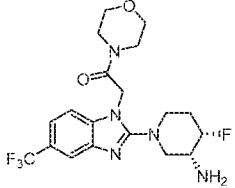
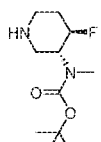
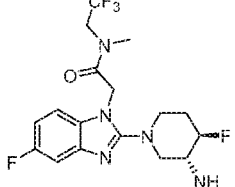
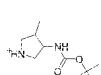
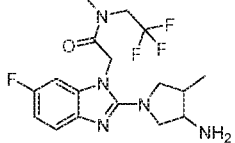
Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
180	44		B		4-((2-((3S,4S)-3-amino-4-methylpiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile 2,2,2-trifluoroacetate	346.2
181	44		B		4-((2-((3S,4R)-3-amino-4-methylpiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile 2,2,2-trifluoroacetate	346.2
182	44		B		4-((2-((3R,4S)-3-amino-4-methylpiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile 2,2,2-trifluoroacetate	346.2
183	44		A		4-((2-((1S,5R)-1-(aminomethyl)-3-azabicyclo[3.1.0]hexan-3-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	344.2
184	44		A		4-((2-((1R,5S)-1-(aminomethyl)-3-azabicyclo[3.1.0]hexan-3-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	344.2
185	44		A		(R)-4-((2-(3-aminopiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	362.2
186	44		A		(R)-4-((2-(3-aminopiperidin-1-yl)-5-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	362.2
442	47		B		2-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)pyrimidine-5-carbonitrile	370.2

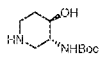
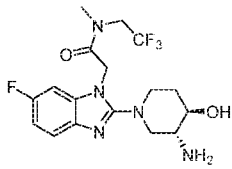
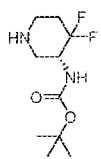
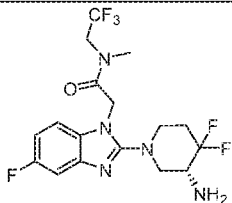
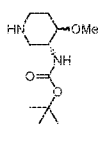
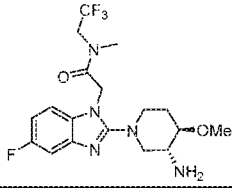
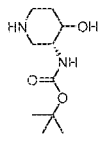
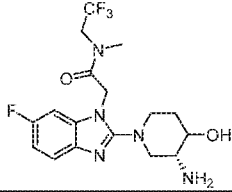
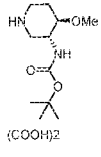
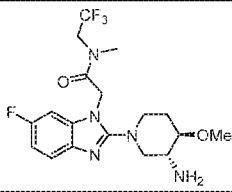
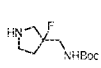
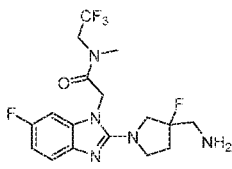
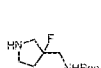
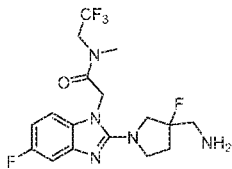
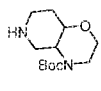
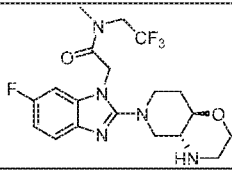
Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
443	47		B		2-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)pyrimidine-5-carbonitrile	370.2
444	48		B		(3R,4R)-4-fluoro-1-((5-methoxypyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	375.4
445	49		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	406.2
446	48		B		(3R,4R)-4-fluoro-1-((5-methoxypyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	375.2
447	52		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4-cyano-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	431.2
448	51		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide	350.2
449	50		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-methoxy-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	418.0
450	51		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-methoxy-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide	350.2

Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
451	5		B		6-((2-((3R,4R)-3-amino-4-methoxypiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	381.2
452	53		B		6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-4-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	399.2
453	54		B		6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(trifluoromethyl)-3H-imidazo[4,5-b]pyridin-3-yl)methyl)nicotinonitrile	420.2
454	17		B		(3R,4R)-1-(1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)-4-methoxypiperidin-3-amine	391.2
455	55		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-bromo-1H-benzo[d]imidazol-1-yl)-1-(azetidin-1-yl)ethan-1-one	412.0
456	17		B		(3R,4R)-1-(1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)-4-methoxypiperidin-3-amine	391.2
457	49		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	406.2

Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
458	54		B		6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(trifluoromethyl)-1H-imidazo[4,5-b]pyridin-1-yl)methyl)nicotinonitrile	420.2
459	56		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)-1-morpholinoethan-1-one	430.2
460	49		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	406.2
461	57		B		2-(2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide	354.2
462	49		B		2-(2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	406.2
463	17		B		6-((2-((3R,4S)-3-amino-4-methoxypiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	381.2
464	56		B		2-(2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)-1-morpholinoethan-1-one	430.2

Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
465	49		B		(R)-2-(2-(3-amino-4,4-difluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	424.2
466	49		B		2-(2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	406.2
467	17		B		(3R,4S)-1-(1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)-4-methoxypiperidin-3-amine	391.2
468	58		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-(trifluoromethoxy)-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide	404.2
469	49		B		2-(6-fluoro-2-((3R,4R)-4-fluoro-3-(methylamino)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	420.2
470	55		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-bromo-1H-benzo[d]imidazol-1-yl)-1-(azetidin-1-yl)ethan-1-one	410.0
471	57		B		2-(2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide	354.2
472	49		B		2-(6-fluoro-2-(1,7-diazaspiro[4.5]decan-7-yl)-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	428.2

Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
473	56		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)-1-morpholinoethan-1-one	430.2
474	58		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(trifluoromethoxy)-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide	404.2
475	59		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(trifluoromethoxy)-1H-benzo[d]imidazol-1-yl)-1-morpholinoethan-1-one	446.2
476	53		B		6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-7-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	399.2
477	17		B		(3R,4S)-1-(1-((5-chloropyrimidin-2-yl)methyl)-5-fluoro-1H-benzo[d]imidazol-2-yl)-4-methoxypiperidin-3-amine	391.2
478	56		B		2-(2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)-1-morpholinoethan-1-one	430.2
479	49		B		2-(5-fluoro-2-((3R,4R)-4-fluoro-3-(methylamino)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	420.2
480	49		B		2-(2-(3-amino-4-methylpyrrolidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-1-morpholinoethan-1-one	388.2

Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
					N-methyl-N-(2,2,2-trifluoroethyl)acetamide	
481	49		B		2-((3R,4R)-3-amino-4-hydroxy piperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	404.2
482	49		B		(R)-2-(2-(3-amino-4,4-difluoropiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	424.2
483	49		B		2-(2-(3R,4R)-3-amino-4-methoxy piperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	418.2
484	49		B		2-(2-(3R)-3-amino-4-hydroxy piperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	404.2
485	49		B		2-(2-(3R,4R)-3-amino-4-methoxy piperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	418.2
486	49		B		2-(2-(3-(aminomethyl)-3-fluoropyrrolidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	406.2
487	49		B		2-(2-(3-(aminomethyl)-3-fluoropyrrolidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	406.2
488	49		B		2-(6-fluoro-2-((4aR,8aR)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-	430.2

Ex. #	Alkylated Intermediate	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
					benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	
489	49		B		(S)-2-(2-(3-aminopyrrolidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	374.2
490	49		B		(R)-2-(2-(3-aminopyrrolidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	374.2
491	49		B		(S)-2-(2-(3-(aminomethyl)pyrrolidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	388.2
492	49		B		2-(6-fluoro-2-((4aR,8aR)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	430.2
493	49		B		2-(5-fluoro-2-((4aS,8aS)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	430.2

[a] hydrolysis of nitrile occurred during SnAr [b] Ritter reactivity observed during Boc deprotection [c] unspecified stereochemistry designates mixtures of enantiomers or diastereomers

Table 3. Characterization data for compounds made following Scheme 8.

5

The column "Separation Stage" indicates after which process step regioisomers formed due to asymmetric benzimidazole substitution at R^1 in Scheme 8 were separated during the preparation of the tabulated final compound (I = after preparation of the alkylated intermediate 1-59 (where at least one R^1 is not hydrogen); B = prior to boc deprotection; or F = final compound).

Ex. #.	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
1	400MHz d ₄ -MeOH	8.85 (dd, J=0.83, 2.07 Hz, 1H), 8.12-8.16 (m, 1H), 7.44 (d, J=8.50 Hz, 1H), 7.37 (dd, J=0.62, 8.29 Hz, 1H), 7.20 (d, J=1.66 Hz, 1H), 7.12-7.16 (m, 1H), 5.48 (s, 2H), 3.50 (br s, 1H), 2.97-3.03 (m, 1H), 2.89-2.96 (m, 1H), 2.78-2.86 (m, 1H), 1.92-2.01 (m, 1H), 1.81 (dt, J=3.94, 8.71 Hz, 1H), 1.57-1.72 (m, 1H), 1.31-1.42 (m, 1H)	B	Chiralpak AD-H, 20% MeOH, Peak 1
2	500MHz d ₄ -MeOH	8.81-8.86 (m, 1H), 8.11-8.17 (m, 1H), 7.44-7.48 (m, 1H), 7.36 (d, J=8.04 Hz, 1H), 7.06-7.10 (m, 2H), 5.49 (s, 2H), 3.52 (br dd, J=1.69, 11.81 Hz, 1H), 2.97-3.06 (m, 1H), 2.90-2.96 (m, 1H), 2.80-2.88 (m, 1H), 1.92-2.01 (m, 1H), 1.82 (br dd, J=4.28, 9.47 Hz, 1H), 1.58-1.71 (m, 1H), 1.29-1.41 (m, 1H)	B	Chiralpak AD-H, 20% MeOH, Peak 2
3	500MHz d ₄ -MeOH	8.75-8.80 (m, 1H), 8.06 (d, J=8.30 Hz, 1H), 7.23-7.31 (m, 1H), 7.11 (d, J=7.27 Hz, 1H), 6.94-7.05 (m, 2H), 5.44 (s, 2H), 3.48 (br d, J=10.12 Hz, 1H), 3.24-3.30 (m, 1H), 3.23-3.28 (m, 1H), 2.94-3.04 (m, 1H), 2.77-2.90 (m, 2H), 1.83-1.96 (m, 1H), 1.71-1.81 (m, 1H), 1.51-1.65 (m, 1H), 1.19-1.35 (m, 1H)	--	--
4	500MHz d ₄ -MeOH	8.83 (s, 1H), 8.11-8.16 (m, 1H), 7.39 (d, J=8.30 Hz, 1H), 7.18 (d, J=7.01 Hz, 1H), 7.02-7.11 (m, 2H), 5.53 (s, 2H), 4.33-4.52 (m, 1H), 3.59-3.66 (m, 1H), 3.50 (br d, J=12.46 Hz, 1H), 3.14-3.22 (m, 1H), 3.09 (dq, J=4.02, 8.69 Hz, 1H), 2.95-3.05 (m, 1H), 2.07-2.22 (m, 1H), 1.76-1.94 (m, 1H)	---	---
5	500MHz d ₄ -MeOH	8.83 (s, 1H), 8.10-8.15 (m, 1H), 7.37 (d, J=8.04 Hz, 1H), 7.17 (d, J=7.01 Hz, 1H), 7.01-7.09 (m, 2H), 5.52 (s, 2H), 3.43 (dd, J=4.15, 12.20 Hz, 1H), 3.20-3.35 (m, 2H), 3.18-3.35 (m, 1H), 3.04-3.17 (m, 1H), 2.10 (ddd, J=4.93, 9.80, 14.34 Hz, 1H), 1.88-2.04 (m, 1H)	--	--
6	500MHz d ₄ -MeOH	8.86 (d, J=1.30 Hz, 1H), 8.14-8.20 (m, 1H), 7.47 (d, J=8.56 Hz, 1H), 7.44 (d, J=8.30 Hz, 1H), 7.23 (d, J=2.08 Hz, 1H), 7.19 (dd, J=1.95, 8.43 Hz, 1H), 5.53 (s, 2H), 4.33-4.50 (m, 1H), 3.53-3.61 (m, 1H), 3.43-3.50 (m, 1H), 3.02-3.20 (m, 2H), 2.95 (dd, J=8.69, 12.33 Hz, 1H), 2.12-2.24 (m, 1H), 1.82-1.94 (m, 1H)	B	Chiralcel OD-H, 25% IPA, peak 1
7	500MHz d ₄ -MeOH	8.86 (d, J=1.30 Hz, 1H), 8.13-8.20 (m, 1H), 7.49 (s, 1H), 7.42 (d, J=8.30 Hz, 1H), 7.12 (s, 2H), 5.54 (s, 2H), 4.43 (s, 1H), 3.57-3.63 (m, 1H), 3.45-3.55 (m, 1H), 3.12-3.20 (m, 1H), 3.03-3.12 (m, 1H), 2.97 (dd, J=8.82, 12.46 Hz, 1H), 2.12-2.24 (m, 1H), 1.80-1.96 (m, 1H)	B	Chiralcel OD-H, 25% IPA, peak 2

Ex. #.	Freq., Solvent	¹ H NMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
8	500MHz d ₄ -MeOH	8.86 (d, J=1.82 Hz, 1H), 8.14-8.19 (m, 1H), 7.47 (d, J=8.56 Hz, 1H), 7.43 (d, J=8.04 Hz, 1H), 7.22 (s, 1H), 7.13-7.20 (m, 1H), 5.53 (s, 2H), 4.75-4.81 (m, 1H), 3.37-3.43 (m, 1H), 3.01-3.29 (m, 4H), 2.08-2.20 (m, 1H), 1.88-2.03 (m, 1H)	B	Chiralcel OD-H, 25% IPA, peak 1
9	500MHz d ₄ -MeOH	8.86 (d, J=1.30 Hz, 1H), 8.14-8.19 (m, 1H), 7.49 (s, 1H), 7.41 (d, J=8.04 Hz, 1H), 7.12 (s, 2H), 5.53 (s, 2H), 3.37-3.49 (m, 2H), 3.28 (dd, J=3.37, 8.04 Hz, 2H), 3.03-3.21 (m, 2H), 2.09-2.18 (m, 1H), 1.89-2.05 (m, 1H)	B	Chiralcel OD-H, 25% IPA, peak 2
10	500MHz d ₄ -MeOH	8.84 (s, 1H), 8.16 (d, J=8.04 Hz, 1H), 7.42-7.47 (m, 1H), 7.19-7.23 (m, 1H), 7.05-7.12 (m, 2H), 5.58 (s, 2H), 3.59 (br d, J=11.42 Hz, 1H), 3.45-3.53 (m, 1H), 3.37 (ddd, J=3.11, 9.54, 12.78 Hz, 1H), 3.16-3.30 (m, 2H), 2.30 (tdd, J=4.70, 9.67, 14.66 Hz, 1H), 2.06-2.22 (m, 1H)	--	--
11	500MHz d ₄ -MeOH	8.80-8.84 (m, 1H), 8.14-8.19 (m, 1H), 7.45-7.51 (m, 2H), 7.41 (d, J=8.04 Hz, 1H), 7.17 (t, J=7.91 Hz, 1H), 5.54-5.60 (m, 2H), 4.35-4.53 (m, 1H), 3.70-3.76 (m, 1H), 3.50-3.64 (m, 1H), 3.19-3.26 (m, 1H), 3.14 (dq, J=4.15, 8.82 Hz, 1H), 2.98-3.08 (m, 1H), 2.11-2.23 (m, 1H), 1.80-1.95 (m, 1H)	--	--
12	500MHz d ₄ -MeOH	8.85 (d, J=1.56 Hz, 1H), 8.15-8.20 (m, 1H), 7.48 (d, J=8.56 Hz, 2H), 7.23 (d, J=1.56 Hz, 1H), 7.19 (dd, J=1.82, 8.56 Hz, 1H), 5.56 (s, 2H), 3.53 (br d, J=12.20 Hz, 1H), 3.40-3.48 (m, 1H), 3.28-3.32 (m, 1H), 3.12-3.27 (m, 2H), 2.23-2.37 (m, 1H), 2.06-2.21 (m, 1H)	F	Chiralcel OD-H, 25% MeOH, peak 1
13	500MHz d ₄ -MeOH	8.85 (d, J=1.04 Hz, 1H), 8.15-8.19 (m, 1H), 7.50 (s, 1H), 7.46 (d, J=8.04 Hz, 1H), 7.07-7.15 (m, 2H), 5.54-5.59 (m, 2H), 3.56 (br d, J=12.20 Hz, 1H), 3.40-3.50 (m, 1H), 3.34-3.39 (m, 1H), 3.13-3.29 (m, 2H), 2.24-2.39 (m, 1H), 2.06-2.22 (m, 1H)	F	Chiralcel OD-H, 25% MeOH, peak 2
14	500MHz d ₄ -MeOH	8.85 (d, J=1.82 Hz, 1H), 8.15-8.20 (m, 1H), 7.64 (d, J=8.30 Hz, 1H), 7.44-7.54 (m, 3H), 5.59-5.64 (m, 2H), 4.36-4.54 (m, 1H), 3.60-3.71 (m, 1H), 3.48-3.56 (m, 1H), 3.14-3.22 (m, 1H), 3.06-3.13 (m, 1H), 2.95-3.03 (m, 1H), 2.12-2.23 (m, 1H), 1.81-1.97 (m, 1H)	B	Chiralcel OD-H, 15% IPA, peak 1
15	500MHz d ₄ -MeOH	8.82-8.87 (m, 1H), 8.15-8.21 (m, 1H), 7.78 (s, 1H), 7.48 (d, J=8.30 Hz, 1H), 7.41 (d, J=8.56 Hz, 1H), 7.31 (d, J=8.30 Hz, 1H), 5.55-5.64 (m, 2H), 4.35-4.54 (m, 1H), 3.60-3.69 (m, 1H), 3.50-3.59 (m, 1H), 3.15-3.22 (m, 1H), 3.06-3.15 (m, 1H), 3.01 (dd, J=8.82, 12.46 Hz, 1H), 2.13-2.27 (m, 1H), 1.83-1.97 (m, 1H)	B	Chiralcel OD-H, 15% IPA, peak 2

Ex. #.	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
16	500MHz d ₄ -MeOH	8.86 (d, J=1.30 Hz, 1H), 8.11-8.18 (m, 1H), 7.53 (d, J=7.79 Hz, 1H), 7.37 (d, J=8.04 Hz, 1H), 7.18-7.25 (m, 1H), 7.11-7.17 (m, 2H), 5.51-5.57 (m, 2H), 4.37-4.53 (m, 1H), 3.57-3.65 (m, 1H), 3.40-3.54 (m, 1H), 3.09-3.21 (m, 2H), 2.99 (dd, J=8.95, 12.33 Hz, 1H), 2.19 (tt, J=4.28, 13.62 Hz, 1H), 1.81-1.98 (m, 1H)	--	--
17	500MHz d ₄ -MeOH	8.90 (d, J=1.30 Hz, 1H), 8.08-8.16 (m, 1H), 7.33-7.38 (m, 1H), 7.25 (d, J=8.04 Hz, 1H), 7.06-7.11 (m, 2H), 6.96-7.02 (m, 1H), 5.45 (s, 2H), 4.14-4.23 (m, 1H), 3.26 (br d, J=13.23 Hz, 1H), 3.04-3.16 (m, 1H), 2.83-2.94 (m, 1H), 2.49-2.60 (m, 2H), 2.43-2.46 (m, 1H), 1.99-2.13 (m, 1H), 1.48-1.57 (m, 1H), 1.38 (qd, J=7.28, 15.02 Hz, 1H)	--	--
18	500MHz d ₄ -MeOH	8.83 (dd, J=1.56, 16.35 Hz, 1H), 8.18-8.25 (m, 1H), 7.50-7.61 (m, 1H), 7.27-7.37 (m, 2H), 5.56 (d, J=3.11 Hz, 2H), 3.04-3.26 (m, 3H), 2.99 (br d, J=8.04 Hz, 2H), 2.11-2.26 (m, 1H), 1.84-2.01 (m, 2H)	--	--
19	500MHz d ₄ -MeOH	8.84 (s, 1H), 8.13-8.21 (m, 1H), 7.52-7.58 (m, 1H), 7.43-7.50 (m, 1H), 7.06-7.18 (m, 2H), 5.50-5.61 (m, 2H), 4.39-4.58 (m, 1H), 3.64 (br d, J=12.46 Hz, 1H), 3.45-3.56 (m, 1H), 3.11-3.22 (m, 2H), 3.01 (dd, J=9.21, 12.33 Hz, 1H), 2.12-2.25 (m, 1H), 1.83-1.97 (m, 1H)	B	Chiralpak AD-H, 15% MeOH, peak 1
20	500MHz d ₄ -MeOH	8.85 (d, J=1.30 Hz, 1H), 8.11-8.21 (m, 1H), 7.45 (d, J=8.30 Hz, 1H), 7.40 (s, 1H), 7.17-7.24 (m, 1H), 7.01-7.08 (m, 1H), 5.51-5.60 (m, 2H), 4.37-4.54 (m, 1H), 3.61-3.68 (m, 1H), 3.45-3.57 (m, 1H), 3.05-3.23 (m, 2H), 3.00 (dd, J=9.08, 12.46 Hz, 1H), 2.13-2.27 (m, 1H), 1.90 (ddd, J=3.63, 9.60, 13.23 Hz, 1H)	B	Chiralpak AD-H, 15% MeOH, peak 2
21	500MHz d ₄ -MeOH	8.84 (d, J=2.08 Hz, 1H), 8.16-8.22 (m, 1H), 7.46-7.54 (m, 2H), 7.35 (d, J=11.16 Hz, 1H), 5.57-5.61 (m, 2H), 4.36-4.53 (m, 1H), 3.64-3.72 (m, 1H), 3.49-3.59 (m, 1H), 3.15-3.24 (m, 1H), 3.07-3.15 (m, 1H), 3.02 (dd, J=8.95, 12.59 Hz, 1H), 2.18 (br dd, J=4.80, 9.21 Hz, 1H), 1.82-1.92 (m, 1H)	B	Phenomenex Lux Cellulose-2, 15% MeOH, peak 1
22	500MHz d ₄ -MeOH	8.83 (d, J=1.30 Hz, 1H), 8.16-8.21 (m, 1H), 7.73 (d, J=6.23 Hz, 1H), 7.52 (d, J=8.30 Hz, 1H), 7.21 (d, J=10.38 Hz, 1H), 5.58 (s, 2H), 4.34-4.53 (m, 1H), 3.63 (br dd, J=1.56, 12.46 Hz, 1H), 3.49 (br s, 1H), 3.05-3.22 (m, 2H), 2.99 (dd, J=8.82, 12.46 Hz, 1H), 2.11-2.26 (m, 1H), 1.89 (ddd, J=3.63, 9.67, 13.43 Hz, 1H)	B	Phenomenex Lux Cellulose-2, 15% MeOH, peak 2

Ex. #.	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
23	500MHz d ₄ -MeOH	8.85 (s, 1H), 8.06-8.13 (m, 1H), 7.51 (d, J=7.79 Hz, 1H), 7.29 (d, J=8.30 Hz, 1H), 7.05-7.22 (m, 3H), 5.49 (s, 2H), 3.30-3.36 (m, 2H), 3.10-3.23 (m, 3H), 2.94-3.09 (m, 1H), 2.38 (qd, J=6.47, 12.52 Hz, 1H), 1.88-2.03 (m, 2H), 1.66-1.88 (m, 2H)	B	Chiralpak AD-H, 30% IPA, peak 1
24	500MHz d ₄ -MeOH	8.85 (s, 1H), 8.18-8.23 (m, 1H), 7.50-7.59 (m, 2H), 7.27-7.33 (m, 1H), 7.21-7.26 (m, 2H), 5.61 (s, 2H), 4.00 (br dd, J=2.47, 12.85 Hz, 1H), 3.80-3.91 (m, 1H), 3.37-3.56 (m, 4H), 3.25 (br d, J=2.34 Hz, 3H), 2.13-2.28 (m, 3H), 1.88-2.07 (m, 3H), 1.69-1.83 (m, 1H)	B	Chiralpak AD-H, 30% IPA, peak 2
25	500MHz d ₄ -MeOH	8.85 (s, 1H), 8.06-8.13 (m, 1H), 7.51 (d, J=7.79 Hz, 1H), 7.29 (d, J=8.30 Hz, 1H), 7.05-7.22 (m, 3H), 5.49 (s, 2H), 3.30-3.36 (m, 2H), 3.10-3.23 (m, 3H), 2.94-3.09 (m, 1H), 2.38 (qd, J=6.47, 12.52 Hz, 1H), 1.88-2.03 (m, 2H), 1.66-1.88 (m, 2H)	B	Chiralpak AD-H, 30% IPA, peak 3
26	500MHz d ₄ -MeOH	8.85 (s, 1H), 8.18-8.23 (m, 1H), 7.50-7.59 (m, 2H), 7.27-7.33 (m, 1H), 7.21-7.26 (m, 2H), 5.61 (s, 2H), 4.00 (br dd, J=2.47, 12.85 Hz, 1H), 3.80-3.91 (m, 1H), 3.37-3.56 (m, 4H), 3.25 (br d, J=2.34 Hz, 3H), 2.13-2.28 (m, 3H), 1.88-2.07 (m, 3H), 1.69-1.83 (m, 1H)	B	Chiralpak AD-H, 30% IPA, peak 4
27	400MHz d ₄ -MeOH	8.83 (dd, J=0.62, 2.07 Hz, 1H), 8.08 (dd, J=2.07, 8.09 Hz, 1H), 7.49-7.54 (m, 1H), 7.32 (d, J=8.29 Hz, 1H), 7.07-7.19 (m, 3H), 5.45-5.52 (m, 2H), 3.38-3.45 (m, 2H), 2.99-3.17 (m, 2H), 1.94-2.14 (m, 2H), 1.57-1.86 (m, 4H)	B	Chiralpak IC, 40% MeOH, peak 1
28	400MHz d ₄ -MeOH	8.83 (dd, J=0.83, 2.07 Hz, 1H), 8.06-8.11 (m, 1H), 7.49-7.55 (m, 1H), 7.32 (d, J=8.29 Hz, 1H), 7.05-7.19 (m, 3H), 5.47-5.52 (m, 2H), 3.37-3.46 (m, 2H), 3.01-3.18 (m, 2H), 1.96-2.18 (m, 2H), 1.56-1.84 (m, 4H)	B	Chiralpak IC, 40% MeOH, peak 2
29	500MHz d ₄ -MeOH	8.49 (d, J=2.34 Hz, 1H), 7.83-7.87 (m, 1H), 7.75-7.79 (m, 2H), 7.66 (d, J=8.30 Hz, 1H), 7.36 (d, J=8.56 Hz, 1H), 5.52 (s, 2H), 4.42-4.59 (m, 1H), 3.77 (dtd, J=1.69, 4.27, 12.62 Hz, 1H), 3.56-3.67 (m, 1H), 3.18-3.26 (m, 2H), 3.09 (s, 3H), 3.02-3.08 (m, 1H), 2.15-2.26 (m, 1H), 1.84-1.96 (m, 1H)	B	Chiralcel OD-H, 25% MeOH, peak 1
30	500MHz d ₄ -MeOH	8.48 (d, J=2.34 Hz, 1H), 8.04-8.08 (m, 1H), 7.83-7.88 (m, 1H), 7.69 (dd, J=1.82, 8.56 Hz, 1H), 7.37 (dd, J=4.02, 8.43 Hz, 2H), 5.48-5.53 (m, 2H), 4.47-4.65 (m, 1H), 3.79 (dtd, J=1.69, 4.27, 12.62 Hz, 1H), 3.58-3.67 (m, 1H), 3.33-3.38 (m, 1H), 3.17-3.25 (m, 1H), 3.07-3.14 (m, 4H), 2.18-2.29 (m, 1H), 1.87-2.03 (m, 1H)	B	Chiralcel OD-H, 25% MeOH, peak 1

Ex. #.	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
31	400MHz d ₄ -MeOH	8.77-8.82 (m, 2H), 7.35-7.43 (m, 1H), 7.28-7.32 (m, 1H), 5.54 (s, 2H), 4.38-4.60 (m, 1H), 3.76 (dtd, J=1.97, 4.31, 12.62 Hz, 1H), 3.56-3.68 (m, 1H), 3.16-3.26 (m, 2H), 2.97-3.10 (m, 1H), 2.12-2.26 (m, 1H), 1.79-1.98 (m, 1H)	--	--
32	400MHz d ₄ -MeOH	8.37 (d, J=2.90 Hz, 1H), 7.57-7.64 (m, 1H), 7.33 (dd, J=4.35, 8.71 Hz, 1H), 7.05 (dd, J=2.07, 8.91 Hz, 1H), 6.73 (ddd, J=2.18, 9.85, 11.61 Hz, 1H), 5.49 (s, 2H), 4.39-4.60 (m, 1H), 3.70 (dtd, J=1.76, 4.28, 12.49 Hz, 1H), 3.49-3.61 (m, 1H), 3.11-3.31 (m, 2H), 3.04 (dd, J=9.12, 12.44 Hz, 1H), 2.13-2.28 (m, 1H), 1.83-2.04 (m, 1H)	B	Regis Whelk-O, 20% MeOH, peak 2
33	400MHz d ₄ -MeOH	8.41 (d, J=2.90 Hz, 1H), 7.57-7.64 (m, 1H), 7.35 (dd, J=4.15, 8.71 Hz, 1H), 6.71-6.85 (m, 2H), 5.41 (s, 2H), 4.32-4.54 (m, 1H), 3.61 (dtd, J=1.66, 4.17, 12.39 Hz, 1H), 3.43-3.53 (m, 1H), 3.06-3.20 (m, 2H), 2.97 (dd, J=8.60, 12.34 Hz, 1H), 2.11-2.25 (m, 1H), 1.80-1.97 (m, 1H)	B	Regis Whelk-O, 20% MeOH, peak 1
34	400MHz d ₄ -MeOH	8.66-8.74 (m, 2H), 6.86-6.92 (m, 1H), 6.72-6.82 (m, 1H), 5.51 (s, 2H), 4.36-4.59 (m, 1H), 3.64 (dtd, J=1.87, 4.28, 12.39 Hz, 1H), 3.47-3.57 (m, 1H), 3.09-3.22 (m, 2H), 2.99 (dd, J=8.91, 12.44 Hz, 1H), 2.07-2.26 (m, 1H), 1.75-1.99 (m, 1H)	B	Regis Whelk-O, 15% MeOH, peak 2
35	400MHz d ₄ -MeOH	8.67-8.72 (m, 2H), 7.03-7.08 (m, 1H), 6.68-6.77 (m, 1H), 5.62 (d, J=0.83 Hz, 2H), 4.44-4.65 (m, 1H), 3.69 (dtd, J=1.76, 4.35, 12.54 Hz, 1H), 3.44-3.58 (m, 1H), 3.24-3.32 (m, 1H), 3.12-3.19 (m, 1H), 3.05 (dd, J=9.43, 12.54 Hz, 1H), 2.17-2.27 (m, 1H), 1.84-2.01 (m, 1H)	B	Regis Whelk-O, 15% MeOH, peak 1
36	500MHz d ₄ -MeOH	8.73 (s, 2H), 7.39-7.44 (m, 1H), 7.35 (dd, J=2.34, 9.34 Hz, 1H), 5.57 (d, J=4.15 Hz, 2H), 5.00-5.16 (m, 1H), 3.72-3.85 (m, 2H), 3.46-3.54 (m, 2H), 3.35-3.44 (m, 1H), 1.98-2.19 (m, 2H)	--	--
37	500MHz d ₄ -MeOH	8.72 (s, 2H), 7.37-7.41 (m, 1H), 7.31 (dd, J=2.47, 9.47 Hz, 1H), 5.55 (s, 2H), 4.41-4.60 (m, 1H), 3.78 (dtd, J=1.82, 4.25, 12.78 Hz, 1H), 3.56-3.70 (m, 1H), 3.16-3.29 (m, 2H), 3.07 (dd, J=9.34, 12.72 Hz, 1H), 2.14-2.24 (m, 1H), 1.83-1.96 (m, 1H)	--	--
38	500MHz d ₄ -MeOH	8.81-8.92 (m, 1 H), 8.23 (dd, J=8.30, 2.08 Hz, 1 H), 7.49-7.66 (m, 2H), 7.17-7.39 (m, 3H), 5.64 (s, 2H), 4.69-4.86 (m, 1H), 3.92-4.06 (m, 1H), 3.61-3.79 (m, 2H), 3.20-3.32 (m, 2H), 2.24-2.41 (m, 1H), 1.92-2.14 (m, 1H)	--	--
39	500MHz d ₄ -MeOH	8.74 - 8.81 (m, 2 H), 7.39 - 7.51 (m, 1 H), 7.00 (dd, J=8.95, 2.47 Hz, 1 H), 6.94 (ddd, J=9.86, 8.82, 2.60 Hz, 1 H), 5.51 (s, 2 H), 4.98 (dt, J=5.26, 2.43 Hz, 1 H), 3.48 (dd, J=11.94, 3.89 Hz, 1 H), 3.19 - 3.41 (m, 5 H), 1.92 - 2.21 (m, 2 H)	B	Chiralpak IC, 20% IPA, peak 1

Ex. #.	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
40	500MHz d ₄ -MeOH	8.78 (s, 2 H), 7.04 - 7.25 (m, 2 H), 6.80 - 6.96 (m, 1 H), 5.45 - 5.61 (m, 2 H), 3.42 - 3.58 (m, 1 H), 3.17 - 3.40 (m, 5 H), 1.88 - 2.23 (m, 2 H)	B	Chiralpak IC, 20% IPA, peak 2
41	500MHz d ₄ -MeOH	8.81 (s, 2H), 7.67-7.71 (m, 1H), 7.61 (d, J=8.30 Hz, 1H), 7.49-7.53 (m, 1H), 5.61 (s, 2H), 3.69-3.77 (m, 1H), 3.58-3.66 (m, 1H), 3.43-3.53 (m, 1H), 3.36-3.43 (m, 1H), 3.23-3.30 (m, 1H), 2.14-2.41 (m, 2H)	B	Chiralpak OJ, 15% MeOH, peak 2
42	500MHz d ₄ -MeOH	8.79 (s, 2H), 7.80-7.86 (m, 1H), 7.42-7.48 (m, 1H), 7.37 (d, J=8.30 Hz, 1H), 5.61 (s, 2H), 3.66-3.74 (m, 1H), 3.55-3.63 (m, 1H), 3.34-3.53 (m, 3H), 3.22-3.30 (m, 1H), 2.29-2.41 (m, 1H), 2.07-2.27 (m, 1H)	B	Chiralpak OJ, 15% MeOH, peak 1
43	400MHz d ₆ -DMSO	8.93 (d, J=1.35 Hz, 1H), 8.32 (dd, J=2.18, 8.19 Hz, 1H), 7.67 (s, 1H), 7.54 (s, 1H), 7.52-7.56 (m, 1H), 7.49 (d, J=7.92 Hz, 1H), 5.56 (s, 2H), 4.22-4.48 (m, 1H), 3.36-3.45 (m, 2H), 2.97-3.09 (m, 1H), 2.72-2.94 (m, 2H), 1.97-2.11 (m, 1H), 1.61-1.77 (m, 1H)	--	--
44	400MHz d ₆ -DMSO	8.96 (s, 1H), 8.27 (dd, J=2.18, 8.19 Hz, 1H), 7.27 (d, J=7.98 Hz, 1H), 7.23 (s, 1H), 6.92 (s, 1H), 5.44 (s, 2H), 4.21-4.48 (m, 1H), 3.35 (br s, 3H), 2.86-3.03 (m, 2H), 2.74 (dd, J=8.60, 12.44 Hz, 1H), 2.24 (s, 3H), 2.20 (s, 3H), 1.93-2.12 (m, 1H), 1.87 (br s, 1H), 1.64-1.82 (m, 1H)	--	--
45	400MHz d ₆ -DMSO	8.92-8.95 (m, 1H), 8.36-8.50 (m, 3H), 7.76 (d, J=8.09 Hz, 1H), 7.53-7.60 (m, 1H), 7.35-7.43 (m, 1H), 7.18 (t, J=9.23 Hz, 1H), 5.65-5.84 (m, 2H), 3.86 (br d, J=10.47 Hz, 1H), 3.26-3.52 (m, 3H), 3.15 (br t, J=9.90 Hz, 1H), 1.82-2.01 (m, 2H), 1.40-1.69 (m, 2H)	B	Chiralcel OD-H, 15% IPA Peak 1
46	400MHz d ₆ -DMSO	8.94 (s, 1H), 8.48 (br s, 2H), 8.40 (dd, J=2.18, 8.19 Hz, 1H), 7.77 (d, J=8.19 Hz, 1H), 7.40 (dd, J=2.85, 8.66 Hz, 2H), 7.14 (dt, J=2.38, 9.33 Hz, 1H), 5.65-5.84 (m, 2H), 3.89 (br d, J=10.57 Hz, 1H), 3.28-3.52 (m, 3H), 3.18 (br t, J=9.80 Hz, 1H), 1.94-2.02 (m, 1H), 1.81-1.93 (m, 1H), 1.47-1.72 (m, 2H)	B	Chiralcel OD-H, 15% IPA Peak 2
47	400MHz d ₆ -DMSO	8.93 (s, 1H), 8.71 (br s, 2H), 8.38 (dd, J=1.75, 8.24 Hz, 1H), 7.73 (d, J=8.17 Hz, 1H), 7.57 (dd, J=4.54, 8.69 Hz, 1H), 7.36 (br d, J=8.30 Hz, 1H), 7.16 (t, J=8.68 Hz, 1H), 5.65-5.82 (m, 2H), 5.06-5.24 (m, 1H), 3.79 (br d, J=12.07 Hz, 1H), 3.62-3.74 (m, 1H), 3.36-3.52 (m, 3H), 3.24-3.33 (m, 1H), 2.09-2.20 (m, 1H), 1.88-2.09 (m, 1H)	B	Chiralcel OD-H, 15% IPA Peak 1

Ex. #.	Freq., Solvent	¹ H NMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
48	400MHz d ₆ -DMSO	8.94 (s, 1H), 8.66 (br s, 3H), 8.37 (dd, <i>J</i> =1.82, 8.17 Hz, 1H), 7.67 (d, <i>J</i> =8.17 Hz, 1H), 7.37 (dd, <i>J</i> =2.14, 9.02 Hz, 1H), 7.31 (br dd, <i>J</i> =4.41, 8.69 Hz, 1H), 7.07 (t, <i>J</i> =8.71 Hz, 1H), 5.60-5.78 (m, 2H), 5.05-5.24 (m, 1H), 3.62-3.78 (m, 2H), 3.36-3.51 (m, 2H), 3.22-3.31 (m, 1H), 2.09-2.18 (m, 1H), 1.93-2.07 (m, 1H)	B	Chiralcel OD-H, 15% IPA Peak 2
49	400MHz d ₆ -DMSO	8.90-8.96 (m, 1H), 8.87 (br s, 2H), 8.40 (dd, <i>J</i> =1.95, 8.17 Hz, 1H), 7.76 (d, <i>J</i> =8.30 Hz, 1H), 7.58 (dd, <i>J</i> =4.54, 8.69 Hz, 1H), 7.39 (br d, <i>J</i> =7.40 Hz, 1H), 7.18 (t, <i>J</i> =8.78 Hz, 1H), 5.68-5.84 (m, 2H), 4.86-5.05 (m, 1H), 4.04 (br d, <i>J</i> =12.46 Hz, 1H), 3.59-3.73 (m, 1H), 3.33-3.53 (m, 2H), 3.22 (br t, <i>J</i> =11.42 Hz, 1H), 2.22-2.32 (m, 1H), 1.75-1.92 (m, 1H)	B	Chiralcel OD-H, 15% IPA Peak 1
50	400MHz d ₆ -DMSO	8.94 (s, 1H), 8.90 (br s, 2H), 8.39 (dd, <i>J</i> =1.62, 8.24 Hz, 1H), 7.76 (d, <i>J</i> =8.17 Hz, 1H), 7.35-7.45 (m, 2H), 7.13 (t, <i>J</i> =8.77 Hz, 1H), 5.68-5.84 (m, 2H), 4.87-5.07 (m, 1H), 4.07 (br d, <i>J</i> =12.72 Hz, 1H), 3.60-3.73 (m, 1H), 3.36-3.53 (m, 2H), 3.25 (br t, <i>J</i> =11.55 Hz, 1H), 2.23-2.32 (m, 1H), 1.78-1.91 (m, 1H)	B	Chiralcel OD-H, 15% IPA Peak 2
51	400MHz d ₆ -DMSO	8.94 (d, <i>J</i> =1.45 Hz, 1H), 8.32 (dd, <i>J</i> =2.18, 8.19 Hz, 1H), 7.72 (d, <i>J</i> =0.93 Hz, 1H), 7.45-7.55 (m, 3H), 5.56 (s, 2H), 3.48 (br d, <i>J</i> =11.71 Hz, 1H), 3.34-3.42 (m, 1H), 2.84-2.95 (m, 1H), 2.61-2.78 (m, 2H), 1.74-1.83 (m, 1H), 1.59-1.72 (m, 1H), 1.40-1.58 (m, 1H), 1.03-1.29 (m, 1H)	B	Chiralpak AD-H, 20% methanol Peak 1
52	400MHz d ₆ -DMSO	8.93 (d, <i>J</i> =1.35 Hz, 1H), 8.32 (dd, <i>J</i> =2.18, 8.19 Hz, 1H), 7.89 (d, <i>J</i> =1.14 Hz, 1H), 7.47-7.54 (m, 1H), 7.42 (d, <i>J</i> =1.45 Hz, 1H), 7.32 (d, <i>J</i> =8.29 Hz, 1H), 5.57 (s, 2H), 3.38-3.50 (m, 1H), 3.29-3.37 (m, 1H), 2.87 (br s, 1H), 2.78 (br s, 1H), 2.66 (br dd, <i>J</i> =9.07, 11.87 Hz, 1H), 1.74-1.85 (m, 1H), 1.62-1.74 (m, 1H), 1.43-1.57 (m, 1H), 1.11-1.31 (m, 1H)	B	Chiralpak AD-H, 20% methanol Peak 2
53	400MHz d ₆ -DMSO	8.93 (dd, <i>J</i> =0.73, 2.07 Hz, 1H), 8.33 (dd, <i>J</i> =2.07, 8.19 Hz, 1H), 7.74 (d, <i>J</i> =0.93 Hz, 1H), 7.48-7.58 (m, 3H), 5.61 (s, 2H), 4.25-4.48 (m, 1H), 3.38-3.57 (m, 2H), 3.03-3.16 (m, 1H), 2.80-2.92 (m, 2H), 1.97-2.13 (m, 1H), 1.61-1.80 (m, 3H)	B	Chiralpak AD-H, 25% methanol Peak 1
54	400MHz d ₆ -DMSO	8.92 (s, 1H), 8.33 (dd, <i>J</i> =2.12, 8.14 Hz, 1H), 7.91 (d, <i>J</i> =1.14 Hz, 1H), 7.54 (d, <i>J</i> =8.29 Hz, 1H), 7.45 (dd, <i>J</i> =1.50, 8.24 Hz, 1H), 7.33 (d, <i>J</i> =8.29 Hz, 1H), 5.61 (s, 2H), 4.25-4.48 (m, 1H), 3.36-3.52 (m, 3H), 3.07 (br s, 1H), 2.79-2.95 (m, 2H), 1.96-2.18 (m, 1H), 1.65-1.80 (m, 2H)	B	Chiralpak AD-H, 25% methanol Peak 2

Ex. #.	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
55	400MHz CDCl ₃	8.88 (d, <i>J</i> =1.35 Hz, 1H), 8.00 (dd, <i>J</i> =2.13, 8.14 Hz, 1H), 7.64 (d, <i>J</i> =8.19 Hz, 1H), 7.45-7.54 (m, 1H), 7.28 (d, <i>J</i> =1.04 Hz, 1H), 7.21-7.26 (m, 1H), 5.36-5.47 (m, 2H), 3.43-3.63 (m, 3H), 3.14-3.33 (m, 2H), 2.27-2.40 (m, 1H), 2.10-2.24 (m, 1H), 1.75 (br s, 2H)	B	Chiralpak AD-H, 20% IPA Peak 1
56	400MHz CDCl ₃	8.89 (d, <i>J</i> =1.35 Hz, 1H), 7.99 (dd, <i>J</i> =2.07, 8.09 Hz, 1H), 7.92 (d, <i>J</i> =0.93 Hz, 1H), 7.42 (dd, <i>J</i> =1.45, 8.29 Hz, 1H), 7.20 (d, <i>J</i> =8.19 Hz, 1H), 7.06 (d, <i>J</i> =8.19 Hz, 1H), 5.40-5.54 (m, 2H), 3.40-3.62 (m, 3H), 3.17-3.35 (m, 2H), 2.29-2.42 (m, 1H), 2.01-2.26 (m, 1H), 1.95 (br s, 2H)	B	Chiralpak AD-H, 20% IPA Peak 2
57	400MHz d ₆ -DMSO	8.93 (s, 1H), 8.31 (br d, <i>J</i> =8.19 Hz, 1H), 7.48 (d, <i>J</i> =8.19 Hz, 1H), 7.35 (s, 1H), 7.24 (s, 1H), 5.53 (s, 2H), 3.39 (br d, <i>J</i> =11.09 Hz, 2H), 3.29 (br d, <i>J</i> =12.44 Hz, 2H), 2.84 (br t, <i>J</i> =10.37 Hz, 1H), 2.57-2.78 (m, 2H), 1.77 (br dd, <i>J</i> =3.89, 8.55 Hz, 1H), 1.65 (br dd, <i>J</i> =4.20, 9.38 Hz, 1H), 1.40-1.61 (m, 1H), 1.05-1.21 (m, 1H)	--	--
58	400MHz d ₆ -DMSO	8.93 (s, 1H), 8.32 (d, <i>J</i> =8.19 Hz, 1H), 7.52 (d, <i>J</i> =8.19 Hz, 1H), 7.36 (s, 1H), 7.26 (s, 1H), 5.58 (s, 2H), 4.24-4.47 (m, 1H), 3.34-3.52 (m, 3H), 2.98-3.10 (m, 1H), 2.78-2.95 (m, 2H), 2.05 (br t, <i>J</i> =12.70 Hz, 1H), 1.84-1.99 (m, 1H), 1.64-1.83 (m, 1H)	--	--
59	400MHz d ₆ -DMSO	8.93 (s, 1H), 8.32 (d, <i>J</i> =8.29 Hz, 1H), 7.52 (d, <i>J</i> =8.09 Hz, 1H), 7.35 (s, 1H), 7.26 (s, 1H), 5.57 (s, 2H), 4.64-4.86 (m, 2H), 3.17-3.38 (m, 2H), 3.05-3.17 (m, 1H), 2.93-3.02 (m, 1H), 2.82-2.93 (m, 1H), 1.92-2.04 (m, 1H), 1.79 (br s, 1H)	--	--
60	400MHz d ₆ -DMSO	8.89-8.96 (m, 1H), 8.33 (d, <i>J</i> =7.79 Hz, 1H), 7.56 (d, <i>J</i> =8.29 Hz, 1H), 7.32-7.40 (m, 1H), 7.28 (s, 1H), 5.54-5.66 (m, 2H), 3.34-3.46 (m, 2H), 3.15-3.26 (m, 1H), 2.96-3.14 (m, 2H), 2.16-2.31 (m, 1H), 1.87-2.08 (m, 2H), 1.78-1.87 (m, 1H)	--	--
61	400MHz d ₆ -DMSO	8.94 (s, 1H), 8.31 (dd, <i>J</i> =2.07, 8.19 Hz, 1H), 7.44 (d, <i>J</i> =8.29 Hz, 1H), 7.02 (d, <i>J</i> =8.78 Hz, 1H), 6.95 (t, <i>J</i> =10.39 Hz, 1H), 5.50 (s, 2H), 3.33 (br d, <i>J</i> =11.82 Hz, 2H), 3.23 (br d, <i>J</i> =12.23 Hz, 2H), 2.66-2.87 (m, 2H), 2.54-2.63 (m, 1H), 1.73-1.90 (m, 1H), 1.60-1.72 (m, 1H), 1.41-1.58 (m, 1H), 1.16 (br s, 1H)	B	Regis Whelk-O s,s, 30% methanol Peak 2
62	400MHz d ₆ -DMSO	8.93 (s, 1H), 8.31 (dd, <i>J</i> =1.97, 8.19 Hz, 1H), 7.48 (d, <i>J</i> =8.29 Hz, 1H), 7.14 (dd, <i>J</i> =1.92, 9.28 Hz, 1H), 6.85 (t, <i>J</i> =10.74 Hz, 1H), 5.50 (s, 2H), 3.34-3.44 (m, 4H), 2.73-2.91 (m, 2H), 2.63 (dd, <i>J</i> =9.07, 11.87 Hz, 1H), 1.74-1.86 (m, 1H), 1.62-1.74 (m, 1H), 1.43-1.60 (m, 1H), 1.11-1.28 (m, 1H)	B	Regis Whelk-O s,s, 30% methanol Peak 1

Ex. #.	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
63	400MHz d ₆ -DMSO	8.93 (s, 1H), 8.32 (dd, <i>J</i> =2.02, 8.24 Hz, 1H), 7.50 (d, <i>J</i> =8.19 Hz, 1H), 7.03 (d, <i>J</i> =8.98 Hz, 1H), 6.98 (t, <i>J</i> =10.69 Hz, 1H), 5.55 (s, 2H), 4.33-4.59 (m, 1H), 3.69-4.05 (m, 2H), 3.31-3.50 (m, 2H), 2.96-3.09 (m, 2H), 2.83 (dd, <i>J</i> =9.02, 12.54 Hz, 1H), 2.02-2.12 (m, 1H), 1.67-1.79 (m, 1H)	B	Chiralcel OJ-H, 15% methanol Peak 2
64	400MHz d ₆ -DMSO	8.92 (s, 1H), 8.32 (dd, <i>J</i> =1.76, 8.19 Hz, 1H), 7.52 (d, <i>J</i> =8.29 Hz, 1H), 7.16 (dd, <i>J</i> =1.92, 9.28 Hz, 1H), 6.87 (t, <i>J</i> =10.73 Hz, 1H), 5.55 (s, 2H), 4.26-4.49 (m, 1H), 3.36-3.45 (m, 2H), 3.02-3.10 (m, 1H), 2.88-2.99 (m, 1H), 2.82 (dd, <i>J</i> =8.60, 12.44 Hz, 1H), 1.92-2.15 (m, 1H), 1.66-1.86 (m, 3H)	B	Chiralcel OJ-H, 15% methanol Peak 1
65	400MHz d ₆ -DMSO	8.94 (s, 1H), 8.31 (dd, <i>J</i> =1.97, 8.19 Hz, 1H), 7.48 (d, <i>J</i> =8.19 Hz, 1H), 7.02 (d, <i>J</i> =8.08 Hz, 1H), 6.96 (t, <i>J</i> =10.40 Hz, 1H), 5.49-5.58 (m, 2H), 4.63-4.83 (m, 1H), 3.04-3.26 (m, 3H), 2.84-2.97 (m, 2H), 1.75-2.01 (m, 2H), 1.65 (br s, 2H)	B	Phenomenex Lux Cellulose-2, 20% methanol Peak 2
66	400MHz d ₆ -DMSO	8.92 (s, 1H), 8.31 (dd, <i>J</i> =1.87, 8.19 Hz, 1H), 7.51 (d, <i>J</i> =8.19 Hz, 1H), 7.16 (dd, <i>J</i> =1.92, 9.28 Hz, 1H), 6.86 (t, <i>J</i> =10.73 Hz, 1H), 5.49-5.59 (m, 2H), 4.81 (br s, 1H), 3.10-3.29 (m, 3H), 2.90-3.02 (m, 2H), 1.81-2.03 (m, 2H), 1.63 (br s, 2H)	B	Phenomenex Lux Cellulose-2, 20% methanol Peak 1
67	400MHz d ₆ -DMSO	8.92 (s, 1H), 8.32 (dd, <i>J</i> =1.97, 8.19 Hz, 1H), 7.55 (d, <i>J</i> =8.19 Hz, 1H), 7.19 (dd, <i>J</i> =1.81, 9.28 Hz, 1H), 6.89 (t, <i>J</i> =10.66 Hz, 1H), 5.59 (s, 2H), 3.33-3.56 (m, 2H), 3.10-3.26 (m, 2H), 2.98-3.10 (m, 1H), 2.21-2.32 (m, 1H), 2.00-2.14 (m, 1H), 1.78 (br s, 2H)	B	Phenomenex Lux Cellulose-2, 20% methanol Peak 1
68	400MHz d ₆ -DMSO	8.93 (s, 1H), 8.33 (dd, <i>J</i> =2.18, 8.19 Hz, 1H), 7.74 (d, <i>J</i> =1.04 Hz, 1H), 7.48-7.58 (m, 3H), 5.61 (s, 2H), 4.25-4.47 (m, 1H), 3.38-3.57 (m, 2H), 3.04-3.17 (m, 1H), 2.80-2.92 (m, 2H), 1.99-2.12 (m, 1H), 1.60-1.79 (m, 3H)	B	Chiralpak AD-H, 25% methanol Peak 1
69	400MHz d ₆ -DMSO	8.92 (s, 1H), 8.33 (dd, <i>J</i> =2.18, 8.19 Hz, 1H), 7.91 (d, <i>J</i> =1.14 Hz, 1H), 7.54 (d, <i>J</i> =8.19 Hz, 1H), 7.45 (dd, <i>J</i> =1.45, 8.29 Hz, 1H), 7.33 (d, <i>J</i> =8.29 Hz, 1H), 5.62 (s, 2H), 4.27-4.48 (m, 1H), 3.36-3.56 (m, 2H), 3.01-3.14 (m, 1H), 2.79-2.96 (m, 2H), 1.96-2.22 (m, 2H), 1.81-1.96 (m, 1H), 1.66-1.81 (m, 1H)	B	Chiralpak AD-H, 25% methanol Peak 2
70	400MHz d ₆ -DMSO	8.96 (d, <i>J</i> =1.45 Hz, 1H), 8.28 (dd, <i>J</i> =2.18, 8.19 Hz, 1H), 7.43 (d, <i>J</i> =7.67 Hz, 1H), 7.32 (d, <i>J</i> =8.29 Hz, 1H), 6.98-7.13 (m, 3H), 5.47 (s, 2H), 3.35 (br dd, <i>J</i> =3.42, 11.71 Hz, 2H), 3.14-3.30 (m, 1H), 2.67-2.89 (m, 2H), 2.58 (dd, <i>J</i> =9.02, 11.71 Hz, 1H), 1.73-1.87 (m, 1H), 1.60-1.72 (m, 1H), 1.42-1.60 (m, 2H), 1.08-1.22 (m, 1H)	--	--

Ex. #.	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
71	400MHz d ₆ - DMSO	9.06 (br s, 3H), 8.88-9.00 (m, 1H), 8.37 (dd, <i>J</i> =2.18, 8.19 Hz, 1H), 7.67 (d, <i>J</i> =8.19 Hz, 1H), 7.38 (dd, <i>J</i> =2.44, 9.17 Hz, 1H), 7.27 (dd, <i>J</i> =4.56, 8.81 Hz, 1H), 7.05 (t, <i>J</i> =9.27 Hz, 1H), 5.61-5.87 (m, 2H), 3.96-4.12 (m, 1H), 3.90 (br d, <i>J</i> =12.85 Hz, 1H), 3.42-3.54 (m, 2H), 3.23-3.34 (m, 1H), 2.45-2.60 (m, 1H), 2.20-2.37 (m, 1H)	B	Chiralcel OD-H, 15% IPA Peak 2
72	400MHz d ₆ - DMSO	8.94 (d, <i>J</i> =1.45 Hz, 1H), 8.31 (dd, <i>J</i> =2.18, 8.19 Hz, 1H), 7.50 (t, <i>J</i> =9.11 Hz, 1H), 7.45 (d, <i>J</i> =8.50 Hz, 1H), 7.36 (dd, <i>J</i> =7.36, 10.78 Hz, 1H), 5.52 (s, 2H), 4.23-4.46 (m, 1H), 3.22-3.45 (m, 3H), 2.81-3.05 (m, 2H), 2.76 (dd, <i>J</i> =8.60, 12.44 Hz, 1H), 1.87-2.12 (m, 1H), 1.63-1.87 (m, 3H)	--	--
73	400MHz d ₆ - DMSO	8.96 (dd, <i>J</i> =0.73, 2.07 Hz, 1H), 8.29 (dd, <i>J</i> =2.18, 8.19 Hz, 1H), 7.45 (d, <i>J</i> =7.54 Hz, 1H), 7.37 (d, <i>J</i> =8.29 Hz, 1H), 7.00-7.13 (m, 3H), 5.51 (s, 2H), 4.63-4.84 (m, 1H), 3.06-3.26 (m, 3H), 2.88-3.00 (m, 2H), 1.79-2.03 (m, 2H), 1.59 (br s, 2H)	--	--
74	400MHz d ₆ - DMSO	8.90 (d, <i>J</i> =1.45 Hz, 1H), 8.37-8.43 (m, 1H), 8.34 (br s, 2H), 7.85 (d, <i>J</i> =8.19 Hz, 1H), 7.46-7.54 (m, 2H), 7.22-7.34 (m, 2H), 5.93 (s, 2H), 3.83-4.11 (m, 4H), 3.60-3.75 (m, 1H), 2.95-3.15 (m, 2H), 1.91 (td, <i>J</i> =4.13, 8.22 Hz, 1H), 1.03 (dd, <i>J</i> =5.29, 7.77 Hz, 1H), 0.52 (t, <i>J</i> =4.87 Hz, 1H)	B	Chiralpak AD-H, 30% isopropanol Peak 1
75	400MHz d ₆ - DMSO	8.90 (d, <i>J</i> =1.97 Hz, 1H), 8.39 (s, 1H), 8.34 (br s, 3H), 7.86 (d, <i>J</i> =8.29 Hz, 1H), 7.47-7.53 (m, 2H), 7.22-7.34 (m, 2H), 5.93 (s, 2H), 4.04-4.13 (m, 1H), 3.83-4.02 (m, 3H), 3.63-3.73 (m, 1H), 2.95-3.20 (m, 2H), 1.91 (td, <i>J</i> =4.09, 8.19 Hz, 1H), 0.98-1.07 (m, 1H), 0.52 (t, <i>J</i> =4.87 Hz, 1H)	B	Chiralpak AD-H, 30% isopropanol Peak 2
76	400MHz d ₆ - DMSO	8.89-8.97 (m, 1H), 8.50 (br s, 2H), 8.41 (dd, <i>J</i> =2.13, 8.24 Hz, 1H), 7.91 (d, <i>J</i> =8.29 Hz, 1H), 7.49 (d, <i>J</i> =8.71 Hz, 2H), 7.23-7.34 (m, 2H), 5.88-6.16 (m, 2H), 4.21 (br dd, <i>J</i> =6.22, 10.88 Hz, 1H), 3.87 (br dd, <i>J</i> =7.26, 10.26 Hz, 1H), 3.42-3.77 (m, 3H), 2.97-3.16 (m, 1H), 2.82-2.94 (m, 1H), 1.71-2.04 (m, 3H), 1.42-1.64 (m, 1H)	B	Phenomenex Lux Cellulose-2, 25% isopropanol w/ 0.2% DEA Peak 1
77	400MHz d ₆ - DMSO	8.92 (d, <i>J</i> =1.45 Hz, 1H), 8.47 (br d, <i>J</i> =1.35 Hz, 3H), 8.41 (dd, <i>J</i> =2.07, 8.19 Hz, 1H), 7.89 (br d, <i>J</i> =8.09 Hz, 1H), 7.49 (d, <i>J</i> =8.09 Hz, 2H), 7.23-7.34 (m, 2H), 5.86-6.14 (m, 2H), 4.10-4.29 (m, 1H), 3.75-4.02 (m, 1H), 3.54-3.73 (m, 3H), 2.97-3.07 (m, 1H), 2.82-2.92 (m, 1H), 1.74-1.99 (m, 3H), 1.41-1.65 (m, 1H)	B	Phenomenex Lux Cellulose-2, 25% isopropanol w/ 0.2% DEA Peak 4

Ex. #.	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
78	400MHz d ₄ -methanol	8.82 (s, 1H), 8.20-8.29 (m, 1H), 7.79 (d, <i>J</i> =8.19 Hz, 1H), 7.28-7.50 (m, 4H), 5.90 (s, 2H), 3.92-4.12 (m, 3H), 3.69-3.76 (m, 1H), 3.55-3.63 (m, 1H), 3.02-3.17 (m, 1H), 2.89-2.96 (m, 2H), 2.28-2.38 (m, 1H), 2.18 (ddt, <i>J</i> =5.34, 7.78, 13.31 Hz, 1H), 1.73-1.85 (m, 1H), 1.60-1.72 (m, 1H)	B	Phenomenex Lux Cellulose-2, 25% isopropanol w/ 0.2% DEA Peak 2
79	400MHz d ₄ -methanol	8.82 (d, <i>J</i> =1.45 Hz, 1H), 8.26 (dd, <i>J</i> =2.07, 8.19 Hz, 1H), 7.78 (d, <i>J</i> =8.09 Hz, 1H), 7.29-7.50 (m, 4H), 5.85-5.93 (m, 2H), 4.05-4.12 (m, 1H), 3.91-4.01 (m, 2H), 3.55-3.77 (m, 2H), 3.01-3.18 (m, 1H), 2.92 (ddt, <i>J</i> =4.28, 4.51, 8.41 Hz, 1H), 2.28-2.37 (m, 1H), 2.13-2.23 (m, 1H), 1.74-1.85 (m, 1H), 1.58-1.71 (m, 1H), 1.43 (s, 1H)	B	Phenomenex Lux Cellulose-2, 25% isopropanol w/ 0.2% DEA Peak 3
80	400MHz d ₆ -DMSO	8.91 (d, <i>J</i> =1.45 Hz, 1H), 8.40 (dd, <i>J</i> =2.18, 8.19 Hz, 1H), 8.28 (br s, 3H), 7.82 (d, <i>J</i> =8.09 Hz, 1H), 7.48 (dd, <i>J</i> =3.21, 7.77 Hz, 2H), 7.28-7.33 (m, 1H), 7.25 (d, <i>J</i> =7.37 Hz, 1H), 5.94 (d, <i>J</i> =3.73 Hz, 2H), 3.87-3.94 (m, 1H), 3.64-3.86 (m, 3H), 2.88 (br t, <i>J</i> =6.27 Hz, 2H), 2.61-2.70 (m, 1H), 2.16 (br d, <i>J</i> =6.22 Hz, 1H), 1.82-1.91 (m, 1H)	B	Chiralpak IC, 40% isopropanol w/ 0.2% DEA Peak 1
81	400MHz d ₆ -DMSO	8.91 (d, <i>J</i> =1.45 Hz, 1H), 8.36-8.43 (m, 1H), 8.33 (br s, 2H), 7.82 (d, <i>J</i> =8.19 Hz, 1H), 7.49 (dd, <i>J</i> =3.84, 7.67 Hz, 2H), 7.21-7.36 (m, 2H), 5.89-5.97 (m, 2H), 3.65-3.93 (m, 5H), 3.47-3.51 (m, 1H), 2.79-2.96 (m, 2H), 2.61-2.72 (m, 1H), 2.12-2.21 (m, 1H), 1.82-1.92 (m, 1H)	B	Chiralpak IC, 40% isopropanol w/ 0.2% DEA Peak 2
82	500MHz DMSO-d ₆	8.92 (s, 1H), 8.54 (br s, 2H), 8.33 (br d, <i>J</i> =7.79 Hz, 1H), 7.72 (s, 1H), 7.57 (br s, 2H), 5.62 (q, <i>J</i> =17.82 Hz, 2H), 5.01-5.20 (m, 1H), 3.59-3.63 (m, 1H), 3.20-3.31 (m, 2H), 3.08 (br t, <i>J</i> =10.96 Hz, 1H), 2.08 (br s, 1H), 1.86-2.03 (m, 1H)	B	--
83	400MHz DMSO-d ₆	8.93 (s, 1H), 8.40 (br s, 2H), 8.33 (dd, <i>J</i> =1.66, 8.09 Hz, 1H), 7.48-7.57 (m, 2H), 7.38 (dd, <i>J</i> =7.46, 10.26 Hz, 1H), 5.50-5.63 (m, 2H), 5.00-5.20 (m, 1H), 3.50 (br s, 1H), 3.24-3.33 (m, 1H), 3.15-3.23 (m, 1H), 3.02-3.14 (m, 1H), 1.87-2.12 (m, 2H)	B	--
84	400MHz DMSO-d ₆	8.90-8.97 (m, 1H), 8.86 (br s, 2H), 8.34 (br d, <i>J</i> =8.29 Hz, 1H), 7.53-7.63 (m, 2H), 7.40 (dd, <i>J</i> =7.31, 10.52 Hz, 1H), 5.54-5.73 (m, 2H), 3.92-4.21 (m, 2H), 3.65-3.78 (m, 2H), 3.33 (br d, <i>J</i> =7.05 Hz, 1H), 3.09-3.21 (m, 1H), 2.15-2.32 (m, 1H)	B	--
85	500 MHz, DMSO-d ₆	8.86-8.99 (m, 2H), 8.56 (d, <i>J</i> =2.21 Hz, 1H), 7.99 (br d, <i>J</i> =8.04 Hz, 1H), 7.47-7.59 (m, 2H), 7.25 (br s, 2H), 7.15-7.23 (m, 1H), 5.50-5.67 (m, 2H), 4.06-4.14 (m, 1H), 3.78-3.95 (m, 3H), 3.25-3.39 (m, 1H), 2.25-2.35 (m, 1H)	B	--

Ex. #.	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
86	500 MHz, DMSO-d ₆	8.55 (d, <i>J</i> =2.21 Hz, 1H), 8.47 (br s, 2H), 7.96 (dd, <i>J</i> =2.34, 8.43 Hz, 1H), 7.50 (d, <i>J</i> =7.78 Hz, 1H), 7.40 (br d, <i>J</i> =7.40 Hz, 1H), 7.09-7.22 (m, 3H), 5.43-5.58 (m, 2H), 5.04-5.22 (m, 1H), 3.72-3.84 (m, 2H), 3.62-3.69 (m, 2H), 3.36-3.43 (m, 2H), 3.19-3.28 (m, 1H), 2.04-2.16 (m, 1H)	B	--
87	500 MHz, DMSO-d ₆	8.93 (d, <i>J</i> =1.95 Hz, 1H), 8.81 (br s, 2H), 8.34 (dd, <i>J</i> =2.08, 8.17 Hz, 1H), 7.59 (d, <i>J</i> =8.17 Hz, 1H), 6.98-7.06 (m, 2H), 5.56-5.75 (m, 2H), 4.00 (dt, <i>J</i> =3.63, 5.51 Hz, 1H), 3.73 (br d, <i>J</i> =12.33 Hz, 1H), 3.38 (br d, <i>J</i> =12.33 Hz, 1H), 3.27-3.34 (m, 1H), 3.10-3.19 (m, 1H), 2.37-2.44 (m, 1H), 2.16-2.33 (m, 1H)	B	--
88	500MHz d ₄ -MeOH	8.84 (d, <i>J</i> =1.82 Hz, 1H), 8.15 (dd, <i>J</i> =2.08, 8.30 Hz, 1H), 7.40-7.52 (m, 2H), 6.91-7.00 (m, 2H), 5.47-5.62 (m, 2H), 3.34-3.54 (m, 2H), 3.08-3.28 (m, 3H), 2.21-2.36 (m, 1H), 2.00-2.21 (m, 1H)	I	YMC Amyose SA, Methanol THF (70:30) 40 %; peak 1
89	500MHz d ₆ -DMSO	8.94 (d, <i>J</i> =1.56 Hz, 1H), 8.33 (dd, <i>J</i> =1.95, 8.17 Hz, 1H), 7.57 (d, <i>J</i> =8.56 Hz, 1H), 7.43 (t, <i>J</i> =7.27 Hz, 2H), 7.18 (t, <i>J</i> =7.91 Hz, 1H), 5.58-5.69 (m, 2H), 3.34-3.28 (m, 3H), 3.02-3.13 (m, 2H), 2.18-2.33 (m, 1H), 1.97-2.13 (m, 1H)	-	
90	600MHz d ₆ -DMSO	8.95 (d, <i>J</i> =1.56 Hz, 1H), 8.34 (dd, <i>J</i> =2.02, 8.25 Hz, 1H), 7.54 (d, <i>J</i> =8.10 Hz, 1H), 7.44 (d, <i>J</i> =8.10 Hz, 1H), 7.41 (d, <i>J</i> =7.79 Hz, 1H), 7.16 (t, <i>J</i> =7.94 Hz, 1H), 5.54-5.67 (m, 2H), 4.26-4.45 (m, 1H), 3.38-3.50 (m, 2H), 3.01-3.10 (m, 1H), 2.79-2.92 (m, 2H), 2.00-2.13 (m, 1H), 1.66-1.80 (m, 1H)	--	--
91	600MHz d ₆ -DMSO	8.95 (d, <i>J</i> =1.25 Hz, 1H), 8.33 (dd, <i>J</i> =2.02, 8.25 Hz, 1H), 7.53 (d, <i>J</i> =8.41 Hz, 1H), 7.43 (d, <i>J</i> =8.10 Hz, 1H), 7.40 (d, <i>J</i> =7.79 Hz, 1H), 7.16 (t, <i>J</i> =7.79 Hz, 1H), 5.54-5.66 (m, 2H), 4.66-4.84 (m, 1H), 3.30 (br d, <i>J</i> =3.74 Hz, 1H), 3.25 (td, <i>J</i> =4.05, 12.77 Hz, 1H), 3.08-3.16 (m, 1H), 2.97-3.05 (m, 1H), 2.83-2.95 (m, 1H), 1.95-2.02 (m, 1H), 1.78-1.94 (m, 1H)	--	--
92	500MHz d ₄ -MeOH	8.79 (d, <i>J</i> =1.30 Hz, 1H), 8.15 (dd, <i>J</i> =2.08, 8.04 Hz, 1H), 8.05 (d, <i>J</i> =1.82 Hz, 1H), 7.77 (d, <i>J</i> =2.08 Hz, 1H), 7.54 (d, <i>J</i> =8.04 Hz, 1H), 5.52-5.64 (m, 2H), 4.30-4.48 (m, 1H), 3.68-3.75 (m, 1H), 3.58-3.67 (m, 1H), 3.14-3.23 (m, 1H), 2.94-3.06 (m, 2H), 2.08-2.19 (m, 1H), 1.75-1.87 (m, 1H)	B	Separated by flash chromatography
93	500MHz d ₄ -MeOH	8.83 (d, <i>J</i> =1.30 Hz, 1H), 8.17-8.22 (m, 2H), 7.66 (d, <i>J</i> =2.34 Hz, 1H), 7.54 (d, <i>J</i> =8.30 Hz, 1H), 5.54 (s, 2H), 4.32-4.50 (m, 1H), 3.64-3.75 (m, 1H), 3.52-3.64 (m, 1H), 3.15-3.27 (m, 1H), 3.02-3.10 (m, 1H), 2.99 (dd, <i>J</i> =8.56, 12.20 Hz, 1H), 2.06-2.23 (m, 1H), 1.78-1.92 (m, 1H)	B	Separated by flash chromatography

Ex. #.	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
94	500MHz d ₄ -MeOH	8.80 (d, <i>J</i> =1.82 Hz, 1H), 8.19 (d, <i>J</i> =2.34 Hz, 1H), 8.12 (dd, <i>J</i> =2.34, 8.04 Hz, 1H), 7.62 (d, <i>J</i> =2.08 Hz, 1H), 7.41 (d, <i>J</i> =8.04 Hz, 1H), 5.49 (s, 2H), 4.34-4.50 (m, 1H), 3.70-3.77 (m, 1H), 3.58-3.66 (m, 1H), 3.21 (ddd, <i>J</i> =2.47, 10.19, 13.04 Hz, 1H), 3.06-3.15 (m, 1H), 2.99-3.05 (m, 1H), 2.10-2.20 (m, 1H), 1.82-1.92 (m, 1H), 1.43 (s, 9H)	B	Separated by flash chromatography
95	500MHz d ₄ -MeOH	8.86 (d, <i>J</i> =1.30 Hz, 1H), 8.13 (dd, <i>J</i> =2.08, 8.30 Hz, 1H), 7.51 (d, <i>J</i> =7.79 Hz, 1H), 7.31 (d, <i>J</i> =8.30 Hz, 1H), 7.16-7.22 (m, 1H), 7.09-7.16 (m, 2H), 5.51 (s, 2H), 3.57-3.63 (m, 1H), 3.37-3.51 (m, 2H), 3.01-3.10 (m, 1H), 2.76-2.92 (m, 2H), 1.95-2.03 (m, 1H), 1.57-1.72 (m, 1H)	--	--
96	500MHz d ₄ -MeOH	8.85 (d, <i>J</i> =1.56 Hz, 1H), 8.13 (dd, <i>J</i> =2.08, 8.30 Hz, 1H), 7.51 (d, <i>J</i> =8.04 Hz, 1H), 7.31 (d, <i>J</i> =8.56 Hz, 1H), 7.16-7.21 (m, 1H), 7.09-7.15 (m, 2H), 5.51 (s, 2H), 3.56-3.64 (m, 1H), 3.37-3.51 (m, 2H), 3.06 (dt, <i>J</i> =2.60, 12.07 Hz, 1H), 2.78-2.92 (m, 2H), 1.99 (br dd, <i>J</i> =2.85, 13.23 Hz, 1H), 1.60-1.71 (m, 1H)	--	--
97	500MHz d ₄ -MeOH	8.86 (s, 1H), 8.08 (dd, <i>J</i> =2.08, 8.30 Hz, 1H), 7.37 (d, <i>J</i> =7.79 Hz, 1H), 7.23 (d, <i>J</i> =8.04 Hz, 1H), 7.07-7.13 (m, 2H), 7.01 (t, <i>J</i> =7.53 Hz, 1H), 5.55 (s, 2H), 3.68 (s, 2H), 3.49-3.61 (m, 6H), 2.15 (t, <i>J</i> =6.88 Hz, 2H)	--	--
98	500MHz d ₄ -MeOH	8.83 (d, <i>J</i> =1.30 Hz, 1H), 8.26 (dd, <i>J</i> =2.08, 8.04 Hz, 1H), 7.80 (d, <i>J</i> =8.30 Hz, 1H), 7.51 (d, <i>J</i> =8.04 Hz, 1H), 7.33-7.47 (m, 3H), 5.95 (d, <i>J</i> =19.72 Hz, 1H), 5.80 (br d, <i>J</i> =18.68 Hz, 1H), 4.17-4.37 (m, 3H), 3.97-4.10 (m, 2H), 3.80 (br t, <i>J</i> =8.95 Hz, 1H), 3.68-3.76 (m, 1H), 3.55 (dd, <i>J</i> =1.95, 13.36 Hz, 1H), 3.32-3.46 (m, 2H)	B	Chiralcel OD-H, 25% MeOH Peak 1
99	500MHz d ₄ -MeOH	8.83 (s, 1H), 8.27 (dd, <i>J</i> =1.82, 8.30 Hz, 1H), 7.80 (d, <i>J</i> =8.56 Hz, 1H), 7.51 (d, <i>J</i> =8.04 Hz, 1H), 7.38-7.47 (m, 2H), 7.35 (br d, <i>J</i> =8.04 Hz, 1H), 5.94 (d, <i>J</i> =18.68 Hz, 1H), 5.80 (br d, <i>J</i> =18.68 Hz, 1H), 4.18-4.36 (m, 3H), 3.95-4.06 (m, 2H), 3.80 (br t, <i>J</i> =8.30 Hz, 1H), 3.67-3.76 (m, 1H), 3.50-3.59 (m, 1H), 3.33-3.47 (m, 2H)	B	Chiralcel OD-H, 25% MeOH Peak 2
100	500MHz d ₄ -MeOH	8.87 (d, <i>J</i> =1.30 Hz, 1H), 8.11 (dd, <i>J</i> =2.08, 8.04 Hz, 1H), 7.38 (d, <i>J</i> =7.79 Hz, 1H), 7.28 (d, <i>J</i> =8.30 Hz, 1H), 7.07-7.16 (m, 2H), 6.99-7.06 (m, 1H), 5.63 (d, <i>J</i> =18.42 Hz, 1H), 5.48 (d, <i>J</i> =18.42 Hz, 1H), 3.93 (dd, <i>J</i> =2.72, 11.81 Hz, 1H), 3.64-3.75 (m, 3H), 3.48-3.63 (m, 2H), 3.43 (dd, <i>J</i> =8.95, 10.77 Hz, 1H), 2.84-3.00 (m, 3H)	B	Chiralcel OD-H, 20% MeOH Peak 1

Ex. #.	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
101	500MHz d ₄ -MeOH	8.87 (d, <i>J</i> =1.56 Hz, 1H), 8.11 (dd, <i>J</i> =2.08, 8.30 Hz, 1H), 7.38 (d, <i>J</i> =8.04 Hz, 1H), 7.28 (d, <i>J</i> =8.30 Hz, 1H), 7.07-7.16 (m, 2H), 6.99-7.06 (m, 1H), 5.63 (d, <i>J</i> =18.42 Hz, 1H), 5.48 (d, <i>J</i> =18.68 Hz, 1H), 3.93 (dd, <i>J</i> =2.60, 11.94 Hz, 1H), 3.64-3.74 (m, 3H), 3.47-3.62 (m, 2H), 3.43 (dd, <i>J</i> =8.95, 10.77 Hz, 1H), 2.85-2.99 (m, 3H)	B	Chiralcel OD-H, 20% MeOH Peak 2
102	500MHz d ₄ -MeOH	8.79-8.88 (m, 1H), 8.12 (dd, <i>J</i> =2.21, 8.17 Hz, 1H), 7.50 (d, <i>J</i> =7.79 Hz, 1H), 7.38 (d, <i>J</i> =8.30 Hz, 1H), 7.06-7.21 (m, 3H), 5.48-5.65 (m, 2H), 3.46 (d, <i>J</i> =11.94 Hz, 1H), 3.35-3.42 (m, 1H), 3.17-3.23 (m, 1H), 3.03-3.12 (m, 1H), 2.12 (ddd, <i>J</i> =4.41, 11.35, 13.30 Hz, 1H), 1.89-2.01 (m, 1H), 1.70-1.80 (m, 1H), 1.59-1.68 (m, 1H)	F	Chiralpak AD-H, 60% MeOH w/ 0.2% DEA Peak 1
103	500MHz d ₄ -MeOH	8.85 (d, <i>J</i> =1.56 Hz, 1H), 8.13 (dd, <i>J</i> =2.08, 8.30 Hz, 1H), 7.51 (d, <i>J</i> =7.79 Hz, 1H), 7.39 (d, <i>J</i> =8.04 Hz, 1H), 7.08-7.22 (m, 3H), 5.51-5.66 (m, 2H), 3.47 (d, <i>J</i> =12.20 Hz, 1H), 3.37-3.43 (m, 1H), 3.21 (br d, <i>J</i> =12.20 Hz, 1H), 3.04-3.11 (m, 1H), 2.07-2.18 (m, 1H), 1.90-2.01 (m, 1H), 1.72-1.81 (m, 1H), 1.58-1.70 (m, 1H)	F	Chiralpak AD-H, 60% MeOH w/ 0.2% DEA Peak 2
104	500MHz d ₄ -MeOH	8.86 (d, <i>J</i> =1.56 Hz, 1H), 8.12 (dd, <i>J</i> =2.08, 8.30 Hz, 1H), 7.51 (d, <i>J</i> =7.78 Hz, 1H), 7.32 (d, <i>J</i> =8.30 Hz, 1H), 7.06-7.23 (m, 3H), 5.48-5.62 (m, 2H), 3.54 (d, <i>J</i> =10.90 Hz, 1H), 3.37 (d, <i>J</i> =10.90 Hz, 1H), 3.24-3.28 (m, 1H), 3.08-3.22 (m, 2H), 3.04 (br d, <i>J</i> =11.94 Hz, 1H), 1.79-1.90 (m, 1H), 1.66-1.77 (m, 1H), 1.61 (ddd, <i>J</i> =4.28, 9.02, 13.43 Hz, 1H), 1.44-1.54 (m, 1H)	B	Chiralcel OD-H, 25% iPrOH w/ 0.2% DEA Peak 1
105	500MHz d ₄ -MeOH	8.86 (d, <i>J</i> =1.30 Hz, 1H), 8.12 (dd, <i>J</i> =2.08, 8.04 Hz, 1H), 7.51 (d, <i>J</i> =7.78 Hz, 1H), 7.33 (d, <i>J</i> =8.04 Hz, 1H), 7.07-7.22 (m, 3H), 5.51-5.62 (m, 2H), 3.54 (d, <i>J</i> =11.16 Hz, 1H), 3.37 (d, <i>J</i> =11.16 Hz, 1H), 3.24-3.28 (m, 1H), 3.09-3.22 (m, 2H), 3.01-3.08 (m, 1H), 1.79-1.90 (m, 1H), 1.67-1.77 (m, 1H), 1.62 (ddd, <i>J</i> =4.41, 9.02, 13.56 Hz, 1H), 1.46-1.56 (m, 1H)	B	Chiralcel OD-H, 25% iPrOH w/ 0.2% DEA Peak 2
106	600MHz DMSO-d ₆	8.94 (d, <i>J</i> =1.48 Hz, 1H), 8.33 (dd, <i>J</i> =2.10, 8.17 Hz, 1H), 7.58-7.63 (m, 2H), 7.51 (d, <i>J</i> =8.25 Hz, 1H), 7.42 (d, <i>J</i> =8.21 Hz, 1H), 5.61-5.68 (m, 2H), 4.75-4.83 (m, 1H), 4.68-4.73 (m, 1H), 3.28-3.32 (m, 3H), 3.24 (td, <i>J</i> =4.03, 12.81 Hz, 1H), 3.05-3.19 (m, 2H), 2.86-3.04 (m, 3H), 2.57-2.65 (m, 1H), 2.33-2.48 (m, 1H), 1.92-2.01 (m, 1H), 1.77-1.91 (m, 1H)	B	SFC: Chiralcel OD-H, 15% methanol.

Ex. #.	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
107	600MHz DMSO-d ₆	9.00 (d, <i>J</i> =1.32 Hz, 1H), 8.39 (dd, <i>J</i> =2.10, 8.25 Hz, 1H), 7.84 (s, 1H), 7.58 (d, <i>J</i> =8.17 Hz, 1H), 7.37-7.45 (m, 2H), 5.63-5.72 (m, 2H), 4.83-4.90 (m, 1H), 4.76-4.81 (m, 1H), 3.33-3.37 (m, 2H), 3.30 (td, <i>J</i> =3.99, 12.65 Hz, 1H), 3.13-3.25 (m, 2H), 2.95-3.11 (m, 2H), 2.01-2.09 (m, 1H), 1.87-2.00 (m, 1H)	B	SFC: Chiralcel OD-H, 15% methanol.
108	600MHz DMSO-d ₆	8.94 (d, <i>J</i> =1.40 Hz, 1H), 8.34 (dd, <i>J</i> =2.14, 8.21 Hz, 1H), 7.62 (s, 1H), 7.63 (d, <i>J</i> =6.89 Hz, 1H), 7.56 (d, <i>J</i> =8.17 Hz, 1H), 7.44 (d, <i>J</i> =8.47 Hz, 1H), 5.65-5.73 (m, 2H), 3.18-3.26 (m, 1H), 2.98-3.12 (m, 2H), 2.17-2.29 (m, 1H), 1.89-2.07 (m, 1H), 1.79 (br s, 2H)	B	SFC: Chiralcel OD-H, 15% methanol.
109	600MHz DMSO-d ₆	8.94 (dd, <i>J</i> =0.66, 2.06 Hz, 1H), 8.34 (dd, <i>J</i> =2.14, 8.21 Hz, 1H), 7.80 (s, 1H), 7.56 (d, <i>J</i> =8.17 Hz, 1H), 7.38 (dd, <i>J</i> =1.21, 8.45 Hz, 1H), 7.33 (d, <i>J</i> =8.41 Hz, 1H), 5.58-5.69 (m, 2H), 3.37-3.44 (m, 1H), 3.20-3.30 (m, 1H), 3.07-3.18 (m, 1H), 2.99-3.06 (m, 1H), 2.21-2.31 (m, 1H), 1.96-2.11 (m, 2H), 1.92 (br s, 1H)	B	SFC: Chiralcel OD-H, 15% methanol.
110	600MHz DMSO-d ₆	8.94 (d, <i>J</i> =1.48 Hz, 1H), 8.49 (br s, 3H), 8.36 (dd, <i>J</i> =2.06, 8.21 Hz, 1H), 7.55 (br d, <i>J</i> =8.10 Hz, 1H), 7.33 (s, 1H), 7.10 (d, <i>J</i> =8.25 Hz, 1H), 6.99 (br d, <i>J</i> =8.17 Hz, 1H), 5.55-5.63 (m, 2H), 4.69-4.81 (m, 1H), 4.24-4.38 (m, 1H), 3.81 (br d, <i>J</i> =12.38 Hz, 1H), 3.61 (br s, 1H), 3.54 (br d, <i>J</i> =12.69 Hz, 1H), 3.10-3.21 (m, 2H), 2.51-2.54 (m, 9H), 2.37 (s, 3H), 2.21 (br t, <i>J</i> =9.81 Hz, 1H), 1.82-1.90 (m, 1H)	B	SFC: Phenomenex Lux Cellulose-2, 25% methanol.
111	600MHz DMSO-d ₆	8.40 (br s, 1H), 8.27 (dd, <i>J</i> =2.06, 8.21 Hz, 1H), 7.47 (br d, <i>J</i> =8.17 Hz, 1H), 6.94-6.98 (m, 1H), 5.44-5.54 (m, 1H), 4.76 (dt, <i>J</i> =4.94, 9.17 Hz, 1H), 3.90-4.72 (m, 3H), 3.69 (br d, <i>J</i> =12.61 Hz, 1H), 3.52 (br s, 1H), 3.42 (br d, <i>J</i> =12.38 Hz, 1H), 2.98-3.12 (m, 1H), 2.42-2.52 (m, 5H), 2.23 (s, 2H), 2.11 (br t, <i>J</i> =9.81 Hz, 1H), 1.72-1.81 (m, 1H)	B	SFC: Phenomenex Lux Cellulose-2, 25% methanol.
112	600MHz DMSO-d ₆	8.95 (dd, <i>J</i> =0.70, 2.02 Hz, 1H), 8.31 (dd, <i>J</i> =2.14, 8.21 Hz, 1H), 7.41 (s, 1H), 7.41 (d, <i>J</i> =6.67 Hz, 1H), 7.29 (s, 1H), 5.43-5.54 (m, 2H), 4.34-4.43 (m, 1H), 4.26-4.34 (m, 1H), 3.25-3.38 (m, 11H), 2.96-3.05 (m, 1H), 2.85-2.91 (m, 1H), 2.76 (dd, <i>J</i> =8.60, 12.50 Hz, 1H), 2.34 (s, 3H), 1.94-2.08 (m, 2H), 1.65-1.83 (m, 1H)	B	SFC: Phenomenex Lux Cellulose-2, 20% methanol
113	600MHz DMSO-d ₆	8.96 (s, 1H), 8.31 (dd, <i>J</i> =2.14, 8.21 Hz, 1H), 7.38-7.53 (m, 2H), 7.15 (s, 1H), 5.38-5.53 (m, 2H), 4.25-4.43 (m, 1H), 3.38-3.40 (m, 1H), 3.29-3.34 (m, 1H), 2.97-3.05 (m, 1H), 2.84-2.92 (m, 1H), 2.76 (dd, <i>J</i> =8.56, 12.53 Hz, 1H), 2.30 (s, 3H), 1.98-2.09 (m, 1H), 1.63-1.80 (m, 3H)	B	SFC: Phenomenex Lux Cellulose-2, 20% methanol

Ex. #.	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
114	600MHz DMSO-d ₆	8.95 (s, 1H), 8.30 (dd, <i>J</i> =2.14, 8.21 Hz, 1H), 7.37 (d, <i>J</i> =8.33 Hz, 1H), 7.31 (d, <i>J</i> =6.93 Hz, 1H), 7.03 (d, <i>J</i> =9.89 Hz, 1H), 5.44-5.52 (m, 2H), 4.35-4.41 (m, 1H), 4.26-4.34 (m, 1H), 3.19-3.33 (m, 1H), 2.93-3.02 (m, 1H), 2.78-2.93 (m, 1H), 2.74 (dd, <i>J</i> =8.64, 12.46 Hz, 1H), 2.25 (d, <i>J</i> =1.48 Hz, 3H), 2.10-2.23 (m, 1H), 1.95-2.09 (m, 2H), 1.66-1.83 (m, 1H)	B	SFC: Phenomenex Lux Cellulose-2, 20% methanol.
115	600MHz DMSO-d ₆	8.92-8.98 (m, 1H), 8.30 (d, <i>J</i> =7.92 Hz, 1H), 7.31-7.44 (m, 2H), 7.22 (d, <i>J</i> =10.43 Hz, 1H), 7.03 (d, <i>J</i> =7.01 Hz, 1H), 5.36-5.51 (m, 2H), 4.35-4.41 (m, 1H), 4.26-4.34 (m, 1H), 3.26-3.44 (m, 1H), 2.85-3.02 (m, 1H), 2.69-2.81 (m, 2H), 2.23-2.27 (m, 1H), 2.21 (d, <i>J</i> =1.56 Hz, 3H), 1.92-2.08 (m, 1H), 1.60-1.92 (m, 1H)	B	SFC: Phenomenex Lux Cellulose-2, 20% methanol.
116	600MHz DMSO-d ₆	8.98 (d, <i>J</i> =1.63 Hz, 1H), 8.31 (dd, <i>J</i> =2.14, 8.21 Hz, 1H), 7.44 (d, <i>J</i> =7.63 Hz, 1H), 7.38 (d, <i>J</i> =8.25 Hz, 1H), 7.07-7.15 (m, 2H), 6.94-7.04 (m, 1H), 5.44-5.50 (m, 2H), 3.38-3.48 (m, 1H), 3.23-3.32 (m, 1H), 2.82-2.91 (m, 1H), 2.52-2.62 (m, 1H), 2.43-2.49 (m, 1H), 2.11 (s, 3H), 1.80-1.88 (m, 1H), 1.68 (td, <i>J</i> =3.67, 13.14 Hz, 1H), 1.50-1.61 (m, 1H), 1.11-1.23 (m, 1H)	B	--
117	600MHz DMSO-d ₆	8.96 (s, 1H), 8.34 (dd, <i>J</i> =2.14, 8.21 Hz, 1H), 7.52 (d, <i>J</i> =7.98 Hz, 2H), 7.27 (s, 1H), 7.15-7.20 (m, 1H), 7.12 (d, <i>J</i> =7.93 Hz, 1H), 7.10 (s, 1H), 5.62 (d, <i>J</i> =17.75 Hz, 1H), 5.55 (d, <i>J</i> =17.75 Hz, 1H), 3.68 (br d, <i>J</i> =11.83 Hz, 1H), 3.34 (br s, 1H), 3.19-3.28 (m, 2H), 3.01 (br t, <i>J</i> =9.42 Hz, 1H), 2.51-2.61 (m, 3H), 1.98-2.06 (m, 1H), 1.83 (dt, <i>J</i> =2.88, 6.50 Hz, 1H), 1.53-1.67 (m, 2H)	--	--
118	600MHz DMSO-d ₆	8.94 (s, 1H), 8.33 (dd, <i>J</i> =2.14, 8.21 Hz, 1H), 7.47 (dd, <i>J</i> =2.18, 8.33 Hz, 2H), 7.05-7.09 (m, 2H), 6.95 (d, <i>J</i> =8.98 Hz, 1H), 5.51-5.58 (m, 2H), 4.47-4.56 (dt, <i>J</i> =4.59, 8.68 Hz, 1H), 3.43-3.57 (m, 1H), 3.37-3.43 (m, 1H), 3.10-3.23 (m, 1H), 2.96-3.03 (m, 1H), 2.87 (dd, <i>J</i> =9.26, 12.61 Hz, 1H), 2.05-2.12 (m, 1H), 1.70-1.79 (m, 1H)	B	SFC: Chiralcel OD-H, 15% methanol.
119	600MHz DMSO-d ₆	8.95 (s, 1H), 8.32 (dd, <i>J</i> =2.14, 8.21 Hz, 1H), 7.45 (d, <i>J</i> =8.33 Hz, 1H), 7.22-7.30 (m, 1H), 7.10-7.18 (m, 1H), 6.87 (dd, <i>J</i> =2.34, 8.56 Hz, 1H), 5.50-5.57 (m, 2H), 4.43 (dt, <i>J</i> =4.59, 8.25 Hz, 1H), 3.40-3.49 (m, 1H), 3.37-3.40 (m, 1H), 2.91-3.07 (m, 1H), 2.81 (dd, <i>J</i> =8.80, 12.53 Hz, 1H), 2.57-2.65 (m, 1H), 2.01-2.11 (m, 1H), 1.68-1.78 (m, 1H)	B	SFC: Chiralcel OD-H, 15% methanol.

Ex. #.	Freq., Solvent	¹ H NMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
120	600MHz DMSO-d ₆	8.95 (d, <i>J</i> =1.95 Hz, 1H), 8.29 (dd, <i>J</i> =2.10, 8.25 Hz, 1H), 7.33 (d, <i>J</i> =8.25 Hz, 1H), 6.96 (t, <i>J</i> =8.02 Hz, 1H), 6.73 (d, <i>J</i> =8.02 Hz, 1H), 6.67 (d, <i>J</i> =8.08 Hz, 1H), 5.44-5.53 (m, 2H), 4.28-4.34 (m, 1H), 3.89 (s, 3H), 3.24-3.42 (m, 1H), 2.85-3.01 (m, 2H), 2.75 (dd, <i>J</i> =8.64, 12.46 Hz, 1H), 1.98-2.16 (m, 1H), 1.95 (br s, 1H), 1.69-1.86 (m, 1H)	--	--
121	600MHz DMSO-d ₆	8.94 (s, 1H), 8.30 (dd, <i>J</i> =1.95, 8.17 Hz, 1H), 7.43 (d, <i>J</i> =8.25 Hz, 1H), 6.91-7.03 (m, 3H), 5.48-5.57 (m, 2H), 4.86-4.78 (m, 1H), 3.64-3.78 (m, 1H), 3.48-3.63 (m, 1H), 3.06-3.17 (m, 1H), 2.99 (br t, <i>J</i> =11.44 Hz, 1H), 2.46-2.49 (m, 1H), 2.14-2.23 (m, 1H), 1.82-1.91 (m, 1H)	--	--
122	600MHz DMSO-d ₆	9.03 (d, <i>J</i> =1.40 Hz, 1H), 8.71-8.78 (m, 1H), 8.28 (br s, 1H), 7.86 (br s, 1H), 7.67 (s, 1H), 7.60 (d, <i>J</i> =8.33 Hz, 1H), 7.42 (d, <i>J</i> =8.47 Hz, 1H), 5.64-5.77 (m, 2H), 4.75-7.1 (m, 1H), 3.30-3.31 (m, 2H), 3.07-3.17 (m, 1H), 2.86-3.02 (m, 1H), 2.28-2.45 (m, 1H), 1.93-2.12 (m, 1H), 1.78-1.93 (m, 1H)	B	SFC: Chiralpak AD-H, 25% methanol
123	600MHz DMSO-d ₆	9.03 (d, <i>J</i> =1.32 Hz, 1H), 8.75 (d, <i>J</i> =1.32 Hz, 1H), 8.27 (s, 1H), 7.86 (br s, 1H), 7.77 (s, 1H), 7.34-7.41 (m, 2H), 5.68 (d, <i>J</i> =1.79 Hz, 2H), 4.77-4.72 (m, 1H), 3.22-3.32 (m, 1H), 3.09-3.20 (m, 1H), 2.89-3.04 (m, 2H), 1.95-2.05 (m, 1H), 1.80-1.94 (m, 1H), 1.76 (br s, 1H)	B	SFC: Chiralpak AD-H, 25% methanol
124	600MHz DMSO-d ₆	8.92 (s, 1H), 8.33 (dd, <i>J</i> =2.14, 8.21 Hz, 1H), 7.70 (s, 1H), 7.52 (d, <i>J</i> =8.47 Hz, 1H), 7.49 (s, 1H), 5.60 (s, 2H), 4.35-4.35 (m, 1H), 3.38-3.51 (m, 1H), 2.98-3.08 (m, 1H), 2.82-2.90 (m, 1H), 2.78 (dd, <i>J</i> =8.64, 12.53 Hz, 1H), 2.00-2.09 (m, 1H), 1.77 (br s, 1H), 1.63-1.74 (m, 1H)	B	SFC: Chiralpak AD-H, 25% methanol
125	600MHz DMSO-d ₆	8.94 (s, 1H), 8.33 (dd, <i>J</i> =2.14, 8.21 Hz, 1H), 7.62 (s, 1H), 7.57 (s, 1H), 7.55 (d, <i>J</i> =8.35 Hz, 1H), 5.54-5.63 (m, 2H), 4.39-4.27 (m, 1H), 3.37-3.46 (m, 2H), 2.98-3.09 (m, 1H), 2.82-2.91 (m, 1H), 2.78 (dd, <i>J</i> =8.60, 12.57 Hz, 1H), 1.98-2.09 (m, 1H), 1.63-1.80 (m, 1H)	B	SFC: Chiralpak AD-H, 25% methanol
126	600MHz DMSO-d ₆	8.93 (s, 1H), 8.34 (dd, <i>J</i> =2.14, 8.21 Hz, 1H), 7.75 (s, 1H), 7.72 (s, 1H), 7.55 (d, <i>J</i> =8.25 Hz, 1H), 5.63-5.71 (m, 2H), 4.37-4.28 (m, 1H), 3.36-3.51 (m, 2H), 3.04-3.11 (m, 1H), 2.79-2.88 (m, 2H), 2.00-2.08 (m, 1H), 1.62-1.78 (m, 1H)	B	SFC: Chiralcel OJ-H, 10% methanol
127	600MHz DMSO-d ₆	¹ H NMR (600 MHz, DMSO-d ₆) δ 8.93 (d, <i>J</i> =1.40 Hz, 1H), 8.34 (dd, <i>J</i> =2.10, 8.17 Hz, 1H), 7.88 (s, 1H), 7.63 (s, 1H), 7.57 (d, <i>J</i> =8.17 Hz, 1H), 5.60-5.67 (m, 2H), 4.37-4.42-4.29 (m, 1H), 3.36-3.45 (m, 1H), 3.14-3.29 (m, 1H), 3.00-3.09 (m, 1H), 2.77-2.89 (m, 2H), 1.95-2.08 (m, 1H), 1.64-1.81 (m, 1H)	B	SFC: Chiralcel OJ-H, 10% methanol.

Ex. #.	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
128	600MHz DMSO-d ₆	8.90-8.99 (m, 1H), 8.26-8.35 (m, 1H), 7.52-7.44 (d, <i>J</i> =7.66 Hz, 1H), 7.33 (d, <i>J</i> =8.30 Hz, 1H), 7.23-7.29 (m, 1H), 7.00-7.19 (m, 1H), 6.99-7.19 (m, 1H), 5.76-5.42 (m, 2H), 2.98-3.15 (m, 2H), 2.72-2.91 (m, 2H), 2.69-2.65 (s, 1H), 2.22-2.39 (m, 1H), 1.71 (br d, <i>J</i> =6.36 Hz, 1H), 1.69 (br d, <i>J</i> =5.19 Hz, 1H), 1.42-1.62 (m, 6H), 1.38 (s, 1H).	--	--
129	600MHz DMSO-d ₆	8.97 (s, 1H), 8.30 (dd, <i>J</i> =2.14, 8.21 Hz, 1H), 7.45 (d, <i>J</i> =7.79 Hz, 1H), 7.33 (d, <i>J</i> =8.17 Hz, 1H), 7.18 (d, <i>J</i> =7.79 Hz, 1H), 7.00-7.14 (m, 2H), 5.47-5.60 (m, 2H), 3.12-3.27 (m, 1H), 3.06 (br d, <i>J</i> =11.99 Hz, 1H), 2.88-3.01 (m, 2H), 2.56-2.64 (m, 1H), 2.51-2.56 (m, 1H), 1.64-1.73 (m, 2H), 1.46-1.59 (m, 1H), 1.21-1.41 (m, 7H)	B	SFC: Phenomenex Lux Cellulose-2, 30% methanol
130	600MHz DMSO-d ₆	8.97 (d, <i>J</i> =1.71 Hz, 1H), 8.30 (dd, <i>J</i> =2.14, 8.21 Hz, 1H), 7.45 (d, <i>J</i> =7.55 Hz, 1H), 7.33 (d, <i>J</i> =8.17 Hz, 1H), 7.18 (d, <i>J</i> =7.86 Hz, 1H), 7.02-7.12 (m, 2H), 5.47-5.58 (m, 2H), 3.12-3.26 (m, 1H), 3.06 (br d, <i>J</i> =12.07 Hz, 1H), 2.87-3.01 (m, 2H), 2.56-2.63 (m, 1H), 2.52-2.55 (m, 1H), 1.63-1.73 (m, 2H), 1.46-1.58 (m, 1H), 1.21-1.41 (m, 7H)	B	SFC: Phenomenex Lux Cellulose-2, 30% methanol
131	600MHz DMSO-d ₆	8.96 (s, 1H), 8.29 (dd, <i>J</i> =2.14, 8.21 Hz, 1H), 7.44 (d, <i>J</i> =7.71 Hz, 1H), 7.35 (d, <i>J</i> =8.25 Hz, 1H), 7.06-7.12 (m, 2H), 6.93-7.04 (m, 1H), 5.41-5.51 (m, 2H), 4.10 (br s, 1H), 3.75 (td, <i>J</i> =2.88, 10.98 Hz, 1H), 3.69 (q, <i>J</i> =3.58 Hz, 1H), 3.37-3.49 (m, 1H), 3.01-3.21 (m, 2H), 2.80-2.94 (m, 2H), 2.43-2.49 (m, 1H), 1.81 (br s, 1H), 1.67-1.79 (m, 1H)	B	SFC: Phenomenex Lux Cellulose-2, 30% methanol.
132	600MHz DMSO-d ₆	8.96 (s, 1H), 8.29 (dd, <i>J</i> =2.14, 8.21 Hz, 1H), 7.45 (d, <i>J</i> =7.97 Hz, 1H), 7.37 (d, <i>J</i> =8.25 Hz, 1H), 7.07-7.13 (m, 2H), 6.98-7.06 (m, 1H), 5.44-5.52 (m, 2H), 4.11 (br s, 1H), 3.80 (td, <i>J</i> =2.86, 11.25 Hz, 1H), 3.74 (br d, <i>J</i> =3.11 Hz, 1H), 3.44-3.54 (m, 1H), 3.14-3.21 (m, 2H), 2.94-3.12 (m, 2H), 2.51-2.62 (m, 1H), 1.83 (br s, 1H), 1.69-1.80 (m, 1H)	B	SFC: Phenomenex Lux Cellulose-2, 30% methanol.
133	600MHz DMSO-d ₆	9.04 (s, 1H), 8.70 (s, 1H), 7.85 (m, 1H), 7.52 (dd, <i>J</i> =7.47, 10.98 Hz, 1H), 7.50 (br dd, <i>J</i> =7.32, 10.35 Hz, 1H), 7.10-7.25 (m, 1H), 5.57 (s, 2H), 4.45-4.60 (m, 1H), 3.62-3.70 (m, 1H), 3.36-3.46 (m, 1H), 2.97 (br t, <i>J</i> =11.21 Hz, 1H), 2.75 (br dd, <i>J</i> =10.12, 12.30 Hz, 1H), 2.33-2.46 (m, 1H), 2.10-2.20 (m, 1H), 1.78-1.86 (m, 1H)	--	--
134	600MHz DMSO-d ₆	9.03 (d, <i>J</i> =1.37 Hz, 1H), 8.74-8.75 (dd, <i>J</i> =1.37, 5.87 Hz, 1H), 8.25 (br d, <i>J</i> =3.97 Hz, 1H), 7.83 (br s, 1H), 7.5-7.68 (s, 1H), 7.60 (d, <i>J</i> =8.32 Hz, 1H), 7.36-7.44 (m, 2H), 5.72 (s, 1H), 5.68 (s, 1H), 4.36-4.45 (m, 1H), 3.38-3.54 (m, 2H), 3.02-3.13 (m, 1H), 2.80-2.95 (m, 2H), 1.99-2.16 (m, 1H), 1.67-1.78 (m, 1H)	--	--

Ex. #.	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
135	600MHz DMSO-d ₆	8.98 (d, <i>J</i> =1.56 Hz, 1H), 8.30 (dd, <i>J</i> =2.14, 8.21 Hz, 1H), 7.44 (d, <i>J</i> =7.79 Hz, 1H), 7.33 (d, <i>J</i> =8.25 Hz, 1H), 7.15 (d, <i>J</i> =7.86 Hz, 1H), 7.10 (t, <i>J</i> =7.76 Hz, 1H), 7.03 (t, <i>J</i> =7.58 Hz, 1H), 5.54-5.60 (m, 1H), 5.44-5.52 (m, 1H), 3.15-3.27 (m, 1H), 3.04-3.13 (m, 2H), 2.75-2.89 (m, 3H), 2.56-2.64 (m, 1H), 1.65-1.76 (m, 1H), 1.54-1.63 (m, 2H), 1.42-1.52 (m, 4H), 1.27-1.41 (m, 1H)	B	SFC: Phenomenex Lux Cellulose-2, 40% methanol
136	600MHz DMSO-d ₆	8.98 (dd, <i>J</i> =0.74, 2.06 Hz, 1H), 8.30 (dd, <i>J</i> =2.14, 8.21 Hz, 1H), 7.44 (d, <i>J</i> =7.55 Hz, 1H), 7.33 (d, <i>J</i> =8.33 Hz, 1H), 7.15 (d, <i>J</i> =7.86 Hz, 1H), 7.10 (dt, <i>J</i> =1.17, 7.59 Hz, 1H), 7.00-7.06 (m, 1H), 5.57 (d, <i>J</i> =17.91 Hz, 1H), 5.48 (d, <i>J</i> =17.91 Hz, 1H), 3.15-3.27 (m, 1H), 3.02-3.14 (m, 2H), 2.75-2.90 (m, 3H), 2.56-2.64 (m, 1H), 1.65-1.76 (m, 1H), 1.54-1.63 (m, 2H), 1.42-1.52 (m, 4H), 1.27-1.40 (m, 1H)	B	SFC: Phenomenex Lux Cellulose-2, 40% methanol.
137	600MHz DMSO-d ₆	8.96 (d, <i>J</i> =1.48 Hz, 1H), 8.29 (dd, <i>J</i> =2.14, 8.21 Hz, 1H), 7.38 (d, <i>J</i> =8.17 Hz, 1H), 7.05 (s, 1H), 7.01 (d, <i>J</i> =8.55 Hz, 1H), 6.67 (dd, <i>J</i> =2.41, 8.72 Hz, 1H), 5.46-5.55 (m, 2H), 3.73 (s, 1H), 3.08-3.24 (m, 2H), 2.97 (br dd, <i>J</i> =9.03, 11.29 Hz, 1H), 2.52-2.57 (m, 1H), 2.19-2.28 (m, 1H), 1.93-2.09 (m, 1H), 1.83 (br s, 1H)	B	SFC: Chiralcel OJ-H, 15% methanol
138	600MHz DMSO-d ₆	8.96 (d, <i>J</i> =1.63 Hz, 1H), 8.29 (dd, <i>J</i> =2.10, 8.17 Hz, 1H), 7.39 (d, <i>J</i> =8.10 Hz, 1H), 7.36 (d, <i>J</i> =8.52 Hz, 1H), 6.78 (s, 1H), 6.74 (d, <i>J</i> =8.78 Hz, 1H), 5.53 (s, 2H), 3.66-3.69 (m, 1H), 3.05-3.17 (m, 2H), 2.90-2.96 (m, 1H), 2.17-2.26 (m, 1H), 1.97-2.07 (m, 1H), 1.75 (br s, 1H)	B	SFC: Chiralcel OJ-H, 15% methanol
139	600MHz DMSO-d ₆	8.95 (d, <i>J</i> =1.95 Hz, 1H), 8.30-8.35 (m, 1H), 7.60 (s, 1H), 7.59 (d, <i>J</i> =10.87 Hz, 1H), 7.50 (d, <i>J</i> =8.17 Hz, 1H), 7.42 (dd, <i>J</i> =1.32, 8.33 Hz, 1H), 5.56-5.63 (m, 2H), 3.49 (br dd, <i>J</i> =3.23, 12.03 Hz, 2H), 2.87-2.94 (m, 1H), 2.57-2.69 (m, 1H), 2.42-2.48 (m, 1H), 2.11 (s, 3H), 1.81-1.87 (m, 1H), 1.64-1.71 (m, 1H), 1.48-1.56 (m, 1H), 1.15-1.28 (m, 1H)	B	SFC: Chiralcel OD-H, 15% methanol w/ 0.2% DEA
140	600MHz DMSO-d ₆	8.95 (d, <i>J</i> =1.63 Hz, 1H), 8.33 (dd, <i>J</i> =2.10, 8.25 Hz, 1H), 7.75 (s, 1H), 7.50 (d, <i>J</i> =8.25 Hz, 1H), 7.29-7.40 (m, 2H), 5.51-5.60 (m, 2H), 3.48 (br dd, <i>J</i> =3.23, 12.03 Hz, 2H), 2.86-2.95 (m, 1H), 2.62 (dd, <i>J</i> =9.03, 12.07 Hz, 1H), 2.43-2.48 (m, 1H), 2.09-2.13 (m, 3H), 1.81-1.88 (m, 1H), 1.69 (td, <i>J</i> =3.79, 13.29 Hz, 1H), 1.51-1.59 (m, 1H), 1.16-1.28 (m, 1H)	B	SFC: Chiralcel OD-H, 15% methanol w/ 0.2% DEA

Ex. #.	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
141	600MHz DMSO-d ₆	8.97 (s, 1H), 8.28 (dd, <i>J</i> =2.02, 8.17 Hz, 1H), 7.43 (d, <i>J</i> =7.79 Hz, 1H), 7.32 (d, <i>J</i> =8.25 Hz, 1H), 7.16 (d, <i>J</i> =7.79 Hz, 1H), 7.09 (t, <i>J</i> =7.24 Hz, 1H), 7.02 (t, <i>J</i> =7.28 Hz, 1H), 5.47-5.57 (m, 2H), 3.08-3.25 (m, 2H), 2.96 (br t, <i>J</i> =8.95 Hz, 1H), 2.77-2.89 (m, 2H), 1.73 (tdd, <i>J</i> =4.41, 8.78, 13.23 Hz, 1H), 1.55 (td, <i>J</i> =3.37, 6.50 Hz, 2H), 1.29-1.48 (m, 2H), 0.93 (s, 1H)	--	--
142	500MHz DMSO-d ₆	8.95 (s, 1H), 8.36 (br d, <i>J</i> =8.19 Hz, 1H), 8.10 (br s, 3H), 7.56 (d, <i>J</i> =8.19 Hz, 1H), 7.15 (d, <i>J</i> =8.81 Hz, 1H), 7.07 (s, 1H), 6.81 (br d, <i>J</i> =8.91 Hz, 1H), 5.52-5.65 (m, 2H), 3.77 (s, 3H), 3.58-3.75 (m, 1H), 3.34 (br d, <i>J</i> =13.27 Hz, 2H), 3.21 (br dd, <i>J</i> =8.71, 12.13 Hz, 1H), 3.07 (br t, <i>J</i> =9.23 Hz, 1H), 1.96 (br s, 1H), 1.83 (br s, 1H), 1.58 (br s, 2H)	B	SFC: Chiralpak IC, 40% isopropanol
143	500MHz DMSO-d ₆	8.95 (s, 1H), 8.35 (d, <i>J</i> =8.09 Hz, 1H), 8.02 (br s, 3H), 7.52 (d, <i>J</i> =8.29 Hz, 1H), 7.42 (d, <i>J</i> =8.50 Hz, 1H), 6.83-6.89 (m, 2H), 5.51-5.66 (m, 2H), 3.48-3.67 (m, 1H), 3.34 (br s, 1H), 3.26 (br d, <i>J</i> =13.48 Hz, 1H), 3.15 (br dd, <i>J</i> =8.34, 12.39 Hz, 1H), 2.94-3.07 (m, 1H), 1.94 (br s, 1H), 1.81 (br s, 1H), 1.56 (br s, 2H)	B	SFC: Chiralpak IC, 40% isopropanol
144	500MHz DMSO-d ₆	8.91 (d, <i>J</i> =1.45 Hz, 1H), 8.41 (br s, 3H), 8.33 (dd, <i>J</i> =2.07, 8.19 Hz, 1H), 7.55 (d, <i>J</i> =8.29 Hz, 1H), 7.15-7.21 (m, 2H), 5.40-5.64 (2, 2H), 4.72-4.84 (dt, <i>J</i> =5.03, 9.36 Hz, 1H), 3.69-3.78 (m, 1H), 3.51 (br s, 1H), 3.43 (br d, <i>J</i> =12.54 Hz, 1H), 2.94-3.12 (m, 2H), 2.12-2.22 (m, 1H), 1.73-1.88 (m, 1H)	--	--
145	500MHz DMSO-d ₆	8.94 (d, <i>J</i> =1.55 Hz, 1H), 8.75 (br s, 3H), 8.37 (dd, <i>J</i> =2.07, 8.19 Hz, 1H), 7.66 (br d, <i>J</i> =7.15 Hz, 1H), 7.21 (br d, <i>J</i> =8.71 Hz, 1H), 7.08 (d, <i>J</i> =2.28 Hz, 1H), 6.84 (br d, <i>J</i> =8.40 Hz, 1H), 5.60-5.76 (m, 2H), 4.86-4.98 (m, 1H), 3.95 (br d, <i>J</i> =6.95 Hz, 1H), 3.59-3.79 (m, 1H), 3.28-3.52 (m, 1H), 3.00-3.27 (m, 2H), 2.19-2.31 (m, 1H), 1.79-1.91 (m, 1H)	B	SFC: Chiralpak AD-H, 20% methanol
146	500MHz DMSO-d ₆	8.94 (d, <i>J</i> =1.45 Hz, 1H), 8.74 (br s, 3H), 8.35 (dd, <i>J</i> =2.07, 8.19 Hz, 1H), 7.60 (br d, <i>J</i> =7.98 Hz, 1H), 7.40-7.47 (m, <i>J</i> =8.71 Hz, 1H), 6.93 (br s, 1H), 6.81-6.90 (m, <i>J</i> =8.60 Hz, 1H), 5.59-5.76 (m, 2H), 4.81-5.01 (m, 1H), 3.86 (br d, <i>J</i> =11.30 Hz, 1H), 3.59-3.79 (m, 1H), 3.33-3.55 (m, 1H), 3.05-3.32 (m, 2H), 2.17-2.33 (m, 1H), 1.70-1.88 (m, 1H)	B	SFC: Chiralpak AD-H, 20% methanol
147	500MHz CDCl ₃	8.87 (s, 2H), 8.05 (d, <i>J</i> =8.19 Hz, 2H), 7.65 (d, <i>J</i> =8.19 Hz, 2H), 5.84 (q, <i>J</i> =6.57 Hz, 2H), 3.08 (s, 6H), 1.78 (d, <i>J</i> =6.63 Hz, 6H), 1.62 (br s, 3H), 1.44 (br s, 2H)	B	SFC: Chiralcel OD-H, 20% methanol

Ex. #.	Freq., Solvent	¹ H NMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
148	500MHz DMSO-d ₆	8.97 (s, 1H), 8.59 (br s, 3H), 8.33 (dd, <i>J</i> =1.95, 8.17 Hz, 1H), 7.48 (br d, <i>J</i> =7.91 Hz, 1H), 7.30-7.44 (m, 1H), 7.04-7.11 (m, 2H), 6.73 (d, <i>J</i> =9.04 Hz, 1H), 5.50-5.63 (m, 2H), 5.10-5.20 (br s, 1H), 3.70-3.80 (m, 1H), 3.44-3.65 (m, 2H), 3.10-3.29 (m, 2H), 1.93-2.16 (m, 2H).	B	SFC: Chiralcel OD-H, 20% methanol
149	500MHz DMSO-d ₆	8.92 (s, 2H), 7.59 (d, <i>J</i> =8.89 Hz, 1H), 7.52 (d, <i>J</i> =9.41 Hz, 1H), 5.60 (d, <i>J</i> =2.02 Hz, 2H), 4.73-4.84 (m, 1H), 3.37-3.49 (m, 1H), 3.11-3.17 (m, 1H), 2.97-3.08 (m, 2H), 2.51-2.55 (m, 1H), 1.93-2.03 (m, 1H), 1.78-1.91 (m, 1H).	--	--
150	500MHz DMSO-d ₆	8.91 (s, 2H), 7.55-7.63 (m, 2H), 5.59-5.69 (m, 2H), 3.87-4.10 (m, 1H), 3.47 (br d, <i>J</i> =13.23 Hz, 1H), 3.32-3.42 (m, 1H), 3.12-3.20 (m, 2H), 2.36 (br d, <i>J</i> =1.69 Hz, 1H), 2.26 (br s, 1H).	B	0.1% NH ₄ OH in ACN and water as mobile phase
151	500MHz DMSO-d ₆	8.89 (s, 2H), 7.52-7.64 (m, 2H), 5.55-5.74 (m, 2H), 3.83-3.95 (m, 1H), 3.32-3.50 (m, 2H), 3.10-3.22 (m, 2H), 2.36-2.44 (m, 1H), 2.11-2.33 (m, 1H)	B	0.1% NH ₄ OH in ACN and water as mobile phase
152	500MHz MeOD	8.82-8.86 (m, 1H), 8.11-8.20 (m, 1H), 7.37-7.46 (m, 2H), 7.21 (d, <i>J</i> =1.82 Hz, 1H), 7.16 (dd, <i>J</i> =1.82, 8.30 Hz, 1H), 5.49 (s, 2H), 3.58-3.63 (m, 1H), 3.42-3.53 (m, 2H), 3.05 (dt, <i>J</i> =2.34, 12.07 Hz, 1H), 2.80-2.91 (m, 2H), 1.95-2.02 (m, 1H), 1.59-1.70 (m, 1H)	I	YMC Amyose SA, Methanol THF (70:30) 40 %; peak 1
153	500MHz MeOD	8.84 (br s, 1H), 8.07-8.20 (m, 1H), 7.37-7.50 (m, 2H), 7.06-7.27 (m, 2H), 5.52 (br s, 2H), 3.93 (br s, 1H), 3.34-3.43 (m, 2H), 3.01-3.16 (m, 2H), 1.85 (br d, <i>J</i> =3.37 Hz, 2H)	I	YMC Amyose SA, Methanol THF (70:30) 40 %; peak 1
154	400MHz d ₆ -DMSO	7.77-7.83 (m, <i>J</i> =7.98 Hz, 2H), 7.48 (d, <i>J</i> =7.67 Hz, 1H), 7.29-7.36 (m, <i>J</i> =7.98 Hz, 2H), 7.03-7.19 (m, 3H), 5.47 (s, 2H), 3.35-3.41 (m, 1H), 3.26-3.30 (m, 1H), 3.11-3.24 (m, 2H), 2.94-3.05 (m, 1H), 2.19-2.34 (m, 1H), 2.01-2.16 (m, 1H), 1.76 (br s, 2H)	--	--
155	400MHz d ₆ -DMSO	8.54 (br d, <i>J</i> =3.01 Hz, 2H), 7.86 (d, <i>J</i> =8.29 Hz, 2H), 7.60 (d, <i>J</i> =7.52 Hz, 1H), 7.44-7.53 (m, <i>J</i> =8.19 Hz, 2H), 7.23-7.39 (m, 3H), 5.66 (br d, <i>J</i> =9.95 Hz, 2H), 4.04 (br d, <i>J</i> =9.95 Hz, 1H), 3.72-3.80 (m, 1H), 3.57-3.64 (m, 1H), 3.31-3.53 (m, 2H), 3.01-3.29 (m, 2H), 1.96-2.08 (m, 1H), 1.47-1.64 (m, 1H)	--	--

Ex. #.	Freq., Solvent	¹ H NMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
156	600MHz DMSO-d ₆	7.79-7.84 (m, <i>J</i> =8.41 Hz, 2H), 7.26-7.32 (m, <i>J</i> =8.41 Hz, 2H), 7.18 (dd, <i>J</i> =2.18, 9.26 Hz, 1H), 6.91 (t, <i>J</i> =10.35 Hz, 1H), 5.43 (s, 2H), 4.39-4.38 (m, 1H), 3.39-3.51 (m, 1H), 3.36-3.14-3.28 (m, 1H), 3.04-3.13 (m, 1H), 2.92-3.03 (m, 1H), 2.84 (dd, <i>J</i> =8.60, 12.65 Hz, 1H), 1.94-2.13 (m, 1H), 1.74-1.91 (m, 1H)	B	SFC: Chiralcel OD-H, 15% methanol.
157	600MHz DMSO-d ₆	δ 7.79-7.84 (m, 2H), 7.28-7.33 (m, <i>J</i> =8.49 Hz, 2H), 7.08 (dd, <i>J</i> =2.22, 8.84 Hz, 1H), 6.99 (dt, <i>J</i> =2.18, 10.59 Hz, 1H), 5.41-5.48 (m, 2H), 4.28-4.36 (m, 1H), 3.37-3.43 (m, 1H), 2.99-3.06 (m, 1H), 2.93 (tdd, <i>J</i> =4.16, 7.88, 14.31 Hz, 1H), 2.79 (dd, <i>J</i> =8.60, 12.50 Hz, 1H), 2.01-2.13 (m, 1H), 1.66-1.80 (m, 1H)	B	SFC: Chiralcel OJ-H, 15% methanol
158	600MHz DMSO-d ₆	7.81-7.84 (m, <i>J</i> =8.25 Hz, 2H), 7.78 (s, 1H), 7.43-7.58 (m, 2H), 7.28-7.33 (m, 2H), 5.51 (s, 2H), 4.39-4.36 (m, 1H), 3.49-3.54 (m, 1H), 3.40-3.48 (m, 1H), 3.03-3.17 (m, 1H), 2.73-2.94 (m, 1H), 1.93-2.11 (m, 1H), 1.82 (br s, 1H), 1.63-1.79 (m, 1H),	B	SFC: Chiralpak AD-H, 25% methanol
159	600MHz DMSO-d ₆	7.94 (s, 1H), 7.78-7.84 (m, <i>J</i> =8.25 Hz, 2H), 7.47 (dd, <i>J</i> =1.01, 8.25 Hz, 1H), 7.36 (d, <i>J</i> =8.33 Hz, 1H), 7.26-7.32 (m, <i>J</i> =8.17 Hz, 2H), 5.47-5.56 (m, 2H), 4.42-4.34 (dt, <i>J</i> =4.32, 8.19 Hz, 1H), 3.44-3.52 (m, 1H), 3.38-3.43 (m, 1H), 3.15-3.28 (m, 1H), 3.04-3.14 (m, 1H), 2.80-2.97 (m, 2H), 2.03-2.12 (m, 1H), 1.70-1.88 (m, 1H)	B	SFC: Chiralpak AD-H, 25% methanol
160	600MHz DMSO-d ₆	7.76-7.85 (m, 3H), 7.46-7.65 (m, 2H), 7.29-7.38 (m, 2H), 5.54 (s, 2H), 3.85-4.05 (m, 1H), 3.35-3.46 (m, 1H), 3.21-3.35 (m, 1H), 3.03-3.20 (m, 1H), 2.54-2.79 (m, 1H), 2.18-2.32 (m, 1H), 1.98-2.14 (m, 1H),	B	SFC: Chiralpak AD-H, 25% methanol
161	600MHz DMSO-d ₆	7.96 (d, <i>J</i> =1.17 Hz, 1H), 7.81 (d, <i>J</i> =8.43 Hz, 2H), 7.48 (dd, <i>J</i> =1.49, 8.24 Hz, 1H), 7.29-7.38 (m, 3H), 5.48-5.57 (m, 2H), 3.34-3.47 (m, 1H), 3.20-3.30 (m, 1H), 3.10-3.19 (m, 1H), 2.96-3.09 (m, 1H), 2.17-2.32 (m, 1H), 1.99-2.15 (m, 1H), 1.79 (br d, <i>J</i> =19.33 Hz, 1H)	B	SFC: Chiralpak AD-H, 25% methanol
162	400MHz d ₆ -DMSO	7.80 (d, <i>J</i> =8.29 Hz, 2H), 7.43 (d, <i>J</i> =7.46 Hz, 1H), 7.30 (d, <i>J</i> =8.29 Hz, 2H), 7.15 (d, <i>J</i> =7.88 Hz, 1H), 6.98-7.11 (m, 2H), 5.39 (s, 2H), 3.57 (s, 1H), 3.38 (br dd, <i>J</i> =3.42, 11.82 Hz, 1H), 3.20-3.28 (m, 1H), 2.78-2.91 (m, 2H), 2.63 (dd, <i>J</i> =9.12, 11.82 Hz, 1H), 2.08-2.28 (m, 1H), 1.78-1.87 (m, 1H), 1.65-1.75 (m, 1H), 1.49-1.63 (m, 1H)	--	--

Ex. #.	Freq., Solvent	¹ H NMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
163	500MHz d ₆ -DMSO	7.81 (d, <i>J</i> =8.30 Hz, 2H), 7.45 (d, <i>J</i> =7.53 Hz, 1H), 7.32 (d, <i>J</i> =8.30 Hz, 2H), 7.07-7.18 (m, 2H), 6.98-7.07 (m, 1H), 5.47 (s, 2H), 3.38-3.48 (m, 1H), 3.05-3.17 (m, 2H), 2.79-2.93 (m, 1H), 1.83 (br s, 1H), 1.60-1.74 (m, 1H), 1.41-1.54 (m, 1H), 0.94 (d, <i>J</i> =6.75 Hz, 3H)	--	--
164	600MHz d ₆ -DMSO	7.81 (d, <i>J</i> =8.10 Hz, 2H), 7.29 (d, <i>J</i> =7.78 Hz, 1H), 7.25 (d, <i>J</i> =8.10 Hz, 2H), 7.14 (d, <i>J</i> =7.79 Hz, 1H), 7.03 (t, <i>J</i> =7.63 Hz, 1H), 6.93 (t, <i>J</i> =7.63 Hz, 1H), 5.51 (s, 2H), 3.51-3.59 (m, 2H), 3.42 (d, <i>J</i> =9.65 Hz, 1H), 3.18 (s, 1H), 3.14 (d, <i>J</i> =9.65 Hz, 1H), 2.43 (d, <i>J</i> =4.36 Hz, 1H), 1.77-1.85 (m, 1H), 1.49-1.56 (m, 1H), 0.96 (s, 3H)	--	--
165	600MHz d ₆ -DMSO	7.82 (d, <i>J</i> =8.10 Hz, 2H), 7.21-7.37 (m, 8H), 7.17 (d, <i>J</i> =7.79 Hz, 1H), 7.04-7.08 (m, 1H), 6.95 (t, <i>J</i> =7.47 Hz, 1H), 5.49-5.58 (m, 2H), 3.94 (dd, <i>J</i> =7.79, 9.65 Hz, 1H), 3.73 (dd, <i>J</i> =6.85, 9.34 Hz, 1H), 3.66 (t, <i>J</i> =9.19 Hz, 1H), 3.42 (q, <i>J</i> =7.16 Hz, 1H), 3.18 (d, <i>J</i> =4.67 Hz, 1H), 3.06 (q, <i>J</i> =7.79 Hz, 1H), 1.72 (br s, 2H)	--	--
166	600MHz d ₆ -DMSO	7.82 (d, <i>J</i> =8.10 Hz, 2H), 7.25-7.32 (m, 3H), 7.11 (d, <i>J</i> =8.10 Hz, 1H), 7.03 (t, <i>J</i> =7.47 Hz, 1H), 6.92 (t, <i>J</i> =7.63 Hz, 1H), 5.50 (s, 2H), 3.57-3.66 (m, 2H), 3.44-3.51 (m, 2H), 3.14 (dd, <i>J</i> =4.83, 9.50 Hz, 1H), 1.95 (qd, <i>J</i> =6.40, 12.26 Hz, 1H), 1.61 (qd, <i>J</i> =6.34, 12.42 Hz, 1H)	--	--
167	400MHz d ₆ -DMSO	7.80 (d, <i>J</i> =8.29 Hz, 2H), 7.43 (d, <i>J</i> =7.46 Hz, 1H), 7.30 (d, <i>J</i> =8.29 Hz, 2H), 7.15 (d, <i>J</i> =7.88 Hz, 1H), 6.98-7.11 (m, 2H), 5.39 (s, 2H), 3.57 (s, 1H), 3.38 (br dd, <i>J</i> =3.42, 11.82 Hz, 1H), 3.20-3.28 (m, 1H), 2.78-2.91 (m, 2H), 2.63 (dd, <i>J</i> =9.12, 11.82 Hz, 1H), 2.08-2.28 (m, 1H), 1.78-1.87 (m, 1H), 1.65-1.75 (m, 1H), 1.49-1.63 (m, 1H)	--	--
168	500MHz d ₆ -DMSO	Mixture of diastereomers: 7.80 (br d, <i>J</i> =7.79 Hz, 2H), 7.27 (br dd, <i>J</i> =7.91, 17.52 Hz, 3H), 7.13 (br d, <i>J</i> =8.04 Hz, 1H), 7.02 (br t, <i>J</i> =8.04 Hz, 1H), 6.93 (br d, <i>J</i> =7.53 Hz, 1H), 5.45-5.57 (m, 2H), 3.56-3.79 (m, 1H), 3.09-3.19 (m, 2H), 1.92-2.05 (m, 1H), 1.71-1.90 (m, 2H), 1.15-1.66 (m, 7H)	--	--
169	600MHz DMSO-d ₆	Mixture of diastereomers: 1.20 - 1.38 (m, 2 H), 1.56 - 1.71 (m, 2 H), 1.88 - 2.07 (m, 1 H), 2.07 - 2.24 (m, 1 H), 2.52 - 2.59 (m, 1 H), 2.62 - 2.72 (m, 1 H), 2.87 (q, <i>J</i> =5.45 Hz, 1 H), 3.06 (br d, <i>J</i> =10.12 Hz, 1 H), 3.12 - 3.21 (m, 4 H), 3.23 - 3.31 (m, 2 H), 3.31 - 3.42 (m, 3 H), 3.43 - 3.56 (m, 1 H), 3.61 (dd, <i>J</i> =10.35, 4.59 Hz, 1 H), 5.47 - 5.55 (m, 2 H), 6.92 - 7.01 (m, 1 H), 7.06 (t, <i>J</i> =7.47 Hz, 1 H), 7.11 - 7.19 (m, 1 H), 7.22 - 7.31 (m, 2 H), 7.37 (d, <i>J</i> =7.79 Hz, 1 H), 7.80 (d, <i>J</i> =7.75 Hz, 2 H)	--	--

Ex. #.	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
170	400MHz MeOD	8.45 (br s, 3H), 7.83 (d, <i>J</i> =8.29 Hz, 2H), 7.49-7.58 (m, 1H), 7.36 (d, <i>J</i> =8.09 Hz, 2H), 7.07-7.25 (m, 3H), 5.49 (s, 2H), 4.71-4.91 (m, 1H), 3.75-3.84 (m, 1H), 3.61-3.73 (m, 1H), 3.36-3.48 (m, 1H), 2.95-3.22 (m, 2H), 2.13-2.25 (m, 1H), 1.72-1.95 (m, 1H)	--	--
171	400MHz MeOD	8.34 (br d, <i>J</i> =1.04 Hz, 3H), 7.82 (d, <i>J</i> =8.29 Hz, 2H), 7.46-7.56 (m, 1H), 7.34 (d, <i>J</i> =8.29 Hz, 2H), 7.07-7.24 (m, 3H), 5.48 (s, 2H), 5.03-5.21 (m, 1H), 3.76-3.87 (m, 1H), 3.52-3.61 (m, 1H), 3.31-3.42 (m, 1H), 3.07-3.28 (m, 2H), 1.89-2.16 (m, 2H)	--	--
172	400MHz MeOD	8.37 (br s, 3H), 7.83 (d, <i>J</i> =8.29 Hz, 2H), 7.48-7.56 (m, 1H), 7.35 (d, <i>J</i> =8.29 Hz, 2H), 7.08-7.23 (m, 3H), 5.48 (s, 2H), 5.01-5.22 (m, 1H), 3.74-3.91 (m, 1H), 3.57 (br dd, <i>J</i> =4.04, 12.75 Hz, 1H), 3.40 (br d, <i>J</i> =11.20 Hz, 1H), 3.08-3.27 (m, 2H), 1.92-2.18 (m, 2H)	--	--
173	400MHz MeOD	7.75-7.84 (m, 2H), 7.39-7.49 (m, 1H), 7.31 (d, <i>J</i> =8.50 Hz, 2H), 7.15-7.21 (m, 1H), 7.11 (dt, <i>J</i> =1.35, 7.52 Hz, 1H), 7.02-7.07 (m, 1H), 5.44 (s, 2H), 4.26-4.48 (m, 1H), 3.33-3.44 (m, 2H), 2.90-3.09 (m, 2H), 2.80 (dd, <i>J</i> =8.71, 12.44 Hz, 1H), 2.00-2.16 (m, 1H), 1.70-1.87 (m, 2H)	--	--
174	400MHz MeOD	7.75-7.83 (m, 2H), 7.52-7.58 (m, 1H), 7.33-7.47 (m, 5H), 5.68-5.89 (m, 2H), 4.00-4.23 (m, 4H), 3.42-3.65 (m, 2H), 2.48-2.64 (m, 1H), 2.24-2.47 (m, 1H)	B	Phenomenex Lux Cellulose-2, 25% MeOH, Peak 1
175	400MHz MeOD	7.76-7.82 (m, 2H), 7.52-7.57 (m, 1H), 7.32-7.46 (m, 5H), 5.68-5.88 (m, 2H), 4.01-4.17 (m, 4H), 3.44-3.65 (m, 2H), 2.50-2.63 (m, 1H), 2.26-2.47 (m, 1H)	B	Phenomenex Lux Cellulose-2, 25% MeOH, Peak 2
176	400MHz MeOD	7.75-7.82 (m, 2H), 7.50-7.55 (m, 1H), 7.39-7.46 (m, 3H), 7.33-7.37 (m, 2H), 5.65-5.86 (m, 2H), 4.08 (dt, <i>J</i> =7.05, 9.74 Hz, 1H), 3.91-4.01 (m, 2H), 3.78 (dd, <i>J</i> =1.14, 10.26 Hz, 1H), 3.22 (d, <i>J</i> =2.28 Hz, 2H), 2.08-2.28 (m, 2H)	B	Chiralpak AD-H, 30% MeOH w/ 0.2% DEA, Peak 1
177	400MHz MeOD	7.74-7.83 (m, 2H), 7.50-7.55 (m, 1H), 7.38-7.48 (m, 3H), 7.31-7.38 (m, 2H), 5.66-5.86 (m, 2H), 4.08 (dt, <i>J</i> =6.95, 9.80 Hz, 1H), 3.89-4.01 (m, 2H), 3.79 (dd, <i>J</i> =1.14, 10.26 Hz, 1H), 3.23 (d, <i>J</i> =2.70 Hz, 2H), 2.11-2.33 (m, 2H)	B	Chiralpak AD-H, 30% MeOH w/ 0.2% DEA, Peak 2

Ex. #.	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
178	400MHz MeOD	7.66-7.74 (m, 2H), 7.36-7.44 (m, 1H), 7.29 (d, J=8.71 Hz, 2H), 7.00-7.16 (m, 3H), 5.48-5.55 (m, 2H), 3.68 (dd, J=7.15, 9.64 Hz, 1H), 3.59 (dd, J=6.12, 7.98 Hz, 2H), 2.70 (d, J=7.26 Hz, 2H), 2.31-2.43 (m, 1H), 2.12 (dd, J=6.01, 12.23 Hz, 1H), 1.70 (dd, J=8.29, 12.44 Hz, 1H), 1.25-1.34 (m, 1H)	--	--
179	400MHz MeOD	7.70 (d, J=8.50 Hz, 2H), 7.36-7.43 (m, 1H), 7.29 (d, J=8.71 Hz, 2H), 6.99-7.17 (m, 3H), 5.46-5.59 (m, 2H), 3.68 (dd, J=7.26, 9.54 Hz, 1H), 3.54-3.64 (m, 2H), 2.69 (d, J=7.26 Hz, 2H), 2.31-2.43 (m, 1H), 2.12 (d, J=6.01 Hz, 1H), 1.61-1.78 (m, 1H)	--	--
180	400MHz d ₆ -DMSO	8.39 (br s, 3H), 7.87 (d, J=8.29 Hz, 2H), 7.53-7.62 (m, 1H), 7.50 (d, J=8.29 Hz, 2H), 7.27-7.36 (m, 1H), 7.22-7.26 (m, 2H), 5.53-5.75 (m, 2H), 3.86-4.00 (m, 1H), 3.41-3.65 (m, 3H), 3.28-3.36 (m, 1H), 3.00-3.17 (m, 2H), 1.89-2.09 (m, 2H), 1.51 (br dd, J=3.01, 12.96 Hz, 1H), 1.00 (d, J=6.63 Hz, 3H)	--	--
181	400MHz d ₆ -DMSO	8.12-8.25 (m, 3H), 7.83 (d, J=8.29 Hz, 2H), 7.48-7.56 (m, 1H), 7.35-7.40 (m, 2H), 7.10-7.26 (m, 3H), 5.49 (br d, J=1.66 Hz, 2H), 3.74-3.87 (m, 1H), 3.39 (br d, J=12.65 Hz, 1H), 2.92-3.13 (m, 3H), 1.64-1.82 (m, 2H), 1.32-1.47 (m, 1H), 1.04 (d, J=6.22 Hz, 3H)	--	--
182	400MHz d ₆ -DMSO	8.12 (br d, J=1.24 Hz, 3H), 7.83 (d, J=8.50 Hz, 2H), 7.48-7.58 (m, 1H), 7.31-7.40 (m, 2H), 7.17-7.25 (m, 2H), 7.07-7.17 (m, 1H), 5.47 (d, J=1.66 Hz, 2H), 3.79 (br d, J=9.74 Hz, 1H), 3.38 (br d, J=12.85 Hz, 1H), 2.89-3.18 (m, 3H), 1.58-1.85 (m, 2H), 1.40 (br d, J=11.40 Hz, 1H), 1.04 (d, J=6.22 Hz, 3H)	--	--
183	400MHz MeOD	7.66-7.75 (m, 2H), 7.39-7.47 (m, 1H), 7.27 (d, J=8.50 Hz, 2H), 7.03-7.20 (m, 3H), 5.44-5.51 (m, 2H), 3.76 (d, J=9.33 Hz, 1H), 3.52-3.69 (m, 3H), 2.90-3.00 (m, 1H), 2.80 (d, J=13.48 Hz, 1H), 1.49-1.58 (m, 1H), 0.84-0.95 (m, 1H), 0.69-0.79 (m, 1H), 0.53 (t, J=4.56 Hz, 1H)	F	Chiralpak AD-H, 20% MeOH w/ 0.2% DEA, Peak 1
184	400MHz MeOD	7.65-7.75 (m, 2H), 7.37-7.45 (m, 1H), 7.27 (d, J=8.29 Hz, 2H), 7.00-7.19 (m, 3H), 5.48 (s, 2H), 3.76 (d, J=9.33 Hz, 1H), 3.51-3.67 (m, 3H), 2.94 (br d, J=13.48 Hz, 1H), 2.81 (s, 1H), 1.53 (td, J=3.81, 7.93 Hz, 1H), 0.74 (dd, J=5.18, 7.88 Hz, 1H), 0.52 (t, J=4.35 Hz, 1H)	F	Chiralpak AD-H, 20% MeOH w/ 0.2% DEA, Peak 2

Ex. #.	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
185	400MHz MeOD	7.70 (d, J=8.50 Hz, 2H), 7.38-7.44 (m, 1H), 7.31 (d, J=8.29 Hz, 2H), 6.82 (dd, J=2.28, 8.71 Hz, 1H), 6.71 (d, J=2.28 Hz, 1H), 5.40 (s, 2H), 3.38-3.46 (m, 1H), 3.21 (td, J=4.17, 11.97 Hz, 1H), 2.88-2.99 (m, 2H), 2.79 (dd, J=8.91, 11.61 Hz, 1H), 1.90-2.01 (m, 1H), 1.76-1.87 (m, 1H), 1.60-1.73 (m, 1H), 1.28-1.40 (m, 1H)	F	Chiralpak IC, 45% IPA w/ 0.2% DEA, peak 1
186	400MHz MeOD	7.69 (d, J=8.29 Hz, 2H), 7.27-7.34 (m, 2H), 7.07 (d, J=2.49 Hz, 1H), 7.00 (d, J=8.71 Hz, 1H), 6.75 (dd, J=2.49, 8.71 Hz, 1H), 5.37 (s, 2H), 3.42-3.50 (m, 1H), 3.26 (br d, J=12.23 Hz, 1H), 2.89-3.02 (m, 2H), 2.81 (dd, J=8.91, 11.61 Hz, 1H), 1.93-2.01 (m, 1H), 1.76-1.86 (m, 1H), 1.59-1.75 (m, 1H), 1.28-1.41 (m, 1H)	F	Chiralpak IC, 45% IPA w/ 0.2% DEA, peak 2
442	500MHz d ₄ -MeOH	9.05-9.18 (m, 2H), 7.39-7.56 (m, 1H), 6.86-7.12 (m, 2H), 5.51-5.68 (m, 2H), 4.40-4.67 (m, 1H), 3.60-3.71 (m, 1H), 3.46-3.56 (m, 1H), 3.28 (dd, J=4.25, 8.40 Hz, 1H), 3.07-3.16 (m, 1H), 3.02 (dd, J=9.43, 12.34 Hz, 1H), 2.17-2.28 (m, 1H), 1.83-1.98 (m, 1H)	B	Chiralpak OD-H, 15% IPA, Peak 1
443	500MHz d ₄ -MeOH	9.06-9.17 (m, 2H), 7.12-7.23 (m, 2H), 6.84-6.93 (m, 1H), 5.57-5.67 (m, 2H), 4.36-4.57 (m, 1H), 3.58-3.69 (m, 1H), 3.48-3.55 (m, 1H), 3.09-3.19 (m, 2H), 2.98 (dd, J=8.82, 12.46 Hz, 1H), 2.18-2.27 (m, 1H), 1.81-1.96 (m, 1H)	B	Chiralpak OD-H, 15% IPA, Peak 2
444	500MHz d ₄ -MeOH	8.47 (s, 2H), 7.39-7.51 (m, 1H), 7.00 (dd, J=2.34, 8.82 Hz, 1H), 6.95 (ddd, J=2.47, 8.76, 9.80 Hz, 1H), 5.36-5.51 (m, 2H), 4.60-4.80 (m, 1H), 3.89-3.99 (m, 3H), 3.77-3.89 (m, 1H), 3.61-3.71 (m, 1H), 3.57 (br dd, J=4.28, 8.95 Hz, 1H), 3.07-3.20 (m, 2H), 2.20-2.36 (m, 1H), 1.91-2.06 (m, 1H)	B	Chiralpak OD-H, 15% MeOH, Peak 1
445	500MHz d ₄ -MeOH	7.37-7.42 (m, 1H), 6.71-6.87 (m, 2H), 5.06-5.16 (m, 2H), 4.47-4.61 (m, 1H), 4.14-4.29 (m, 2H), 3.77-3.85 (m, 3H), 3.48-3.55 (m, 1H), 3.02-3.09 (m, 1H), 2.94-3.00 (m, 1H), 2.17-2.25 (m, 1H), 1.91-2.01 (m, 1H)	B	Chiralpak IC, 20% MeOH, Peak 1
446	500MHz d ₄ -MeOH	8.39-8.49 (m, 2H), 7.10-7.24 (m, 2H), 6.77-6.93 (m, 1H), 5.34-5.49 (m, 2H), 4.35-4.57 (m, 1H), 3.70 (dtd, J=1.82, 4.17, 12.42 Hz, 1H), 3.51-3.60 (m, 1H), 3.13-3.23 (m, 2H), 3.01 (dd, J=8.82, 12.46 Hz, 1H), 2.14-2.28 (m, 1H), 1.78-1.99 (m, 1H)	B	Chiralpak OD-H, 15% MeOH, Peak 2
447	500MHz d ₄ -MeOH	7.26-7.43 (m, 2H), 5.07-5.23 (m, 2H), 4.42-4.59 (m, 1H), 4.12-4.24 (m, 1H), 3.61-3.70 (m, 1H), 3.44-3.56 (m, 1H), 3.19-3.27 (m, 1H), 2.99-3.11 (m, 1H), 2.12-2.27 (m, 1H), 1.86-1.99 (m, 1H)	--	--

Ex. #.	Freq., Solvent	¹ H NMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
448	500MHz d ₄ -MeOH	7.37-7.40 (m, 1H), 6.79-6.87 (m, 2H), 5.03 (s, 2H), 4.47-4.57 (m, 1H), 4.38-4.61 (m, 2H), 3.83 (s, 3H), 3.47-3.57 (m, 2H), 3.23 (s, 3H), 3.05-3.11 (m, 1H), 3.03 (s, 3H), 2.96 (br dd, J=8.95, 12.07 Hz, 1H), 2.15-2.28 (m, 2H), 1.87-2.08 (m, 3H)	B	Chiralpak OD-H, 15% MeOH, Peak 1
449	500MHz d ₄ -MeOH	7.37-7.42 (m, 1H), 6.71-6.87 (m, 2H), 5.06-5.16 (m, 2H), 4.47-4.61 (m, 1H), 4.14-4.29 (m, 2H), 3.77-3.85 (m, 3H), 3.48-3.55 (m, 1H), 3.02-3.09 (m, 1H), 2.94-3.00 (m, 1H), 2.17-2.25 (m, 1H), 1.91-2.01 (m, 1H)	B	Chiralpak IC, 15% MeOH, Peak 2
450	500MHz d ₄ -MeOH	7.11 (d, J=8.82 Hz, 1H), 7.05 (d, J=2.34 Hz, 1H), 6.80-6.85 (m, 1H), 5.01 (s, 2H), 4.44-4.58 (m, 1H), 3.82 (s, 3H), 3.53-3.60 (m, 1H), 3.41-3.47 (m, 2H), 3.21 (s, 3H), 3.07-3.14 (m, 1H), 3.02 (s, 3H), 2.93-2.99 (m, 1H), 2.18-2.28 (m, 1H), 1.91-2.03 (m, 1H)	B	Chiralpak OD-H, 15% MeOH, Peak 2
451	600MHz DMSO – d ₆	8.95 (d, J=1.48 Hz, 1H), 8.30 (dd, J=2.10, 8.25 Hz, 1H), 7.41 (td, J=4.55, 8.80 Hz, 2H), 7.09 (dd, J=2.41, 9.19 Hz, 1H), 6.92 (t, J=9.42 Hz, 1H), 5.49 (s, 2H), 3.40 (br s, 1H), 3.24-3.36 (m, 3H), 3.17 (s, 1H), 2.86-2.98 (m, 2H), 2.60-2.75 (m, 2H), 1.89-2.04 (m, 1H), 1.26-1.43 (m, 1H)	--	--
452	600MHz DMSO – d ₆	8.94 (d, J=1.40 Hz, 1H), 8.29 (dd, J=2.14, 8.21 Hz, 1H), 7.37 (d, J=8.17 Hz, 1H), 6.69 (dd, J=2.26, 8.88 Hz, 1H), 6.59 (dd, J=2.22, 12.18 Hz, 1H), 5.48 (s, 2H), 4.25-4.38 (m, 1H), 3.89 (s, 3H), 3.22-3.29 (m, 1H), 2.84-2.98 (m, 2H), 2.62-2.76 (m, 1H), 1.99-2.07 (m, 1H), 1.79 (br s, 1H), 1.64-1.76 (m, 1H)	--	--
453	600MHz DMSO – d ₆	8.90 (s, 1H), 8.34 (dd, J=2.14, 8.21 Hz, 1H), 7.90 (d, J=8.10 Hz, 1H), 7.64 (d, J=8.35 Hz, 1H), 7.61 (d, J=8.06 Hz, 1H), 5.64 (s, 2H), 4.30-4.44 (m, 1H), 3.59-3.68 (m, 2H), 3.13-3.28 (m, 1H), 2.77-2.90 (m, 2H), 1.99-2.08 (m, 1H), 1.57-1.70 (m, 1H)	B	Chiralpak AD-H, 25% IPA, peak 1
454	600MHz DMSO – d ₆	8.91 (s, 2H), 7.40 (dd, J=4.90, 8.64 Hz, 1H), 7.11 (dd, J=2.49, 9.26 Hz, 1H), 6.91 (ddd, J=2.57, 8.68, 10.08 Hz, 1H), 5.45-5.52 (m, 2H), 3.27-3.29 (m, 3H), 2.86-2.97 (m, 2H), 2.61-2.71 (m, 2H), 1.96-2.05 (m, 1H), 1.58 (br s, 2H), 1.31-1.48 (m, 1H)	B	Chiralpak AD-H, 25% IPA, peak 1
455	500MHz DMSO – d ₆	7.47 (d, J=1.82 Hz, 1H), 7.35 (d, J=8.30 Hz, 1H), 7.22 (dd, J=1.75, 8.37 Hz, 1H), 4.75 (s, 2H), 4.24-4.31 (m, 2H), 3.95 (t, J=7.66 Hz, 2H), 3.33-3.38 (m, 1H), 2.97-3.06 (m, 2H), 2.80 (dd, J=8.30, 12.59 Hz, 1H), 2.36 (s, 1H), 2.29 (quin, J=7.62 Hz, 2H), 2.08-2.17 (m, 1H), 1.74-1.94 (m, 1H)	--	--

Ex. #.	Freq., Solvent	¹ H NMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
456	600MHz DMSO – d ₆	8.91 (s, 2H), 7.22 (dd, <i>J</i> =2.41, 9.81 Hz, 1H), 7.14 (dd, <i>J</i> =4.79, 8.68 Hz, 1H), 6.85 (ddd, <i>J</i> =2.49, 8.70, 9.91 Hz, 1H), 5.49 (d, <i>J</i> =2.10 Hz, 2H), 3.36-3.43 (m, 2H), 3.28-3.30 (m, 3H), 2.90-2.99 (m, 1H), 2.66-2.72 (m, 2H), 1.98-2.06 (m, 1H), 1.62 (br s, 1H), 1.33-1.42 (m, 1H)	--	--
457	600MHz DMSO – d ₆	7.38-7.43 (m, 1H), 7.12 (dd, <i>J</i> =2.49, 9.26 Hz, 1H), 6.90-6.96 (m, 1H), 5.07-5.16 (m, 2H), 4.23-4.50 (m, 1H), 4.23 (q, <i>J</i> =9.45 Hz, 1H), 3.21-3.29 (m, 3H), 2.93-3.01 (m, 3H), 2.72-2.81 (m, 1H), 1.96-2.12 (m, 1H), 1.72-1.90 (m, 3H)	B	Chiralpak AD-H, 25% IPA, peak 1
458	600MHz DMSO – d ₆	8.93 (dd, <i>J</i> =0.66, 2.06 Hz, 1H), 8.34 (dd, <i>J</i> =2.14, 8.21 Hz, 1H), 7.72 (d, <i>J</i> =8.10 Hz, 1H), 7.61 (d, <i>J</i> =8.56 Hz, 1H), 7.49 (d, <i>J</i> =8.10 Hz, 1H), 5.66 (d, <i>J</i> =1.71 Hz, 2H), 4.32-4.43 (m, 1H), 3.50-3.64 (m, 2H), 3.15-3.28 (m, 1H), 2.85-2.94 (m, 2H), 2.04-2.12 (m, 1H), 1.66-1.77 (m, 1H)	B	Chiralpak AD-H, 25% IPA, peak 1
459	600MHz DMSO – d ₆	7.66 (s, 1H), 7.57 (d, <i>J</i> =8.25 Hz, 1H), 7.41 (dd, <i>J</i> =1.25, 8.33 Hz, 1H), 5.11-5.21 (m, 2H), 4.38-4.49 (m, 1H), 3.64-3.72 (m, 2H), 3.61 (td, <i>J</i> =4.74, 9.75 Hz, 4H), 3.44-3.53 (m, 2H), 3.34-3.41 (m, 1H), 3.17 (d, <i>J</i> =4.90 Hz, 1H), 3.09 (ddd, <i>J</i> =2.84, 9.48, 12.59 Hz, 1H), 2.95-3.05 (m, 1H), 2.86 (dd, <i>J</i> =8.06, 12.65 Hz, 1H), 2.09-2.19 (m, 1H), 1.75-1.93 (m, 1H)	B	Chiralpak AD-H, 25% IPA, peak 1
460	600MHz DMSO – d ₆	7.23 (d, <i>J</i> =9.81 Hz, 1H), 7.16-7.20 (m, 1H), 6.92 (t, <i>J</i> =8.84 Hz, 1H), 5.08-5.17 (m, 2H), 4.32-4.51 (m, 1H), 4.23 (q, <i>J</i> =9.55 Hz, 2H), 3.34-3.39 (m, 1H), 3.25-3.30 (m, 4H), 2.93-3.05 (m, 2H), 2.74-2.85 (m, 1H), 2.03-2.13 (m, 1H), 1.71-1.89 (m, 1H)	B	Chiralpak AD-H, 25% IPA, peak 2
461	600MHz DMSO – d ₆	7.39 (d, <i>J</i> =8.41 Hz, 1H), 7.33 (d, <i>J</i> =2.02 Hz, 1H), 7.09 (dd, <i>J</i> =2.10, 8.41 Hz, 1H), 4.94-5.05 (m, 2H), 4.70-4.84 (m, 1H), 3.14-3.28 (m, 2H), 3.10-3.13 (m, 6H), 2.91-3.06 (m, 2H), 2.89 (s, 1H), 1.87-2.05 (m, 1H), 1.68 (br s, 1H)	B	Chiralpak AD-H, 25% IPA, peak 1
462	600MHz DMSO – d ₆	8.42 (br s, 2H), 7.44-7.48 (m, 1H), 7.20 (dd, <i>J</i> =2.37, 9.23 Hz, 1H), 6.99 (t, <i>J</i> =9.27 Hz, 1H), 5.10-5.21 (m, 2H), 5.04-5.10 (m, 1H), 4.36-4.55 (m, 1H), 4.23 (q, <i>J</i> =9.52 Hz, 2H), 3.78 (br s, 1H), 3.48 (br dd, <i>J</i> =4.01, 12.42 Hz, 1H), 3.26-3.34 (m, 1H), 3.02-3.17 (m, 2H), 2.99 (s, 1H), 2.51-2.65 (m, 1H), 1.95-2.12 (m, 2H)	B	Chiralpak AD-H, 25% IPA, peak 1
463	600MHz DMSO – d ₆	8.95 (d, <i>J</i> =1.32 Hz, 1H), 8.30 (dd, <i>J</i> =2.10, 8.17 Hz, 1H), 7.38-7.45 (m, 2H), 7.07 (dd, <i>J</i> =2.49, 9.19 Hz, 1H), 6.92 (ddd, <i>J</i> =2.57, 8.66, 10.10 Hz, 1H), 5.47-5.57 (m, 2H), 3.24-3.31 (m, 3H), 3.13-3.23 (m, 2H), 2.99-3.10 (m, 2H), 2.89-2.98 (m, 2H), 1.75-1.89 (m, 1H), 1.53-1.67 (m, 1H)	--	--

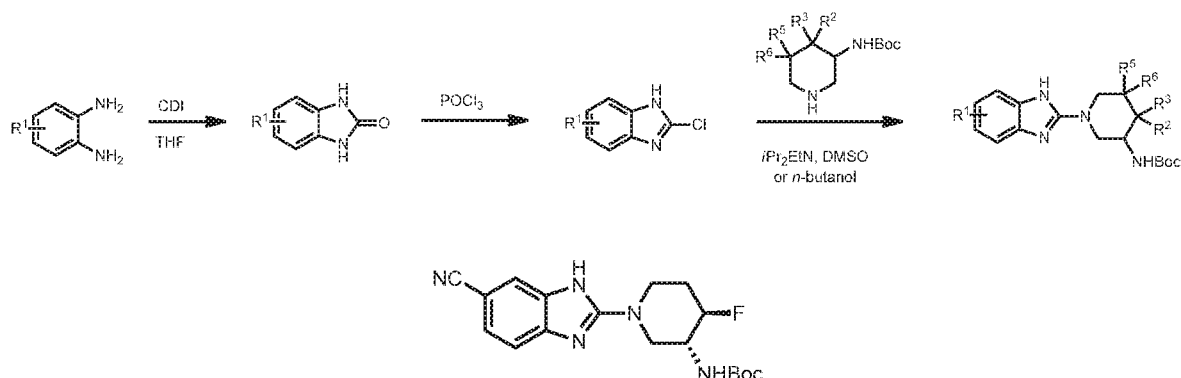
Ex. #.	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
464	600MHz DMSO – d ₆	8.44 (br s, 2H), 7.74 (s, 1H), 7.62 (d, <i>J</i> =8.33 Hz, 1H), 7.46 (d, <i>J</i> =8.21 Hz, 1H), 5.14-5.24 (m, 2H), 4.88 (dt, <i>J</i> =4.87, 9.32 Hz, 1H), 4.69-4.83 (m, 1H), 4.42-4.55 (m, 1H), 3.73-3.83 (m, 1H), 3.69 (br d, <i>J</i> =4.36 Hz, 3H), 3.57-3.65 (m, 4H), 3.37-3.56 (m, 3H), 2.99-3.17 (m, 2H), 2.24 (br t, <i>J</i> =9.46 Hz, 1H), 1.83-1.92 (m, 1H)	B	Chiralpak AD-H, 25% IPA, peak 1
465	600MHz DMSO – d ₆	8.73 (br s, 2H), 7.46-7.50 (m, 1H), 7.21-7.23 (m, 1H), 6.98-7.02 (m, 1H), 5.17-5.22 (m, 1H), 4.36-4.53 (m, 1H), 4.13-4.32 (m, 2H), 3.95-4.13 (m, 2H), 3.64 (br d, <i>J</i> =12.53 Hz, 1H), 3.25-3.34 (m, 3H), 3.09-3.15 (m, 1H), 2.52-2.65 (m, 3H)	B	Chiralpak AD-H, 25% IPA, peak 1
466	600MHz DMSO – d ₆	8.38 (br s, 2H), 7.23-7.30 (m, 1H), 6.99 (t, <i>J</i> =9.27 Hz, 1H), 5.05-5.21 (m, 2H), 4.49 (q, <i>J</i> =8.93 Hz, 1H), 4.23 (q, <i>J</i> =9.52 Hz, 2H), 3.79 (br s, 1H), 3.44-3.66 (m, 1H), 3.30-3.37 (m, 1H), 3.28 (s, 2H), 3.06-3.18 (m, 1H), 2.52-2.55 (m, 3H), 1.93-2.11 (m, 1H)	B	Chiralpak AD-H, 25% IPA, peak 1
467	600MHz DMSO – d ₆	8.91 (s, 2H), 7.40 (dd, <i>J</i> =4.87, 8.68 Hz, 1H), 7.07 (dd, <i>J</i> =2.53, 9.30 Hz, 1H), 6.91 (ddd, <i>J</i> =2.53, 8.62, 10.10 Hz, 1H), 5.46-5.57 (m, 2H), 3.25-3.31 (m, 3H), 3.12-3.22 (m, 1H), 2.90-3.08 (m, 4H), 1.84 (dtd, <i>J</i> =3.58, 7.67, 13.31 Hz, 1H), 1.49-1.64 (m, 1H), 1.40 (br s, 1H)	B	Chiralpak AD-H, 25% IPA, peak 1
468	600MHz DMSO – d ₆	7.47 (d, <i>J</i> =8.56 Hz, 1H), 7.31 (s, 1H), 7.06 (dd, <i>J</i> =1.21, 8.60 Hz, 1H), 4.97-5.07 (m, 2H), 4.34-4.45 (m, 1H), 3.32 (s, 1H), 3.12 (s, 3H), 2.95-3.09 (m, 2H), 2.89 (s, 3H), 2.76-2.85 (m, 1H), 2.06-2.15 (m, 1H), 1.72-1.89 (m, 2H)	B	SFC: Chiralpak AD-H analytical column, 15% methanol with 0.2% DEA
469	600MHz DMSO – d ₆	9.07 (br s, 2H), 7.44-7.48 (m, 1H), 7.21 (dd, <i>J</i> =2.57, 9.26 Hz, 1H), 6.96-7.03 (m, 1H), 5.06-5.19 (m, 2H), 4.92 – 5.03 (m, 1H), 4.23 (q, <i>J</i> =9.58 Hz, 2H), 3.56-3.86 (m, 2H), 3.46 (br s, 1H), 3.29 (s, 3H), 3.11 (br dd, <i>J</i> =9.89, 12.61 Hz, 1H), 2.92-3.04 (m, 1H), 2.68 (br s, 3H), 2.16-2.25 (m, 1H), 1.82-1.95 (m, 1H)	--	--
470	600MHz DMSO – d ₆	7.58 (d, <i>J</i> =1.82 Hz, 1H), 7.17-7.24 (m, 2H), 4.70-4.77 (m, 2H), 4.46-4.35 (m, 1H), 4.21-4.29 (m, 2H), 3.94 (t, <i>J</i> =7.72 Hz, 2H), 3.33-3.41 (m, 2H), 2.97-3.08 (m, 2H), 2.82 (dd, <i>J</i> =8.30, 12.59 Hz, 1H), 2.28 (quin, <i>J</i> =7.72 Hz, 2H), 2.14 (ddd, <i>J</i> =4.61, 8.66, 17.09 Hz, 1H), 1.73-1.88 (m, 1H)	B	SFC: Chiralpak IC, 45% methanol Peak 2
471	600MHz DMSO – d ₆	7.44 (d, <i>J</i> =2.02 Hz, 1H), 7.19 (d, <i>J</i> =8.49 Hz, 1H), 7.07 (dd, <i>J</i> =2.02, 8.41 Hz, 1H), 4.93-5.04 (m, 2H), 4.79-4.84 (m, 1H), 4.70-4.76 (m, 1H), 3.10-3.23 (m, 6H), 2.94-3.10 (m, 2H), 2.88 (s, 2H), 1.86-2.05 (m, 1H), 1.75 (br s, 1H)	B	SFC: Chiralpak IC, 30% methanol Peak 2

Ex. #.	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
472	600MHz DMSO – d ₆	7.21 (d, <i>J</i> =9.28 Hz, 1H), 6.96-7.03 (m, 2H), 5.09-5.17 (m, 2H), 4.17-4.40 (m, 1H), 3.39-3.56 (m, 1H), 3.13-3.25 (m, 2H), 3.00 (s, 1H), 2.89 (br t, <i>J</i> =10.63 Hz, 1H), 2.52-2.55 (m, 2H), 2.35-2.46 (m, 2H), 1.92-2.00 (m, 2H), 1.73-1.86 (m, 1H), 1.19-1.29 (m, 1H),	--	--
473	600MHz DMSO – d ₆	7.74 (s, 1H), 7.37-7.46 (m, 2H), 5.08-5.18 (m, 2H), 4.36-4.50 (m, 1H), 3.56-3.72 (m, 6H), 3.42-3.54 (m, 2H), 3.35-3.41 (m, 2H), 2.98-3.11 (m, 2H), 2.85 (dd, <i>J</i> =8.17, 12.61 Hz, 1H), 2.03-2.19 (m, 1H), 1.75-1.91 (m, 1H)	B	SFC: IC, 15% methanol Peak 2
474	600MHz DMSO – d ₆	7.39 (s, 1H), 7.26 (d, <i>J</i> =8.56 Hz, 1H), 7.05 (d, <i>J</i> =8.79 Hz, 1H), 4.98-5.11 (m, 2H), 3.35-3.41 (m, 1H), 3.11-3.17 (m, 3H), 2.96-3.10 (m, 2H), 2.89 (s, 3H), 2.77-2.86 (m, 1H), 2.07-2.17 (m, 1H), 1.73-1.90 (m, 3H)	B	SFC: Chiralpak AD-H analytical column, 15% methanol with 0.2% DEA. Peak 2
475	600MHz DMSO – d ₆	7.40 (s, 1H), 7.29 (d, <i>J</i> =8.64 Hz, 1H), 7.06 (d, <i>J</i> =8.63 Hz, 1H), 4.98-5.12 (m, 2H), 4.37-4.48 (m, 1H), 3.56-3.71 (m, 5H), 3.41-3.54 (m, 2H), 3.37-3.41 (m, 1H), 3.12-3.26 (m, 2H), 2.93-3.09 (m, 2H), 2.79-2.90 (m, 1H), 2.05-2.22 (m, 1H), 1.75-1.87 (m, 1H)	B	Chiralcel OD-H column Peak 2
476	600MHz DMSO – d ₆	8.90 (s, 1H), 8.27 (dd, <i>J</i> =2.10, 8.25 Hz, 1H), 7.30 (d, <i>J</i> =8.33 Hz, 1H), 6.87 (dd, <i>J</i> =2.18, 9.34 Hz, 1H), 6.57 (dd, <i>J</i> =2.18, 11.91 Hz, 1H), 5.48-5.56 (m, 2H), 4.37-4.45 (m, 1H), 3.55 (s, 3H), 3.38-3.48 (m, 2H), 3.17 (s, 1H), 2.96-3.06 (m, 2H), 2.81 (dd, <i>J</i> =8.91, 12.57 Hz, 1H), 2.01-2.11 (m, 1H), 1.68-1.80 (m, 1H)	B	SFC: Chiralpak AD-H, 25% methanol Peak 1
477	600MHz DMSO – d ₆	8.91 (s, 2H), 7.22 (dd, <i>J</i> =2.49, 9.81 Hz, 1H), 7.10 (dd, <i>J</i> =4.75, 8.72 Hz, 1H), 6.84 (ddd, <i>J</i> =2.49, 8.70, 9.91 Hz, 1H), 5.46-5.58 (m, 2H), 3.26-3.31 (m, 3H), 2.98-3.24 (m, 4H), 2.93 (td, <i>J</i> =3.28, 6.75 Hz, 1H), 1.86 (dtd, <i>J</i> =3.54, 7.61, 13.38 Hz, 1H), 1.58-1.66 (m, 1H), 1.40 (br s, 1H)	B	SFC: Phenomenex Lux Cellulose-2, 15% methanol. Peak 2
478	600MHz DMSO – d ₆	8.47 (br s, 2H), 7.78 (s, 1H), 7.44-7.50 (m, 2H), 5.09-5.23 (m, 2H), 4.80 - 4.88 (m, 1H), 3.72-3.84 (m, 1H), 3.69 (br d, <i>J</i> =4.52 Hz, 3H), 3.57-3.66 (m, 4H), 3.38-3.53 (m, 2H), 3.13 (br dd, <i>J</i> =10.32, 12.57 Hz, 1H), 3.05 (br t, <i>J</i> =11.60 Hz, 1H), 2.24 (br t, <i>J</i> =9.54 Hz, 1H), 1.85-1.93 (m, 1H), 1.15-1.27 (m, 1H)	B	SFC: Chiralpak IC, 15% methanol. Peak 2

Ex. #.	Freq., Solvent	¹ H NMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
479	600MHz DMSO – d ₆	7.26-7.29 (m, 1H), 7.25 (t, <i>J</i> =6.83 Hz, 1H), 6.99 (t, <i>J</i> =9.32 Hz, 1H), 5.05-5.21 (m, 2H), 4.87-5.01 (m, 1H), 4.23 (q, <i>J</i> =9.55 Hz, 2H), 3.69-3.79 (m, 1H), 3.58 (dt, <i>J</i> =4.36, 8.99 Hz, 1H), 3.27-3.30 (m, 3H), 3.06-3.14 (m, 1H), 2.97-3.03 (m, 2H), 2.65 (s, 3H), 2.16-2.25 (m, 1H), 1.81-1.95 (m, 1H)	B	FC using an (2xChiralpak IC 2x25 cm, 5 μm column), Peak2
480	600MHz DMSO – d ₆	8.23-8.31 (br s, 1H), 6.90-7.33 (m, 3H), 5.13-5.26 (m, 2H), 4.11-4.29 (m, 1H), 3.82-3.91 (m, 1H), 3.63 (br d, <i>J</i> =9.19 Hz, 1H), 3.45-3.59 (m, 1H), 3.36 (td, <i>J</i> =8.29, 16.43 Hz, 1H), 3.28 (s, 3H), 3.10-3.23 (m, 1H), 2.52-2.55 (m, 1H), 2.34-2.47 (m, 1H), 0.97-1.19 (m, 3H)	--	--
481	600MHz DMSO – d ₆	7.28-7.59 (m, 1H), 7.05-7.16 (m, 1H), 6.75-6.95 (m, 1H), 4.77-4.93 (m, 1H), 4.08-4.53 (m, 1H), 4.02-4.32 (m, 1H), 3.32-3.32 (m, 2H), 3.21-3.30 (m, 1H), 2.76-2.93 (m, 1H), 2.53-2.70 (m, 1H), 1.68-1.86 (m, 1H), 1.45-1.63 (m, 1H), 1.02-1.18 (m, 1H), -0.05-0.15 (m, 1H)	--	--
482	600MHz DMSO – d ₆	8.70 (br s, 2H), 7.26-7.32 (m, 1H), 7.02 (ddd, <i>J</i> =2.53, 8.86, 9.79 Hz, 1H), 5.15-5.24 (m, 1H), 4.12-4.30 (m, 2H), 4.03-4.12 (m, 1H), 3.68 (br d, <i>J</i> =11.91 Hz, 5H), 3.26-3.40 (m, 3H), 3.11-3.18 (m, 1H), 2.65 (br s, 1H), 2.58-2.63 (m, 1H), 2.52-2.56 (m, 4H)	B	SFC with Chiralcel OD-H, 10% methanol Peak2
483	600MHz DMSO – d ₆	8.70 (br s, 2H), 7.26-7.32 (m, 2H), 7.02 (ddd, <i>J</i> =2.53, 8.86, 9.79 Hz, 1H), 5.15-5.24 (m, 2H), 4.12-4.30 (m, 2H), 4.03-4.12 (m, 2H), 3.68 (br d, <i>J</i> =11.91 Hz, 2H), 3.26-3.40 (m, 4H), 3.11-3.18 (m, 1H), 2.65 (br s, 1H), 2.58-2.63 (m, 1H).	B	SFC: Chiralpak IC, 25% isopropanol. Peak2
484	600MHz DMSO – d ₆	8.14 (br s, 2H), 7.22-7.27 (m, 2H), 7.11-7.19 (m, 1H), 5.03-5.15 (m, 2H), 4.23 (dq, <i>J</i> =3.35, 9.37 Hz, 1H), 3.58-3.69 (m, 2H), 3.27 (s, 3H), 3.15-3.25 (m, 2H), 2.96-3.03 (m, 2H), 2.85-2.93 (m, 1H), 1.79-2.00 (m, 1H), 1.55-1.61 (m, 1H)	B	SFC: Chiralpak IC, 25% isopropanol. Peak1
485	600MHz DMSO – d ₆	8.14 (br s, 2H), 7.23-7.28 (m, 2H), 6.98 (t, <i>J</i> =9.21 Hz, 1H), 5.03-5.18 (m, 2H), 4.23 (q, <i>J</i> =9.47 Hz, 2H), 3.63-3.82 (m, 1H), 3.47 (br s, 1H), 3.29-3.42 (m, 1H), 3.28 (s, 2H), 2.97-3.11 (m, 2H), 2.87-2.96 (m, 1H), 2.52-2.55 (m, 4H), 2.14-2.31 (m, 1H), 1.38-1.50 (m, 1H)	B	SFC using an Chiralpak IC 2x25 cm, 5 micron, a mobile phase of 25% isopropanol Peak 2
486	600MHz DMSO – d ₆	8.23 (br s, 2H), 7.15-7.28 (m, 1H), 6.98-7.14 (m, 2H), 6.78-6.91 (m, 1H), 5.09-5.28 (m, 1H), 4.16-4.29 (m, 1H), 3.50-3.89 (m, 3H), 3.40-3.49 (m, 1H), 3.26-3.30 (m, 2H), 2.54 (s, 2H), 2.15-2.33 (m, 1H)	B	SFC: Chiralpak AD-H analytical column, 25% isopropanol Peak1

Ex. #.	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
487	600MHz DMSO – d ₆	8.23 (br s, 2H), 7.14-7.28 (m, 1H), 7.12 (br s, 1H), 6.99-7.10 (m, 1H), 5.16-5.29 (m, 1H), 4.16-4.29 (m, 1H), 3.64-3.83 (m, 2H), 3.41 (br s, 2H), 3.37-3.39 (m, 1H), 3.26-3.29 (m, 2H), 2.52-2.55 (m, 2H), 2.15-2.33 (m, 1H)	B	SFC: Chiralpak AD-H analytical column, 25% isopropanol Peak2
488	600MHz DMSO – d ₆	7.36-7.43 (m, 1H), 7.09 (dd, <i>J</i> =2.49, 9.34 Hz, 1H), 6.87-6.96 (m, 1H), 5.03-5.09 (m, 2H), 4.17-4.28 (m, 2H), 3.73-3.79 (m, 1H), 3.71 (br d, <i>J</i> =3.11 Hz, 1H), 3.40-3.49 (m, 2H), 3.23-3.29 (m, 1H), 2.89-3.08 (m, 6H), 2.51-2.57 (m, 1H), 1.72-1.82 (m, 1H)	B	SFC using two Regis WHELK-O s,s 2x25 cm, 5 micron columns Peak2
489	600MHz DMSO – d ₆	7.16-7.21 (m, 1H), 7.05 (dd, <i>J</i> =2.49, 9.42 Hz, 1H), 6.78-6.84 (m, 1H), 5.07-5.19 (m, 2H), 4.20-4.46 (m, 2H), 3.52-3.65 (m, 2H), 3.40-3.51 (m, 2H), 3.26 (s, 3H), 3.07-3.14 (m, 1H), 1.87-2.00 (m, 1H), 1.62 (qd, <i>J</i> =6.18, 12.45 Hz, 1H)	--	--
490	600MHz DMSO – d ₆	7.16-7.21 (m, 1H), 7.05 (dd, <i>J</i> =2.49, 9.42 Hz, 1H), 6.78-6.84 (m, 1H), 5.07-5.19 (m, 2H), 4.16-4.31 (m, 2H), 3.92 (br s, 1H), 3.77 (br s, 1H), 3.44-3.58 (m, 3H), 3.25-3.29 (m, 1H), 2.99 (s, 1H), 2.52-2.55 (m, 1H), 2.28 (qd, <i>J</i> =7.20, 13.97 Hz, 1H), 2.00 (br d, <i>J</i> =4.83 Hz, 1H)	--	--
491	600MHz DMSO – d ₆	7.17-7.23 (m, 1H), 7.08 (dd, <i>J</i> =2.49, 9.42 Hz, 1H), 6.79-6.89 (m, 1H), 5.07-5.21 (m, 2H), 4.16-4.41 (m, 2H), 3.39-3.58 (m, 2H), 3.14-3.27 (m, 2H), 2.94-3.03 (m, 1H), 2.68 (br d, <i>J</i> =6.93 Hz, 2H), 2.52-2.57 (m, 1H), 2.27-2.34 (m, 1H), 1.95-2.04 (m, 1H), 1.65 (qd, <i>J</i> =8.03, 12.28 Hz, 1H)	--	--
492	600MHz DMSO – d ₆	1.79 (br dd, <i>J</i> =8.64, 3.11 Hz, 1H) 1.84 (br s, 1H) 2.88 - 2.97 (m, 2H) 2.97 - 3.13 (m, 4H) 3.17 (s, 1H), 3.24 - 3.28 (m, 3H) 3.38 - 3.53 (m, 2H) 3.68 - 3.80 (m, 2H) 4.17 - 4.28 (m, 2H) 4.48 (q, <i>J</i> =8.93 Hz, 1H) 5.00 (s, 1H) 5.07 (s, 1H) 6.87 - 6.94 (m, 1H) 7.15 (dd, <i>J</i> =8.68, 4.79 Hz, 1H) 7.18 - 7.25 (m, 1H)	--	--
493	600MHz DMSO – d ₆	1.65 - 1.82 (m, 2H) 1.84 (br s, 1H) 2.52 - 2.56 (m, 1H) 2.90 - 2.96 (m, 2H) 2.98 - 3.13 (m, 5H) 3.17 (s, 1H) 3.24 - 3.28 (m, 3H) 3.38 - 3.53 (m, 3H) 3.69 - 3.79 (m, 2H) 4.09 (br s, 1H) 4.16 - 4.29 (m, 2H) 4.48 (q, <i>J</i> =9.16 Hz, 1H) 5.00 (s, 1H) 5.07 (s, 2H) 6.88 - 6.94 (m, 1H) 7.13 - 7.25 (m, 2H)	--	--

Scheme 9

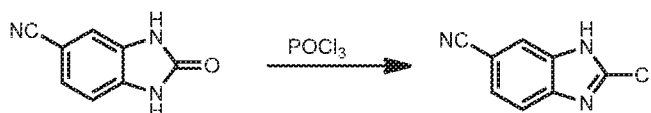


Intermediate 60: tert-butyl ((3R,4R)-1-(6-cyano-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl)carbamate



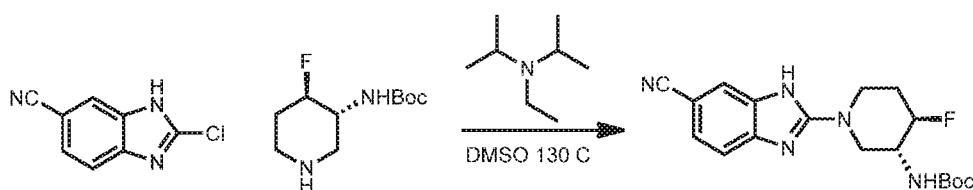
Step 1. 2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-carbonitrile

To a solution of 1,2-diamino-4-cyanobenzene (1.00 mL, 7.51 mmol) in tetrahydrofuran (5 mL) was added 1,1'-carbonyldiimidazole (1.22 g, 7.51 mmol). The reaction was stirred at ambient temperature for one hour, concentrated, then triturated with water. The brown precipitate was collected by vacuum filtration to provide 2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-carbonitrile as a brown powder. MS (ESI, pos. ion) m/z: 160.2 [M+1]



Step 2. 2-chloro-1H-benzo[d]imidazole-6-carbonitrile

To a suspension of 2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-carbonitrile (XVIII, 1.19 g, 7.48 mmol, 1 equiv) in acetonitrile (5 mL) was added phosphorus(v) oxychloride (1.398 mL, 14.95 mmol). The reaction was stirred at 110 °C for 16 hours, then cooled to room temperature. It was diluted with acetonitrile and then slowly added to a cold, rapidly-stirring beaker of saturated aqueous sodium bicarbonate (50 mL). The mixture was extracted with ethyl acetate; which was dried over anhydrous magnesium sulfate, filtered, and concentrated to provide 2-chloro-1H-benzo[d]imidazole-6-carbonitrile as a tan powder. (ESI, pos. ion) m/z: 178.2 [M+1]



Step 3. **tert-butyl ((3R,4R)-1-(6-cyano-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl)carbamate (Intermediate 60)**

N,N-diisopropylethylamine (3.93 mL, 22.52 mmol), 2-chloro-1H-benzo[d]imidazole-6-carbonitrile (2 g, 11.26 mmol), tert-butyl ((3R,4R)-4-fluoropiperidin-3-yl)carbamate (2.95 g, 13.51 mmol), and 1-butanol (25 mL) were combined in a flask and heated to 130 °C for 48 hours. The mixture was concentrated, then loaded onto a 125g RediSep ISCO cartridge, eluting with 0-4% MeOH in DCM to provide the title compound as a light brown foam. (ESI, pos. ion) m/z: 360.2 [M+1]

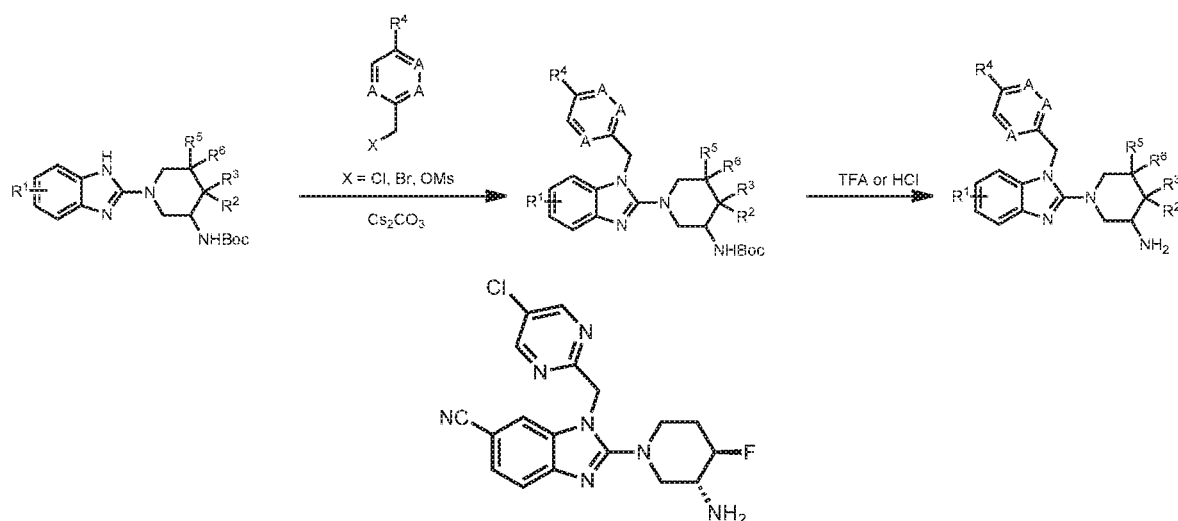
The following intermediates were synthesized using a sequence analogous to that described for intermediate 60 and general scheme 9 above:

Table 4. SnAr Intermediates prepared following Scheme 9

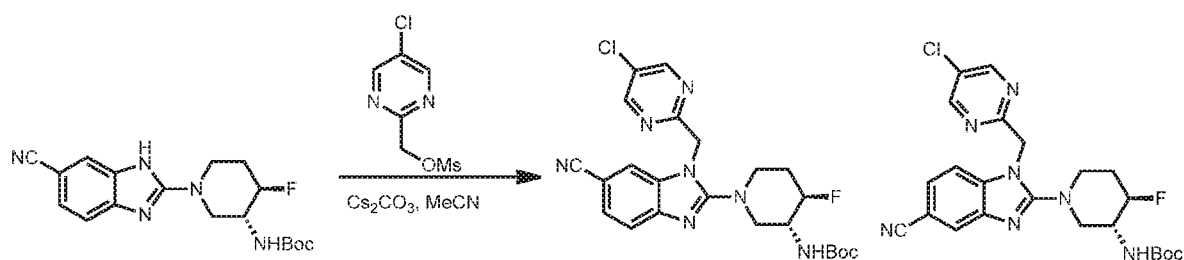
Int #	Structure	Compound Name	MS MH+
60		tert-butyl ((3R,4R)-1-(6-cyano-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl)carbamate	360.2
61		(S)-tert-butyl (1-(1H-benzo[d]imidazol-2-yl)piperidin-3-yl)(methyl)carbamate	331.3
62		tert-butyl ((3R,4R)-1-(4,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl)carbamate	371.2
63		tert-butyl 6-(4,6-difluoro-1H-benzo[d]imidazol-2-yl)hexahydro-2H-pyrido[4,3-b][1,4]oxazine-4(3H)-carboxylate	396.2
64		tert-butyl ((3R,4R)-1-(6-cyano-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl)(methyl)carbamate	374.2
65		tert-butyl ((3R,4R)-4-fluoro-1-(6-fluoro-1H-benzo[d]imidazol-2-yl)piperidin-3-yl)carbamate	353.2
66		(R)-tert-butyl (1-(6-chloro-1H-benzo[d]imidazol-2-yl)-4,4-difluoropiperidin-3-yl)carbamate	387.2
67		tert-butyl ((3R,4R)-1-(1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl)carbamate	335.0
68		tert-butyl ((3R,4R)-1-(5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl)carbamate	371.2
69		tert-butyl ((3R,4R)-1-(6-chloro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl)carbamate	369.2

Int #	Structure	Compound Name	MS MH+
70		(R)-tert-butyl 1-(4,6-difluoro-1H-benzo[d]imidazol-2-yl)-4,4-difluoropiperidin-3-yl carbamate	389.2
71		(S)-tert-butyl 1-(1H-benzo[d]imidazol-2-yl)piperidin-3-yl carbamate	317.2
72		(R)-tert-butyl 1-(1H-benzo[d]imidazol-2-yl)piperidin-3-yl carbamate	317.2
73		(R)-tert-butyl 1-(1H-benzo[d]imidazol-2-yl)-4,4-difluoropiperidin-3-yl carbamate	353.2
74		tert-butyl ((3R,4S)-1-(6-cyano-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl) carbamate	360.2
75		tert-butyl ((3R,4R)-1-(6-fluoro-1H-benzo[d]imidazol-2-yl)-4-hydroxypiperidin-3-yl) carbamate	351.2
76		tert-butyl ((3R,4S)-1-(5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl) carbamate	371.0
77		tert-butyl ((3R,4S)-4-fluoro-1-(6-(trifluoromethyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-yl) carbamate	403.2
78		(R)-tert-butyl 1-(5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4,4-difluoropiperidin-3-yl carbamate	389.2
79		tert-butyl ((3R,4S)-1-(1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl) carbamate	335.2
80		tert-butyl ((3R,4S)-1-(6-fluoro-1H-benzo[d]imidazol-2-yl)-4-hydroxypiperidin-3-yl) carbamate	351.2
81		tert-butyl ((3R,4R)-4-fluoro-1-(6-(trifluoromethyl)-1H-imidazo[4,5-b]pyridin-2-yl)piperidin-3-yl) carbamate	404.2
82		tert-butyl ((3R,4R)-4-fluoro-1-(6-fluoro-4-methoxy-1H-benzo[d]imidazol-2-yl)piperidin-3-yl) carbamate	383.2
83		tert-butyl ((3R,4R)-4-fluoro-1-(6-(trifluoromethyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-yl) carbamate	403.2

Int #	Structure	Compound Name	MS MH+
84		tert-butyl ((3R,4R)-4-fluoro-1-(6-fluoro-1H-imidazo[4,5-b]pyridin-2-yl)piperidin-3-yl)carbamate	354.2
85		(R)-tert-butyl (4,4-difluoro-1-(6-fluoro-1H-benzo[d]imidazol-2-yl)piperidin-3-yl)carbamate	371.2

Scheme 10. Advancement of S_NAr intermediates to final products

Example 187: 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile



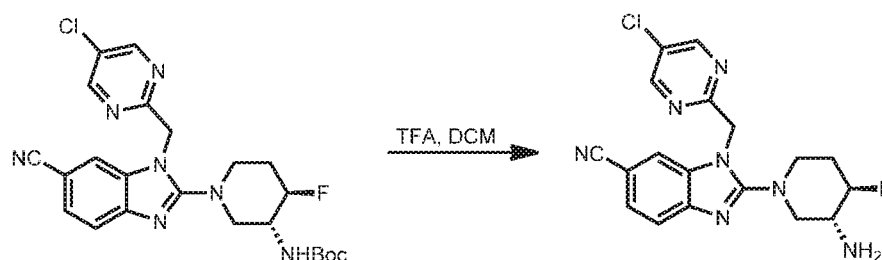
Step 1. $tert$ -butyl ((3R,4R)-1-(1-((5-chloropyrimidin-2-yl)methyl)-6-cyano-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl)carbamate

Cesium carbonate (0.707 mg, 2.170 mmol), $tert$ -butyl ((3R,4R)-1-(6-cyano-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl)carbamate (390 mg, 1.085 mmol), (5-chloropyrimidin-2-yl)methyl methanesulfonate (290 mg, 1.302 mmol), and acetonitrile (10 mL) were combined in a vial and stirred overnight. The mixture was poured into water and extracted with DCM (3X). The organics were combined, dried over Na_2SO_4 , filtered, and concentrated. The brown solid was dissolved in DCM, loaded onto a 20g plug of silica and flushed with EtOAc (~4 column volumes). The EtOAc was concentrated to provide $tert$ -butyl ((3R,4R)-1-

(1-((5-chloropyrimidin-2-yl)methyl)-6-cyano-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl)carbamate and tert-butyl ((3R,4R)-1-(1-((5-chloropyrimidin-2-yl)methyl)-5-cyano-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl)carbamate as a mixture of isomers. The isomers were separated using chiral SFC (Chiralcel AD, 25% IPA, *peak 1*). (ESI, pos. ion) m/z: 486.2 [M+1]

5

Boc Deprotection using TFA (Procedure B)



Step 2. 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile (Example 187)

10 tert-Butyl ((3R,4R)-1-(1-((5-chloropyrimidin-2-yl)methyl)-6-cyano-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl)carbamate (150 mg, 0.309 mmol) was loaded into a vial. DCM (5 mL), then TFA (2 mL) was added. After 1 hour, the mixture was poured onto an SCX column, prewetted with methanol, flushed with methanol, then eluted with methanolic ammonia. The residue was redissolved in MeCN/H₂O, frozen, and lyophilized to provide the title compound as a white solid. ¹H NMR (500 MHz, MeOD) δ 8.80 (s, 2H), 7.65-7.69 (m, 1H), 7.54-7.61 (m, 1H), 7.49 (d, J=8.30 Hz, 1H), 5.57 (s, 2H), 4.42-4.60 (m, 1H), 3.72-3.80 (m, 1H), 3.64 (br d, J=13.23 Hz, 1H), 3.15-3.27 (m, 2H), 3.06 (dd, J=9.21, 12.59 Hz, 1H), 2.13-2.27 (m, 1H), 1.80-1.99 (m, 1H). (ESI, pos. ion) m/z: 386.2 [M+1]

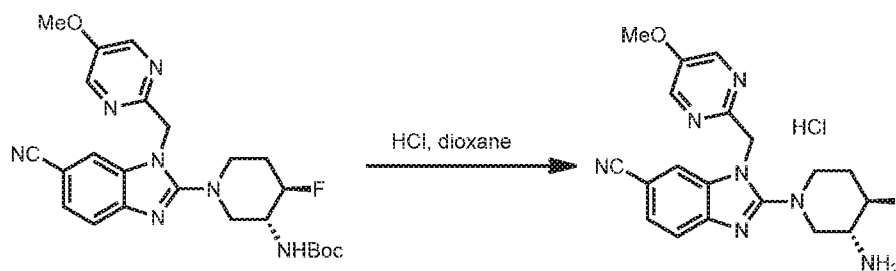
15

Note: In some cases, the free base was redissolved in DCM, and HCl was added to crash out the HCl salt.

20 *This is noted in the table as a TFA deprotection, but HCl product.*

Alternative Boc Deprotection with HCl (Procedure A)

Step 2. 2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-methoxypyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile hydrochloride (Example 242)

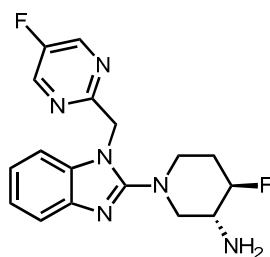


25

tert-Butyl ((3R,4R)-1-(6-cyano-1-((5-methoxypyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl)carbamate (69 mg) was dissolved in dioxane (2 mL), and 4 N HCl in dioxane (500 uL) was added. The reaction was stirred at ambient temperature overnight, then concentrated in vacuo to provide the title compound as a white solid. ¹H NMR (500 MHz, MeOD) δ 8.52 (s, 2H), 7.94 (s, 1H), 7.66-7.74 (m, 2H), 5.54-5.67 (m, 2H), 4.77-4.93 (m, 1H), 4.21-4.30 (m, 1H), 4.01 (br d, J=12.98 Hz, 1H), 3.96 (s, 3H), 3.71-3.78 (m, 1H), 3.43-3.50 (m, 2H), 2.32-2.46 (m, 1H), 1.98-2.14 (m, 1H). (ESI, pos. ion) m/z: 382.2 [M+1].

Note: HCl salt was sometimes free based using an aqueous work up or using ion exchange chromatography. Isolation of salt or free base is specified in table.

The following compounds were made in a manner analogous to that outlined in Schemes 9 and 10:

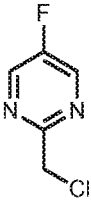
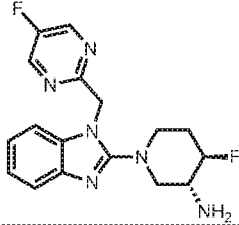
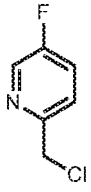
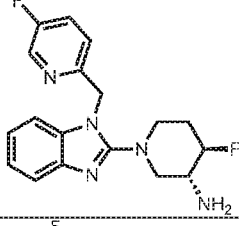
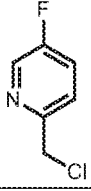
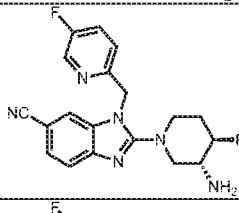
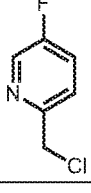
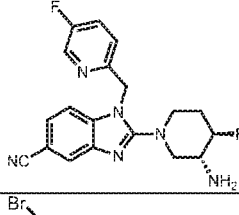
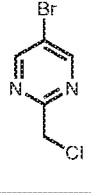
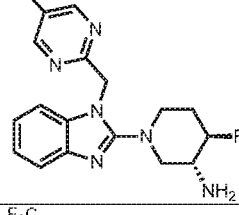
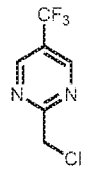
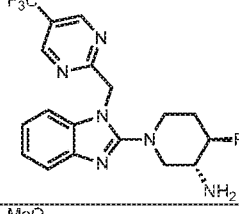
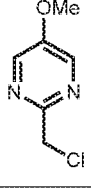
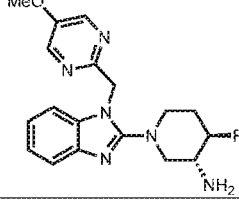


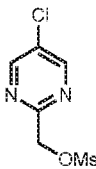
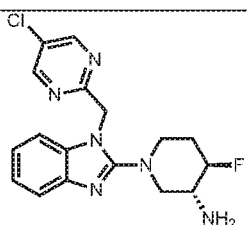
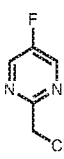
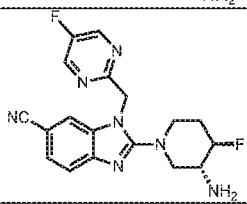
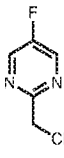
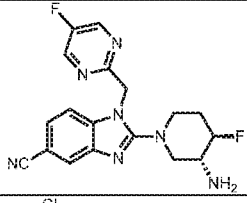
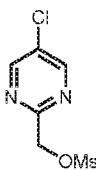
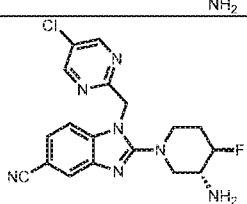
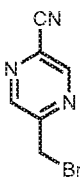
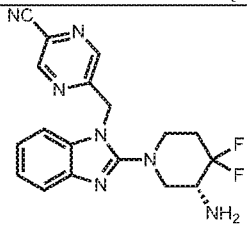
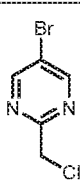
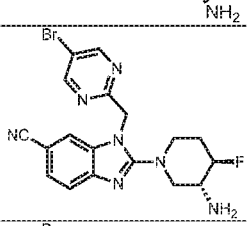
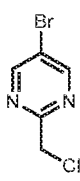
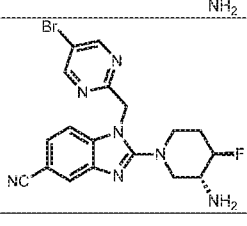
Example 188: (3R,4R)-4-fluoro-1-(1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine was synthesized on 0.3 mmol scale following a sequence analogous to that described above. The Boc deprotection was accomplished using the TFA procedure. ¹H NMR (500 MHz, MeOD) δ 8.68-8.74 (s, 2H), 7.47-7.52 (m, 1H), 7.14-7.20 (m, 2H), 7.08-7.13 (m, 1H), 5.53 (s, 2H), 4.34-4.52 (m, 1H), 3.64 (dtd, J=1.95, 4.14, 12.36 Hz, 1H), 3.48-3.57 (m, 1H), 3.04-3.21 (m, 2H), 2.98 (dd, J=8.82, 12.20 Hz, 1H), 2.12-2.25 (m, 1H), 1.82-1.92 (m, 1H). (ESI, pos. ion) m/z: 345.2 [M+1].

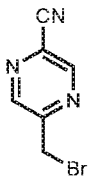
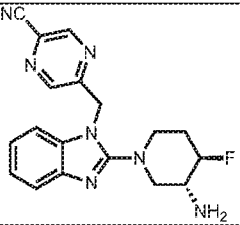
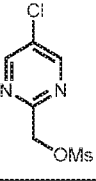
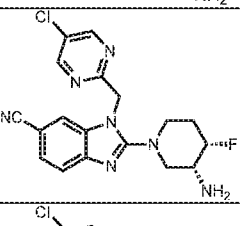
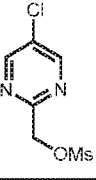
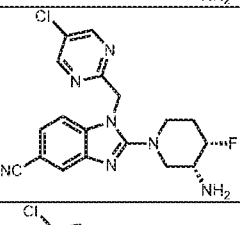
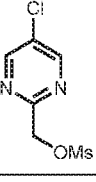
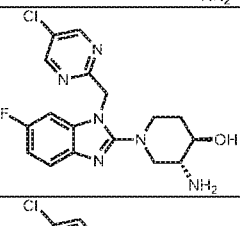
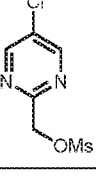
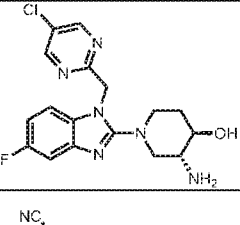
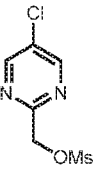
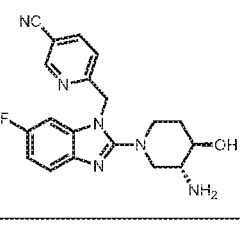
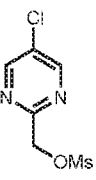
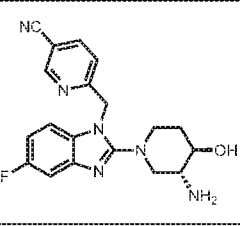
The following Examples were synthesized using a sequence analogous to that described for examples 239-240 and general scheme 9-10 above:

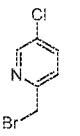
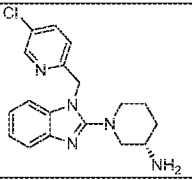
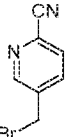
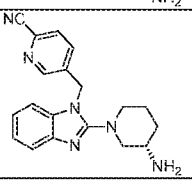
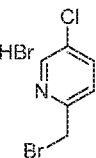
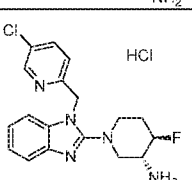
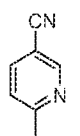
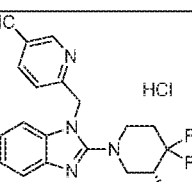
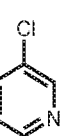
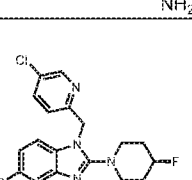
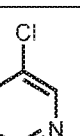
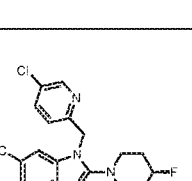
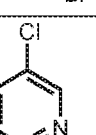
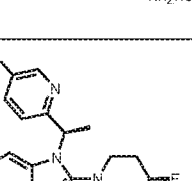
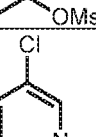
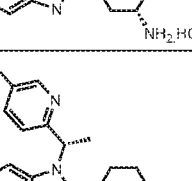
Table 5. Compounds made following schemes 9-10

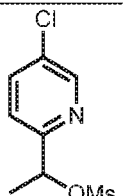
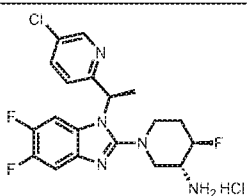
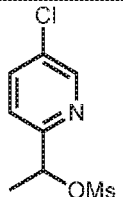
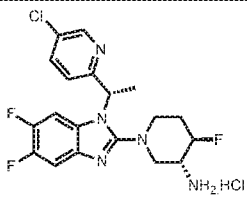
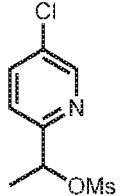
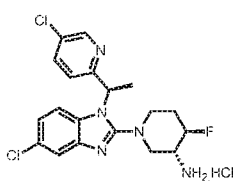
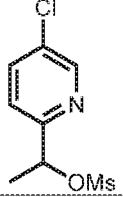
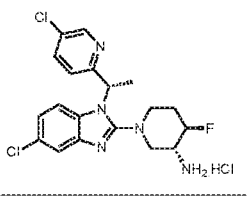
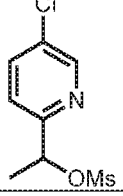
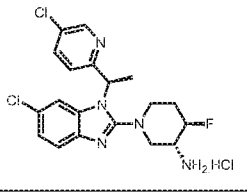
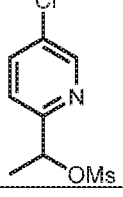
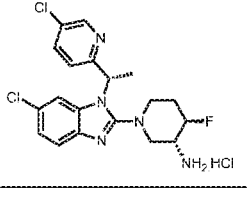
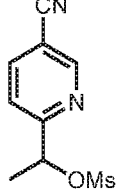
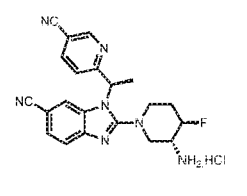
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
187	60		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile	386.0

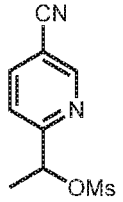
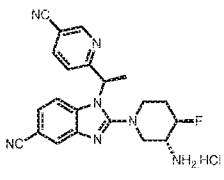
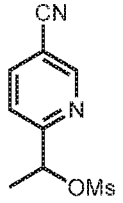
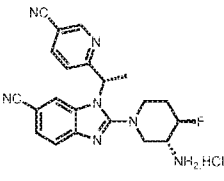
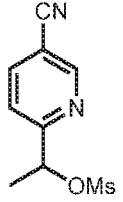
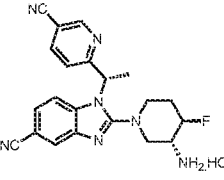
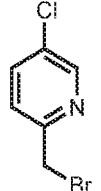
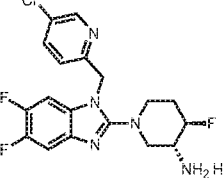
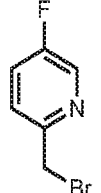
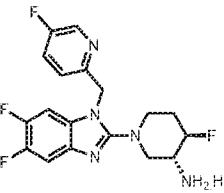
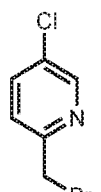
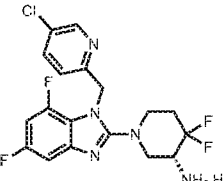
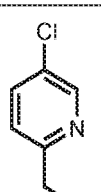
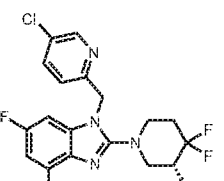
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
188	67		B		(3R,4R)-4-fluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	345.2
189	67		B		(3R,4R)-4-fluoro-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	344.2
190	60		B		2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile	369.0
191	60		B		2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile	369.2
192	67		B		(3R,4R)-1-((5-bromopyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	405.0
193	67		B		(3R,4R)-4-fluoro-1-((5-(trifluoromethyl)pyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	395.2
194	67		B		(3R,4R)-4-fluoro-1-((5-methoxypyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	357.2

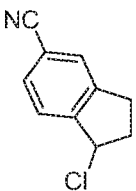
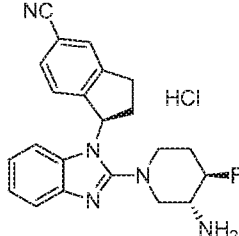
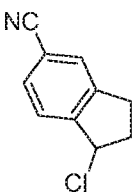
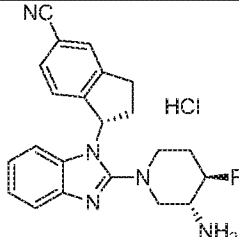
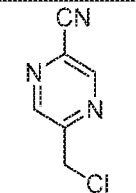
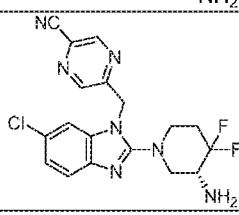
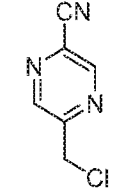
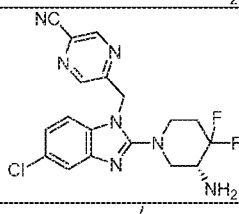
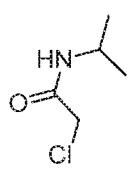
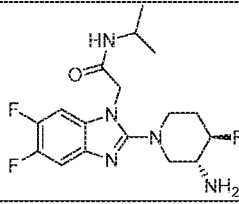
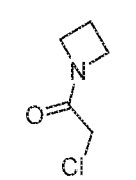
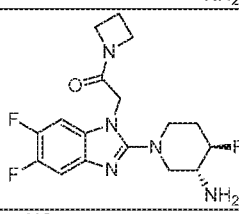
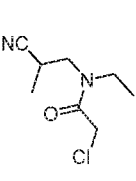
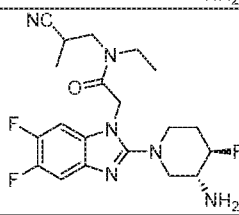
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
195	67		B		(3R,4R)-1-(1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	361.8
196	60		B		2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile	370.0
197	60		B		2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile	370.0
198	60		B		2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-cyanopyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile	386.0
199	73		B		2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile	370.0
200	60		B		2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-bromopyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile	432.0
201	60		B		2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-bromopyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile	432.0

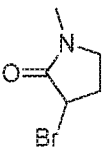
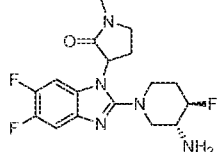
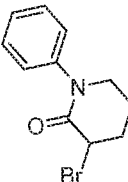
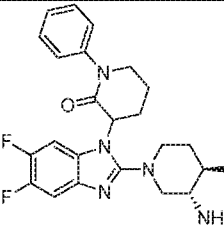
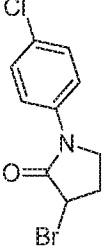
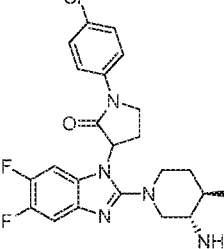
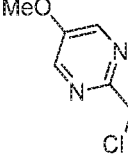
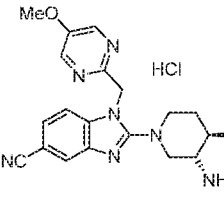
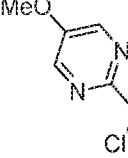
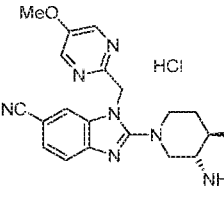
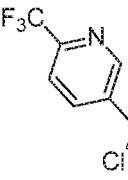
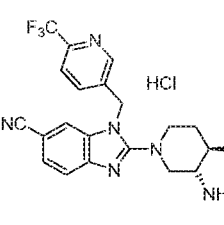
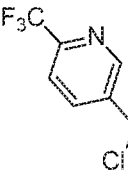
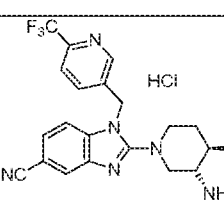
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
202	67		B		5-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)pyrazine-2-carbonitrile	352.2
203	74		B		2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile	386.2
204	74		B		2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile	386.2
205	75		B		(3R,4R)-3-amino-1-(1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)piperidin-4-ol	377.0
206	75		B		(3R,4R)-3-amino-1-(1-((5-chloropyrimidin-2-yl)methyl)-5-fluoro-1H-benzo[d]imidazol-2-yl)piperidin-4-ol	377.0
207	75		B		6-((2-((3R,4R)-3-amino-4-hydroxypiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	367.2
208	75		B		6-((2-((3R,4R)-3-amino-4-hydroxypiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	367.2

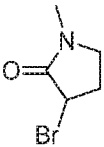
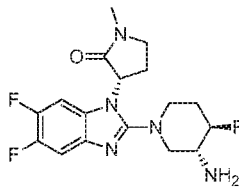
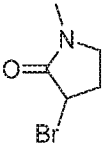
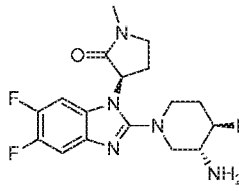
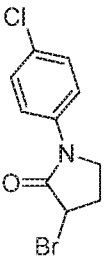
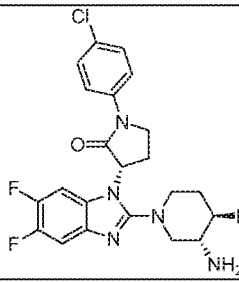
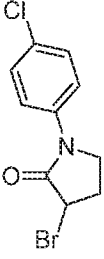
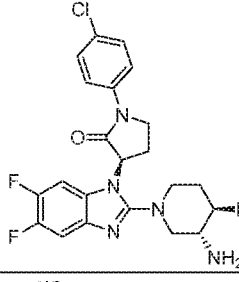
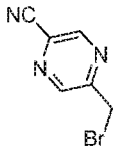
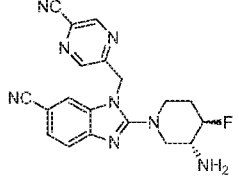
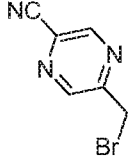
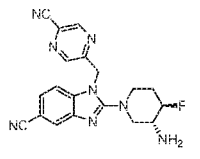
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
209	71		B		(S)-1-(1-((5-chloropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	342.0
210	71		B		(S)-5-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)picolinonitrile	333.2
211	67		A		(3R,4R)-1-(1-((5-chloropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride	360.0
212	73		A		(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride	369.0
213	60		B ^a		2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyridin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile hydrochloride	385.0
214	60		B ^a		2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyridin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile hydrochloride	385.0
215	67		B ^a		(3R,4R)-1-(1-((R)-1-(5-chloropyridin-2-yl)ethyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride	374.2
216	67		B ^a		(3R,4R)-1-(1-((S)-1-(5-chloropyridin-2-yl)ethyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride	374.2

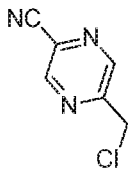
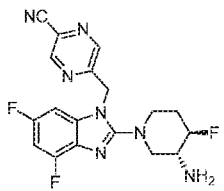
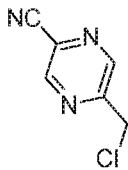
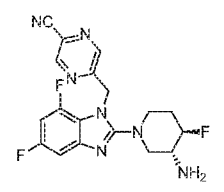
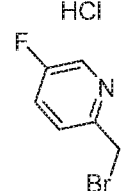
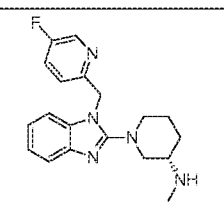
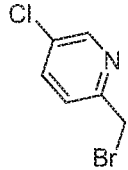
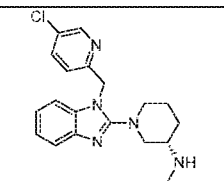
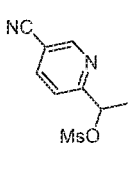
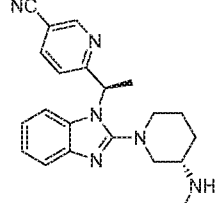
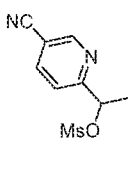
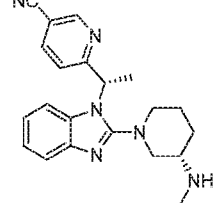
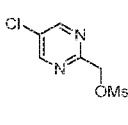
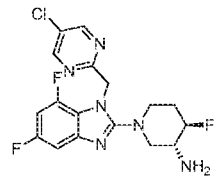
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
217	68		B ^a		(3R,4R)-1-(1-((R)-1-(5-chloropyridin-2-yl)ethyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride	410.2
218	68		B ^a		(3R,4R)-1-(1-((S)-1-(5-chloropyridin-2-yl)ethyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride	410.2
219	69		B ^a		(3R,4R)-1-(5-chloro-1-((R)-1-(5-chloropyridin-2-yl)ethyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride	408.0
220	69		B ^a		(3R,4R)-1-(5-chloro-1-((S)-1-(5-chloropyridin-2-yl)ethyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride	408.0
221	69		B ^a		(3R,4R)-1-(6-chloro-1-((R)-1-(5-chloropyridin-2-yl)ethyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride	408.0
222 a	69		B ^a		(3R,4R)-1-(6-chloro-1-((S)-1-(5-chloropyridin-2-yl)ethyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride	408.0
223	60		B ^a		2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((R)-1-(5-cyanopyridin-2-yl)ethyl)-1H-benzo[d]imidazole-6-carbonitrile hydrochloride	390.2

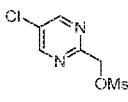
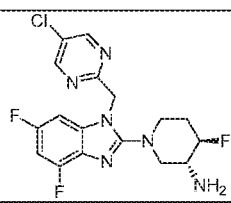
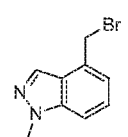
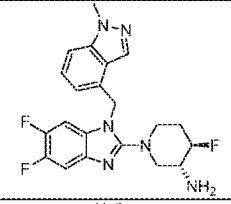
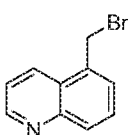
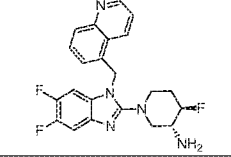
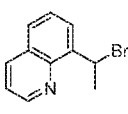
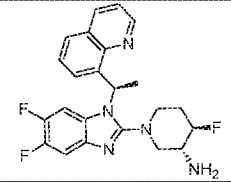
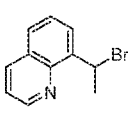
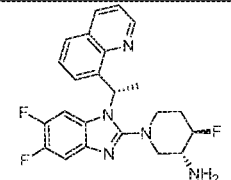
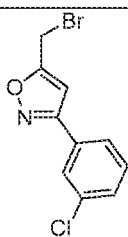
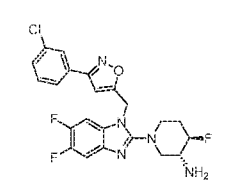
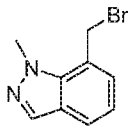
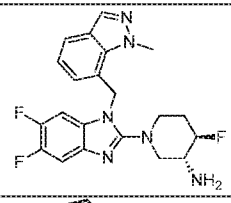
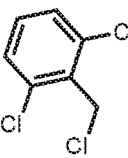
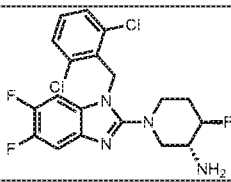
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
224	60		B ^a		2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((R)-1-(5-cyanopyridin-2-yl)ethyl)-1H-benzo[d]imidazole-5-carbonitrile hydrochloride	390.2
225	60		B ^a		2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((S)-1-(5-cyanopyridin-2-yl)ethyl)-1H-benzo[d]imidazole-6-carbonitrile hydrochloride	390.2
226	60		B ^a		2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((S)-1-(5-cyanopyridin-2-yl)ethyl)-1H-benzo[d]imidazole-5-carbonitrile hydrochloride	390.2
227	68		B ^a		(3R,4R)-1-(1-((5-chloropyridin-2-yl)methyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride	396.2
228	68		B ^a		(3R,4R)-1-(5,6-difluoro-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride	380.2
229	70		B ^a		(R)-1-(1-((5-chloropyridin-2-yl)methyl)-5,7-difluoro-1H-benzo[d]imidazol-2-yl)-4,4-difluoropiperidin-3-amine hydrochloride	414.2
230	70		B ^a		(R)-1-(1-((5-chloropyridin-2-yl)methyl)-4,6-difluoro-1H-benzo[d]imidazol-2-yl)-4,4-difluoropiperidin-3-amine hydrochloride	414.2

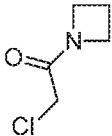
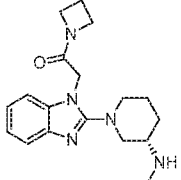
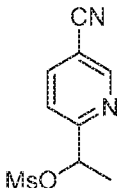
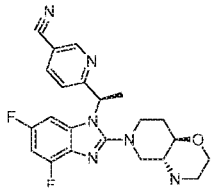
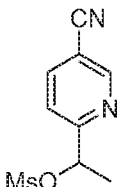
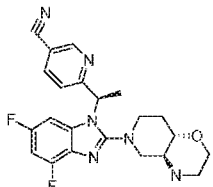
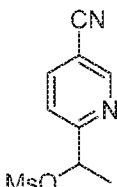
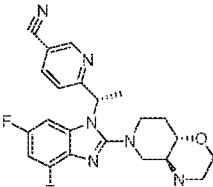
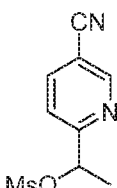
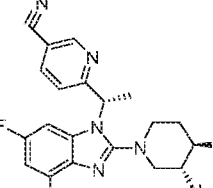
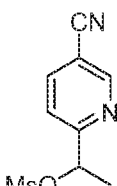
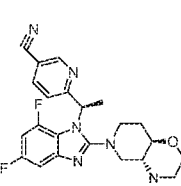
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
231	67		A		(R)-1-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)-2,3-dihydro-1H-indene-5-carbonitrile hydrochloride	376.2
232	67		A		(S)-1-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)-2,3-dihydro-1H-indene-5-carbonitrile hydrochloride	376.2
233	66		A		(R)-5-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)pyrazine-2-carbonitrile	404.0
234	66		A		(R)-5-((2-(3-amino-4,4-difluoropiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)methyl)pyrazine-2-carbonitrile	404.0
235	68		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-isopropylacetamide	370.2
236	68		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(azetidin-1-yl)ethanone	368.2
237	68		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(2-cyanopropyl)-N-ethylacetamide	423.2

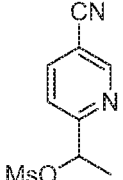
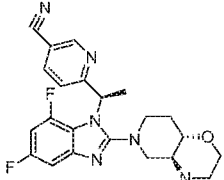
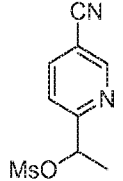
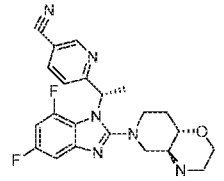
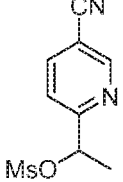
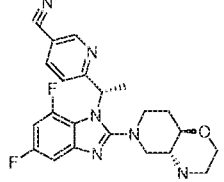
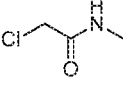
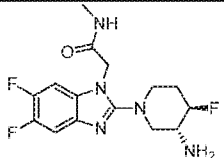
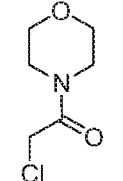
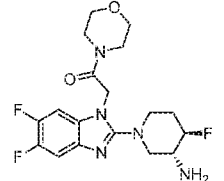
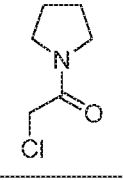
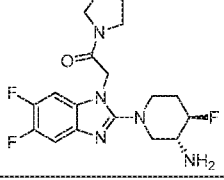
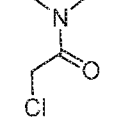
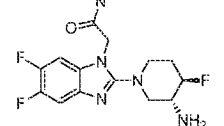
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
238	68		B		3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-methylpyrrolidin-2-one	368.2
239	68		B		3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-phenylpiperidin-2-one	444.2
240	68		B		3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-chlorophenyl)pyrrolidin-2-one	464.2
241	60		A		2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-methoxypyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile hydrochloride	382.2
242	60		A		2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-methoxypyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile hydrochloride	382.2
243	60		A		2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((6-(trifluoromethyl)pyridin-3-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile hydrochloride	419.2
244	60		A		2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((6-(trifluoromethyl)pyridin-3-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile hydrochloride	419.2

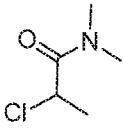
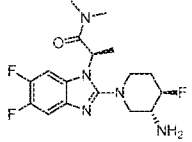
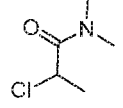
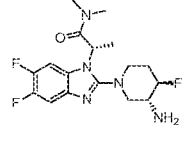
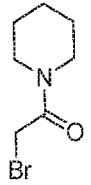
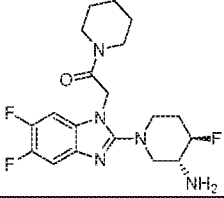
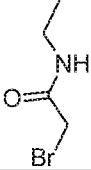
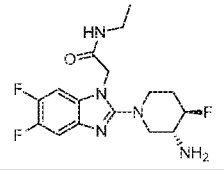
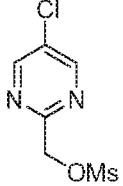
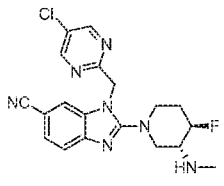
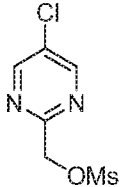
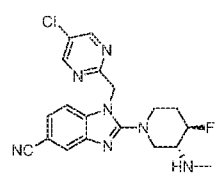
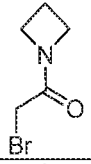
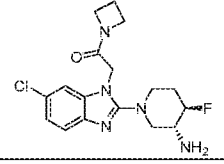
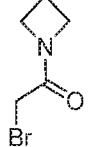
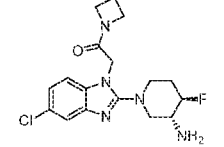
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
					carbonitrile hydrochloride	
245	68		B		(S)-3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-methylpyrrolidin-2-one	368.2
246	68		B		(R)-3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-methylpyrrolidin-2-one	368.2
247	68		B		(S)-3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-chlorophenyl)pyrrolidin-2-one	464.2
248	68		B		(R)-3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-chlorophenyl)pyrrolidin-2-one	464.2
249	60		B		2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-1-((5-cyano-2-pyrazinyl)methyl)-1H-benzimidazole-6-carbonitrile	377.2
250	60		B		2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-1-((5-cyano-2-pyrazinyl)methyl)-1H-benzimidazole-5-carbonitrile	377.2

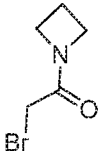
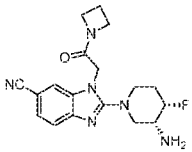
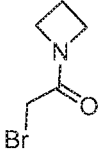
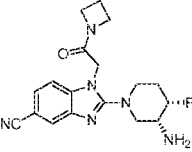
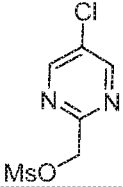
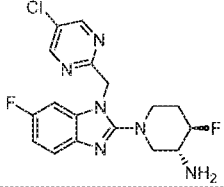
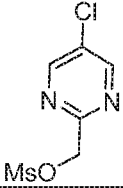
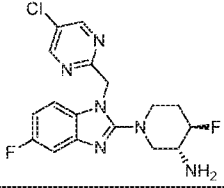
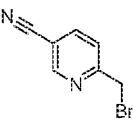
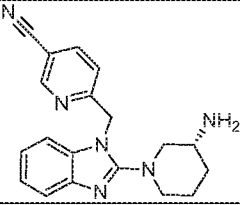
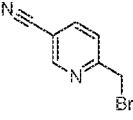
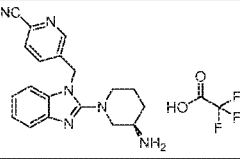
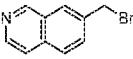
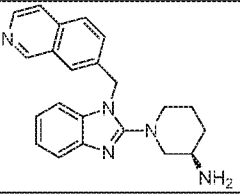
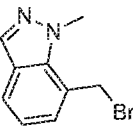
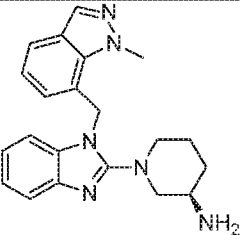
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
251	62		B		5-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-4,6-difluoro-1H-benzimidazol-1-yl)methyl)-2-pyrazinecarbonitrile	388.2
252	62		B		5-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,7-difluoro-1H-benzimidazol-1-yl)methyl)-2-pyrazinecarbonitrile	388.2
253	61		B		(3S)-1-(1-((5-fluoro-2-pyridinyl)methyl)-1H-benzimidazol-2-yl)-N-methyl-3-piperidinamine	340.2
254	61		B		(3S)-1-(1-((5-chloro-2-pyridinyl)methyl)-1H-benzimidazol-2-yl)-N-methyl-3-piperidinamine	356.2
255	61		B		6-((1R)-1-(2-((3S)-3-(methylamino)-1-piperidinyl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile	361.2
256	61		B		6-((1S)-1-(2-((3S)-3-(methylamino)-1-piperidinyl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile	361.2
257	62		B		(3R,4R)-1-(1-((5-chloro-2-pyrimidinyl)methyl)-5,7-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	397.2

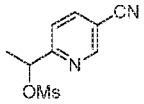
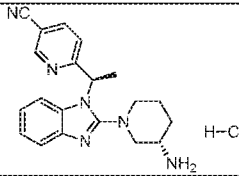
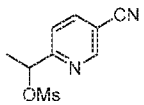
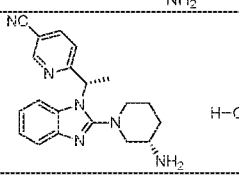
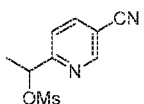
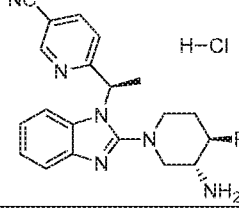
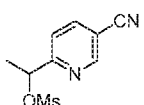
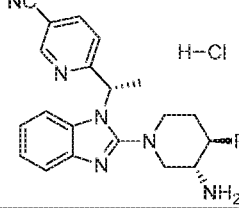
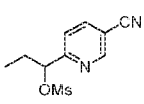
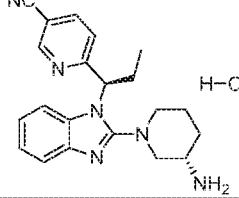
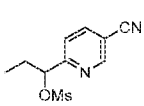
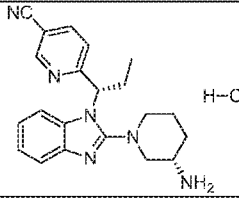
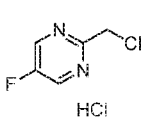
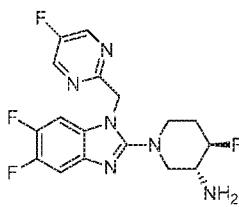
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
258	62		B		(3R,4R)-1-(1-((5-chloro-2-pyrimidinyl)methyl)-4,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	397.2
259	68		B		(3R,4R)-1-(5,6-difluoro-1-((1-methyl-1H-indazol-4-yl)methyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	415.2
260	68		B		(3R,4R)-1-(5,6-difluoro-1-(5-quinolinylmethyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	412.2
261	68		B		(3R,4R)-1-(5,6-difluoro-1-((1R)-1-(8-quinolinyl)ethyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	426.2
262	68		B		(3R,4R)-1-(5,6-difluoro-1-((1S)-1-(8-quinolinyl)ethyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	426.2
263	68		B		(3R,4R)-1-(1-((3-(3-chlorophenyl)-1,2-oxazol-5-yl)methyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	462.2
264	68		B		(3R,4R)-1-(5,6-difluoro-1-((1-methyl-1H-indazol-7-yl)methyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	415.2
265	68		B		(3R,4R)-1-(1-(2,6-dichlorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	429.0

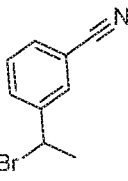
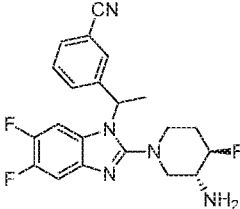
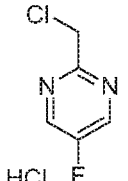
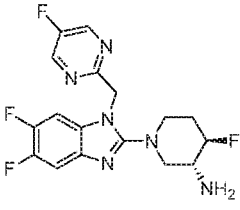
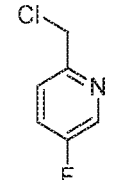
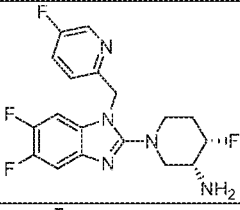
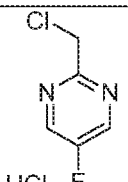
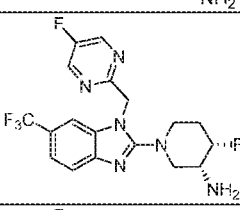
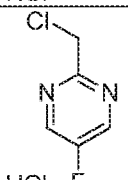
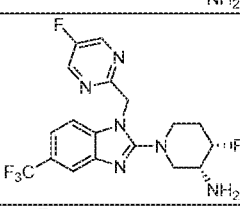
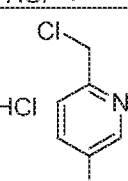
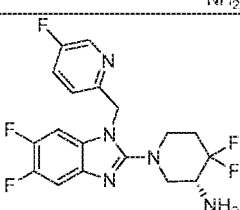
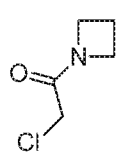
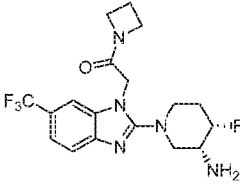
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
266	61		B		1-(1-azetidinyl)-2-(2-((3S)-3-(methylamino)-1-piperidinyl)-1H-benzimidazol-1-yl)ethanone	328.2
267	63		B		6-((1R)-1-(4,6-difluoro-2-((4aR,8aR)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile	425.2
268	63		B		6-((1R)-1-(4,6-difluoro-2-((4aS,8aS)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile	425.2
269	63		B		6-((1S)-1-(4,6-difluoro-2-((4aS,8aS)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile	425.2
270	63		B		6-((1S)-1-(4,6-difluoro-2-((4aR,8aR)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile	425.2
271	63		B		6-((1R)-1-(5,7-difluoro-2-((4aR,8aR)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile	425.2

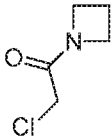
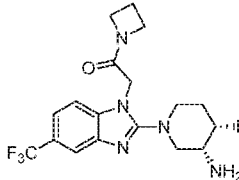
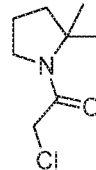
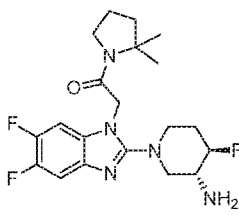
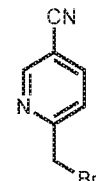
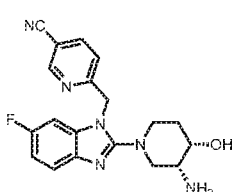
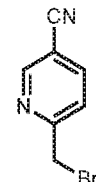
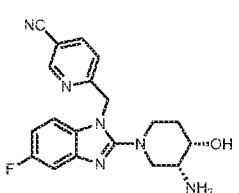
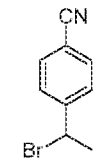
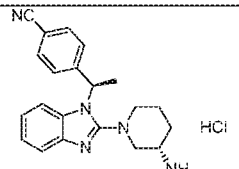
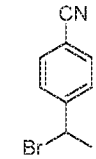
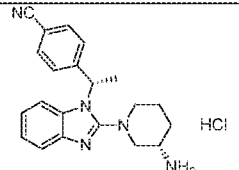
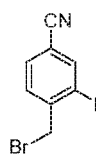
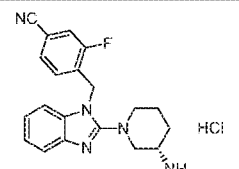
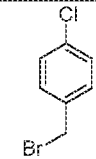
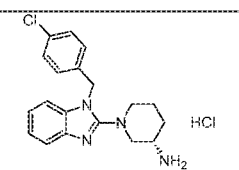
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
272	63		B		6-((1R)-1-(5,7-difluoro-2-((4aS,8aS)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile	425.2
273	63		B		6-((1S)-1-(5,7-difluoro-2-((4aS,8aS)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile	425.2
274	63		B		6-((1S)-1-(5,7-difluoro-2-((4aR,8aR)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile	425.2
275	68		B		2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)-N-methylacetamide	342.2
276	68		B		2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)-1-(4-morpholinyl)ethanone	398.2
277	68		B		2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)-1-(1-pyrrolidinyl)ethanone	382.2
278	68		B		2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)-N,N-dimethylacetamide	356.2

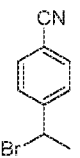
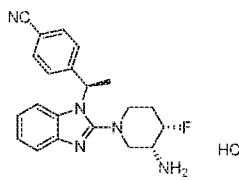
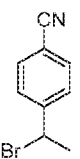
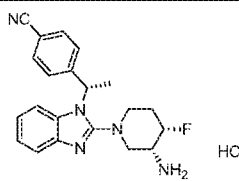
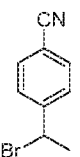
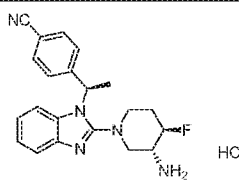
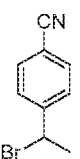
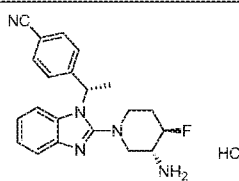
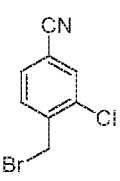
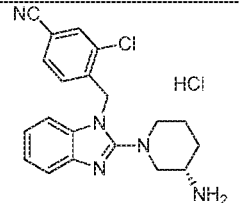
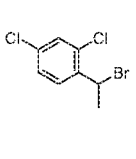
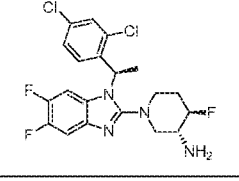
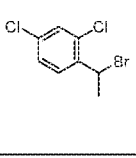
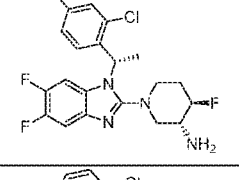
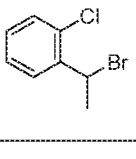
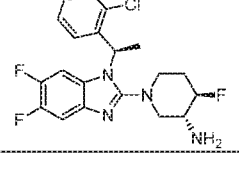
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
279	68		B		(2R)-2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)-N,N-dimethylpropanamide	370.2
280	68		B		(2S)-2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)-N,N-dimethylpropanamide	370.2
281	68		B		2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)-1-(1-piperidinyl)ethanone	396.2
282	68		B		2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)-N-ethylacetamide	356.2
283	64		B		1-((5-chloro-2-pyrimidinyl)methyl)-2-((3R,4R)-4-fluoro-3-(methylamino)-1-piperidinyl)-1H-benzimidazole-6-carbonitrile	400.0
284	64		B		1-((5-chloro-2-pyrimidinyl)methyl)-2-((3R,4R)-4-fluoro-3-(methylamino)-1-piperidinyl)-1H-benzimidazole-5-carbonitrile	400.0
285	69		B		2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-6-chloro-1H-benzimidazol-1-yl)-1-(1-azetidinyl)ethanone	366.2
286	69		B		2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5-chloro-1H-benzimidazol-1-yl)-1-(1-azetidinyl)ethanone	366.2

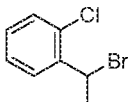
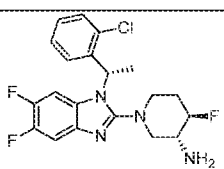
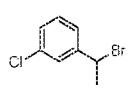
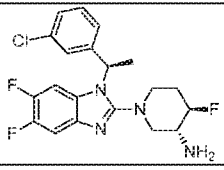
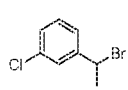
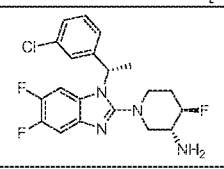
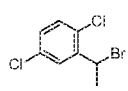
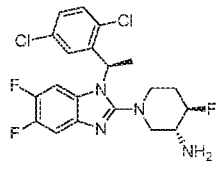
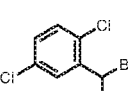
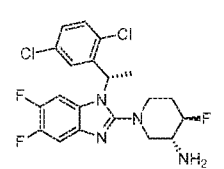
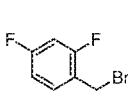
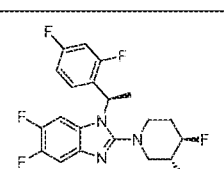
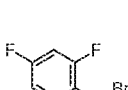
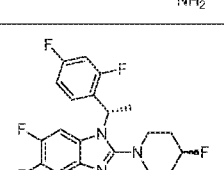
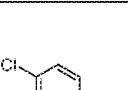
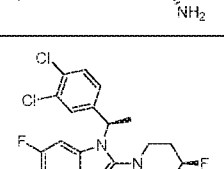
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
287	74		B		2-((3R,4S)-3-amino-4-fluoro-1-piperidinyl)-1-(2-(1-azetidiny)-2-oxoethyl)-1H-benzimidazole-6-carbonitrile	357.2
288	74		B		2-((3R,4S)-3-amino-4-fluoro-1-piperidinyl)-1-(2-(1-azetidiny)-2-oxoethyl)-1H-benzimidazole-5-carbonitrile	357.2
289	65		B		(3R,4R)-1-(1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	379.0
290	65		B		(3R,4R)-1-(1-((5-chloropyrimidin-2-yl)methyl)-5-fluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	379.0
291	71		A		(R)-6-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	333.2
292	72		A		(R)-5-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)picolinonitrile 2,2,2-trifluoroacetate	333.0
293	72		A		(R)-1-(1-(isoquinolin-7-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	358.2
294	72		A		(R)-1-(1-(1-methyl-1H-indazol-7-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	361.2

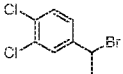
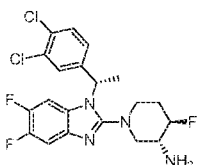
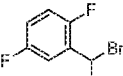
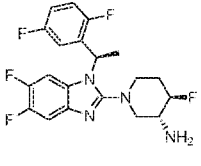
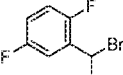
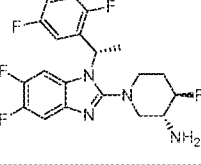
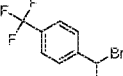
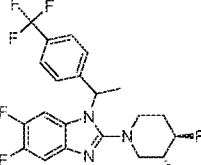
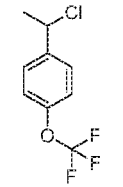
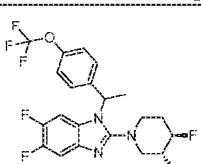
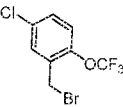
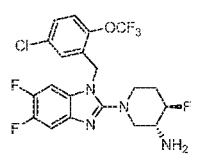
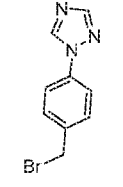
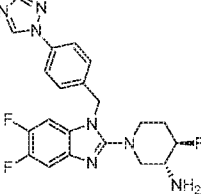
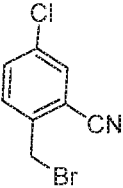
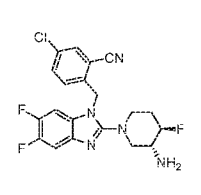
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
295	71		A		6-((R)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile hydrochloride	347.2
296	71		A		6-((S)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile hydrochloride	347.2
297	67		B		6-((R)-1-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile hydrochloride	365.0
298	67		B		6-((S)-1-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile hydrochloride	365.0
299	71		B		6-((R)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)propyl)nicotinonitrile hydrochloride	361.2
300	71		B		6-((S)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)propyl)nicotinonitrile hydrochloride	361.2
301	68		B		(3R,4R)-1-(5,6-difluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	381.2

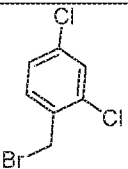
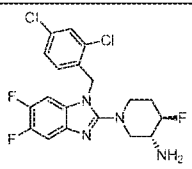
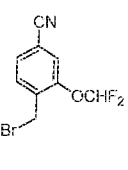
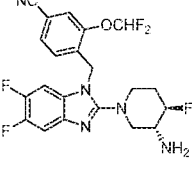
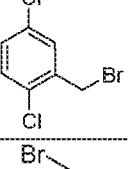
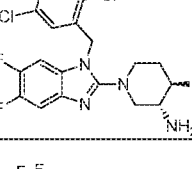
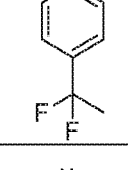
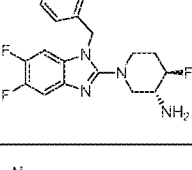
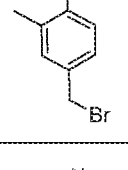
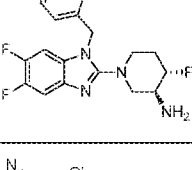
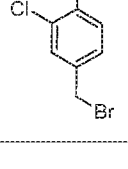
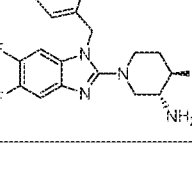
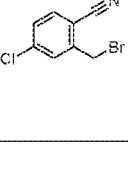
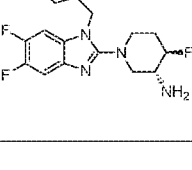
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
302	68		B		3-(1-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile	400.2
303	68		B		(3R,4R)-1-(5,6-difluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	381.0
304	76		B		(3R,4S)-1-(5,6-difluoro-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	380.2
305	77		B		(3R,4S)-4-fluoro-1-(1-((5-fluoropyrimidin-2-yl)methyl)-6-(trifluoromethyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	413.2
306	77		B		(3R,4S)-4-fluoro-1-(1-((5-fluoropyrimidin-2-yl)methyl)-5-(trifluoromethyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	413.2
307	78		B		(R)-1-(5,6-difluoro-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4,4-difluoropiperidin-3-amine	398.0
308	77		B		2-(2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)-1-(azetidin-1-yl)ethan-1-one	400.2

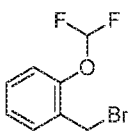
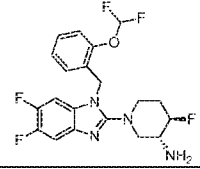
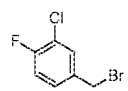
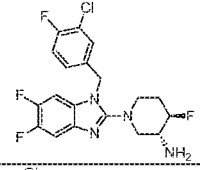
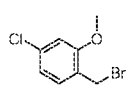
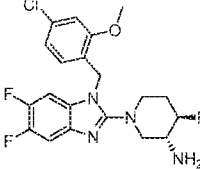
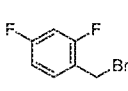
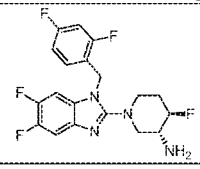
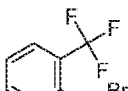
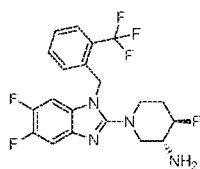
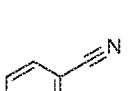
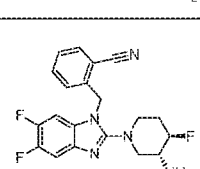
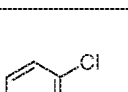
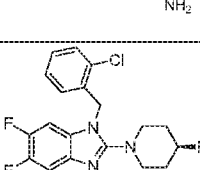
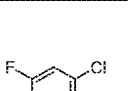
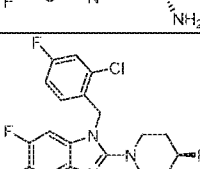
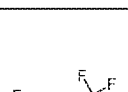
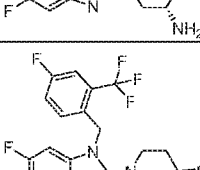
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
309	77		B		2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)-1-(azetidin-1-yl)ethan-1-one	400.2
310	68		B		2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(2,2-dimethylpyrrolidin-1-yl)ethan-1-one	410.2
311	80		B		6-((2-((3R,4S)-3-amino-4-hydroxypiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	367.2
312	80		B		6-((2-((3R,4S)-3-amino-4-hydroxypiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile	367.2
313	71		A		4-((R)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile hydrochloride	346.2
314	71		A		4-((S)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile hydrochloride	346.2
315	71		A		(S)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-3-fluorobenzonitrile hydrochloride	350.0
316	71		A		(S)-1-(1-(4-chlorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine hydrochloride	341.0

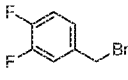
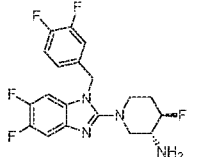
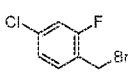
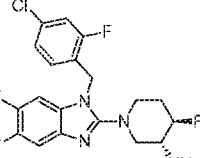
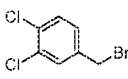
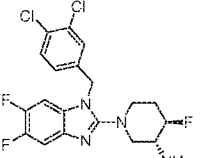
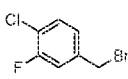
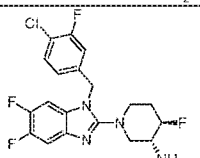
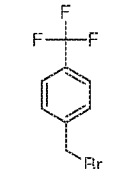
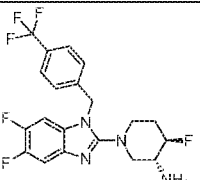
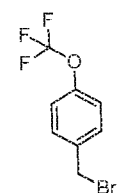
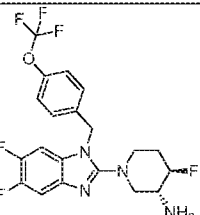
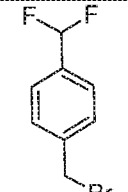
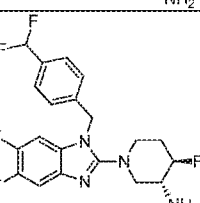
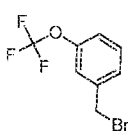
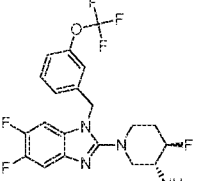
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
317	79		A		4-((R)-1-(2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile hydrochloride	364.0
318	79		A		4-((S)-1-(2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile hydrochloride	364.0
319	67		A		4-((R)-1-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile hydrochloride	364.2
320	67		A		4-((S)-1-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile hydrochloride	364.2
321	71		A		(S)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-3-chlorobenzonitrile hydrochloride	366.0
322	68		B		(3R,4R)-1-(1-((1R)-1-(2,4-dichlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	453.2
323	68		B		(3R,4R)-1-(1-((1S)-1-(2,4-dichlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	453.2
324	68		B		(3R,4R)-1-(1-((1R)-1-(2-chlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	409.2

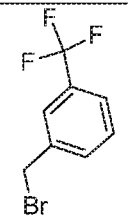
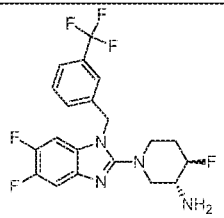
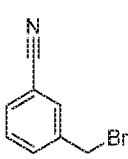
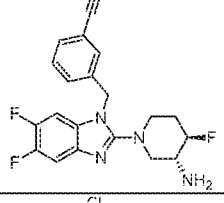
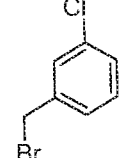
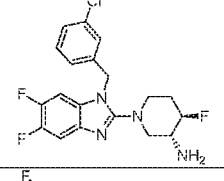
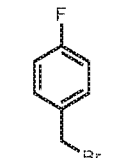
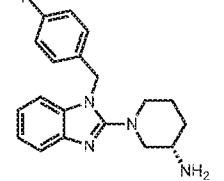
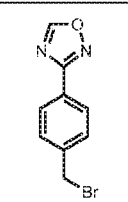
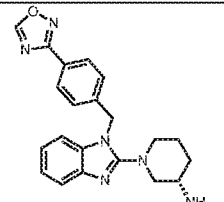
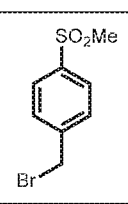
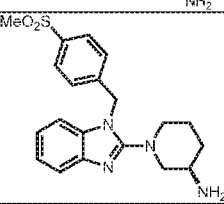
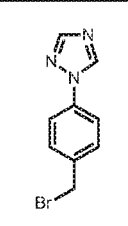
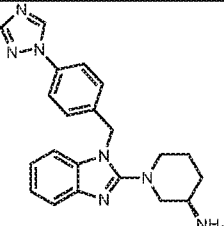
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
325	68		B		(3R,4R)-1-(1-((1S)-1-(2-chlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	409.2
326	68		B		(3R,4R)-1-(1-((1R)-1-(3-chlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	409.2
327	68		B		(3R,4R)-1-(1-((1S)-1-(3-chlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	409.2
328	68		B		(3R,4R)-1-(1-((1R)-1-(2,5-dichlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	443.0
329	68		B		(3R,4R)-1-(1-((1S)-1-(2,5-dichlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	443.0
330	68		B		(3R,4R)-1-(1-((1R)-1-(2,4-difluorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	411.2
331	68		B		(3R,4R)-1-(1-((1S)-1-(2,4-difluorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	411.2
332	68		B		(3R,4R)-1-(1-((1R)-1-(3,4-dichlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	443.0

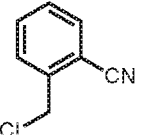
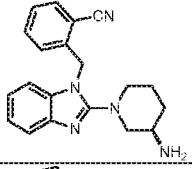
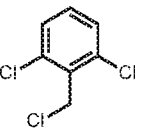
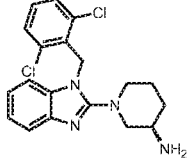
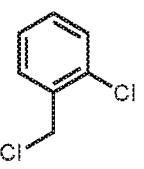
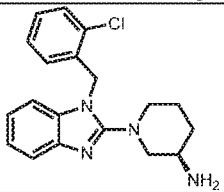
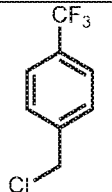
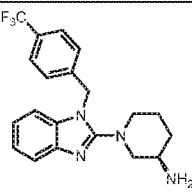
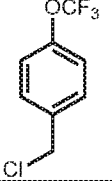
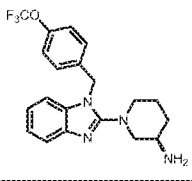
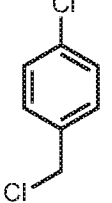
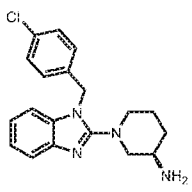
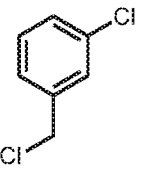
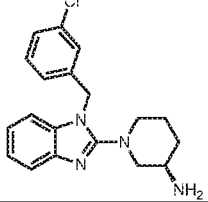
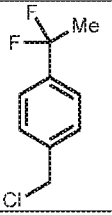
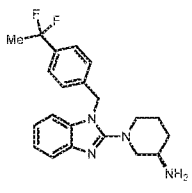
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
333	68		B		(3R,4R)-1-(1-((1S)-1-(3,4-dichlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	443.0
334	68		B		(3R,4R)-1-(1-((1R)-1-(2,5-difluorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	411.2
335	68		B		(3R,4R)-1-(1-((1S)-1-(2,5-difluorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	411.2
336b	68		B		(3R,4R)-1-(5,6-difluoro-1-((1R)-1-(4-(trifluoromethyl)phenyl)ethyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	443.2
337b	68		B		(3R,4R)-1-(5,6-difluoro-1-((1R)-1-(4-(trifluoromethoxy)phenyl)ethyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	459.2
338	68		B		(3R,4R)-1-(1-(5-chloro-2-(trifluoromethoxy)benzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	479.2
339	68		B		(3R,4R)-1-(5,6-difluoro-1-(4-(1H-1,2,4-triazol-1-yl)benzyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	428.2
340	68		B		2-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)-5-chlorobenzonitrile	420.2

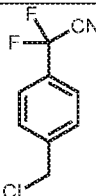
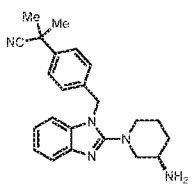
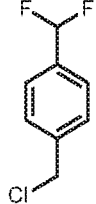
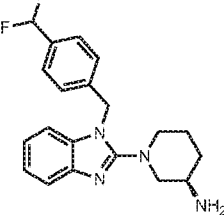
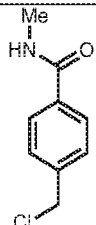
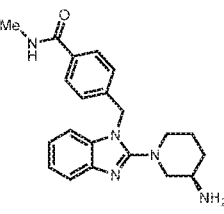
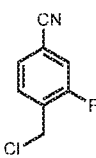
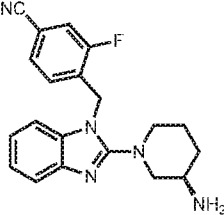
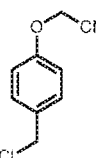
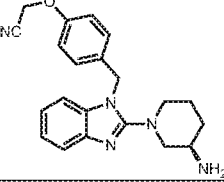
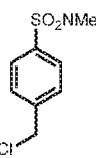
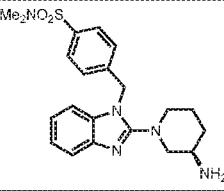
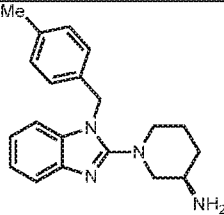
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
341	68		B		(3R,4R)-1-(1-(2,4-dichlorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	429.2
342	68		B		4-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)-3-(difluoromethoxy)benzonitrile	452.2
343	68		B		(3R,4R)-1-(1-(2,5-dichlorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	429.0
344	68		B		(3R,4R)-1-(1-(4-(1,1-difluoroethyl)benzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	425.2
345	68		B		4-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)-2-methylbenzonitrile	400.2
346	68		B		4-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)-2-chlorobenzonitrile	420.2
347	68		B		2-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)-4-chlorobenzonitrile	420.2

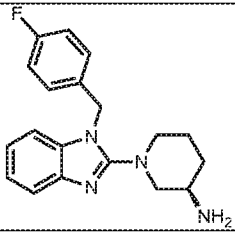
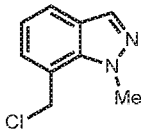
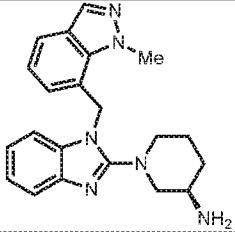
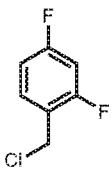
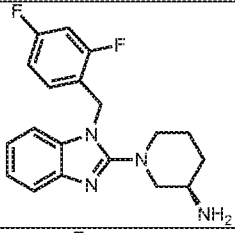
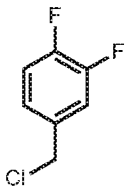
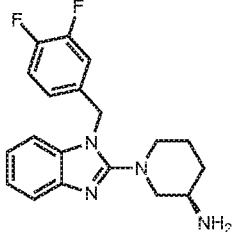
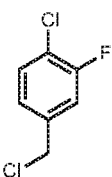
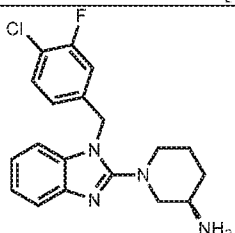
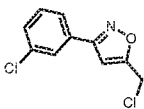
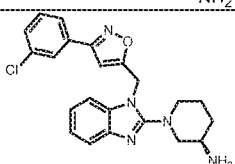
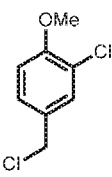
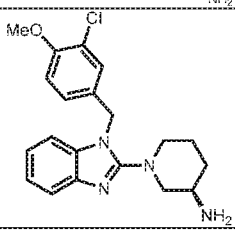
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
348	68		B		(3R,4R)-1-(1-(2-(difluoromethoxy)benzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	427.2
349	68		B		(3R,4R)-1-(1-(3-chloro-4-fluorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	413.0
350	68		B		(3R,4R)-1-(1-(4-chloro-2-methoxybenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	425.2
351	68		B		(3R,4R)-1-(1-(2,4-difluorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	397.2
352	68		B		(3R,4R)-1-(1-(2,2,2-trifluorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	429.2
353	68		B		2-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)benzonitrile	386.2
354	68		B		(3R,4R)-1-(1-(2-chlorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	395.0
355	68		B		(3R,4R)-1-(1-(2-chloro-4-fluorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	413.0
356	68		B		(3R,4R)-1-(1-(5,6-difluoro-1-(trifluoromethyl)benzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	447.2

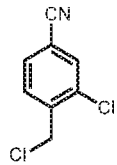
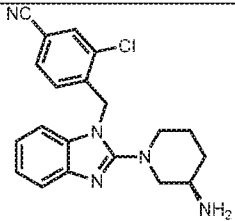
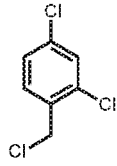
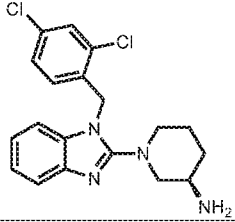
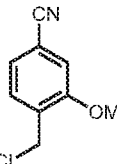
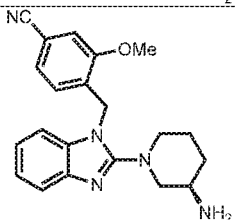
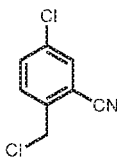
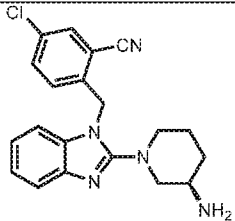
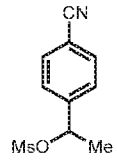
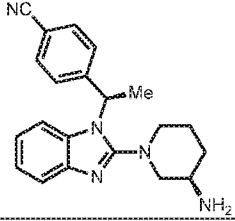
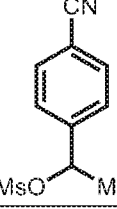
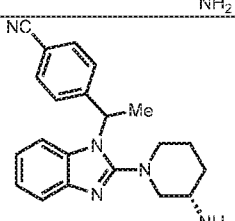
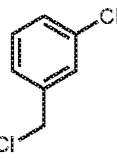
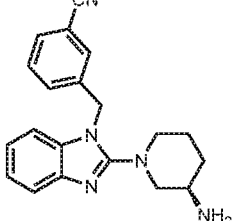
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
357	68		B		(3R,4R)-1-(1-(3,4-difluorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	397.2
358	68		B		(3R,4R)-1-(1-(4-chloro-2-fluorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	413.0
359	68		B		(3R,4R)-1-(1-(3,4-dichlorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	429.0
360	68		B		(3R,4R)-1-(1-(4-chloro-3-fluorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	413.2
361	68		B		(3R,4R)-1-(5,6-difluoro-1-(4-(trifluoromethyl)benzyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	429.2
362	68		B		(3R,4R)-1-(5,6-difluoro-1-(4-(trifluoromethoxy)benzyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	445.2
363	68		B		(3R,4R)-1-(1-(4-(difluoromethyl)benzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	411.2
364	68		B		(3R,4R)-1-(5,6-difluoro-1-(3-(trifluoromethoxy)benzyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	445.2

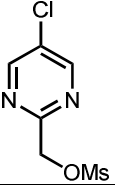
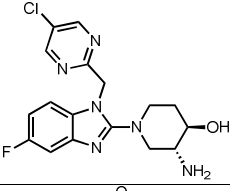
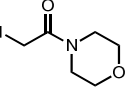
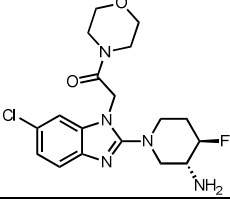
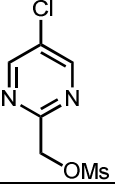
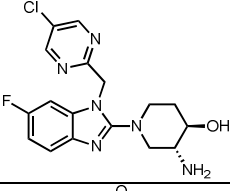
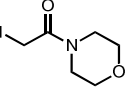
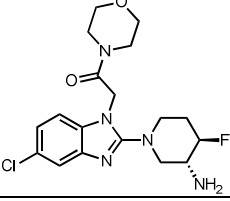
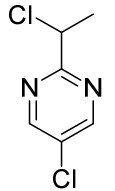
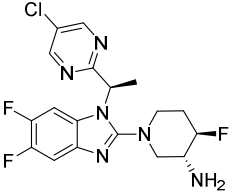
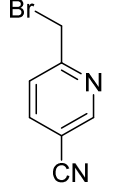
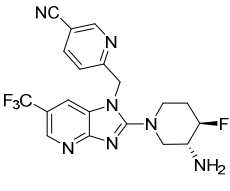
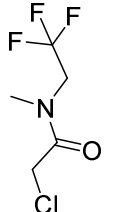
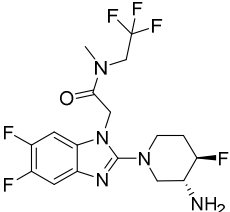
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
365	68		B		(3R,4R)-1-(5,6-difluoro-1-(3-(trifluoromethyl)benzyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	429.2
366	68		B		3-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)benzonitrile	386.2
367	68		B		(3R,4R)-1-(1-(3-chlorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine	395.2
368	71		B		(S)-1-(1-(4-fluorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	325.3
369	71		B		(S)-1-(1-(4-(1,2,4-oxadiazol-3-yl)benzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	375.2
370	72		B		(R)-1-(1-(4-(methylsulfonyl)benzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	385.2
371	72		B		(R)-1-(1-(4-(1H-1,2,4-triazol-1-yl)benzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	374.0

Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
372	72		A		(R)-2-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	332.2
373	72		A		(R)-1-(1-(2,6-dichlorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	376.2
374	72		A		(R)-1-(1-(2-chlorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	341.2
375	72		A		(R)-1-(1-(4-(trifluoromethyl)benzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	375.2
376	72		A		(R)-1-(1-(4-(trifluoromethoxy)benzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	391.0
377	72		A		(R)-1-(1-(4-chlorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	341.2
378	72		A		(R)-1-(1-(3-chlorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	341.2
379	72		A		(R)-1-(1-(4-(1,1-difluoroethyl)benzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	371.2

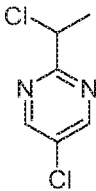
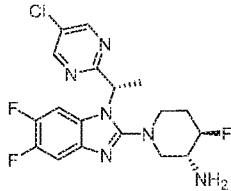
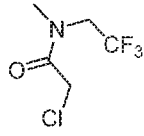
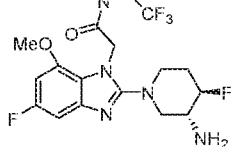
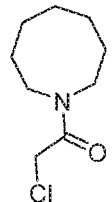
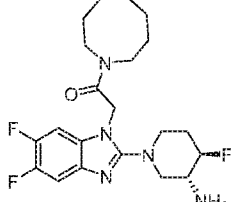
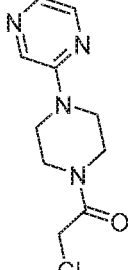
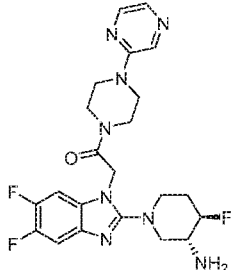
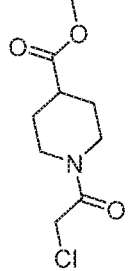
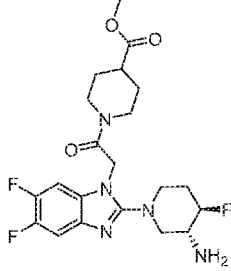
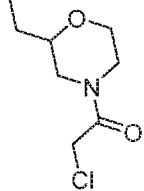
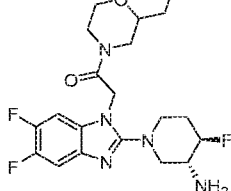
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
380	72		A		(R)-2-(4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)phenyl)-2-methylpropanenitrile	374.2
381	72		A		(R)-1-(1-(4-(difluoromethyl)benzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	357.0
382	72		A		(R)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-N-methylbenzamide	364.2
383	72		A		(R)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-3-fluorobenzonitrile	350.2
384	72		A		(R)-2-(4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)phenoxy)acet nitrile	362.2
385	72		A		(R)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-N,N-dimethylbenzenesulfonamide	414.2
386	72		A		(R)-1-(1-(4-methylbenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	321.2

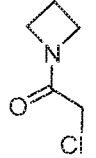
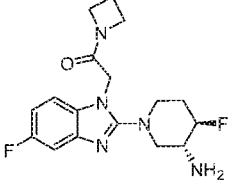
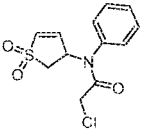
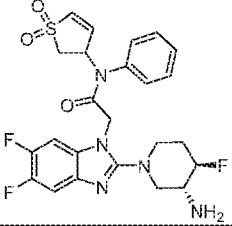
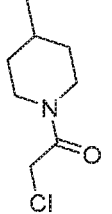
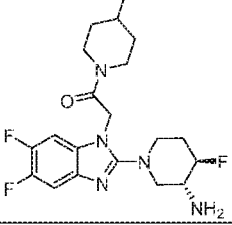
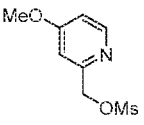
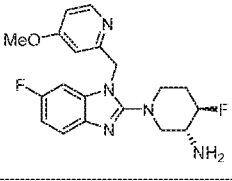
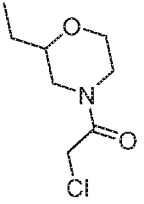
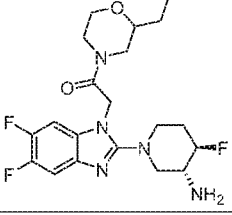
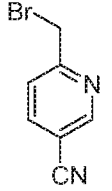
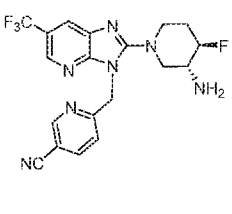
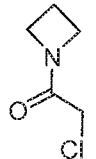
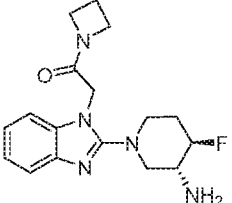
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
387	72		A		(R)-1-(1-(4-fluorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	324.4
388	72		A		(R)-1-(1-((1-methyl-1H-indazol-7-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	361.2
389	72		A		(R)-1-(1-(2,4-difluorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	343.2
390	72		A		(R)-1-(1-(3,4-difluorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	343.2
391	72		A		(R)-1-(1-(4-chloro-3-fluorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	359.2
392	72		A		(R)-1-(1-((3-(3-chlorophenyl)isoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	408.2
393	72		A		(R)-1-(1-(3-chloro-4-methoxybenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	371.2

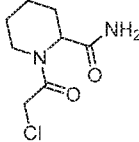
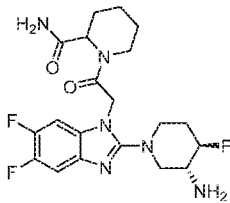
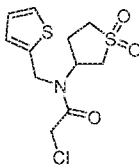
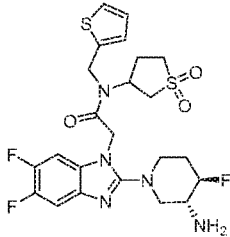
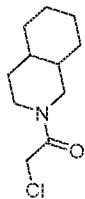
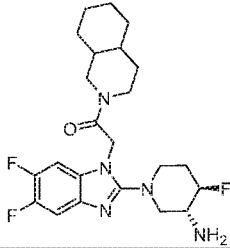
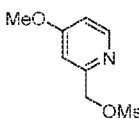
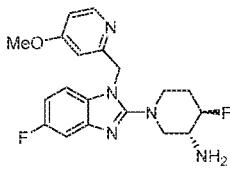
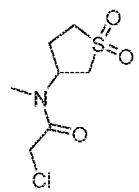
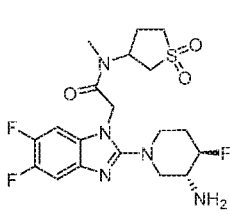
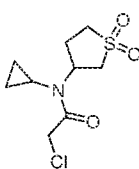
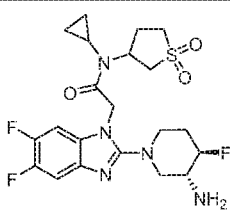
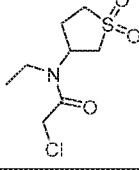
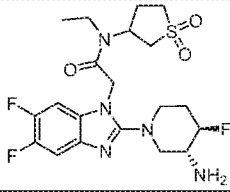
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
394	72		A		(R)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-3-chlorobenzonitrile	366.2
395	72		A		(R)-1-(1-(2,4-dichlorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	376.2
396	72		A		(R)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-3-methoxybenzonitrile	362.2
397	72		A		(R)-2-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-5-chlorobenzonitrile	366.2
398	72		A		4-((R)-1-(2-((R)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile	347.2
399	71		A		4-(1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile	346.2
400	72		A		(R)-3-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	332.2

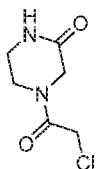
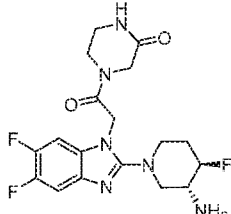
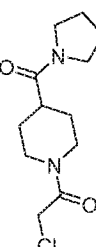
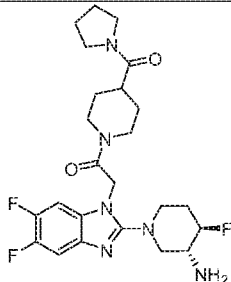
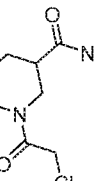
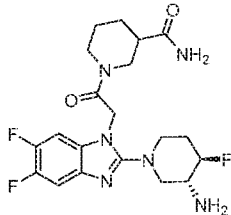
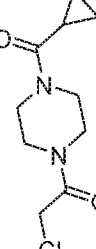
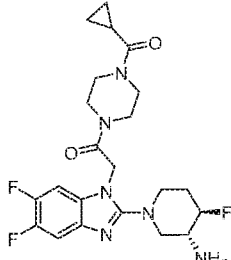
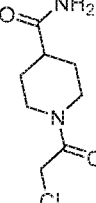
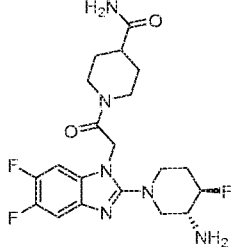
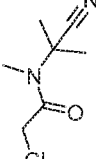
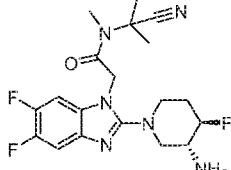
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
494			B		(3R,4R)-3-amino-1-((5-chloropyrimidin-2-yl)methyl)-5-fluoro-1H-benzo[d]imidazol-2-yl)piperidin-4-ol	377.2
495			B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)-1-morpholinoethanone	396.2
496	75		B		(3R,4R)-3-amino-1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)piperidin-4-ol	377.2
497	69		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)-1-morpholinoethanone	396.2
498	68		B		(3R,4R)-1-((R)-1-(5-chloropyrimidin-2-yl)ethyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	411.0
499	81		B		6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-(trifluoromethyl)-1H-imidazo[4,5-b]pyridin-1-yl)methyl)nicotinonitrile	420.2
500	68		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	424.2

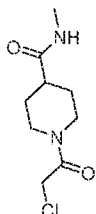
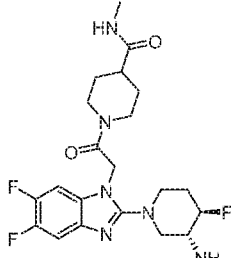
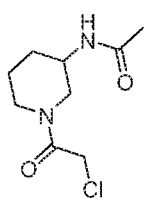
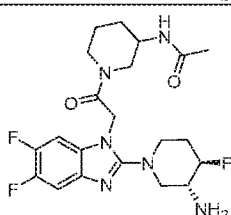
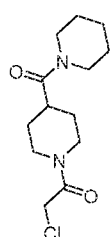
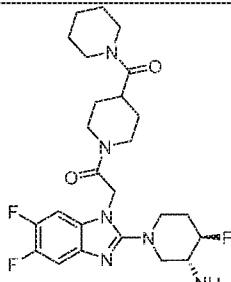
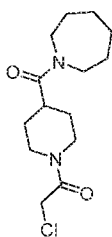
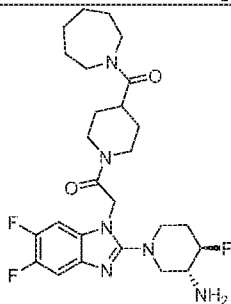
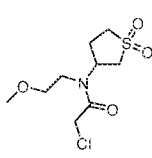
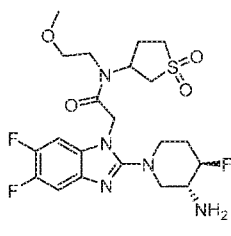
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
501	68		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(thiazol-2-yl)acetamide	425.2
502	69		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide	354.2
503	65		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-1-(azetidin-1-yl)ethan-1-one	350.2
504	68		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(3-(trifluoromethyl)piperidin-1-yl)ethan-1-one	464.2
505	68		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)ethan-1-one	450.2
506	69		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide	354.2
507	68		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(2-methylmorpholino)ethan-1-one	412.2

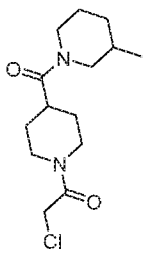
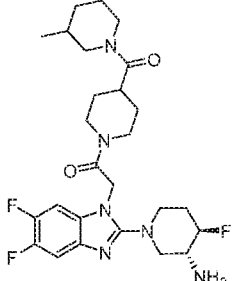
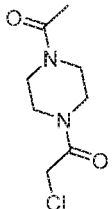
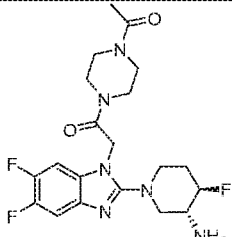
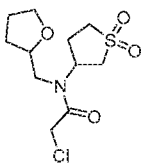
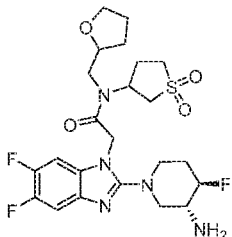
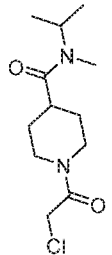
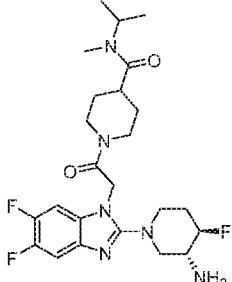
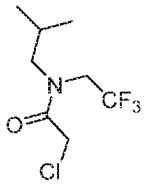
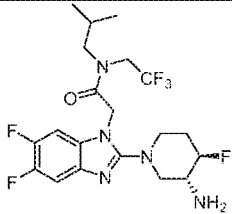
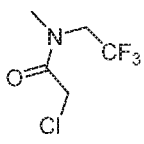
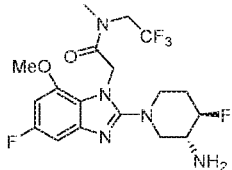
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
508	68		B		(3R,4R)-1-(1-((R)-1-(5-chloropyrimidin-2-yl)ethyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	411.0
509	82		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-7-methoxy-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	436.2
510	68		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(azocan-1-yl)ethan-1-one	424.2
511	68		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-(pyrazin-2-yl)piperazin-1-yl)ethan-1-one	475.2
512	68		B		methyl 1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)piperidine-4-carboxylate	454.2
513	68		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(2-ethylmorpholino)ethan-1-one	426.2

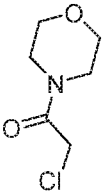
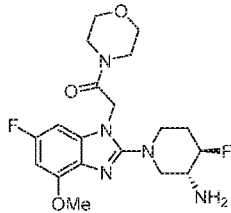
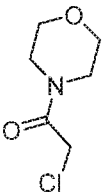
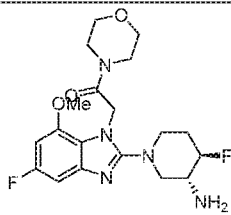
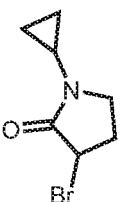
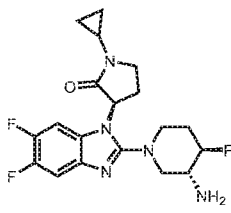
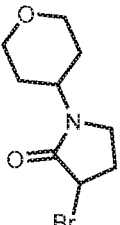
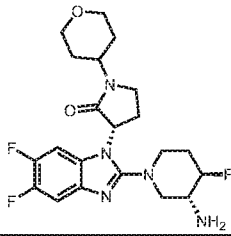
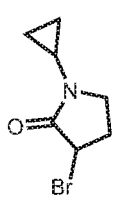
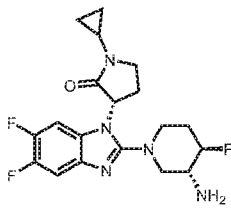
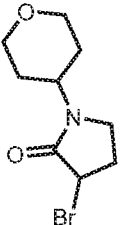
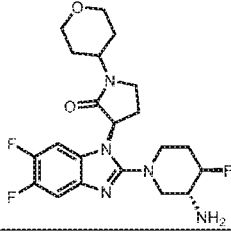
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
514	65		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)-1-(azetidin-1-yl)ethan-1-one	350.2
515	68		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(1,1-dioxido-2,3-dihydrothiophen-3-yl)-N-phenylacetamide	520.2
516	68		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-methylpiperidin-1-yl)ethan-1-one	410.2
517	65		B		(3R,4R)-4-fluoro-1-(6-fluoro-1-((4-methoxypyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	375.2
518	68		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(2-ethylmorpholino)ethan-1-one	426.2
519	81		B		6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-(trifluoromethyl)-3H-imidazo[4,5-b]pyridin-3-yl)methyl)nicotinonitrile	420.2
520	65		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)-1-(azetidin-1-yl)ethan-1-one	332.2

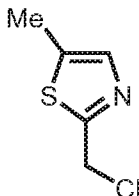
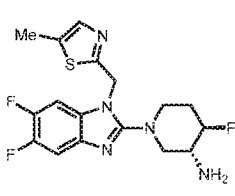
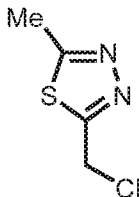
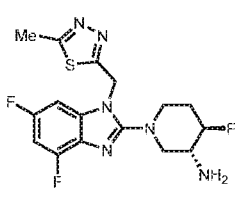
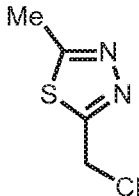
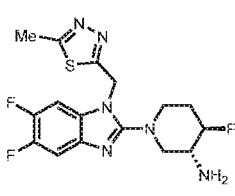
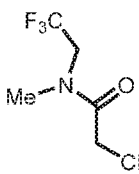
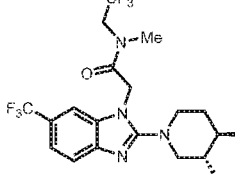
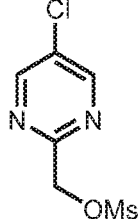
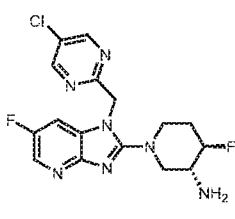
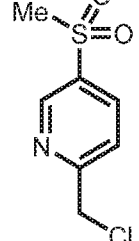
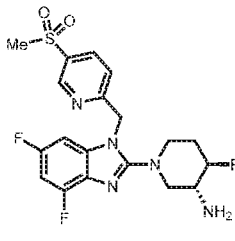
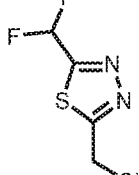
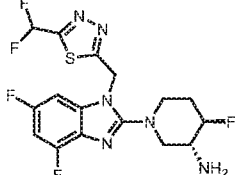
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
521	68		B		1-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)piperidine-2-carboxamide	439.2
522	68		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(1,1-dioxido-2,3-dihydrothiophen-3-yl)-N-(thiophen-2-ylmethyl)acetamide	542.2
523	68		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(octahydroisoquinolin-2(1H)-yl)ethan-1-one	450.2
524	65		B		(3R,4R)-4-fluoro-1-(5-fluoro-1-(4-methoxypyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	375.2
525	68		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(1,1-dioxido-2,3-dihydrothiophen-3-yl)-N-methylacetamide	460.2
526	68		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-cyclopropyl-N-(1,1-dioxido-2,3-dihydrothiophen-3-yl)acetamide	486.2
527	68		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(1,1-dioxido-2,3-dihydrothiophen-3-yl)-N-ethylacetamide	474.2

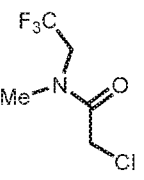
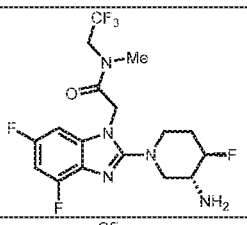
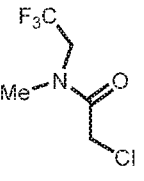
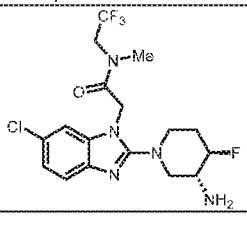
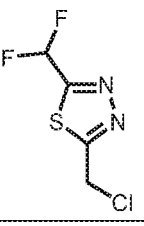
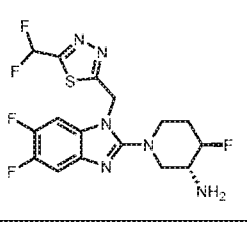
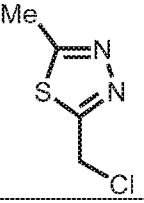
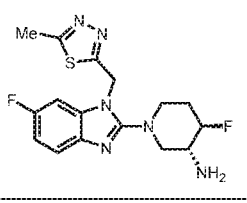
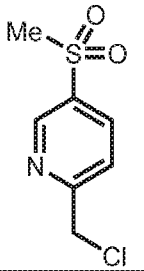
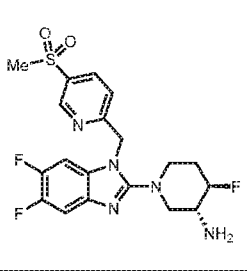
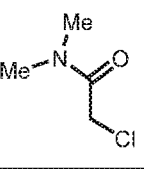
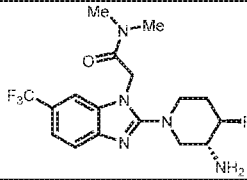
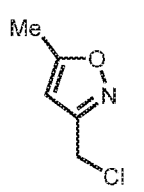
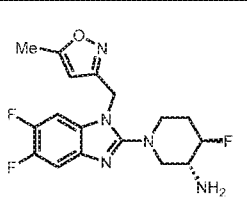
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
					en-3-yl)-N-ethylacetamide	
528	68		B		4-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)piperazin-2-one	411.2
529	68		B		2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-(pyrrolidine-1-carbonyl)piperidin-1-yl)ethan-1-one	493.2
530	68		B		1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)piperidine-3-carboxamide	439.2
531	68		B		2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-(cyclopropanecarbonyl)piperazin-1-yl)ethan-1-one	465.2
532	68		B		1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)piperidine-4-carboxamide	439.2
533	68		B		2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(2-cyanopropan-2-yl)-N-methylacetamide	409.2

Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
534	68		B		1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)-N-methylpiperidine-4-carboxamide	453.2
535	68		B		N-(1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)piperidin-3-yl)acetamide	453.2
536	68		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-(piperidine-1-carbonyl)piperidin-1-yl)ethan-1-one	507.2
537	68		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-(azepane-1-carbonyl)piperidin-1-yl)ethan-1-one	521.2
538	68		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(1,1-dioxidotetrahydrothiophen-3-yl)-N-(2-methoxyethyl)acetamide	504.2

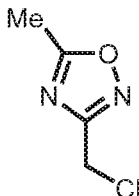
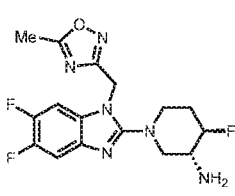
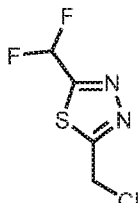
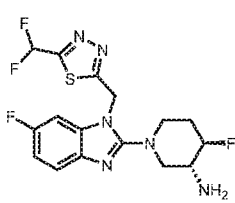
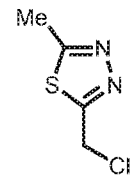
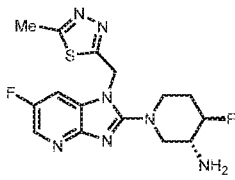
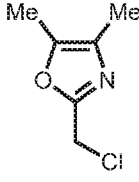
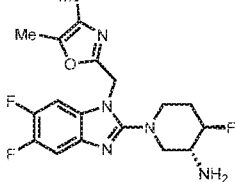
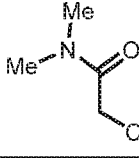
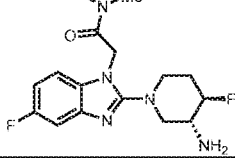
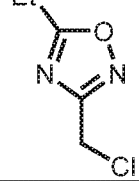
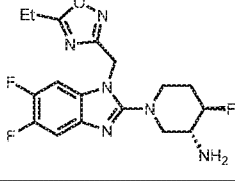
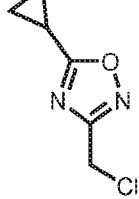
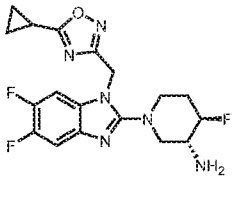
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
539	68		B		2-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-(3-methylpiperidine-1-carbonyl)piperidin-1-yl)ethan-1-one	521.2
540	68		B		1-(4-acetylpiperazin-1-yl)-2-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)ethan-1-one	439.2
541	68		B		2-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(1,1-dioxidotetrahydrothiophen-3-yl)-N-((tetrahydrofuran-2-yl)methyl)acetamide	530.2
542	68		B		1-(2-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)-N-isopropyl-N-methylpiperidine-4-carboxamide	495.2
543	68		B		2-((2-((3R,4R)-3-amino-4-methoxypiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	418.2
544	82		B		2-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-7-methoxy-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	436.2

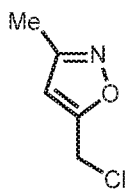
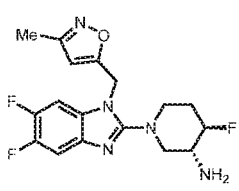
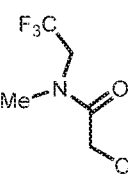
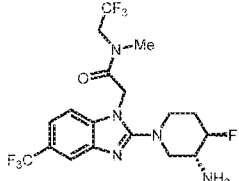
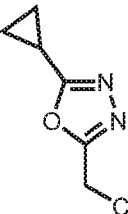
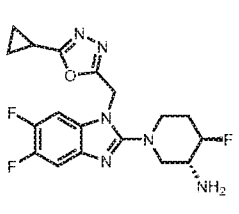
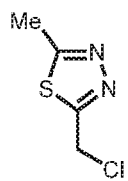
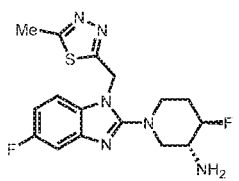
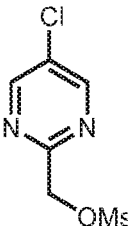
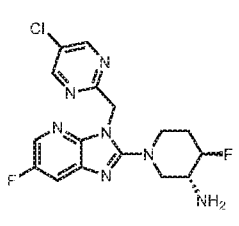
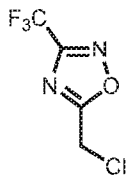
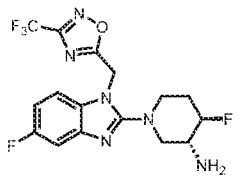
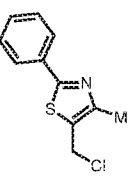
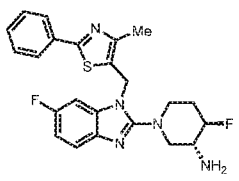
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
545	82		B		2-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-4-methoxy-1H-benzo[d]imidazol-1-yl)-1-morpholinoethan-1-one	410.2
546	82		B		2-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-7-methoxy-1H-benzo[d]imidazol-1-yl)-1-morpholinoethan-1-one	410.2
547	68		A		(R)-3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-cyclopropylpyrrolidin-2-one	394.2
548	68		A		(S)-3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(tetrahydro-2H-pyran-4-yl)pyrrolidin-2-one	438.2
549	68		A		(S)-3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-cyclopropylpyrrolidin-2-one	394.2
550	68		A		(R)-3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(tetrahydro-2H-pyran-4-yl)pyrrolidin-2-one	438.2

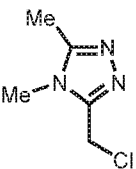
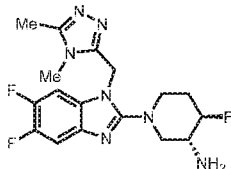
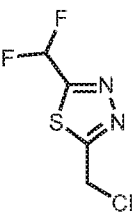
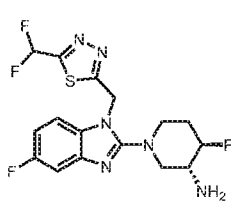
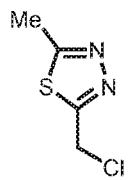
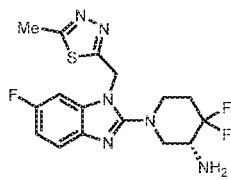
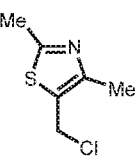
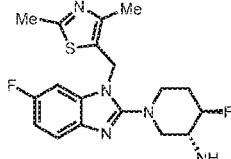
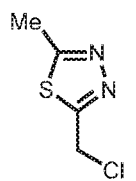
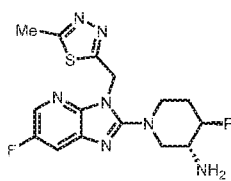
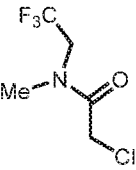
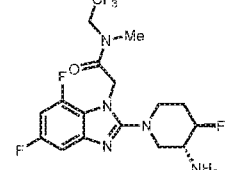
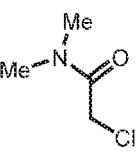
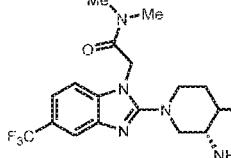
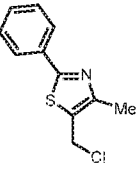
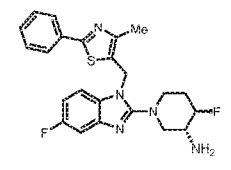
Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
551	68		B		(3R,4R)-1-((5,6-difluoro-1-((5-methylthiazol-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	382.2
552	62		B		(3R,4R)-1-((4,6-difluoro-1-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	383.2
553	68		B		(3R,4R)-1-((5,6-difluoro-1-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	383.2
554	83		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	456.2
555	84		B		(3R,4R)-1-((1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-imidazo[4,5-b]pyridin-2-yl)-4-fluoropiperidin-3-amine	380.0
556	62		B		(3R,4R)-1-((4,6-difluoro-1-((5-(methylsulfonyl)pyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	440.2
557	62		B		(3R,4R)-1-((1-((5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)methyl)-4,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	419.2

Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
					4-fluoropiperidin-3-amine	
558	62		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	424.2
559	69		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	422.2
560	68		B		(3R,4R)-1-(1-((5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)methyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	419.0
561	65		B		(3R,4R)-4-fluoro-1-(6-fluoro-1-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	365.2
562	68		B		(3R,4R)-1-(5,6-difluoro-1-((5-(methylsulfonyl)pyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	440.2
563	83		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide	388.2
564	68		B		(3R,4R)-1-(5,6-difluoro-1-((5-methylisoxazol-3-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	366.2

Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
565	62		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4,6-difluoro-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide	356.2
566	65		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide	338.2
567	68		B		(3R,4R)-1-(5,6-difluoro-1-((5-methyloxazol-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	366.2
568	68		B		(3R,4R)-1-(5,6-difluoro-1-((4-methylthiazol-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	382.0
569	65		B		(3R,4R)-4-fluoro-1-(6-fluoro-1-((3-(trifluoromethyl)-1,2,4-oxadiazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	403.2
570	69		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	422.2
571	68		B		(3R,4R)-1-(5,6-difluoro-1-((5-methyl-1,3,4-oxadiazol-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	367.2

Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
572	68		B		(3R,4R)-1-((5,6-difluoro-1-((5-methyl-1,2,4-oxadiazol-3-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	367.2
573	65		B		(3R,4R)-1-((1-((5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	401.2
574	84		B		(3R,4R)-4-fluoro-1-((6-fluoro-1-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)-1H-imidazo[4,5-b]pyridin-2-yl)piperidin-3-amine	366.2
575	68		B		(3R,4R)-1-((1-((4,5-dimethyloxazol-2-yl)methyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	380.2
576	65		B		2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide	338.2
577	68		B		(3R,4R)-1-((1-((5-ethyl-1,2,4-oxadiazol-3-yl)methyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	381.2
578	68		B		(3R,4R)-1-((1-((5-cyclopropyl-1,2,4-oxadiazol-3-yl)methyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	393.2

Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
579	68		B		(3R,4R)-1-((5,6-difluoro-1-((3-methylisoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	366.2
580	83		B		2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	456.2
581	68		B		(3R,4R)-1-((1-((5-cyclopropyl-1,3,4-oxadiazol-2-yl)methyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	393.2
582	65		B		(3R,4R)-4-fluoro-1-((5-fluoro-1-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	365.2
583	84		B		(3R,4R)-1-((3-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-3H-imidazo[4,5-b]pyridin-2-yl)-4-fluoropiperidin-3-amine	380.2
584	65		B		(3R,4R)-4-fluoro-1-((5-fluoro-1-((3-(trifluoromethyl)-1,2,4-oxadiazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	403.0
585	65		B		(3R,4R)-4-fluoro-1-((6-fluoro-1-((4-methyl-2-phenylthiazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	440.2

Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
586	68		B		(3R,4R)-1-(1-((4,5-dimethyl-1H-1,2,4-triazol-3-yl)methyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	380.2
587	65		B		(3R,4R)-1-(1-((5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)methyl)-5-fluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	401.2
588	85		B		(R)-4,4-difluoro-1-(6-fluoro-1-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	383.2
589	65		B		(3R,4R)-1-(1-((2,4-dimethylthiazol-5-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	378.2
590	84		B		(3R,4R)-4-fluoro-1-(6-fluoro-3-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)-3H-imidazo[4,5-b]pyridin-2-yl)piperidin-3-amine	366.2
591	62		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,7-difluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	424.2
592	83		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide	388.2
593	65		B		(3R,4R)-4-fluoro-1-(5-fluoro-1-((4-methyl-2-phenylthiazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	440.2

Ex. #	SnAr Intermediate	Electrophile	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
594	62		B		2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,7-difluoro-1H-benzo[d]imidazol-1-yl)-N,N-dimethylacetamide	356.2
595	62		B		(3R,4R)-1-((5,7-difluoro-1-((5-(methylsulfonyl)pyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	440.2
596	65		B		(3R,4R)-1-((1-((2,4-dimethylthiazol-5-yl)methyl)-5-fluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	378.2
597	85		B		(R)-4,4-difluoro-1-((5-fluoro-1-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	383.2
598	62		B		(3R,4R)-1-((1-((5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)methyl)-5,7-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	419.2
599	62		B		(3R,4R)-1-((5,7-difluoro-1-((5-methyl-1,3,4-thiadiazol-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine	383.2

[a] Boc was removed using TFA. The free base was redissolved in DCM, and HCl was added to crash out the HCl salt. [b] unspecified stereochemistry denotes a mixture of enantiomers or diastereomers.

Table 6. Characterization data for compounds made following schemes 9-10

5

The column "Separation Stage" indicates after which process step regioisomers formed due to asymmetric benzimidazole substitution at R^1 in Scheme 10 were separated during the preparation of the tabulated final compound (1 = after preparation of the *N*-aralkyl-2-piperidinyl-benzimidazole intermediate

in the first step of Scheme 10 (where at least one R^1 is not hydrogen); B = prior to boc deprotection; or F = final compound).

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
187	500MHz d ₄ -MeOH	8.80 (s, 2H), 7.65-7.69 (m, 1H), 7.54-7.61 (m, 1H), 7.49 (d, J=8.30 Hz, 1H), 5.57 (s, 2H), 4.42-4.60 (m, 1H), 3.72-3.80 (m, 1H), 3.64 (br d, J=13.23 Hz, 1H), 3.15-3.27 (m, 2H), 3.06 (dd, J=9.21, 12.59 Hz, 1H), 2.13-2.27 (m, 1H), 1.80-1.99 (m, 1H)	B	Chiralpak AD-H, 25% IPA, peak 1
188	500MHz d ₄ -MeOH	8.68-8.74 (s, 2H), 7.47-7.52 (m, 1H), 7.14-7.20 (m, 2H), 7.08-7.13 (m, 1H), 5.53 (s, 2H), 4.34-4.52 (m, 1H), 3.64 (dtd, J=1.95, 4.14, 12.36 Hz, 1H), 3.48-3.57 (m, 1H), 3.04-3.21 (m, 2H), 2.98 (dd, J=8.82, 12.20 Hz, 1H), 2.12-2.25 (m, 1H), 1.82-1.92 (m, 1H)	--	--
189	400MHz d ₄ -MeOH	8.40 (d, J=2.90 Hz, 1H), 7.47-7.58 (m, 2H), 7.21 (dd, J=4.35, 8.71 Hz, 1H), 7.13-7.17 (m, 1H), 7.06-7.13 (m, 2H), 4.32-4.55 (m, 1H), 3.62 (dtd, J=1.66, 4.17, 12.39 Hz, 1H), 3.41-3.52 (m, 1H), 3.04-3.18 (m, 2H), 2.92-3.01 (m, 1H), 2.07-2.22 (m, 1H), 1.80-1.97 (m, 1H)	--	--
190	400MHz d ₄ -MeOH	8.40 (d, J=2.90 Hz, 1H), 7.61 (dt, J=2.90, 8.50 Hz, 1H), 7.52-7.56 (m, 2H), 7.42-7.46 (m, 1H), 7.40 (dd, J=4.35, 8.71 Hz, 1H), 5.46 (s, 2H), 4.32-4.54 (m, 1H), 3.67-3.75 (m, 1H), 3.55-3.65 (m, 1H), 3.21 (ddd, J=2.90, 10.21, 12.80 Hz, 1H), 3.06-3.14 (m, 1H), 2.98-3.05 (m, 1H), 2.10-2.25 (m, 1H), 1.89 (ddd, J=3.52, 9.69, 13.53 Hz, 1H)	B	Chiralpak AD-H, 20% MeOH, Peak 1
191	400MHz d ₄ -MeOH	8.39 (d, J=2.90 Hz, 1H), 7.75-7.78 (m, 1H), 7.61 (dt, J=2.90, 8.50 Hz, 1H), 7.35-7.42 (m, 2H), 7.27 (d, J=8.29 Hz, 1H), 5.45-5.50 (m, 2H), 4.32-4.54 (m, 1H), 3.68 (dtd, J=1.66, 4.02, 12.28 Hz, 1H), 3.51-3.63 (m, 1H), 3.15-3.25 (m, 1H), 3.10 (ddd, J=3.94, 7.72, 9.48 Hz, 1H), 2.96-3.06 (m, 1H), 2.13-2.27 (m, 1H), 1.81-1.97 (m, 1H)	B	Chiralpak AD-H, 20% MeOH, Peak 2
192	500MHz d ₄ -MeOH	8.98 (s, 2H), 7.42-7.47 (m, 1H), 7.07-7.15 (m, 2H), 7.01-7.06 (m, 1H), 5.49 (s, 2H), 4.33-4.51 (m, 1H), 3.37-3.50 (m, 2H), 2.99-3.07 (m, 2H), 2.82 (br dd, J=8.95, 12.07 Hz, 1H), 2.00-2.16 (m, 1H), 1.65-1.79 (m, 1H)	--	--
193	400MHz CDCl ₃	8.97 (s, 2H), 7.60-7.67 (m, 1H), 7.16-7.23 (m, 1H), 7.03-7.15 (m, 2H), 5.45-5.56 (m, 2H), 4.29-4.56 (m, 1H), 3.64-3.76 (m, 1H), 3.51-3.63 (m, 1H), 3.14-3.33 (m, 2H), 3.03 (dd, J=8.60, 12.54 Hz, 1H), 2.08-2.24 (m, 1H), 1.83-2.03 (m, 1H)	--	--

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
194	400MHz CDCl ₃	8.36-8.39 (m, 2H), 7.60 (d, J=8.50 Hz, 1H), 7.14-7.20 (m, 2H), 7.06-7.14 (m, 1H), 5.36 (d, J=2.07 Hz, 2H), 4.34-4.56 (m, 1H), 3.90 (s, 3H), 3.63-3.78 (m, 2H), 3.14-3.31 (m, 2H), 3.04 (dd, J=8.40, 12.54 Hz, 1H), 2.11-2.25 (m, 1H), 1.90-2.05 (m, 1H)	--	--
195	400MHz d ₄ -MeOH	8.76 (s, 2H), 7.44-7.54 (m, 1H), 7.06-7.19 (m, 3H), 5.50 (br s, 2H), 4.32-4.53 (m, 1H), 3.62 (br d, J=12.23 Hz, 1H), 3.51 (br d, J=12.02 Hz, 1H), 3.02-3.21 (m, 2H), 2.89-3.01 (m, 1H), 2.12-2.26 (m, 1H), 1.81-1.98 (m, 1H)	--	--
196	500MHz d ₄ -MeOH	8.70-8.75 (m, 2H), 7.65-7.69 (m, 1H), 7.58 (d, J=8.30 Hz, 1H), 7.45-7.52 (m, 1H), 5.58 (s, 2H), 4.43-4.65 (m, 1H), 3.76-3.83 (m, 1H), 3.67 (br d, J=12.98 Hz, 1H), 3.16-3.32 (m, 2H), 3.09 (dd, J=9.34, 12.46 Hz, 1H), 2.15-2.29 (m, 1H), 1.86-1.99 (m, 1H)	B	Chiralpak AD-H, 20% MeOH, peak 1
197	500MHz d ₄ -MeOH	8.72 (s, 2H), 7.77-7.82 (m, 1H), 7.41-7.45 (m, 1H), 7.32-7.38 (m, 1H), 5.59 (s, 2H), 4.33-4.51 (m, 1H), 3.65-3.71 (m, 1H), 3.53-3.63 (m, 1H), 3.16-3.24 (m, 1H), 3.05-3.14 (m, 1H), 2.96-3.04 (m, 1H), 2.14-2.28 (m, 1H), 1.89 (ddd, J=3.63, 9.67, 13.43 Hz, 1H)	B	Chiralpak AD-H, 20% MeOH, peak 2
198	400MHz d ₄ -MeOH	8.70-8.89 (m, 1H), 7.72-7.98 (m, 1H), 7.17-7.54 (m, 2H), 5.31-5.67 (m, 2H), 4.39-4.66 (m, 1H), 3.57-3.82 (m, 2H), 3.01-3.25 (m, 3H), 2.15-2.35 (m, 1H), 1.93 (td, J=1.22, 9.80 Hz, 1H)	B	Chiralpak AD-H, 25% IPA, peak 2
199	400MHz d ₄ -MeOH	8.90 (d, J=1.45 Hz, 1H), 8.75-8.78 (m, 1H), 7.48-7.56 (m, 1H), 7.08-7.23 (m, 4H), 5.66 (s, 2H), 3.39-3.59 (m, 3H), 3.13-3.30 (m, 2H), 2.25-2.40 (m, 1H), 2.04-2.25 (m, 1H)	--	--
200	400MHz d ₄ -MeOH	8.88 (s, 2H), 7.63-7.68 (m, 1H), 7.53-7.59 (m, 1H), 7.45-7.50 (m, 1H), 5.53 (s, 2H), 4.36-4.58 (m, 1H), 3.72 (br dd, J=1.45, 12.65 Hz, 1H), 3.58-3.66 (m, 1H), 3.10-3.26 (m, 2H), 2.99-3.07 (m, 1H), 2.13-2.27 (m, 1H), 1.82-1.95 (m, 1H)	B	Chiralpak AD-H, 25% IPA, peak 1
201	400MHz d ₄ -MeOH	8.86-8.90 (m, 2H), 7.80-7.84 (m, 1H), 7.45 (dd, J=1.24, 8.29 Hz, 1H), 7.34-7.39 (m, 1H), 5.56 (s, 2H), 4.33-4.53 (m, 1H), 3.62-3.70 (m, 1H), 3.53-3.60 (m, 1H), 3.14-3.23 (m, 1H), 3.02-3.13 (m, 1H), 2.94-3.02 (m, 1H), 2.18-2.26 (m, 1H), 1.80-1.96 (m, 1H)	B	Chiralpak AD-H, 25% IPA, peak 1
202	400MHz CDCl ₃	9.11 (s, 1H), 8.92 (s, 1H), 8.30-8.39 (m, 3H), 7.47-7.53 (m, 1H), 7.23 (d, J=7.88 Hz, 1H), 7.14-7.19 (m, 1H), 7.11 (d, J=7.26 Hz, 1H), 5.68 (s, 2H), 4.81-4.92 (m, 1H), 3.59-3.74 (m, 2H), 3.45-3.55 (m, 1H), 3.03-3.16 (m, 2H), 2.14-2.24 (m, 1H), 1.80-1.93 (m, 1H)	--	--

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
203	500MHz d ₄ -MeOH	8.79 (s, 2 H), 7.75 - 7.89 (m, 1 H), 7.45 (dd, J=8.30, 1.30 Hz, 1 H), 7.36 (d, J=8.04 Hz, 1 H), 5.55 - 5.60 (m, 2 H), 3.44 - 3.54 (m, 2 H), 3.35 - 3.42 (m, 2 H), 3.06 - 3.25 (m, 3 H), 1.89 - 2.18 (m, 2 H)	B	Chiralpak OJ, 15% MeOH, peak 1
204	500MHz d ₄ -MeOH	8.80 (s, 2 H), 7.65 - 7.69 (m, 1 H), 7.56 - 7.61 (m, 1 H), 7.51 (dd, J=8.30, 1.56 Hz, 1 H), 5.57 (s, 2 H), 3.37 - 3.57 (m, 3 H), 3.06 - 3.26 (m, 3 H), 2.09 - 2.18 (m, 1 H), 1.90 - 2.08 (m, 2 H)	B	Chiralpak OJ, 15% MeOH, peak 2
205	500MHz d ₄ -MeOH	8.78 (s, 2H), 7.39-7.48 (m, 1H), 6.99 (dd, J=2.47, 8.95 Hz, 1H), 6.90-6.95 (m, 1H), 5.48 (s, 2H), 3.64 (dd, J=1.82, 7.79 Hz, 1H), 3.42-3.53 (m, 2H), 3.05 (dt, J=2.60, 12.07 Hz, 1H), 2.83-2.90 (m, 2H), 2.01 (qd, J=3.62, 13.01 Hz, 1H), 1.62-1.71 (m, 1H)	B	Chiralpak AD-H, 25% MeOH, peak 2
206	500MHz d ₄ -MeOH	8.75-8.79 (m, 2H), 7.12-7.22 (m, 2H), 6.82-6.93 (m, 1H), 5.49 (s, 2H), 3.65-3.72 (m, 1H), 3.53-3.62 (m, 1H), 3.44-3.52 (m, 1H), 3.08 (dt, J=2.60, 12.20 Hz, 1H), 2.86-2.97 (m, 2H), 2.02 (qd, J=3.61, 13.04 Hz, 1H), 1.62-1.75 (m, 1H)	B	Chiralpak AD-H, 25% MeOH, peak 1
207	500MHz d ₄ -MeOH	8.82-8.85 (m, 1H), 8.09-8.15 (m, 1H), 7.36 (d, J=8.04 Hz, 1H), 7.18 (dd, J=2.34, 9.34 Hz, 1H), 7.09 (dd, J=4.54, 8.69 Hz, 1H), 6.87 (dt, J=2.47, 9.28 Hz, 1H), 5.46-5.51 (m, 2H), 3.58-3.66 (m, 1H), 3.46-3.54 (m, 1H), 3.38-3.44 (m, 1H), 3.02-3.14 (m, 1H), 2.73-2.90 (m, 2H), 1.93-2.04 (m, 1H), 1.58-1.72 (m, 1H)	B	Chiralpak AD-H, 25% IPA, peak 1
208	500MHz d ₄ -MeOH	8.84 (d, J=1.30 Hz, 1H), 8.09-8.18 (m, 1H), 7.41-7.47 (m, 1H), 7.37 (d, J=8.30 Hz, 1H), 6.90-7.00 (m, 2H), 5.48 (s, 2H), 3.50-3.59 (m, 1H), 3.36-3.47 (m, 2H), 3.04 (dt, J=2.60, 11.94 Hz, 1H), 2.72-2.87 (m, 2H), 1.91-2.04 (m, 1H), 1.56-1.69 (m, 1H)	B	Chiralpak AD-H, 25% IPA, peak 2
209	400MHz d ₆ -DMSO	8.56 (d, J=2.1 Hz, 1H), 7.93 (dd, J=2.5, 8.4 Hz, 1H), 7.52 - 7.31 (m, 2H), 7.25 (d, J=8.4 Hz, 1H), 7.14 - 7.01 (m, 2H), 5.47 - 5.34 (m, 2H), 3.55 (br dd, J=3.2, 12.2 Hz, 1H), 3.27 - 3.18 (m, 2H), 3.17 - 2.90 (m, 2H), 2.01 - 1.89 (m, 1H), 1.79 (br dd, J=3.4, 9.9 Hz, 1H), 1.64 - 1.45 (m, 2H)	--	--
210	400MHz d ₆ -DMSO	8.72 (d, J=1.66 Hz, 1H), 8.31 (br s, 2H), 8.02 (d, J=8.09 Hz, 1H), 7.83-7.89 (m, 1H), 7.57 (d, J=7.77 Hz, 1H), 7.27 (m, 3H), 5.54-5.61 (m, 2H), 3.70 (br dd, J=2.80, 12.44 Hz, 1H), 3.48 (br s, 1H), 3.27-3.44 (m, 2H), 3.07-3.16 (m, 1H), 1.96-2.10 (m, 1H), 1.83-1.94 (m, 1H), 1.59-1.73 (m, 2H)	--	--

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
211	400MHz d ₆ - DMSO	8.92 (br s, 3H), 8.55 (d, <i>J</i> =2.18 Hz, 1H), 8.03 (dd, <i>J</i> =2.49, 8.40 Hz, 1H), 7.67 (d, <i>J</i> =8.40 Hz, 1H), 7.60 (d, <i>J</i> =7.77 Hz, 1H), 7.28-7.44 (m, 3H), 5.64-5.78 (m, 2H), 4.88-5.10 (m, 1H), 4.18 (br d, <i>J</i> =12.65 Hz, 1H), 3.77 (br d, <i>J</i> =13.58 Hz, 1H), 3.54-3.63 (m, 1H), 3.43-3.53 (m, 1H), 3.21-3.42 (m, 1H), 2.26-2.37 (m, 1H), 1.82-1.94 (m, 1H)	--	--
212	400MHz d ₆ - DMSO	9.12 (br s, 3H), 8.94 (s, 1H), 8.40 (d, <i>J</i> =8.19 Hz, 1H), 7.77 (d, <i>J</i> =8.19 Hz, 1H), 7.61 (d, <i>J</i> =7.88 Hz, 1H), 7.25-7.39 (m, 3H), 5.72-5.93 (m, 2H), 4.03 (br d, <i>J</i> =12.75 Hz, 2H), 3.57-3.70 (m, 2H), 3.42 (br t, <i>J</i> =10.78 Hz, 1H), 2.53-2.62 (m, 1H), 2.23-2.38 (m, 1H)	--	--
213	500MHz DMSO- d ₆	8.57 (br s, 2H), 8.50-8.55 (m, 1H), 7.94-8.00 (m, 2H), 7.43-7.51 (m, 2H), 7.35 (d, <i>J</i> =8.30 Hz, 1H), 5.54 (d, <i>J</i> =7.66 Hz, 2H), 4.81 (dt, <i>J</i> =4.87, 9.11 Hz, 1H), 3.83-3.92 (m, 1H), 3.50-3.58 (m, 2H), 3.16 (br dd, <i>J</i> =10.19, 12.65 Hz, 1H), 3.06 (br t, <i>J</i> =11.74 Hz, 1H), 2.20 (br t, <i>J</i> =9.54 Hz, 1H), 1.76-1.88 (m, 1H)	B	Chiralpak AD-H, 25% IPA, peak 2
214	500MHz DMSO- d ₆	8.66 (br s, 2H), 8.54 (d, <i>J</i> =2.21 Hz, 1H), 7.98 (dd, <i>J</i> =2.34, 8.43 Hz, 1H), 7.78 (s, 1H), 7.57-7.63 (m, <i>J</i> =8.30 Hz, 1H), 7.51-7.57 (m, <i>J</i> =8.30 Hz, 1H), 7.46 (d, <i>J</i> =8.43 Hz, 1H), 5.49-5.62 (m, 2H), 4.79-4.99 (m, 1H), 3.95 (br d, <i>J</i> =12.98 Hz, 1H), 3.71-3.84 (m, 2H), 3.20 (br t, <i>J</i> =11.48 Hz, 1H), 3.07 (br t, <i>J</i> =11.81 Hz, 1H), 2.21 (br t, <i>J</i> =9.67 Hz, 1H), 1.80 (br t, <i>J</i> =9.93 Hz, 1H)	B	Chiralpak AD-H, 25% IPA, peak 2
215	500MHz DMSO- d ₆	8.59 (br d, <i>J</i> =2.47 Hz, 3H), 7.86-7.91 (m, 1H), 7.45 (d, <i>J</i> =7.91 Hz, 1H), 7.33 (s, 1H), 7.27-7.32 (m, 1H), 7.02-7.09 (m, 1H), 6.92-6.97 (m, 2H), 5.86 (q, <i>J</i> =6.96 Hz, 1H), 4.76-4.99 (m, 1H), 3.65-3.76 (m, 2H), 3.37 (br s, 1H), 3.14-3.22 (m, 1H), 3.07 (br t, <i>J</i> =11.16 Hz, 1H), 2.19-2.27 (m, 1H), 1.89-1.98 (m, 1H), 1.86 (d, <i>J</i> =7.14 Hz, 3H)	B	Chiralpak IC, 20% methanol, peak 1
216	500MHz DMSO- d ₆	8.63 (d, <i>J</i> =1.95 Hz, 1H), 7.89 (br dd, <i>J</i> =1.88, 8.50 Hz, 1H), 7.47 (d, <i>J</i> =7.92 Hz, 1H), 7.28 (d, <i>J</i> =8.43 Hz, 1H), 7.07 (t, <i>J</i> =6.55 Hz, 1H), 6.94-7.00 (m, 2H), 5.87 (q, <i>J</i> =7.01 Hz, 1H), 4.71-4.90 (m, 1H), 3.66-3.77 (m, 1H), 3.58-3.64 (m, 1H), 3.40-3.48 (m, 1H), 3.02-3.18 (m, 2H), 2.20-2.28 (m, 1H), 1.96-2.02 (m, 1H), 1.92 (d, <i>J</i> =7.14 Hz, 3H)	B	Chiralpak IC, 20% methanol, peak 2
217	500MHz DMSO- d ₆	8.56 (d, <i>J</i> =2.34 Hz, 1H), 8.53 (br s, 2H), 7.90 (dd, <i>J</i> =2.47, 8.43 Hz, 1H), 7.50 (dd, <i>J</i> =7.59, 10.96 Hz, 1H), 7.39 (d, <i>J</i> =8.43 Hz, 1H), 7.13 (dd, <i>J</i> =7.33, 10.83 Hz, 1H), 5.83 (q, <i>J</i> =7.09 Hz, 1H), 4.75-4.93 (m, 1H), 3.65 (br dd, <i>J</i> =4.48, 9.15 Hz, 2H), 3.29 (br d, <i>J</i> =11.94 Hz, 1H), 3.07-3.18 (m, 1H), 3.02 (br t, <i>J</i> =11.03 Hz, 1H), 2.16-2.24 (m, 1H), 1.85-1.92 (m, 1H), 1.83 (d, <i>J</i> =7.14 Hz, 3H)	B	Chiralcel OZ-H, 15% methanol, peak 1

Ex. #	Freq., Solvent	¹ H NMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
218	500MHz DMSO- <i>d</i> ₆	8.65 (br s, 2H), 8.62 (d, <i>J</i> =2.34 Hz, 1H), 7.94 (dd, <i>J</i> =2.47, 8.56 Hz, 1H), 7.55 (dd, <i>J</i> =7.66, 11.03 Hz, 1H), 7.39 (d, <i>J</i> =8.56 Hz, 1H), 7.15-7.21 (m, 1H), 5.87 (q, <i>J</i> =7.09 Hz, 1H), 4.80-4.97 (m, 1H), 3.62-3.79 (m, 2H), 3.16 (dd, <i>J</i> =10.12, 11.94 Hz, 1H), 3.03 (br t, <i>J</i> =11.55 Hz, 1H), 2.25 (br t, <i>J</i> =9.41 Hz, 1H), 1.94-2.03 (m, 1H), 1.91 (d, <i>J</i> =7.27 Hz, 3H)	B	Chiralcel OZ-H, 15% methanol, peak 2
219	500MHz DMSO- <i>d</i> ₆	8.58 (br s, 1H), 8.58 (br s, 2H), 7.91 (dd, <i>J</i> =2.47, 8.56 Hz, 1H), 7.44 (d, <i>J</i> =8.36 Hz, 1H), 7.39 (d, <i>J</i> =8.39 Hz, 1H), 7.02-7.09 (m, 2H), 5.84 (q, <i>J</i> =7.09 Hz, 1H), 4.73-4.97 (m, 1H), 3.68 (br dd, <i>J</i> =4.09, 10.70 Hz, 2H), 3.32 (br d, <i>J</i> =11.42 Hz, 1H), 3.10-3.21 (m, 1H), 3.05 (br t, <i>J</i> =11.03 Hz, 1H), 2.16-2.27 (m, 1H), 1.86-1.93 (m, 1H), 1.83 (d, <i>J</i> =7.14 Hz, 3H)	B	Regis Whelk-O s,s, 20% methanol, peak 1
220	500MHz DMSO- <i>d</i> ₆	8.64 (d, <i>J</i> =2.46 Hz, 1H), 8.56 (br s, 2H), 7.95 (dd, <i>J</i> =2.47, 8.56 Hz, 1H), 7.46-7.51 (m, <i>J</i> =8.43 Hz, 1H), 7.35-7.43 (m, <i>J</i> =8.56 Hz, 1H), 7.05-7.16 (m, 2H), 5.87 (q, <i>J</i> =7.14 Hz, 1H), 4.78-4.99 (m, 1H), 3.75 (br d, <i>J</i> =12.20 Hz, 2H), 3.37-3.50 (m, 1H), 3.13-3.21 (m, 1H), 3.07 (br t, <i>J</i> =11.55 Hz, 1H), 2.25 (br t, <i>J</i> =9.34 Hz, 1H), 1.95-2.04 (m, 1H), 1.92 (d, <i>J</i> =7.14 Hz, 3H)	B	Regis Whelk-O s,s, 20% methanol, peak 2
221	500MHz DMSO- <i>d</i> ₆	8.62 (br s, 1H), 8.60 (br s, 2H), 7.95 (dd, <i>J</i> =2.47, 8.43 Hz, 1H), 7.54 (d, <i>J</i> =1.56 Hz, 1H), 7.40 (d, <i>J</i> =8.56 Hz, 1H), 6.97-7.05 (m, 2H), 5.88 (q, <i>J</i> =7.01 Hz, 1H), 4.77-5.04 (m, 1H), 3.76 (br s, 3H), 3.57 (s, 1H), 3.44 (br d, <i>J</i> =12.07 Hz, 1H), 3.18-3.32 (m, 1H), 3.13 (br t, <i>J</i> =11.16 Hz, 1H), 2.23-2.32 (m, 1H), 1.92-2.01 (m, 1H), 1.89 (d, <i>J</i> =7.01 Hz, 3H)	B	Regis Whelk-O s,s, 20% methanol, peak 3
222	500MHz DMSO- <i>d</i> ₆	8.62 (br d, <i>J</i> =2.34 Hz, 3H), 7.92 (dd, <i>J</i> =2.47, 8.56 Hz, 1H), 7.54 (s, 1H), 7.35 (d, <i>J</i> =8.56 Hz, 1H), 6.99-7.05 (m, 2H), 5.87 (q, <i>J</i> =7.01 Hz, 1H), 4.80-5.01 (m, 1H), 3.78 (br dd, <i>J</i> =5.00, 11.87 Hz, 2H), 3.44-3.53 (m, 1H), 3.20 (dd, <i>J</i> =10.38, 12.07 Hz, 1H), 3.10 (br t, <i>J</i> =11.48 Hz, 1H), 2.27 (br t, <i>J</i> =9.41 Hz, 1H), 1.95-2.04 (m, 1H), 1.92 (d, <i>J</i> =7.14 Hz, 3H)	B	Regis Whelk-O s,s, 20% methanol, peak 4
223	500MHz DMSO- <i>d</i> ₆	9.00 (s, 1H), 8.63 (br s, 3H), 8.38 (dd, <i>J</i> =1.69, 8.30 Hz, 1H), 7.58-7.70 (m, 3H), 7.52 (d, <i>J</i> =8.30 Hz, 1H), 6.00 (q, <i>J</i> =7.01 Hz, 1H), 4.81-5.00 (m, 1H), 3.74-3.83 (m, 1H), 3.65-3.74 (m, 1H), 3.42 (br d, <i>J</i> =11.68 Hz, 1H), 3.24 (br dd, <i>J</i> =9.80, 12.39 Hz, 1H), 3.13 (br t, <i>J</i> =11.16 Hz, 1H), 2.23-2.32 (m, 1H), 1.94 (br d, <i>J</i> =7.14 Hz, 4H)	B	Phenomenex Lux Cellulose-2, 20% isopropanol, peak 1

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
224	500MHz DMSO- <i>d</i> ₆	9.00 (s, 1H), 8.69-8.73 (m, 2H), 8.36 (dd, <i>J</i> =1.88, 8.24 Hz, 1H), 8.00 (s, 1H), 7.66 (d, <i>J</i> =8.30 Hz, 1H), 7.41 (d, <i>J</i> =8.43 Hz, 1H), 7.17 (d, <i>J</i> =8.43 Hz, 1H), 6.04 (q, <i>J</i> =6.96 Hz, 1H), 4.86-5.04 (m, 1H), 3.77 (br d, <i>J</i> =12.72 Hz, 1H), 3.65-3.73 (m, 1H), 3.42 (br d, <i>J</i> =11.94 Hz, 1H), 3.26 (br dd, <i>J</i> =9.60, 12.59 Hz, 1H), 3.12 (br t, <i>J</i> =11.09 Hz, 1H), 2.25-2.34 (m, 1H), 1.90-1.99 (m, 4H)	B	Phenomenex Lux Cellulose-2, 20% isopropanol, peak 2
225	500MHz DMSO- <i>d</i> ₆	8.98-9.02 (m, 1H), 8.62 (br d, <i>J</i> =3.24 Hz, 2H), 8.36 (dd, <i>J</i> =1.88, 8.24 Hz, 1H), 7.63 (dd, <i>J</i> =3.18, 8.24 Hz, 2H), 7.59 (s, 1H), 7.52 (d, <i>J</i> =8.17 Hz, 1H), 5.96 (q, <i>J</i> =6.96 Hz, 1H), 4.79-4.98 (m, 1H), 3.74-3.86 (m, 1H), 3.68-3.72 (m, 1H), 3.46 (br d, <i>J</i> =11.94 Hz, 1H), 3.14-3.26 (m, 1H), 3.09 (br t, <i>J</i> =12.00 Hz, 1H), 2.19-2.30 (m, 1H), 1.97 (br d, <i>J</i> =7.27 Hz, 4H)	B	Phenomenex Lux Cellulose-2, 20% isopropanol, peak 3
226	500MHz DMSO- <i>d</i> ₆	8.92-8.96 (m, 1H), 8.58 (br s, 3H), 8.28 (dd, <i>J</i> =1.95, 8.30 Hz, 1H), 7.94 (s, 1H), 7.53 (d, <i>J</i> =8.30 Hz, 1H), 7.34 (dd, <i>J</i> =1.30, 8.43 Hz, 1H), 7.23 (s, 1H), 7.07-7.16 (m, 2H), 7.03 (s, 1H), 5.94 (q, <i>J</i> =6.92 Hz, 1H), 4.72-4.93 (m, 1H), 3.68-3.79 (m, 1H), 3.58-3.68 (m, 1H), 3.40 (br d, <i>J</i> =12.85 Hz, 1H), 3.15 (br t, <i>J</i> =11.35 Hz, 1H), 3.04 (br t, <i>J</i> =11.74 Hz, 1H), 2.20 (br t, <i>J</i> =9.54 Hz, 1H), 1.95 (m, 1H), 1.91 (d, <i>J</i> =7.01 Hz, 3H)	B	Phenomenex Lux Cellulose-2, 20% isopropanol, peak 4
227	500MHz DMSO- <i>d</i> ₆	8.54 (br d, <i>J</i> =2.21 Hz, 1H), 8.52 (br s, 2H), 7.96 (dd, <i>J</i> =2.47, 8.43 Hz, 1H), 7.54 (dd, <i>J</i> =7.53, 10.90 Hz, 1H), 7.33-7.44 (m, 2H), 5.37-5.52 (m, 2H), 4.73-4.92 (m, 1H), 3.75-3.83 (m, 1H), 3.51-3.62 (m, 1H), 3.45 (br d, <i>J</i> =12.20 Hz, 1H), 3.12 (br dd, <i>J</i> =10.64, 12.33 Hz, 1H), 3.01 (br t, <i>J</i> =11.61 Hz, 1H), 2.14-2.23 (m, 1H), 1.76-1.90 (m, 1H)	B	--
228	500MHz DMSO- <i>d</i> ₆	8.52 (br s, 2H), 8.49 (d, <i>J</i> =2.85 Hz, 1H), 7.76 (dt, <i>J</i> =2.98, 8.69 Hz, 1H), 7.53 (dd, <i>J</i> =7.40, 11.03 Hz, 1H), 7.44 (t, <i>J</i> =6.74 Hz, 1H), 7.37 (t, <i>J</i> =8.28 Hz, 1H), 5.38-5.51 (m, 2H), 4.73-4.95 (m, 1H), 3.75-3.83 (m, 1H), 3.47 (br d, <i>J</i> =12.98 Hz, 1H), 3.12 (dd, <i>J</i> =10.19, 12.52 Hz, 1H), 3.01 (br t, <i>J</i> =11.42 Hz, 1H), 2.15-2.23 (m, 1H), 1.77-1.87 (m, 1H)	B	--
229	400MHz DMSO- <i>d</i> ₆	8.80 (br s, 2H), 8.52 (d, <i>J</i> =2.38 Hz, 1H), 7.96 (dd, <i>J</i> =2.44, 8.45 Hz, 1H), 7.39 (d, <i>J</i> =8.40 Hz, 1H), 7.21 (dd, <i>J</i> =2.13, 9.17 Hz, 1H), 6.95 (t, <i>J</i> =10.40 Hz, 1H), 5.45-5.58 (m, 2H), 3.76 (br d, <i>J</i> =12.02 Hz, 1H), 3.31-3.47 (m, 2H), 3.17-3.26 (m, 1H), 2.33 (m, 3H)	B	Regis Whelk-O s,s, 15% methanol, peak 1
230	500MHz DMSO- <i>d</i> ₆	8.87 (br s, 2H), 8.55 (s, 1H), 7.97 (br d, <i>J</i> =8.17 Hz, 1H), 7.46 (br d, <i>J</i> =8.30 Hz, 1H), 6.95-7.04 (m, 2H), 5.41-5.63 (m, 2H), 3.95-4.06 (m, 1H), 3.77 (br d, <i>J</i> =12.20 Hz, 1H), 3.30-3.45 (m, 2H), 3.18 (br t, <i>J</i> =10.19 Hz, 1H), 2.19-2.35 (m, 1H)	B	Regis Whelk-O s,s, 15% methanol, peak 2

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
231	500MHz d ₄ -MeOH	7.86 (s, 1H), 7.65 (d, <i>J</i> =8.04 Hz, 1H), 7.55 (d, <i>J</i> =7.79 Hz, 1H), 7.42 (t, <i>J</i> =7.66 Hz, 1H), 7.16-7.26 (m, 2H), 6.64 (br dd, <i>J</i> =1.82, 9.08 Hz, 1H), 6.27 (br t, <i>J</i> =8.69 Hz, 1H), 4.89-5.03 (m, 1H), 4.13-4.24 (m, 1H), 3.92-4.01 (m, 1H), 3.79-3.90 (m, 1H), 3.50-3.64 (m, 2H), 3.39-3.48 (m, 1H), 3.24-3.30 (m, 1H), 2.97-3.08 (m, 1H), 2.70 (qd, <i>J</i> =9.45, 13.43 Hz, 1H), 2.52 (dt, <i>J</i> =4.67, 7.79 Hz, 1H), 2.17-2.34 (m, 1H)	B	Phenomenex Lux Cellulose-2, 30% MeOH Peak 1
232	500MHz d ₄ -MeOH	7.86 (s, 1H), 7.64 (d, <i>J</i> =8.04 Hz, 1H), 7.54 (d, <i>J</i> =7.78 Hz, 1H), 7.40 (t, <i>J</i> =7.79 Hz, 1H), 7.14-7.22 (m, 2H), 6.65 (br d, <i>J</i> =7.53 Hz, 1H), 6.27 (br t, <i>J</i> =9.08 Hz, 1H), 4.88-5.00 (m, 1H), 4.08-4.16 (m, 1H), 3.86-3.99 (m, 2H), 3.39-3.58 (m, 3H), 3.24-3.30 (m, 1H), 3.01-3.11 (m, 1H), 2.62-2.77 (m, 1H), 2.44-2.56 (m, 1H), 2.10-2.27 (m, 1H)	B	Phenomenex Lux Cellulose-2, 30% MeOH Peak 2
233	500MHz d ₄ -MeOH	8.90 (d, <i>J</i> =1.30 Hz, 1H), 8.82 (d, <i>J</i> =1.30 Hz, 1H), 7.46 (d, <i>J</i> =8.56 Hz, 1H), 7.28 (d, <i>J</i> =2.08 Hz, 1H), 7.18 (dd, <i>J</i> =1.95, 8.43 Hz, 1H), 5.65 (s, 2H), 3.38-3.51 (m, 2H), 3.28 (br d, <i>J</i> =3.37 Hz, 1H), 3.16-3.25 (m, 1H), 3.08-3.15 (m, 1H), 2.23-2.36 (m, 1H), 2.07-2.22 (m, 1H)	B	Chiralpak IC, 15% MeOH, Peak 1
234	500MHz d ₄ -MeOH	8.91 (d, <i>J</i> =1.30 Hz, 1H), 8.82 (d, <i>J</i> =1.04 Hz, 1H), 7.50 (d, <i>J</i> =1.82 Hz, 1H), 7.15-7.19 (m, 1H), 7.09-7.15 (m, 1H), 5.67 (s, 2H), 3.42-3.55 (m, 2H), 3.33-3.38 (m, 1H), 3.20-3.28 (m, 1H), 3.13-3.20 (m, 1H), 2.25-2.38 (m, 1H), 2.09-2.23 (m, 1H)	B	Chiralpak IC, 15% MeOH, Peak 2
235	600MHz d ₆ -DMSO	8.30 (br d, <i>J</i> =7.79 Hz, 1H), 7.46 (dd, <i>J</i> =7.47, 11.21 Hz, 1H), 7.36 (dd, <i>J</i> =7.32, 10.74 Hz, 1H), 4.64 (s, 2H), 4.30-4.46 (m, 1H), 3.84-3.93 (m, 1H), 3.37-3.43 (m, 1H), 2.93-3.05 (m, 2H), 2.79 (dd, <i>J</i> =8.72, 12.46 Hz, 1H), 2.06-2.17 (m, 1H), 1.75-1.85 (m, 1H), 1.10 (dd, <i>J</i> =1.87, 6.54 Hz, 6H)	--	--
236	600MHz d ₆ -DMSO	7.46 (dd, <i>J</i> =7.47, 11.21 Hz, 1H), 7.38 (dd, <i>J</i> =7.32, 10.74 Hz, 1H), 4.73 (s, 2H), 4.33-4.47 (m, 1H), 4.27 (dt, <i>J</i> =4.67, 7.63 Hz, 2H), 3.89-3.99 (m, 2H), 3.34-3.40 (m, 2H), 2.95-3.06 (m, 2H), 2.80 (dd, <i>J</i> =8.25, 12.61 Hz, 1H), 2.26-2.34 (m, 2H), 2.06-2.18 (m, 1H), 1.75-1.85 (m, 1H)	--	--
237	600MHz d ₆ -DMSO	7.44-7.52 (m, 1H), 7.28-7.38 (m, 1H), 5.02-5.12 (m, 2H), 4.32-4.47 (m, 1H), 3.55-3.86 (m, 2H), 3.18-3.55 (m, 5H), 2.93-3.07 (m, 2H), 2.74-2.84 (m, 1H), 2.03-2.17 (m, 1H), 1.71-1.84 (m, 1H), 1.01-1.36 (m, 6H) (mixture of 2 diastereomers/rotamers)	--	--
238	600MHz d ₆ -DMSO	7.53 (dd, <i>J</i> =7.47, 11.21 Hz, 1H), 7.09-7.20 (m, 1H), 5.28 (t, <i>J</i> =9.96 Hz, 1H), 4.30-4.48 (m, 1H), 3.56-3.64 (m, 1H), 3.42-3.50 (m, 1H), 3.30-3.42 (m, 2H), 2.97-3.09 (m, 2H), 2.88 (s, 3H), 2.76-2.85 (m, 1H), 2.54-2.59 (m, 1H), 2.27-2.37 (m, 1H), 2.07-2.19 (m, 1H), 1.76-1.93 (m, 1H)	--	--

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
239	600MHz d ₆ -DMSO	7.45-7.54 (m, 2H), 7.39-7.44 (m, 2H), 7.35-7.38 (m, 2H), 7.27 (dt, <i>J</i> =0.93, 7.32 Hz, 1H), 5.21-5.32 (m, 1H), 4.32-4.50 (m, 1H), 4.08-4.20 (m, 1H), 3.61-3.68 (m, 1H), 3.29-3.39 (m, 2H), 2.97-3.11 (m, 2H), 2.73-2.90 (m, 1H), 2.51-2.63 (m, 1H), 2.07-2.32 (m, 4H), 1.82-1.92 (m, 1H)	--	--
240	600MHz d ₆ -DMSO	7.76-7.81 (m, 2H), 7.53-7.58 (m, 1H), 7.48-7.53 (m, 2H), 7.34-7.41 (m, 1H), 5.59 (dd, <i>J</i> =9.65, 11.21 Hz, 1H), 4.34-4.49 (m, 1H), 4.06 (br t, <i>J</i> =9.19 Hz, 1H), 3.92-4.00 (m, 1H), 3.34-3.43 (m, 2H), 3.01-3.09 (m, 2H), 2.82 (ddd, <i>J</i> =8.88, 12.69, 14.87 Hz, 1H), 2.64-2.72 (m, 1H), 2.54-2.61 (m, 1H), 2.10-2.20 (m, 1H), 1.80-1.90 (m, 1H)	--	--
241	500MHz d ₄ -MeOH	8.51 (s, 2H), 7.95 (d, <i>J</i> =0.78 Hz, 1H), 7.65-7.70 (m, 1H), 7.59-7.64 (m, 1H), 5.57-5.68 (m, 2H), 4.77-4.95 (m, 1H), 4.23-4.32 (m, 1H), 3.98-4.06 (m, 1H), 3.95 (s, 3H), 3.71-3.80 (m, 1H), 3.42-3.53 (m, 2H), 2.34-2.44 (m, 1H), 2.01-2.15 (m, 1H)	B	Chiralcel OJ-H, 15% MeOH Peak 2
242	500MHz d ₄ -MeOH	8.52 (s, 2H), 7.94 (s, 1H), 7.66-7.74 (m, 2H), 5.54-5.67 (m, 2H), 4.77-4.93 (m, 1H), 4.21-4.30 (m, 1H), 4.01 (br d, <i>J</i> =12.98 Hz, 1H), 3.96 (s, 3H), 3.71-3.78 (m, 1H), 3.43-3.50 (m, 2H), 2.32-2.46 (m, 1H), 1.98-2.14 (m, 1H)	B	Chiralcel OJ-H, 15% MeOH Peak 1
243	600MHz d ₆ -DMSO	8.82 (br d, <i>J</i> =3.89 Hz, 3H), 8.73 (s, 1H), 7.94 (d, <i>J</i> =1.04 Hz, 1H), 7.86-7.90 (m, 1H), 7.80-7.85 (m, 1H), 7.64-7.68 (m, 1H), 7.56-7.63 (m, 1H), 5.58-5.72 (m, 2H), 4.87-5.04 (m, 1H), 3.94-4.03 (m, 1H), 3.57-3.64 (m, 2H), 3.31 (dd, <i>J</i> =10.12, 12.98 Hz, 1H), 3.16 (br t, <i>J</i> =11.42 Hz, 1H), 2.20-2.32 (m, 1H), 1.79-1.96 (m, 1H)	B	Chiralpak AD-H, 20% MeOH Peak 1
244	600MHz d ₆ -DMSO	8.73 (br d, <i>J</i> =4.15 Hz, 3H), 8.71 (d, <i>J</i> =1.56 Hz, 1H), 8.01 (d, <i>J</i> =1.30 Hz, 1H), 7.83-7.91 (m, 1H), 7.79 (dd, <i>J</i> =1.43, 8.17 Hz, 1H), 7.51-7.60 (m, 1H), 7.37-7.51 (m, 1H), 5.55-5.73 (m, 2H), 4.81-5.03 (m, 1H), 3.85-3.96 (m, 1H), 3.58-3.66 (m, 1H), 3.49-3.54 (m, 1H), 3.25 (dd, <i>J</i> =9.86, 12.98 Hz, 1H), 3.11 (br t, <i>J</i> =11.42 Hz, 1H), 2.20-2.31 (m, 1H), 1.82-1.95 (m, 1H)	B	Chiralpak AD-H, 20% MeOH Peak 2
245	500MHz d ₄ -MeOH	7.36 (dd, <i>J</i> =7.27, 10.64 Hz, 1H), 7.06 (dd, <i>J</i> =7.01, 10.12 Hz, 1H), 5.39 (t, <i>J</i> =9.99 Hz, 1H), 4.34-4.52 (m, 1H), 3.67-3.74 (m, 1H), 3.57-3.65 (m, 1H), 3.48 (br dd, <i>J</i> =3.76, 7.14 Hz, 2H), 3.08-3.20 (m, 2H), 3.01 (s, 3H), 2.95 (dd, <i>J</i> =8.95, 12.33 Hz, 1H), 2.64-2.74 (m, 1H), 2.46 (qd, <i>J</i> =9.81, 12.88 Hz, 1H), 2.18-2.29 (m, 1H), 1.92-2.03 (m, 1H)	F	Chiralpak IC, 25% MeOH, w/ 0.2% DEA Peak 1

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
246	500MHz d ₄ -MeOH	7.36 (dd, <i>J</i> =7.27, 10.64 Hz, 1H), 7.06 (dd, <i>J</i> =7.01, 10.12 Hz, 1H), 5.39 (t, <i>J</i> =9.99 Hz, 1H), 4.36-4.52 (m, 1H), 3.67-3.74 (m, 1H), 3.58-3.65 (m, 1H), 3.52-3.58 (m, 1H), 3.38-3.46 (m, 1H), 3.11-3.20 (m, 2H), 3.01 (s, 3H), 2.93 (dd, <i>J</i> =8.56, 12.46 Hz, 1H), 2.61-2.71 (m, 1H), 2.45 (qd, <i>J</i> =9.74, 13.07 Hz, 1H), 2.18-2.29 (m, 1H), 1.92-2.04 (m, 1H)	F	Chiralpak IC, 25% MeOH, w/ 0.2% DEA Peak 2
247	500MHz d ₄ -MeOH	7.78 (d, <i>J</i> =9.08 Hz, 2H), 7.46 (d, <i>J</i> =9.08 Hz, 2H), 7.40 (dd, <i>J</i> =7.27, 10.64 Hz, 1H), 7.21 (br dd, <i>J</i> =6.88, 10.25 Hz, 1H), 5.63 (dd, <i>J</i> =9.47, 11.03 Hz, 1H), 4.37-4.55 (m, 1H), 4.06-4.20 (m, 2H), 3.55-3.63 (m, 1H), 3.41-3.49 (m, 1H), 3.14-3.23 (m, 2H), 2.96 (dd, <i>J</i> =8.82, 12.20 Hz, 1H), 2.75-2.84 (m, 1H), 2.58-2.73 (m, 1H), 2.19-2.33 (m, 1H), 1.92-2.06 (m, 1H)	F	Chiralcel OD-H, 30% MeOH, w/ 0.2% DEA Peak 1
248	500MHz d ₄ -MeOH	7.77 (d, <i>J</i> =8.82 Hz, 2H), 7.43-7.49 (m, 2H), 7.40 (dd, <i>J</i> =7.27, 10.64 Hz, 1H), 7.17-7.24 (m, 1H), 5.59-5.67 (m, 1H), 4.37-4.54 (m, 1H), 4.06-4.20 (m, 2H), 3.48-3.56 (m, 2H), 3.12-3.21 (m, 2H), 2.95-3.07 (m, 1H), 2.78-2.87 (m, 1H), 2.62-2.72 (m, 1H), 2.20-2.31 (m, 1H), 1.94-2.06 (m, 1H)	F	Chiralcel OD-H, 30% MeOH, w/ 0.2% DEA Peak 2
249	DMSO-d ₆	9.09 (d, <i>J</i> =1.48 Hz, 1H), 8.96 (d, <i>J</i> =1.40 Hz, 1H), 7.78 (d, <i>J</i> =1.48 Hz, 1H), 7.56 (d, <i>J</i> =8.29 Hz, 1H), 7.50 (d, <i>J</i> =8.50 Hz, 1H), 5.66-5.76 (m, 2H), 4.39-4.37 (m, 1H), 3.39-3.49 (m, 2H), 3.06-3.17 (m, 1H), 2.80-2.95 (m, 2H), 2.00-2.14 (m, 2H), 1.67-1.83 (m, 1H)	B	SFC: Chiralpak AD-H, 30% methanol.
250	DMSO-d ₆	9.08 (d, <i>J</i> =1.40 Hz, 1H), 8.97 (d, <i>J</i> =1.40 Hz, 1H), 7.93 (d, <i>J</i> =1.48 Hz, 1H), 7.46 (d, <i>J</i> =8.36 Hz, 1H), 7.39 (d, <i>J</i> =8.21 Hz, 1H), 5.67-5.76 (m, 2H), 4.38-4.34 (m, 1H), 3.37-3.46 (m, 2H), 3.02-3.12 (m, 1H), 2.79-2.98 (m, 2H), 2.00-2.16 (m, 1H), 1.68-1.79 (m, 1H)	B	SFC: Chiralpak AD-H, 25% methanol
251	DMSO-d ₆	9.10 (d, <i>J</i> =1.40 Hz, 1H), 8.97 (d, <i>J</i> =1.32 Hz, 1H), 7.17 (dd, <i>J</i> =2.18, 9.26 Hz, 1H), 6.89 (t, <i>J</i> =10.46 Hz, 1H), 5.63-5.70 (m, 2H), 4.26-4.31 (m, 1H), 3.37-3.51 (m, 2H), 3.03-3.12 (m, 1H), 2.92-3.01 (m, 1H), 2.79-2.91 (m, 1H), 1.99-2.17 (m, 1H), 1.70-1.84 (m, 1H)	B	SFC: Chiralpak AD-H, 30% methanol
252	DMSO-d ₆	9.02-9.15 (m, 1H), 8.93-8.98 (m, 1H), 7.17 (d, <i>J</i> =8.96 Hz, 1H), 6.82-6.94 (m, 1H), 5.61-5.70 (m, 2H), 4.34 (dt, <i>J</i> =4.28, 8.25 Hz, 1H), 3.37-3.44 (m, 1H), 3.03-3.10 (m, 1H), 2.87-2.886 (m, 2H), 2.32-2.47 (m, 1H), 2.02-2.18 (m, 1H), 1.69-1.83 (m, 1H)	B	SFC: Chiralpak AD-H, 25% methanol

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
253	DMSO-d ₆	10.99-11.51 (m, 1H), 8.46-8.48 (m, 1H), 7.65-7.72 (m, 1H), 7.51-7.57 (m, 1H), 7.13-7.20 (m, 2H), 6.84-6.95 (m, 2H), 4.09-4.26 (m, 1H), 3.88-4.08 (m, 1H), 3.74-3.82 (m, 2H), 2.80-3.00 (m, 2H), 2.58-2.67 (m, 1H), 2.20-2.26 (m, 3H), 1.93-2.00 (m, 1H), 1.74-1.84 (m, 1H), 1.47-1.55 (m, 2H)	--	--
254	DMSO-d ₆	8.48-8.64 (s, 1H), 7.83-7.99 (m, 1H), 7.43-7.58 (m, 1H), 7.26 (d, <i>J</i> =8.30 Hz, 1H), 7.01-7.20 (m, 2H), 6.89 (br dd, <i>J</i> =3.05, 5.51 Hz, 2H), 4.55 (s, 1H), 4.01 (br d, <i>J</i> =12.20 Hz, 1H), 3.74-3.83 (m, 1H), 3.55-3.69 (m, 1H), 2.82-3.04 (m, 2H), 2.58-2.66 (m, 1H), 2.35-2.47 (m, 1H), 2.25 (s, 2H), 1.95 (br s, 1H), 1.80 (br dd, <i>J</i> =3.18, 6.16 Hz, 1H), 1.44-1.63 (m, 1H),	--	--
255	DMSO-d ₆	9.04 (d, <i>J</i> =2.02 Hz, 1H), 8.30 (d, <i>J</i> =8.16 Hz, 1H), 7.40-7.47 (m, 2H), 7.05 (t, <i>J</i> =7.59 Hz, 1H), 6.92-7.00 (m, 2H), 5.81-5.87 (m, 1H), 3.37-3.48 (m, 1H), 2.85-2.94 (m, 2H), 2.52-2.69 (m, 3H), 2.37-2.47 (m, 1H), 2.15 (s, 3H), 1.85-1.95 (m, 2H), 1.71-1.82 (m, 1H), 1.59-1.69 (m, 1H), 1.14-1.26 (m, 1H)	B	SFC: Chiralpak IC, 25% methanol
256	DMSO-d ₆	9.04 (d, <i>J</i> =1.48 Hz, 1H), 8.29 (d, <i>J</i> =8.18 Hz, 1H), 7.45 (d, <i>J</i> =8.80 Hz, 1H), 7.41 (d, <i>J</i> =8.07 Hz, 1H), 7.05 (ddd, <i>J</i> =1.87, 6.46, 8.02 Hz, 1H), 6.90-7.00 (m, 2H), 5.80-5.88 (m, 1H), 3.38-3.50 (m, 2H), 3.21-3.28 (m, 1H), 2.82-2.94 (m, 1H), 2.67 (dd, <i>J</i> =9.07, 11.64 Hz, 1H), 2.51-2.62 (m, 2H), 2.25 (s, 2H), 2.15 (s, 1H), 1.91 (d, <i>J</i> =7.16 Hz, 4H), 1.62-1.80 (m, 2H), 1.18-1.28 (m, 1H)	B	SFC: Chiralpak IC, 25% methanol
257	DMSO-d ₆	8.92 (s, 2H), 7.15 (dd, <i>J</i> =2.18, 9.34 Hz, 1H), 6.86 (t, <i>J</i> =10.48 Hz, 1H), 5.51-5.60 (m, 2H), 4.298-4.44 (m, 1H), 3.34-3.42 (m, 2H), 3.02-3.10 (m, 1H), 2.88-2.97 (m, 1H), 2.81 (dd, <i>J</i> =8.45, 12.57 Hz, 1H), 2.04-2.12 (m, 1H), 1.66-1.82 (m, 1H)	B	SFC/MS with MeOH as co- solvent at 10% iso-cratic Column: 4- Ethylpyridine 21.2x150mm
258	DMSO-d ₆	8.92 (s, 2H), 7.06 (dd, <i>J</i> =2.26, 8.88 Hz, 1H), 6.95 (dt, <i>J</i> =2.18, 10.63 Hz, 1H), 5.50-5.57 (m, 2H), 4.26-4.43 (m, 1H), 3.25-3.42 (m, 1H), 2.93-3.09 (m, 2H), 2.86 (br s, 1H), 2.76 (br dd, <i>J</i> =8.60, 12.34 Hz, 1H), 2.00-2.09 (m, 1H), 1.62-1.73 (m, 1H)	B	SFC/MS with MeOH as co- solvent at 10% iso-cratic Column: 4- Ethylpyridine 21.2x150mm

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
259	DMSO-d ₆	7.85 (d, <i>J</i> =0.78 Hz, 1H), 7.57 (d, <i>J</i> =8.49 Hz, 1H), 7.50 (dd, <i>J</i> =7.43, 11.17 Hz, 1H), 7.33 (dd, <i>J</i> =7.08, 8.41 Hz, 1H), 7.25 (dd, <i>J</i> =7.32, 10.67 Hz, 1H), 6.77 (d, <i>J</i> =6.70 Hz, 1H), 5.59-5.66 (m, 2H), 4.27-4.41 (m, 1H), 4.03 (s, 3H), 3.42-3.59 (m, 1H), 2.99-3.12 (m, 1H), 2.89-2.98 (m, 1H), 2.83 (dd, <i>J</i> =8.68, 12.57 Hz, 1H), 2.29-2.47 (m, 1H), 1.94-2.11 (m, 1H), 1.67-1.77 (m, 1H)	--	--
260	DMSO-d ₆	8.97 (dd, <i>J</i> =1.56, 4.20 Hz, 1H), 8.61 (d, <i>J</i> =8.02 Hz, 1H), 7.97 (d, <i>J</i> =8.49 Hz, 1H), 7.67 (t, <i>J</i> =7.95 Hz, 1H), 7.61-7.65 (m, 1H), 7.53 (dd, <i>J</i> =7.47, 11.13 Hz, 1H), 7.25 (dd, <i>J</i> =7.32, 10.67 Hz, 1H), 7.00 (d, <i>J</i> =7.19 Hz, 1H), 5.79-5.86 (m, 2H), 4.27-4.40 (m, 1H), 3.37-3.52 (m, 2H), 3.01-3.10 (m, 1H), 2.89-2.99 (m, 1H), 2.83 (dd, <i>J</i> =8.49, 12.53 Hz, 1H), 2.02 (dddd, <i>J</i> =4.28, 8.60, 12.62, 16.77 Hz, 1H), 1.67-1.83 (m, 1H)	--	--
261	DMSO-d ₆	8.91 (dd, <i>J</i> =1.71, 4.13 Hz, 1H), 8.40 (dd, <i>J</i> =1.48, 8.25 Hz, 1H), 7.98 (d, <i>J</i> =8.10 Hz, 1H), 7.87 (d, <i>J</i> =7.16 Hz, 1H), 7.65 (t, <i>J</i> =7.71 Hz, 1H), 7.57 (dd, <i>J</i> =4.17, 8.21 Hz, 1H), 7.37-7.52 (m, 2H), 6.75 (q, <i>J</i> =7.19 Hz, 1H), 4.33-4.41 (m, 1H), 3.35-3.46 (m, 2H), 2.96-3.09 (m, 2H), 2.72 (dd, <i>J</i> =8.76, 12.34 Hz, 1H), 2.52-2.56 (m, 1H), 1.97-2.10 (m, 4H), 1.63-1.79 (m, 1H)	B	SFC: Chiralpak IC column, 20% methanol.
262	DMSO-d ₆	8.91 (dd, <i>J</i> =1.71, 4.13 Hz, 1H), 8.39 (dd, <i>J</i> =1.56, 8.25 Hz, 1H), 7.98 (d, <i>J</i> =8.02 Hz, 1H), 7.86 (d, <i>J</i> =7.16 Hz, 1H), 7.65 (t, <i>J</i> =7.71 Hz, 1H), 7.56 (dd, <i>J</i> =4.13, 8.25 Hz, 1H), 7.46 (dd, <i>J</i> =7.63, 11.13 Hz, 1H), 7.39 (dd, <i>J</i> =7.36, 11.25 Hz, 1H), 6.73 (q, <i>J</i> =7.14 Hz, 1H), 4.28-4.36 (m, 1H), 3.36-3.46 (m, 1H), 3.14-3.28 (m, 2H), 2.83-2.97 (m, 2H), 2.52-2.55 (m, 1H), 2.38 (br s, 1H), 1.91-2.05 (m, 4H), 1.68-1.85 (m, 1H)	B	SFC: Chiralpak IC column, 20% methanol.
263	DMSO-d ₆	7.92 (t, <i>J</i> =1.71 Hz, 1H), 7.84 (td, <i>J</i> =1.31, 7.65 Hz, 1H), 7.51-7.59 (m, 4H), 7.14 (s, 1H), 5.57 (s, 2H), 4.29-4.50 (m, 1H), 3.36-3.49 (m, 3H), 2.99-3.13 (m, 1H), 2.87 (dd, <i>J</i> =8.37, 12.57 Hz, 1H), 2.04-2.20 (m, 1H), 1.77-1.92 (m, 1H)	--	--
264	DMSO-d ₆	8.06 (s, 1H), 7.68 (d, <i>J</i> =8.02 Hz, 1H), 7.54 (t, <i>J</i> =9.20 Hz, 1H), 7.18 (dd, <i>J</i> =7.59, 10.47 Hz, 1H), 6.99 (t, <i>J</i> =7.59 Hz, 1H), 6.48 (d, <i>J</i> =7.30 Hz, 1H), 5.98 (d, <i>J</i> =17.36 Hz, 1H), 5.91 (d, <i>J</i> =17.36 Hz, 1H), 4.36-4.45 (m, 1H), 4.31-4.35 (m, 3H), 3.40-3.57 (m, 2H), 3.08-3.13 (m, 1H), 2.90-2.97 (m, 1H), 2.86 (dd, <i>J</i> =8.14, 12.57 Hz, 1H), 2.54-2.66 (m, 1H), 1.99-2.07 (m, 1H), 1.67-1.83 (m, 1H)	--	--

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
265	DMSO-d ₆	7.47-7.56 (m, 3H), 7.42 (dd, <i>J</i> =7.67, 8.52 Hz, 1H), 6.75 (dd, <i>J</i> =7.24, 10.82 Hz, 1H), 5.50-5.56 (m, 2H), 4.29-4.47 (m, 1H), 3.40-3.51 (m, 1H), 3.35-3.40 (m, 1H), 3.01-3.14 (m, 1H), 2.91-3.01 (m, 1H), 2.82 (dd, <i>J</i> =8.76, 12.42 Hz, 1H), 2.08-2.17 (m, 1H), 1.72-1.84 (m, 1H)	--	--
266	DMSO-d ₆	7.37-7.41 (m, 1H), 7.18 (d, <i>J</i> =7.38 Hz, 1H), 7.07 (t, <i>J</i> =6.39 Hz, 2H), 4.62-4.71 (m, 2H), 4.25 (t, <i>J</i> =7.63 Hz, 2H), 3.89-3.97 (m, 2H), 3.40-3.48 (m, 1H), 3.23-3.29 (m, 1H), 2.83-2.91 (m, 1H), 2.52-2.65 (m, 1H), 2.25-2.32 (m, 1H), 1.83-1.93 (m, 1H), 1.71-1.79 (m, 1H), 1.60-1.69 (m, 1H), 1.21-1.33 (m, 1H)	--	--
267	DMSO-d ₆	9.53 (br s, 1H), 8.97 (d, <i>J</i> =1.63 Hz, 1H), 8.33 (d, <i>J</i> =8.66 Hz, 1H), 7.55 (d, <i>J</i> =8.47 Hz, 1H), 7.23 (dd, <i>J</i> =2.22, 9.07 Hz, 1H), 6.88 (t, <i>J</i> =10.52 Hz, 1H), 5.82-5.96 (m, 1H), 4.02 (br dd, <i>J</i> =3.93, 7.90 Hz, 2H), 3.61-3.79 (m, 1H), 3.57 (br s, 1H), 3.50 (br dd, <i>J</i> =4.09, 12.42 Hz, 1H), 3.28 (br s, 1H), 3.13-3.26 (m, 1H), 3.09 (br d, <i>J</i> =12.77 Hz, 1H), 2.51-2.66 (m, 2H), 1.97 (br s, 2H), 1.84-1.93 (m, 3H)	B	SFC: Chiralpak IC, 15% methanol (initial purification). Chiralpak AD-H, 10% methanol (reprocess of fraction A). -
268	DMSO-d ₆	9.46 (br s, 1H), 8.93-9.04 (m, 1H), 8.33 (d, <i>J</i> =8.76 Hz, 1H), 7.55 (d, <i>J</i> =8.51 Hz, 1H), 7.23 (dd, <i>J</i> =2.18, 9.03 Hz, 1H), 6.89 (t, <i>J</i> =10.51 Hz, 1H), 5.85-5.96 (m, 1H), 3.92-4.07 (m, 2H), 3.83 (br s, 2H), 3.55-3.79 (m, 1H), 3.50 (br dd, <i>J</i> =4.13, 12.46 Hz, 1H), 3.25-3.33 (m, 1H), 3.13-3.25 (m, 1H), 3.09 (br d, <i>J</i> =12.53 Hz, 1H), 2.51-2.56 (m, 2H), 1.96 (br s, 2H), 1.83-1.92 (m, 3H)	B	SFC: Chiralpak IC, 15% methanol (initial purification). Chiralpak AD-H, 10% methanol (reprocess of fraction A). -
269	DMSO-d ₆	9.44 (br s, 1H), 8.94-8.99 (m, 1H), 8.30-8.35 (m, 1H), 7.49-7.56 (m, 1H), 7.23 (dd, <i>J</i> =2.26, 9.03 Hz, 1H), 6.89 (t, <i>J</i> =10.49 Hz, 1H), 5.86-5.94 (m, 1H), 3.95-4.09 (m, 2H), 3.71-3.80 (m, 2H), 3.57-3.69 (m, 1H), 3.50 (br dd, <i>J</i> =4.09, 12.26 Hz, 1H), 3.12-3.26 (m, 2H), 3.09 (br d, <i>J</i> =12.77 Hz, 1H), 2.51-2.62 (m, 2H), 1.91-1.97 (m, 1H), 1.85-1.91 (m, 3H)	B	SFC: Chiralpak IC, 15% methanol (initial purification). - Lux-Cellulose 2, 15% methanol (reprocess of fraction B). -

Ex. #	Freq., Solvent	¹ H NMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
270	DMSO-d ₆	9.45 (br s, 1H), 8.97 (d, <i>J</i> =1.48 Hz, 1H), 8.29-8.36 (m, 1H), 7.48-7.56 (m, 1H), 7.23 (dd, <i>J</i> =2.18, 9.03 Hz, 1H), 6.89 (t, <i>J</i> =10.48 Hz, 1H), 5.85-5.94 (m, 1H), 3.97-4.07 (m, 2H), 3.71-3.80 (m, 2H), 3.57-3.69 (m, 1H), 3.29 (br s, 1H), 3.12-3.26 (m, 1H), 3.09 (br d, <i>J</i> =12.53 Hz, 1H), 2.52-2.55 (m, 2H), 1.96-2.06 (m, 1H), 1.94 (br s, 1H), 1.83-1.91 (m, 3H)	B	SFC: Chiralpak IC, 15% methanol (initial purification). - Lux-Cellulose 2, 15% methanol (reprocess of fraction B).
271	DMSO-d ₆	9.32 (br s, 1H), 8.86 (br s, 1H), 8.32-8.37 (m, 1H), 7.55-7.59 (m, 1H), 6.99 (dt, <i>J</i> =2.06, 10.53 Hz, 1H), 6.79 (dd, <i>J</i> =1.99, 8.99 Hz, 1H), 5.92 (q, <i>J</i> =7.16 Hz, 1H), 3.95-4.10 (m, 2H), 3.81 (br d, <i>J</i> =9.50 Hz, 1H), 3.70-3.78 (m, 1H), .61-3.69 (m, 1H), 3.39-3.48 (m, 2H), 3.07-3.17 (m, 1H), 2.52-2.55 (m, 2H), 1.87-1.99 (m, 5H)	B	SFC: Chiralpak IC, 15% methanol (initial purification). - Chiralcel OZ- H, 25% methanol (reprocess of fraction C). -
272	DMSO-d ₆	9.33 (br s, 1H), 8.88 (br s, 1H), 8.35 (br d, <i>J</i> =8.17 Hz, 1H), 7.57 (d, <i>J</i> =8.25 Hz, 1H), 6.97-7.10 (m, 1H), 6.79 (br d, <i>J</i> =8.88 Hz, 1H), 5.89-5.98 (m, 1H), 3.99-4.07 (m, 2H), 3.78-3.84 (m, 1H), 3.70-3.78 (m, 1H), 3.64 (br t, <i>J</i> =11.29 Hz, 1H), 3.41-3.53 (m, 1H), 3.24 (br s, 1H), 3.07-3.17 (m, 1H), 2.54 (s, 2H), 1.86-1.99 (m, 5H)	B	SFC: Chiralpak IC, 15% methanol (initial purification). - fraction C). Regis Whelk- O s.s, 20% methanol (reprocess of peaks C1-C3).
273	DMSO-d ₆	9.33 (br s, 1H), 8.90 (br d, <i>J</i> =18.92 Hz, 1H), 8.32-8.37 (m, 1H), 7.57 (dd, <i>J</i> =6.89, 7.67 Hz, 1H), 6.99 (t, <i>J</i> =10.22 Hz, 1H), 6.79 (br d, <i>J</i> =8.95 Hz, 1H), 5.87-5.94 (m, 1H), 3.97-4.09 (m, 2H), 3.81 (br d, <i>J</i> =8.95 Hz, 1H), 3.70-3.78 (m, 1H), 3.61-3.69 (m, 1H), 3.57-3.69 (m, 1H), 3.29 (br s, 1H), 3.15 (br d, <i>J</i> =14.09 Hz, 1H), 2.52-2.56 (m, 2H), 2.00 (br d, <i>J</i> =5.99 Hz, 1H), 1.92 (d, <i>J</i> =7.16 Hz, 4H)	B	SFC: Chiralpak IC, 15% methanol (initial purification). - Regis Whelk- O s.s, 30% methanol (reprocess of fraction D).

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
274	DMSO-d ₆	9.33 (br s, 1H), 8.80-8.96 (m, 1H), 8.32-8.37 (m, 1H), 7.57 (t, <i>J</i> =7.49 Hz, 1H), 6.99 (dt, <i>J</i> =2.02, 10.51 Hz, 1H), 6.79 (br d, <i>J</i> =9.03 Hz, 1H), 5.87-5.94 (m, 1H), 3.96-4.08 (m, 2H), 3.80 (br s, 1H), 3.70-3.78 (m, 1H), 3.55-3.69 (m, 1H), 3.40-3.53 (m, 1H), 3.15 (br d, <i>J</i> =14.17 Hz, 1H), 3.10 (br d, <i>J</i> =13.39 Hz, 1H), 2.51-2.55 (m, 2H), 1.92 (d, <i>J</i> =7.16 Hz, 5H)	B	SFC: Chiralpak IC, 15% methanol (initial purification). - Regis Whelk- O s.s, 30% methanol (reprocess of fraction D).
275	DMSO-d ₆	8.27 (br d, <i>J</i> =7.21 Hz, 1H), 7.47 (dd, <i>J</i> =7.47, 11.21 Hz, 1H), 7.34 (dd, <i>J</i> =7.32, 10.67 Hz, 1H), 4.62-4.69 (m, 2H), 4.32-4.44 (m, 2H), 3.33-3.50 (m, 1H), 3.17 (br s, 1H), 2.96-3.11 (m, 2H), 2.77-2.85 (m, 1H), 2.66 (d, <i>J</i> =4.59 Hz, 3H), 2.07-2.15 (m, 1H), 1.75-1.83 (m, 1H)	--	--
276	DMSO-d ₆	7.46 (t, <i>J</i> =9.25 Hz, 1H), 7.40 (t, <i>J</i> =8.98 Hz, 1H), 4.98-5.07 (m, 2H), 4.35-4.47 (m, 1 H), 3.63-3.73 (m, 2H), 3.56-3.62 (m, 4H), 3.38-3.54 (m, 2H), 3.22-3.37 (m, 2H), 3.17 (br s, 1H), 2.94-3.10 (m, 1H), 2.80 (dd, <i>J</i> =8.14, 12.57 Hz, 1H), 2.06-2.17 (m, 1H), 1.75-1.84 (m, 1H)	--	--
277	DMSO-d ₆	7.46 (dd, <i>J</i> =7.47, 11.13 Hz, 1H), 7.38 (dd, <i>J</i> =7.32, 10.74 Hz, 1H), 4.84-4.94 (m, 2H), 4.35-4.44 (m, 1H), 3.51-3.66 (m, 2H), 3.23-3.41 (m, 2H), 2.94-3.11 (m, 4H), 2.80 (dd, <i>J</i> =8.21, 12.57 Hz, 2H), 2.29-2.47 (m, 1H), 2.02-2.18 (m, 2H), 1.96 (quin, <i>J</i> =6.83 Hz, 1H), 1.75-1.86 (m, 1H)	--	--
278	DMSO-d ₆	7.46 (dd, <i>J</i> =7.47, 11.21 Hz, 1H), 7.37 (dd, <i>J</i> =7.36, 10.78 Hz, 1H), 4.93-5.02 (m, 2H), 4.32-4.44 (m, 1H), 3.24-3.42 (m, 1H), 3.17 (br s, 1H), 3.11 (s, 6H), 2.94-3.06 (m, 1H), 2.88 (s, 1H), 2.79 (dd, <i>J</i> =8.21, 12.65 Hz, 1H), 2.05-2.16 (m, 1H), 1.74-1.84 (m, 1H)	--	--
279	DMSO-d ₆	7.53 (dd, <i>J</i> =7.55, 11.13 Hz, 1H), 7.39 (dd, <i>J</i> =7.43, 11.09 Hz, 1H), 5.51 (q, <i>J</i> =6.98 Hz, 1H), 4.39-4.47 (dt, <i>J</i> =4.13, 7.94 Hz, 1H), 3.07-3.26 (m, 3H), 2.72-2.81 (m, 7H), 2.52-2.56 (m, 1H), 2.10-2.28 (m, 1H), 1.71-1.86 (m, 1H), 1.61 (d, <i>J</i> =7.01 Hz, 3H)	B	SFC: Chiralpak IC analytical column, 15% methanol with 0.2% DEA
280	DMSO-d ₆	7.53 (dd, <i>J</i> =7.55, 11.13 Hz, 1H), 7.39 (dd, <i>J</i> =7.43, 11.09 Hz, 1H), 5.51 (q, <i>J</i> =6.98 Hz, 1H), 4.39-4.47 (dt, <i>J</i> =4.13, 7.94 Hz, 1H), 3.07-3.26 (m, 3H), 2.72-2.81 (m, 7H), 2.52-2.56 (m, 1H), 2.10-2.28 (m, 1H), 1.71-1.86 (m, 1H), 1.61 (d, <i>J</i> =7.01 Hz, 3H)	B	SFC: Chiralpak IC analytical column, 15% methanol with 0.2% DEA

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
281	DMSO-d ₆	7.46 (dd, <i>J</i> =7.47, 11.21 Hz, 1H), 7.37 (dd, <i>J</i> =7.36, 10.78 Hz, 1H), 4.99 (d, <i>J</i> =2.34 Hz, 2H), 4.31-4.39 (m, 1H), 3.40-3.54 (m, 3H), 3.19-3.29 (m, 1H), 2.93-3.04 (m, 2H), 2.78 (dd, <i>J</i> =8.25, 12.53 Hz, 1H), 2.06-2.16 (m, 1H), 1.71-1.83 (m, 3H), 1.54-1.66 (m, 4H), 1.40-1.53 (m, 2H)	--	--
282	DMSO-d ₆	8.31-8.41 (m, 1H), 7.47 (dd, <i>J</i> =7.47, 11.21 Hz, 1H), 7.35 (dd, <i>J</i> =7.28, 10.70 Hz, 1H), 4.61-4.68 (m, 2H), 4.32-4.47 (m, 1H), 3.35-3.45 (m, 1H), 3.11-3.28 (m, 2H), 2.95-3.08 (m, 2H), 2.80 (dd, <i>J</i> =8.68, 12.65 Hz, 1H), 2.03-2.18 (m, 1H), 1.99 (br s, 1H), 1.56-1.91 (m, 1H), 1.06 (t, <i>J</i> =7.24 Hz, 3H)	--	--
283	DMSO-d ₆	8.94 (s, 2H), 7.80 (d, <i>J</i> =1.09 Hz, 1H), 7.55 (d, <i>J</i> =8.39 Hz, 1H), 7.50 (d, <i>J</i> =8.39 Hz, 1H), 5.54-5.62 (m, 2H), 4.44-4.57 (m, 1H), 3.45-3.56 (m, 2H), 3.07-3.13 (m, 1H), 2.81 (dd, <i>J</i> =8.56, 12.92 Hz, 1H), 2.52-2.64 (m, 1H), 2.17 (s, 3H), 1.95-2.10 (m, 1H), 1.70-1.82 (m, 1H)	B	SFC: Chiralpak AD-H analytical column, 30% methanol
284	DMSO-d ₆	8.94 (s, 2H), 7.91 (d, <i>J</i> =1.01 Hz, 1H), 7.46 (dd, <i>J</i> =1.56, 8.25 Hz, 1H), 7.39 (d, <i>J</i> =8.25 Hz, 1H), 5.60 (s, 2H), 4.42-4.57 (m, 1H), 3.47-3.54 (m, 1H), 3.37-3.46 (m, 1H), 3.04-3.11 (m, 1H), 2.79 (dd, <i>J</i> =8.52, 12.81 Hz, 1H), 2.52-2.65 (m, 1H), 2.18 (s, 3H), 1.95-2.11 (m, 1H), 1.71-1.84 (m, 1H)	B	SFC: Chiralpak AD-H analytical column, 30% methanol
285	DMSO-d ₆	7.42 (d, <i>J</i> =8.49 Hz, 1H), 7.38 (d, <i>J</i> =2.02 Hz, 1H), 7.12-7.15 (m, 1H), 4.73-4.80 (m, 2H), 4.57-4.69 (m, 1H), 3.95 (t, <i>J</i> =7.71 Hz, 2H), 3.51-3.56 (m, 1H), 3.31-3.44 (m, 2H), 3.28 (br s, 1H), 3.17 (s, 1H), 2.99-3.10 (m, 1H), 2.95 (br dd, <i>J</i> =9.34, 12.61 Hz, 1H), 2.25-2.32 (m, 2H), 2.06-2.23 (m, 1H), 1.72-1.89 (m, 1H)	B	SFC: Chiralpak IC analytical column, 45% methanol.
286	DMSO-d ₆	7.47 (d, <i>J</i> =1.95 Hz, 1H), 7.25 (d, <i>J</i> =8.49 Hz, 1H), 7.13 (dd, <i>J</i> =1.95, 8.49 Hz, 1H), 4.72-4.79 (m, 2H), 4.58-4.70 (dt, <i>J</i> =4.59, 8.68 Hz, 1H), 4.23-4.29 (m, 1H), 3.94 (t, <i>J</i> =7.71 Hz, 1H), 3.51-3.59 (m, 1H), 3.31-3.47 (m, 2H), 3.28 (br s, 1H), 3.17 (s, 1H), 3.01-3.12 (m, 1H), 2.96 (br dd, <i>J</i> =9.23, 12.65 Hz, 2H), 2.13-2.31 (m, 1H), 1.79-1.89 (m, 1H)	B	SFC: Chiralpak IC analytical column, 45% methanol.
287	DMSO-d ₆	7.77 (d, <i>J</i> =1.01 Hz, 1H), 7.46-7.54 (m, 2H), 4.74-4.86 (m, 3H), 4.25-4.36 (m, 2H), 3.96 (t, <i>J</i> =7.71 Hz, 2H), 3.12-3.29 (m, 3H), 3.01-3.09 (m, 2H), 2.30 (quin, <i>J</i> =7.69 Hz, 2H), 2.01-2.08 (m, 1H), 1.80-1.99 (m, 1H)	B	SFC: Chiralpak IC analytical column, 35% methanol
288	DMSO-d ₆	7.86-7.92 (m, 1H), 7.46-7.52 (m, 1H), 7.33-7.42 (m, 1H), 4.74-4.86 (m, 3H), 4.25-4.36 (m, 2H), 3.96 (t, <i>J</i> =7.71 Hz, 2H), 3.12-3.29 (m, 3H), 3.01-3.09 (m, 2H), 2.30 (quin, <i>J</i> =7.69 Hz, 2H), 2.01-2.08 (m, 1H), 1.80-1.99 (m, 1H)	B	SFC: Chiralpak IC analytical column, 35% methanol

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
289	DMSO-d ₆	8.92 (s, 2H), 7.42 (dd, <i>J</i> =4.87, 8.68 Hz, 1H), 7.11 (dd, <i>J</i> =2.49, 9.26 Hz, 1H), 6.92 (ddd, <i>J</i> =2.57, 8.68, 10.08 Hz, 1H), 5.47-5.56 (m, 2H), 4.26-4.42 (m, 1H), 3.35-3.49 (m, 2H), 2.93-3.03 (m, 1H), 2.82-2.92 (m, 1H), 2.74 (dd, <i>J</i> =8.60, 12.42 Hz, 1H), 1.97-2.12 (m, 1H), 1.64-1.82 (m, 1H)	B	SFC: Chiralcel OD-H, 15% isopropanol
290	DMSO-d ₆	8.92 (s, 2H), 7.24 (dd, <i>J</i> =2.45, 9.77 Hz, 1H), 7.14 (dd, <i>J</i> =4.75, 8.72 Hz, 1H), 6.87 (ddd, <i>J</i> =2.49, 8.70, 9.91 Hz, 1H), 5.51 (d, <i>J</i> =2.10 Hz, 2H), 4.27-4.34 (m, 1H), 3.35-3.44 (m, 2H), 2.98-3.06 (m, 1H), 2.83-2.93 (m, 1H), 2.78 (dd, <i>J</i> =8.60, 12.57 Hz, 1H), 1.99-2.09 (m, 1H), 1.64-1.79 (m, 1H)	B	SFC: Chiralcel OD-H, 15% isopropanol
291	500MHz DMSO-d ₆	8.96 (s, 1H), 8.28 (br dd, <i>J</i> =1.95, 8.17 Hz, 1H), 7.36-7.50 (m, 1H), 7.32 (br d, <i>J</i> =8.04 Hz, 1H), 7.05-7.20 (m, 2H), 6.98-7.05 (m, 1H), 5.47 (s, 2H), 3.3 (m, 1H), 2.83 (br t, <i>J</i> =10.06 Hz, 2H), 2.74 (br s, 1H), 2.60-2.67 (m, 1H), 1.79 (br d, <i>J</i> =8.30 Hz, 1H), 1.66 (br s, 1H), 1.51 (br d, <i>J</i> =10.77 Hz, 1H), 1.15 (br d, <i>J</i> =10.64 Hz, 1H)	--	--
292	500MHz DMSO-d ₆	8.67 (d, <i>J</i> =1.66 Hz, 1H), 8.02 (br d, <i>J</i> =7.98 Hz, 3H), 7.77 (dd, <i>J</i> =1.97, 8.09 Hz, 1H), 7.52 (d, <i>J</i> =7.77 Hz, 1H), 7.13-7.28 (m, 3H), 5.54 (s, 2H), 3.57-3.65 (m, 1H), 3.45 (br s, 1H), 3.30 (br d, <i>J</i> =12.75 Hz, 1H), 3.18 (dd, <i>J</i> =8.50, 12.44 Hz, 1H), 2.98-3.07 (m, 1H), 1.99 (br d, <i>J</i> =9.02 Hz, 1H), 1.83 (br s, 1H), 1.54-1.70 (m, 2H)	--	--
293	500MHz DMSO-d ₆	9.23 (s, 1H), 8.48 (br d, <i>J</i> =5.71 Hz, 1H), 7.95 (br d, <i>J</i> =8.17 Hz, 1H), 7.88 (s, 1H), 7.79 (br d, <i>J</i> =5.58 Hz, 1H), 7.57 (br d, <i>J</i> =8.43 Hz, 1H), 7.44 (br d, <i>J</i> =7.66 Hz, 1H), 7.17 (br d, <i>J</i> =7.91 Hz, 1H), 7.08 (br t, <i>J</i> =7.46 Hz, 1H), 6.97-7.04 (m, 1H), 5.49 (s, 2H), 2.78-2.95 (m, 2H), 2.53-2.72 (m, 2H), 1.82 (br d, <i>J</i> =10.25 Hz, 2H), 1.68 (br s, 1H), 1.61 (br s, 1H), 1.18 (br d, <i>J</i> =9.73 Hz, 1H)	--	--
294	500MHz DMSO-d ₆	8.05 (s, 1H), 7.67 (br d, <i>J</i> =7.92 Hz, 1H), 7.46 (br d, <i>J</i> =7.78 Hz, 1H), 7.08 (br t, <i>J</i> =6.75 Hz, 1H), 6.92-7.03 (m, 3H), 6.59 (br d, <i>J</i> =6.88 Hz, 1H), 5.83-5.96 (m, 2H), 4.32 (s, 3H), 3.37-3.59 (m, 1H), 2.86-2.99 (m, 1H), 2.82 (br s, 1H), 2.53-2.76 (m, 1H), 1.78 (br s, 2H), 1.65 (br s, 1H), 1.58 (br s, 1H), 1.19 (br d, <i>J</i> =9.99 Hz, 1H)	--	--
295	500MHz DMSO-d ₆	9.03 (s, 1H), 8.29 (br d, <i>J</i> =6.74 Hz, 1H), 7.36-7.51 (m, 2H), 6.99-7.12 (m, 1H), 6.94 (d, <i>J</i> =3.94 Hz, 2H), 5.82-5.99 (m, 1H), 4.03 (q, <i>J</i> =7.15 Hz, 1H), 3.39 (br d, <i>J</i> =10.78 Hz, 1H), 3.17 (br d, <i>J</i> =12.65 Hz, 1H), 2.81-3.05 (m, 2H), 1.75-1.95 (m, 4H), 1.54-1.70 (m, 1H), 1.31-1.47 (m, 1H), 1.17 (t, <i>J</i> =7.10 Hz, 1H)	B	SFC: Chiralpak IC, 20% methanol w/ 0.2% DEA

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
296	500MHz DMSO-d ₆	9.04 (d, <i>J</i> =1.55 Hz, 1H), 8.24-8.31 (m, 1H), 7.36-7.48 (m, 2H), 7.01-7.09 (m, 1H), 6.89-6.99 (m, 2H), 5.83-5.96 (m, 1H), 3.35-3.53 (m, 2H), 3.21 (br d, <i>J</i> =12.13 Hz, 1H), 3.12 (br s, 1H), 2.77-3.02 (m, 2H), 1.75-1.95 (m, 1H), 1.67 (br d, <i>J</i> =9.23 Hz, 1H), 1.29-1.46 (m, 1H).	B	SFC: Chiralpak IC, 20% methanol w/ 0.2% DEA
297	500MHz DMSO-d ₆	9.03 (d, <i>J</i> =1.55 Hz, 1H), 8.80 (br s, 3H), 8.36 (dd, <i>J</i> =2.07, 8.29 Hz, 1H), 7.66 (br d, <i>J</i> =8.29 Hz, 1H), 7.56 (d, <i>J</i> =7.98 Hz, 1H), 7.39 (br s, 1H), 7.00-7.15 (m, 2H), 6.04 (q, <i>J</i> =6.77 Hz, 1H), 4.92-5.05 (m, 1H), 3.84 (br d, <i>J</i> =12.75 Hz, 1H), 3.75 (br s, 1H), 3.62-3.71 (m, 1H), 3.32-3.54 (m, 1H), 3.06-3.30 (m, 1H), 2.77-3.05 (m, 1H), 2.53-2.75 (m, 1H), 2.27-2.47 (m, 1H), 1.91-2.02 (m, 4H).	B	SFC: Chiralpak IC, 20% methanol w/ 0.2% DEA
298	500MHz DMSO-d ₆	9.02 (d, <i>J</i> =1.45 Hz, 1H), 8.80 (br s, 3H), 8.35 (dd, <i>J</i> =2.18, 8.29 Hz, 1H), 7.63 (d, <i>J</i> =7.56 Hz, 1H), 7.58 (d, <i>J</i> =7.48 Hz, 1H), 7.20-7.29 (m, 1H), 7.03-7.15 (m, 2H), 6.01 (q, <i>J</i> =6.91 Hz, 1H), 4.90-5.02 (m, 1H), 3.91 (s, 1H), 3.87 (br s, 1H), 3.65-3.81 (m, 1H), 3.59-3.64 (m, 1H), 3.26 (br t, <i>J</i> =11.25 Hz, 1H), 2.32 (br d, <i>J</i> =3.84 Hz, 1H), 2.01 (d, <i>J</i> =7.05 Hz, 4H).	B	SFC: Chiralpak IC, 20% methanol w/ 0.2% DEA
299	500MHz DMSO-d ₆	9.07 (d, <i>J</i> =1.55 Hz, 1H), 8.36-8.52 (m, 4H), 7.84 (d, <i>J</i> =8.19 Hz, 1H), 7.63 (d, <i>J</i> =7.98 Hz, 1H), 7.28-7.39 (m, 1H), 7.21 (br d, <i>J</i> =3.63 Hz, 2H), 5.90 (br dd, <i>J</i> =4.77, 10.47 Hz, 1H), 4.02 (br d, <i>J</i> =14.10 Hz, 1H), 3.89 (br s, 1H), 3.59-3.81 (m, 1H), 3.33-3.54 (m, 2H), 3.10-3.32 (m, 2H), 2.56 (br dd, <i>J</i> =7.20, 13.73 Hz, 1H), 2.31 (qd, <i>J</i> =7.03, 10.63 Hz, 1H), 2.08 (br s, 1H), 1.96-2.05 (m, 1H), 1.74 (br d, <i>J</i> =8.60 Hz, 1H), 1.60 (br d, <i>J</i> =4.35 Hz, 1H), 0.59 (br t, <i>J</i> =7.15 Hz, 3H).	B	SFC: Chiralpak IC, 25% methanol w/ 0.2% DEA
300	500MHz DMSO-d ₆	9.06 (d, <i>J</i> =1.56 Hz, 1H), 8.51 (br s, 3H), 8.38-8.48 (m, 1H), 7.79 (br d, <i>J</i> =8.40 Hz, 1H), 7.61 (d, <i>J</i> =8.09 Hz, 1H), 7.26-7.34 (m, 1H), 7.13-7.22 (m, 2H), 5.71 (br dd, <i>J</i> =5.65, 9.80 Hz, 1H), 3.67-3.78 (m, 1H), 3.42-3.50 (m, 1H), 3.16 (s, 1H), 3.10 (br s, 1H), 2.55-2.69 (m, 1H), 2.26-2.45 (m, 2H), 1.98-2.12 (m, 1H), 1.86 (br s, 2H), 1.65 (br s, 1H), 1.10-1.31 (m, 1H), 0.64-0.71 (m, 3H).	B	SFC: Chiralpak IC, 25% methanol w/ 0.2% DEA
301	500MHz DMSO-d ₆	8.87 (s, 2H), 8.40 (br s, 2H), 7.53 (dd, <i>J</i> =7.43, 11.02 Hz, 1H), 7.39 (t, <i>J</i> =8.98 Hz, 1H), 5.50-5.60 (m, 2H), 4.72-4.84 (m, 1H), 3.62-3.75 (m, 1H), 3.42-3.59 (m, 1H), 3.17-3.29 (m, 1H), 2.95-3.08 (m, 2H), 2.13-2.20 (m, 1H), 1.73-1.82 (m, 1H).	--	--
302	500MHz DMSO-d ₆	7.85 (s, 1H), 7.77 (d, <i>J</i> =7.71 Hz, 1H), 7.49-7.56 (m, 2H), 7.44 (d, <i>J</i> =8.32 Hz, 1H), 7.20 (t, <i>J</i> =8.97 Hz, 1H), 5.83 (q, <i>J</i> =7.08 Hz, 1H), 4.36-4.46 (m, 1H), 4.03-4.16 (m, 1H), 3.35-3.39 (m, 1H), 3.14-3.19 (m, 1H), 2.99-3.13 (m, 1H), 2.78-2.92 (m, 1H), 2.08-2.20 (m, 1H), 1.76-1.94 (m, 4H).	--	--

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
303	500MHz DMSO-d ₆	8.88 (s, 2H), 7.50 (dd, <i>J</i> =7.43, 11.09 Hz, 1H), 7.38 (t, <i>J</i> =8.94 Hz, 1H), 5.49-5.58 (m, 2H), 4.45- 4.54 (dt, <i>J</i> =4.55, 8.66 Hz, 1H), 3.43-3.61 (m, 1H), 3.38-3.42 (m, 1H), 3.05-3.24 (m, 1H), 2.95-3.03 (m, 1H), 2.86 (dd, <i>J</i> =9.19, 12.61 Hz, 1H), 1.98-2.11 (m, 1H), 1.66-1.76 (m, 1H)	--	--
304	500MHz DMSO-d ₆	8.50 (d, <i>J</i> =2.88 Hz, 1H), 7.73 (dt, <i>J</i> =2.96, 8.72 Hz, 1H), 7.48 (dd, <i>J</i> =7.47, 11.21 Hz, 1H), 7.30-7.38 (m, 2H), 5.36-5.43 (m, 2H), 4.65-4.82 (m, 1H), 6 3.16-3.29 (m, 2H), 3.04-3.14 (m, 1H), 2.88-3.00 (m, 2H), 1.94-2.01 (m, 1H), 1.80-1.92 (m, 1H).	--	--
305	500MHz DMSO-d ₆	8.88 (s, 2H), 7.65 (s, 1H), 7.58 (d, <i>J</i> =8.43 Hz, 1H), 7.41 (dd, <i>J</i> =1.25, 8.33 Hz, 1H), 5.59-5.67 (m, 2H), 4.66-4.73 (m, 1H), 3.24-3.30 (m, 2H), 3.07-3.18 (m, 1H), 2.83-2.99 (m, 2H), 1.92-2.00 (m, 1H), 1.75-1.90 (m, 1H).	B	SFC: Chiralpak AD-H, 25% methanol
306	500MHz DMSO-d ₆	8.88 (s, 2H), 7.75 (s, 1H), 7.36 (s, 2H), 5.55-5.64 (m, 2H), 4.70-4.76-4.81 (m, 1H), 3.24-3.31 (m, 2H), 3.08-3.18 (m, 1H), 2.86-3.00 (m, 2H), 1.93-2.03 (m, 1H), 1.76-1.92 (m, 1H).	B	SFC: Chiralpak AD-H, 25% methanol
307	500MHz DMSO-d ₆	8.46-8.51 (m, 1H), 7.74 (t, <i>J</i> =8.73 Hz, 1H), 7.51 (t, <i>J</i> =9.21 Hz, 1H), 7.41 (d, <i>J</i> =8.81 Hz, 1H), 7.34 (t, <i>J</i> =9.19 Hz, 1H), 5.40-5.47 (m, 2H), 3.50 (br d, <i>J</i> =12.46 Hz, 1H), 3.15-3.23 (m, 1H), 3.10 (td, <i>J</i> =4.45, 16.87 Hz, 1H), 2.97-3.02 (m, 1H), 2.52-2.59 (m, 1H), 2.18-2.29 (m, 1H), 1.98-2.11 (m, 1H).	--	--
308	500MHz DMSO-d ₆	7.63 (s, 1H), 7.56 (d, <i>J</i> =8.25 Hz, 1H), 7.41 (dd, <i>J</i> =1.28, 8.29 Hz, 1H), 4.76-4.89 (m, 3H), 4.26-4.33 (m, 2H), 3.96 (t, <i>J</i> =7.75 Hz, 2H), 3.15-3.29 (m, 2H), 2.97-3.13 (m, 2H), 2.30 (td, <i>J</i> =7.66, 15.43 Hz, 2H), 1.90-2.09 (m, 1H)	B	SFC: Chiralpak IC, 15% methanol.
309	500MHz DMSO-d ₆	7.73 (s, 1H), 7.41 (s, 2H), 4.75-4.88 (m, 3H), 4.24-4.34 (m, 2H), 3.95 (t, <i>J</i> =7.71 Hz, 2H), 3.14-3.28 (m, 3H), 2.98-3.12 (m, 2H), 2.29 (td, <i>J</i> =7.69, 15.45 Hz, 2H), 1.91-2.09 (m, 2H)	B	SFC: Chiralpak IC, 15% methanol.
310	500MHz DMSO-d ₆	7.45 (dd, <i>J</i> =7.47, 11.13 Hz, 1H), 7.37 (dd, <i>J</i> =7.32, 10.74 Hz, 1H), 4.77-4.86 (m, 2H), 4.32-4.46 (m, 1H), 3.59-3.67 (m, 2H), 2.94-3.12 (m, 2H), 2.78 (dd, <i>J</i> =8.29, 12.57 Hz, 1H), 2.00-2.13 (m, 1H), 1.84-1.94 (m, 3H), 1.71-1.84 (m, 4H), 1.35 (d, <i>J</i> =2.96 Hz, 6H).	--	--
311	500MHz MeOD	8.86 (s, 1H), 8.14-8.20 (m, 1H), 7.48 (br dd, <i>J</i> =5.06, 8.69 Hz, 1H), 7.43 (br d, <i>J</i> =8.30 Hz, 1H), 6.93-7.01 (m, 2H), 5.46-5.58 (m, 2H), 3.94-4.01 (m, 1H), 3.34-3.48 (m, 3H), 3.20-3.26 (m, 1H), 3.09 (br dd, <i>J</i> =5.32, 12.07 Hz, 1H), 1.87 (q, <i>J</i> =5.71 Hz, 2H)	B	Cel2, 20% MeOH, 0.2% DEA, peak 1

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
312	500MHz MeOD	8.86 (s, 1H), 8.16 (br dd, J=1.95, 8.17 Hz, 1H), 7.42 (br d, J=8.56 Hz, 1H), 7.21 (br dd, J=2.34, 9.34 Hz, 1H), 7.11 (br dd, J=4.54, 8.69 Hz, 1H), 6.86-6.94 (m, 1H), 5.48-5.58 (m, 2H), 3.95-4.06 (m, 1H), 3.35-3.52 (m, 3H), 3.11-3.20 (m, 1H), 1.81-1.92 (m, 2H)	B	Cel2, 20% MeOH, 0.2% DEA, peak 2
313	400MHz d ₆ -DMSO	8.45 (br s, 2H), 7.89 (d, J=8.40 Hz, 2H), 7.55-7.64 (m, 3H), 7.31 (t, J=7.62 Hz, 1H), 7.18 (t, J=7.62 Hz, 1H), 7.08 (d, J=8.19 Hz, 1H), 5.98 (q, J=6.98 Hz, 1H), 3.64-3.74 (m, 2H), 3.44-3.51 (m, 1H), 3.31-3.38 (m, 1H), 3.11-3.20 (m, 1H), 1.96-2.05 (m, 2H), 1.93 (d, J=7.05 Hz, 3H), 1.64-1.79 (m, 2H)	B	Chiralpak IC, 30% IPA Peak 1
314	400MHz d ₆ -DMSO	8.40 (br s, 3H), 7.85 (d, J=8.50 Hz, 2H), 7.55-7.61 (m, 1H), 7.52 (d, J=8.29 Hz, 2H), 7.25 (br t, J=7.62 Hz, 1H), 7.04-7.15 (m, 2H), 5.89 (q, J=7.05 Hz, 1H), 3.72-3.78 (m, 2H), 3.31-3.38 (m, 2H), 3.13-3.22 (m, 1H), 2.02-2.08 (m, 1H), 2.00 (d, J=7.05 Hz, 3H), 1.89-1.97 (m, 1H), 1.62-1.79 (m, 2H)	B	Chiralpak IC, 30% IPA Peak 2
315	400MHz d ₆ -DMSO	8.43 (br s, 3H), 7.97 (dd, J=1.14, 10.06 Hz, 1H), 7.70 (d, J=7.59 Hz, 1H), 7.58 (d, J=7.88 Hz, 1H), 7.39-7.48 (m, 1H), 7.23-7.38 (m, 3H), 5.52-5.65 (m, 2H), 3.79 (br d, J=10.16 Hz, 1H), 3.34-3.51 (m, 3H), 3.11-3.22 (m, 1H), 1.95-2.04 (m, 1H), 1.83-1.95 (m, 1H), 1.58-1.75 (m, 2H)	--	--
316	400MHz d ₆ -DMSO	8.55 (br s, 3H), 7.60 (d, J=7.77 Hz, 1H), 7.45 (d, J=7.92 Hz, 2H), 7.27-7.39 (m, 5H), 5.47-5.62 (m, 2H), 3.92 (br d, J=10.37 Hz, 1H), 3.64-3.74 (m, 1H), 3.41-3.53 (m, 2H), 3.18-3.29 (m, 1H), 1.96-2.05 (m, 1H), 1.86-1.96 (m, 1H), 1.57-1.76 (m, 2H)	--	--
317	400MHz d ₆ -DMSO	8.67 (br s, 3H), 7.87 (d, J=8.40 Hz, 2H), 7.51-7.62 (m, 3H), 7.26 (t, J=7.00 Hz, 1H), 7.04-7.17 (m, 2H), 5.94-6.01 (m, 1H), 5.10-5.30 (m, 1H), 3.84-3.97 (m, 1H), 3.57-3.68 (m, 2H), 3.23-3.37 (m, 2H), 2.18-2.29 (m, 1H), 2.07-2.18 (m, 1H), 1.95 (d, J=7.05 Hz, 3H)	B	Chiralpak IC, 25% IPA Peak 1
318	400MHz d ₆ -DMSO	8.85 (br s, 3H), 7.85 (d, J=8.40 Hz, 2H), 7.52-7.63 (m, 3H), 7.22-7.35 (m, 1H), 7.06-7.18 (m, 2H), 5.94 (q, J=7.05 Hz, 1H), 5.13-5.34 (m, 1H), 3.83-4.00 (m, 1H), 3.72-3.80 (m, 1H), 3.51-3.61 (m, 1H), 3.40 (br s, 2H), 2.24 (br d, J=2.38 Hz, 2H), 1.99-2.05 (m, 3H)	B	Chiralpak IC, 25% IPA Peak 2
319	400MHz d ₆ -DMSO	8.83 (br s, 3H), 7.87 (d, J=8.40 Hz, 2H), 7.53-7.62 (m, 3H), 7.28 (t, J=7.06 Hz, 1H), 7.14 (t, J=7.77 Hz, 1H), 7.05 (d, J=8.09 Hz, 1H), 5.98 (q, J=6.88 Hz, 1H), 4.89-5.11 (m, 1H), 3.87 (br d, J=12.75 Hz, 1H), 3.78 (br d, J=6.84 Hz, 1H), 3.42-3.61 (m, 2H), 3.18-3.29 (m, 1H), 2.29-2.38 (m, 1H), 1.98-2.07 (m, 1H), 1.95 (d, J=6.95 Hz, 3H)	B	Chiralpak IC, 25% IPA Peak 1

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
320	400MHz d ₆ - DMSO	8.86 (br s, 3H), 7.85 (d, <i>J</i> =8.40 Hz, 2H), 7.50-7.61 (m, 3H), 7.25 (t, <i>J</i> =7.52 Hz, 1H), 7.04-7.15 (m, 2H), 5.94 (q, <i>J</i> =6.81 Hz, 1H), 4.87-5.09 (m, 1H), 3.91 (br d, <i>J</i> =12.75 Hz, 1H), 3.79 (br s, 1H), 3.47-3.55 (m, 1H), 3.35-3.44 (m, 1H), 3.22-3.31 (m, 1H), 2.27-2.38 (m, 1H), 2.02-2.08 (m, 1H), 1.99 (d, <i>J</i> =7.15 Hz, 3H)	B	Chiralpak IC, 25% IPA Peak 2
321	400MHz d ₆ - DMSO	8.48 (br s, 3H), 8.21 (d, <i>J</i> =1.45 Hz, 1H), 7.84 (dd, <i>J</i> =1.45, 8.09 Hz, 1H), 7.61 (d, <i>J</i> =7.98 Hz, 1H), 7.31-7.45 (m, 2H), 7.19-7.29 (m, 2H), 5.45-5.60 (m, 2H), 3.73-3.82 (m, 1H), 3.42-3.54 (m, 2H), 3.34 (br d, <i>J</i> =13.06 Hz, 1H), 3.17 (br t, <i>J</i> =9.43 Hz, 1H), 1.95-2.06 (m, 1H), 1.83-1.94 (m, 1H), 1.59-1.78 (m, 2H)	--	--
322	600MHz DMSO- d ₆	7.91 (d, <i>J</i> =8.49 Hz, 2H), 7.48-7.56 (m, 2H), 7.19 (dd, <i>J</i> =7.32, 10.90 Hz, 1H), 5.88 (q, <i>J</i> =7.06 Hz, 1H), 4.32-4.48 (m, 1H), 3.35-3.41 (m, 1H), 3.24-3.28 (m, 1H), 3.17-3.22 (m, 3H), 2.99-3.09 (m, 1H), 2.87 (dd, <i>J</i> =8.52, 12.50 Hz, 1H), 2.51-2.57 (m, 1H), 2.08-2.19 (m, 1H), 1.98 (br d, <i>J</i> =7.08 Hz, 1H), 1.74-1.90 (m, 1H)	B	SFC: Chiralcel OJ-H, 15% methanol.
323	600MHz DMSO- d ₆	7.90 (d, <i>J</i> =7.91 Hz, 2H), 7.47-7.56 (m, 2H), 7.20 (dd, <i>J</i> =7.28, 10.86 Hz, 1H), 5.88 (q, <i>J</i> =7.06 Hz, 1H), 4.32-4.41 (m, 1H), 3.36-3.43 (m, 1H), 3.16-3.27 (m, 1H), 2.99-3.13 (m, 1H), 2.80 (dd, <i>J</i> =8.56, 12.46 Hz, 1H), 2.51-2.62 (m, 1H), 2.08-2.26 (m, 1H), 1.93 (d, <i>J</i> =7.16 Hz, 3H), 1.79-1.91 (m, 1H)	B	SFC: Chiralcel OJ-H, 15% methanol.
324	600MHz DMSO- d ₆	7.74 (d, <i>J</i> =7.73 Hz, 1H), 7.42-7.52 (m, 3H), 7.33-7.41 (m, 2H), 5.87 (q, <i>J</i> =7.14 Hz, 1H), 4.31-4.42 (m, 1H), 3.20-3.27 (m, 1H), 3.17 (s, 1H), 2.91-3.00 (m, 2H), 2.78 (dd, <i>J</i> =8.88, 12.30 Hz, 1H), 1.99-2.14 (m, 1H), 1.94 (d, <i>J</i> =7.24 Hz, 4H), 1.69-1.87 (m, 1H)	B	SFC: Chiralpak AD-H, 10% methanol.
325	600MHz DMSO- d ₆	7.72 (d, <i>J</i> =8.01 Hz, 1H), 7.51 (dd, <i>J</i> =7.67, 11.09 Hz, 1H), 7.41-7.46 (m, 2H), 7.32-7.40 (m, 2H), 5.87 (q, <i>J</i> =7.11 Hz, 1H), 4.31-4.41 (m, 1H), 3.25-3.40 (m, 1H), 3.17 (s, 1H), 3.11 (br d, <i>J</i> =12.61 Hz, 1H), 2.92-3.07 (m, 1H), 2.74 (dd, <i>J</i> =8.99, 12.34 Hz, 1H), 2.01-2.17 (m, 1H), 1.94 (d, <i>J</i> =7.16 Hz, 4H), 1.71-1.89 (m, 1H)	B	SFC: Chiralpak AD-H, 10% methanol.
326	600MHz DMSO- d ₆	7.52 (dd, <i>J</i> =7.63, 11.06 Hz, 1H), 7.33-7.39 (m, 3H), 7.19 (dd, <i>J</i> =7.28, 10.94 Hz, 1H), 7.08-7.15 (m, 1H), 5.74-5.82 (m, 1H), 4.34-4.45 (m, 1H), 3.35-3.42 (m, 1H), 2.97-3.08 (m, 2H), 2.86 (dd, <i>J</i> =8.68, 12.42 Hz, 1H), 2.05-2.20 (m, 1H), 1.78-1.96 (m, 5H)	B	SFC: Chiralpak AD-H, 10% methanol.

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
327	600MHz DMSO-d ₆	7.52 (dd, <i>J</i> =7.59, 11.09 Hz, 1H), 7.34-7.38 (m, 3H), 7.19 (dd, <i>J</i> =7.32, 10.90 Hz, 1H), 7.08-7.16 (m, 1H), 5.73-5.82 (m, 1H), 4.35-4.45 (m, 1H), 3.34-3.43 (m, 2H), 3.21-3.28 (m, 1H), 3.00-3.10 (m, 1H), 2.81 (dd, <i>J</i> =8.52, 12.42 Hz, 1H), 2.07-2.21 (m, 1H), 1.78-1.96 (m, 5H)	B	SFC: Chiralpak AD-H, 10% methanol.
328	600MHz DMSO-d ₆	7.77 (s, 1H), 7.41-7.54 (m, 4H), 5.83 (q, <i>J</i> =7.14 Hz, 1H), 4.28-4.40 (m, 1H), 3.10 (br d, <i>J</i> =12.38 Hz, 1H), 2.90-3.04 (m, 2H), 2.72 (dd, <i>J</i> =8.87, 12.30 Hz, 1H), 2.00-2.16 (m, 1H), 1.95 (d, <i>J</i> =7.16 Hz, 3H), 1.68-1.87 (m, 2H)	B	SFC: Chiralcel OD-H column, 10% isopropanol.
329	600MHz DMSO-d ₆	7.79 (s, 1H), 7.42-7.54 (m, 4H), 5.84 (q, <i>J</i> =7.14 Hz, 1H), 4.27-4.41 (m, 1H), 3.16-3.27 (m, 1H), 2.87-3.00 (m, 2H), 2.78 (dd, <i>J</i> =9.03, 12.38 Hz, 1H), 2.00-2.13 (m, 1H), 1.95 (d, <i>J</i> =7.16 Hz, 3H), 1.69-1.86 (m, 2H)	B	SFC: Chiralcel OD-H column, 10% isopropanol.
330	600MHz DMSO-d ₆	7.75-7.80 (m, 1H), 7.48 (dd, <i>J</i> =7.63, 11.06 Hz, 1H), 7.26 (dd, <i>J</i> =7.28, 11.02 Hz, 1H), 7.14-7.20 (m, 2H), 5.89 (q, <i>J</i> =6.95 Hz, 1H), 4.40-4.47 (m, 1H), 4.33-4.39 (m, 1H), 3.27-3.30 (m, 2H), 2.94-3.01 (m, 2H), 2.86 (dd, <i>J</i> =8.95, 12.46 Hz, 1H), 2.02-2.14 (m, 1H), 1.85-2.00 (m, 5H)	B	SFC: 15 Chiralpak AD-H, 15% isopropanol
331	600MHz DMSO-d ₆	7.74-7.82 (m, 1H), 7.48 (dd, <i>J</i> =7.67, 11.09 Hz, 1H), 7.26 (dd, <i>J</i> =7.32, 11.05 Hz, 1H), 7.14-7.20 (m, 2H), 5.88 (q, <i>J</i> =7.11 Hz, 1H), 4.34-4.48 (m, 1H), 3.28-3.39 (m, 1H), 3.23 (br dd, <i>J</i> =5.41, 7.43 Hz, 2H), 3.03-3.13 (m, 1H), 2.78 (dd, <i>J</i> =8.37, 12.42 Hz, 1H), 2.07-2.22 (m, 1H), 1.94 (d, <i>J</i> =7.16 Hz, 3H), 1.64-1.86 (m, 1H)	B	SFC: 15 Chiralpak AD-H, 15% isopropanol
332	600MHz DMSO-d ₆	7.57 (s, 1H), 7.59 (d, <i>J</i> =11.19 Hz, 1H), 7.52 (dd, <i>J</i> =7.59, 11.09 Hz, 1H), 7.26 (dd, <i>J</i> =7.28, 10.94 Hz, 1H), 7.10 (d, <i>J</i> =8.54 Hz, 1H), 5.77 (q, <i>J</i> =7.16 Hz, 1H), 4.32-4.45 (m, 1H), 3.24-3.38 (m, 1H), 2.96-3.09 (m, 2H), 2.85 (dd, <i>J</i> =8.56, 12.46 Hz, 1H), 2.05-2.21 (m, 1H), 1.77-1.94 (m, 5H)	B	SFC: Chiralpak AD-H 25 cm column, 20% isopropanol
333	600MHz DMSO-d ₆	7.51-7.61 (m, 3H), 7.26 (t, <i>J</i> =9.06 Hz, 1H), 7.10 (d, <i>J</i> =8.29 Hz, 1H), 5.74-5.81 (m, 1H), 4.31-4.45 (m, 1H), 3.21-3.28 (m, 1H), 2.98-3.12 (m, 2H), 2.80 (dd, <i>J</i> =8.49, 12.46 Hz, 1H), 2.09-2.20 (m, 1H), 1.78-1.93 (m, 5H)	B	SFC: Chiralpak AD-H 25 cm column, 20% isopropanol
334	600MHz DMSO-d ₆	7.62 (ddd, <i>J</i> =3.15, 5.99, 9.15 Hz, 1H), 7.48 (dd, <i>J</i> =7.59, 11.09 Hz, 1H), 7.35 (dd, <i>J</i> =7.32, 11.05 Hz, 1H), 7.13-7.25 (m, 2H), 5.91 (q, <i>J</i> =7.14 Hz, 1H), 4.32-4.44 (m, 1H), 3.25-3.29 (m, 1H), 2.92-3.03 (m, 2H), 2.87 (dd, <i>J</i> =8.84, 12.26 Hz, 1H), 1.99-2.14 (m, 1H), 1.86-1.96 (m, 5H), 1.83 (br s, 1H)	B	SFC: Chiralpak AD-H, 15% isopropanol.

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
335	600MHz DMSO-d ₆	7.72 (d, <i>J</i> =8.17 Hz, 2H), 7.53 (dd, <i>J</i> =7.55, 10.90 Hz, 1H), 7.45 (br d, <i>J</i> =7.08 Hz, 2H), 7.17 (t, <i>J</i> =8.84 Hz, 1H), 5.87 (q, <i>J</i> =6.95 Hz, 1H), 4.31-4.40 (m, 1H), 3.35-3.41 (m, 2H), 3.21-3.26 (m, 1H), 3.17 (s, 1H), 2.97-3.10 (m, 2H), 2.77-2.94 (m, 1H), 2.02-2.18 (m, 1H), 1.93 (d, <i>J</i> =7.16 Hz, 3H), 1.72-1.90 (m, 3H)	B	SFC: Chiralpak AD-H, 15% isopropanol.
336	600MHz DMSO-d ₆	7.72 (d, <i>J</i> =8.17 Hz, 2H), 7.53 (dd, <i>J</i> =7.55, 10.90 Hz, 1H), 7.45 (br d, <i>J</i> =7.08 Hz, 2H), 7.17 (t, <i>J</i> =8.84 Hz, 1H), 5.87 (q, <i>J</i> =6.95 Hz, 1H), 4.31-4.45 (m, 1H), 3.21-3.26 (m, 1H), 3.17 (s, 1H), 2.97-3.10 (m, 1H), 2.77-2.94 (m, 1H), 2.02-2.18 (m, 1H), 1.93 (d, <i>J</i> =7.16 Hz, 3H), 1.72-1.90 (m, 2H)	B	SFC: Regis Whelk-O s.s, 15% methanol.
337	600MHz DMSO-d ₆	7.51 (dd, <i>J</i> =7.59, 10.78 Hz, 1H), 7.32-7.39 (m, 4H), 7.15 (dd, <i>J</i> =7.32, 10.90 Hz, 1H), 5.81 (q, <i>J</i> =7.08 Hz, 1H), 4.34-4.45 (m, 1H), 3.22-3.39 (m, 1H), 2.96-3.12 (m, 2H), 2.77-2.94 (m, 1H), 2.07-2.19 (m, 1H), 1.78-1.93 (m, 5H)	B	SFC: Regis Whelk-O s.s, 15% methanol.
338	600MHz DMSO-d ₆	8.87 (s, 2H), 7.48 (dd, <i>J</i> =7.47, 11.13 Hz, 1H), 7.37 (dd, <i>J</i> =7.32, 10.74 Hz, 1H), 5.39-5.55 (m, 2H), 4.68-4.77 (m, 1H), 3.14-3.28 (m, 1H), 3.01-3.11 (m, 1H), 2.83-2.94 (m, 2H), 1.88-2.01 (m, 1H), 1.69-1.87 (m, 1H), 1.63 (br s, 1H)	B	--
339	600MHz DMSO-d ₆	8.50 (d, <i>J</i> =2.88 Hz, 1H), 7.73 (dt, <i>J</i> =2.96, 8.72 Hz, 1H), 7.48 (dd, <i>J</i> =7.47, 11.21 Hz, 1H), 7.30-7.38 (m, 2H), 5.36-5.43 (m, 2H), 4.75-4.82 (m, 1H), 4.65-4.74 (m, 1H), 3.16-3.29 (m, 1H), 3.04-3.14 (m, 1H), 2.88-3.00 (m, 2H), 1.94-2.01 (m, 1H), 1.80-1.92 (m, 1H), 1.59 (br s, 1H)	B	--
340	600MHz DMSO-d ₆	8.12 (d, <i>J</i> =2.26 Hz, 1H), 7.71 (dd, <i>J</i> =2.26, 8.49 Hz, 1H), 7.54 (dd, <i>J</i> =7.47, 11.06 Hz, 1H), 7.36 (t, <i>J</i> =8.91 Hz, 1H), 6.97 (d, <i>J</i> =8.56 Hz, 1H), 5.45-5.54 (m, 3H), 4.36-4.43 (m, 1H), 4.28-4.35 (m, 1H), 3.27-3.35 (m, 1H), 3.17 (s, 1H), 2.99-3.07 (m, 1H), 2.86-2.98 (m, 1H), 2.76 (dd, <i>J</i> =8.68, 12.57 Hz, 1H), 2.01-2.17 (m, 1H), 1.66-1.82 (m, 1H)	B	--
341	600MHz DMSO-d ₆	8.12 (d, <i>J</i> =2.26 Hz, 1H), 7.71 (dd, <i>J</i> =2.26, 8.49 Hz, 1H), 7.54 (dd, <i>J</i> =7.47, 11.06 Hz, 1H), 7.36 (t, <i>J</i> =8.91 Hz, 1H), 6.97 (d, <i>J</i> =8.56 Hz, 1H), 5.45-5.54 (m, 2H), 4.28-4.43 (m, 1H), 3.27-3.35 (m, 1H), 3.17 (s, 1H), 2.99-3.07 (m, 1H), 2.86-2.98 (m, 1H), 2.76 (dd, <i>J</i> =8.68, 12.57 Hz, 1H), 2.01-2.17 (m, 1H), 1.66-1.82 (m, 1H)	B	--
342	600MHz DMSO-d ₆	7.80 (s, 1H), 7.65 (dd, <i>J</i> =1.44, 7.98 Hz, 1H), 7.49-7.57 (m, 1H), 7.38 (s, 1H), 7.32 (dd, <i>J</i> =7.24, 10.67 Hz, 1H), 6.97 (d, <i>J</i> =8.02 Hz, 1H), 5.33-5.40 (m, 2H), 4.29-4.42 (m, 1H), 3.36-3.45 (m, 1H), 3.16-3.28 (m, 1H), 2.98-3.05 (m, 1H), 2.86-2.95 (m, 1H), 2.76 (dd, <i>J</i> =8.72, 12.61 Hz, 1H), 1.98-2.10 (m, 1H), 1.65-1.79 (m, 1H)	B	--

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
343	600MHz DMSO-d ₆	7.51-7.59 (m, 2H), 7.44 (dd, <i>J</i> =2.57, 8.56 Hz, 1H), 7.37 (dd, <i>J</i> =7.28, 10.70 Hz, 1H), 6.89 (d, <i>J</i> =2.49 Hz, 1H), 5.31-5.38 (m, 2H), 4.29-4.41 (m, 1H), 3.35-3.46 (m, 1H), 3.25-3.29 (m, 1H), 2.99-3.05 (m, 1H), 2.85-2.96 (m, 1H), 2.77 (dd, <i>J</i> =8.64, 12.53 Hz, 1H), 1.91-2.09 (m, 1H), 1.65-1.76 (m, 1H)	B	--
344	600MHz DMSO-d ₆	7.48-7.56 (m, 3H), 7.39 (dd, <i>J</i> =7.32, 10.67 Hz, 1H), 7.24 (d, <i>J</i> =8.25 Hz, 2H), 5.33-5.42 (m, 2H), 4.31-4.43 (m, 1H), 3.43 (ddd, <i>J</i> =3.39, 7.07, 8.86 Hz, 1H), 3.36-3.39 (m, 1H), 3.17 (d, <i>J</i> =4.75 Hz, 1H), 2.92-3.08 (m, 1H), 2.81 (dd, <i>J</i> =8.56, 12.61 Hz, 1H), 1.98-2.11 (m, 1H), 1.93 (t, <i>J</i> =18.84 Hz, 3H), 1.63-1.87 (m, 1H)	B	--
345	600MHz DMSO-d ₆	7.74 (s, 1H), 7.52-7.60 (m, 2H), 7.22 (dd, <i>J</i> =7.36, 10.63 Hz, 1H), 6.68 (d, <i>J</i> =8.02 Hz, 1H), 5.31-5.40 (m, 2H), 4.09-4.41 (m, 1H), 3.36-3.45 (m, 1H), 3.15-3.24 (m, 1H), 3.00-3.07 (m, 1H), 2.87-2.98 (m, 1H), 2.78 (dd, <i>J</i> =8.33, 12.61 Hz, 1H), 2.34-2.39 (m, 3H), 1.98-2.10 (m, 1H), 1.61-1.79 (m, 1H)	B	--
346	600MHz DMSO-d ₆	8.16 (d, <i>J</i> =1.63 Hz, 1H), 7.75 (dd, <i>J</i> =1.60, 8.06 Hz, 1H), 7.55 (dd, <i>J</i> =7.43, 11.09 Hz, 1H), 7.37 (dd, <i>J</i> =7.32, 10.67 Hz, 1H), 6.89 (d, <i>J</i> =8.10 Hz, 1H), 5.38-5.46 (m, 2H), 4.29-4.40 (m, 1H), 3.26 (br s, 2H), 2.98-3.06 (m, 1H), 2.83-2.97 (m, 1H), 2.75 (dd, <i>J</i> =8.60, 12.57 Hz, 1H), 1.98-2.16 (m, 1H), 1.62-1.79 (m, 1H)	B	--
347	600MHz DMSO-d ₆	8.12 (d, <i>J</i> =2.26 Hz, 1H), 7.71 (dd, <i>J</i> =2.26, 8.49 Hz, 1H), 7.54 (dd, <i>J</i> =7.44, 11.09 Hz, 1H), 7.36 (dd, <i>J</i> =7.28, 10.70 Hz, 1H), 6.97 (d, <i>J</i> =8.56 Hz, 1H), 5.46-5.53 (m, 2H), 4.24-4.43 (m, 1H), 3.09-3.24 (m, 2H), 2.99-3.06 (m, 1H), 2.83-2.98 (m, 1H), 2.76 (dd, <i>J</i> =8.60, 12.57 Hz, 1H), 2.02-2.10 (m, 1H), 1.67-1.86 (m, 1H)	B	--
348	600MHz DMSO-d ₆	7.51 (dd, <i>J</i> =7.47, 11.21 Hz, 1H), 7.35-7.42 (m, 1H), 7.15-7.28 (m, 4H), 6.86 (d, <i>J</i> =7.65 Hz, 1H), 5.30 (s, 2H), 4.19-4.43 (m, 1H), 3.37-3.49 (m, 2H), 2.98-3.09 (m, 1H), 2.89-2.97 (m, 1H), 2.78 (dd, <i>J</i> =8.80, 12.61 Hz, 1H), 1.95-2.09 (m, 1H), 1.65-1.83 (m, 1H)	B	--
349	600MHz DMSO-d ₆	7.44-7.52 (m, 3H), 7.36 (t, <i>J</i> =8.95 Hz, 1H), 7.09 (ddd, <i>J</i> =2.18, 4.63, 8.52 Hz, 1H), 5.28-5.35 (m, 2H), 4.27-4.47 (m, 1H), 3.38-3.47 (m, 1H), 3.09-3.23 (m, 1H), 2.93-3.07 (m, 2H), 2.80 (dd, <i>J</i> =8.60, 12.57 Hz, 1H), 2.00-2.14 (m, 1H), 1.69-1.88 (m, 1H)	B	--

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
350	600MHz DMSO-d ₆	7.49 (dd, <i>J</i> =7.43, 11.17 Hz, 1H), 7.25 (dd, <i>J</i> =7.32, 10.67 Hz, 1H), 7.14 (d, <i>J</i> =1.95 Hz, 1H), 6.93 (dd, <i>J</i> =1.95, 8.17 Hz, 1H), 6.71 (d, <i>J</i> =8.17 Hz, 1H), 5.18 (s, 2H), 4.24-4.43 (m, 1H), 3.84 (s, 3H), 3.36-3.48 (m, 1H), 3.11-3.28 (m, 1H), 2.97-3.06 (m, 1H), 2.89-2.97 (m, 1H), 2.77 (dd, <i>J</i> =8.80, 12.61 Hz, 1H), 1.96-2.09 (m, 1H), 1.64-1.82 (m, 1H)	B	--
351	600MHz DMSO-d ₆	7.50 (dd, <i>J</i> =7.47, 11.13 Hz, 1H), 7.39 (dd, <i>J</i> =7.24, 10.74 Hz, 1H), 7.29 (t, <i>J</i> =9.79 Hz, 1H), 7.00-7.08 (m, 2H), 5.34 (s, 2H), 4.29-4.45 (m, 1H), 3.37-3.50 (m, 2H), 2.99-3.07 (m, 1H), 2.90-2.98 (m, 1H), 2.78 (dd, <i>J</i> =8.64, 12.53 Hz, 1H), 2.04-2.12 (m, 1H), 1.69-1.87 (m, 1H)	B	--
352	600MHz DMSO-d ₆	7.84 (d, <i>J</i> =7.55 Hz, 1H), 7.51-7.61 (m, 3H), 7.30 (t, <i>J</i> =8.69 Hz, 1H), 6.75 (d, <i>J</i> =7.71 Hz, 1H), 5.45 (s, 2H), 4.22-4.39 (m, 1H), 3.34-3.42 (m, 1H), 3.22-3.28 (m, 1H), 2.95-3.09 (m, 1H), 2.83-2.92 (m, 1H), 2.62-2.78 (m, 1H), 1.89-2.03 (m, 1H), 1.58-1.74 (m, 1H)	B	--
353	600MHz DMSO-d ₆	7.91 (dd, <i>J</i> =1.01, 7.71 Hz, 1H), 7.64 (dt, <i>J</i> =1.21, 7.73 Hz, 1H), 7.49-7.56 (m, 2H), 7.33 (dd, <i>J</i> =7.28, 10.70 Hz, 1H), 6.98 (d, <i>J</i> =7.86 Hz, 1H), 5.49-5.55 (m, 2H), 4.26-4.42 (m, 1H), 3.36-3.46 (m, 1H), 3.09-3.26 (m, 1H), 2.99-3.07 (m, 1H), 2.86-2.96 (m, 1H), 2.77 (dd, <i>J</i> =8.68, 12.57 Hz, 1H), 1.92-2.09 (m, 1H), 1.64-1.82 (m, 1H)	B	--
354	600MHz DMSO-d ₆	7.54 (s, 1H), 7.51-7.53 (m, 1H), 7.35 (dt, <i>J</i> =1.56, 7.67 Hz, 1H), 7.23-7.31 (m, 2H), 6.78-6.82 (m, 1H), 5.32-5.40 (m, 2H), 4.24-4.44 (m, 1H), 3.36-3.51 (m, 1H), 2.99-3.14 (m, 1H), 2.87-2.96 (m, 1H), 2.77 (dd, <i>J</i> =8.60, 12.57 Hz, 1H), 2.00-2.07 (m, 1H), 1.85-1.98 (m, 1H), 1.65-1.78 (m, 1H)	B	--
355	600MHz DMSO-d ₆	7.50-7.57 (m, 2H), 7.29 (t, <i>J</i> =9.13 Hz, 1H), 7.17 (dt, <i>J</i> =2.65, 8.49 Hz, 1H), 6.86-6.90 (m, 1H), 5.29-5.36 (m, 2H), 4.19-4.46 (m, 1H), 3.35-3.48 (m, 1H), 3.26-3.29 (m, 1H), 2.99-3.14 (m, 1H), 2.87-2.95 (m, 1H), 2.77 (dd, <i>J</i> =8.72, 12.61 Hz, 1H), 2.01-2.09 (m, 1H), 1.63-1.79 (m, 1H)	B	--
356	600MHz DMSO-d ₆	7.76 (dd, <i>J</i> =2.65, 9.03 Hz, 1H), 7.57 (dd, <i>J</i> =7.47, 11.13 Hz, 1H), 7.46 (dt, <i>J</i> =2.65, 8.45 Hz, 1H), 7.33 (dd, <i>J</i> =7.28, 10.63 Hz, 1H), 6.81 (dd, <i>J</i> =5.29, 8.64 Hz, 1H), 5.38-5.45 (m, 2H), 4.25-4.41 (m, 1H), 3.34-3.49 (m, 1H), 3.23-3.29 (m, 1H), 2.95-3.01 (m, 1H), 2.83-2.91 (m, 1H), 2.74 (dd, <i>J</i> =8.91, 12.57 Hz, 1H), 1.97-2.04 (m, 1H), 1.62-1.80 (m, 1H)	B	--

Ex. #	Freq., Solvent	¹ H NMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
357	600MHz DMSO-d ₆	7.36-7.52 (m, 3H), 7.29 (t, <i>J</i> =9.45 Hz, 1H), 6.92-6.98 (m, 1H), 5.27-5.34 (m, 2H), 4.26-4.48 (m, 1H), 3.38-3.49 (m, 1H), 3.36-3.38 (m, 1H), 2.93-3.07 (m, 2H), 2.81 (dd, <i>J</i> =8.60, 12.57 Hz, 1H), 2.05-2.13 (m, 1H), 1.71-1.89 (m, 1H)	B	--
358	600MHz DMSO-d ₆	7.46-7.54 (m, 2H), 7.39 (dd, <i>J</i> =7.32, 10.67 Hz, 1H), 7.24 (dd, <i>J</i> =1.87, 8.33 Hz, 1H), 6.96 (t, <i>J</i> =8.29 Hz, 1H), 5.35 (s, 2H), 4.27-4.44 (m, 1H), 3.36-3.49 (m, 2H), 3.00-3.17 (m, 1H), 2.89-2.98 (m, 1H), 2.78 (dd, <i>J</i> =8.68, 12.57 Hz, 1H), 2.02-2.13 (m, 1H), 1.67-1.84 (m, 1H)	B	--
359	600MHz DMSO-d ₆	7.58 (d, <i>J</i> =8.33 Hz, 1H), 7.44-7.53 (m, 3H), 7.04 (dd, <i>J</i> =2.02, 8.33 Hz, 1H), 5.30-5.36 (m, 2H), 4.30-4.46 (m, 1H), 3.38-3.51 (m, 2H), 2.93-3.07 (m, 2H), 2.80 (dd, <i>J</i> =8.64, 12.61 Hz, 1H), 2.05-2.13 (m, 1H), 1.68-1.86 (m, 1H)	B	--
360	600MHz DMSO-d ₆	¹ H NMR (600 MHz, DMSO-d ₆) δ 7.55 (t, <i>J</i> =8.15 Hz, 1H), 7.51 (t, <i>J</i> =9.00 Hz, 1H), 7.43 (t, <i>J</i> =8.77 Hz, 1H), 7.26 (dd, <i>J</i> =1.87, 10.20 Hz, 1H), 6.94 (dd, <i>J</i> =1.44, 8.29 Hz, 1H), 5.30-5.37 (m, 2H), 4.32-4.46 (m, 1H), 3.38-3.52 (m, 2H), 3.00-3.08 (m, 1H), 2.92-3.00 (m, 1H), 2.80 (dd, <i>J</i> =8.60, 12.57 Hz, 1H), 1.96-2.13 (m, 1H), 1.69-1.87 (m, 1H)	B	--
361	600MHz DMSO-d ₆	7.68-7.74 (m, <i>J</i> =8.17 Hz, 2H), 7.52 (dd, <i>J</i> =7.43, 11.17 Hz, 1H), 7.41 (dd, <i>J</i> =7.32, 10.67 Hz, 1H), 7.31-7.36 (m, <i>J</i> =8.02 Hz, 2H), 5.40-5.47 (m, 2H), 4.31-4.45 (m, 1H), 3.39-3.53 (m, 2H), 3.00-3.07 (m, 1H), 2.91-2.99 (m, 1H), 2.80 (dd, <i>J</i> =8.60, 12.57 Hz, 1H), 2.03-2.11 (m, 1H), 1.66-1.83 (m, 1H)	B	--
362	600MHz DMSO-d ₆	7.50 (dd, <i>J</i> =7.43, 11.17 Hz, 1H), 7.43 (dd, <i>J</i> =7.32, 10.74 Hz, 1H), 7.34 (d, <i>J</i> =8.17 Hz, 2H), 7.27 (d, <i>J</i> =8.06 Hz, 2H), 5.32-5.40 (m, 2H), 4.23-4.50 (m, 1H), 3.39-3.46 (m, 1H), 3.36 (br s, 1H), 2.99-3.11 (m, 1H), 2.91-2.99 (m, 1H), 2.80 (dd, <i>J</i> =8.68, 12.57 Hz, 1H), 1.99-2.12 (m, 1H), 1.65-1.81 (m, 1H)	B	--
363	600MHz DMSO-d ₆	7.48-7.58 (m, 3H), 7.38 (dd, <i>J</i> =7.32, 10.67 Hz, 1H), 7.27 (d, <i>J</i> =8.10 Hz, 2H), 7.00 (t, <i>J</i> =55.86 Hz, 1H), 5.35-5.43 (m, 2H), 4.20-4.48 (m, 1H), 3.42 (ddd, <i>J</i> =3.39, 7.08, 8.91 Hz, 1H), 3.36-3.38 (m, 1H), 2.99-3.08 (m, 1H), 2.91-2.99 (m, 1H), 2.80 (dd, <i>J</i> =8.60, 12.57 Hz, 1H), 1.98-2.11 (m, 1H), 1.65-1.82 (m, 1H)	B	--
364	600MHz DMSO-d ₆	7.43-7.52 (m, 3H), 7.27 (br d, <i>J</i> =8.17 Hz, 1H), 7.19 (s, 1H), 7.11 (d, <i>J</i> =7.79 Hz, 1H), 5.35-5.43 (m, 2H), 4.31-4.42 (m, 1H), 3.39-3.47 (m, 1H), 3.36-3.38 (m, 1H), 2.98-3.07 (m, 1H), 2.94 (tdd, <i>J</i> =4.20, 7.94, 14.40 Hz, 1H), 2.80 (dd, <i>J</i> =8.68, 12.57 Hz, 1H), 1.69-1.86 (m, 1H)	B	--

Ex. #	Freq., Solvent	¹ H NMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
365	600MHz DMSO-d ₆	¹ H NMR (600 MHz, DMSO-d ₆) δ 7.65 (d, <i>J</i> =8.23 Hz, 1H), 7.62 (s, 1H), 7.46-7.57 (m, 3H), 7.34 (d, <i>J</i> =7.71 Hz, 1H), 5.39-5.47 (m, 2H), 4.20-4.48 (m, 1H), 3.39-3.47 (m, 1H), 3.35-3.38 (m, 1H), 2.91-3.06 (m, 2H), 2.80 (dd, <i>J</i> =8.68, 12.57 Hz, 1H), 1.98-2.11 (m, 1H), 1.69-1.85 (m, 1H)	B	--
366	600MHz DMSO-d ₆	7.76 (d, <i>J</i> =7.71 Hz, 1H), 7.70 (s, 1H), 7.48-7.57 (m, 2H), 7.44 (t, <i>J</i> =8.87 Hz, 1H), 7.40 (d, <i>J</i> =8.08 Hz, 1H), 5.34-5.42 (m, 2H), 4.27-4.50 (m, 1H), 3.38-3.48 (m, 1H), 3.15-3.26 (m, 1H), 3.00-3.13 (m, 1H), 2.91-3.00 (m, 1H), 2.80 (dd, <i>J</i> =8.60, 12.57 Hz, 1H), 1.99-2.16 (m, 1H), 1.72-1.87 (m, 1H)	B	--
367	600MHz DMSO-d ₆	7.50 (dd, <i>J</i> =7.43, 11.17 Hz, 1H), 7.43 (dd, <i>J</i> =7.32, 10.74 Hz, 1H), 7.35 (s, 1H), 7.35 (d, <i>J</i> =5.66 Hz, 1H), 7.27 (s, 1H), 7.01-7.06 (m, 1H), 5.30-5.37 (m, 2H), 4.26-4.51 (m, 1H), 3.39-3.49 (m, 1H), 3.36-3.38 (m, 1H), 2.92-3.07 (m, 2H), 2.80 (dd, <i>J</i> =8.64, 12.53 Hz, 1H), 1.96-2.14 (m, 1H), 1.72-1.84 (m, 1H)	B	--
368	400MHz d ₄ -MeOH	7.47-7.53 (m, 1H), 7.09-7.23 (m, 5H), 7.00-7.08 (m, 2H), 5.30 (s, 2H), 3.48-3.55 (m, 1H), 3.24-3.30 (m, 1H), 2.92-3.06 (m, 2H), 2.86 (dd, <i>J</i> =8.81, 11.71 Hz, 1H), 1.92-2.04 (m, 1H), 1.82 (td, <i>J</i> =4.07, 13.42 Hz, 1H), 1.64-1.76 (m, 1H), 1.30-1.45 (m, 1H)	--	--
369	600MHz D ₆ -DMSO	7.98-8.03 (m, 2H), 7.44 (d, <i>J</i> =7.79 Hz, 1H), 7.34 (d, <i>J</i> =8.41 Hz, 2H), 7.16-7.18 (m, 1H), 7.07-7.11 (m, 1H), 6.99-7.04 (m, 1H), 5.39 (s, 2H), 2.81-2.95 (m, 2H), 2.69 (br d, <i>J</i> =2.49 Hz, 1H), 1.81-1.88 (m, 1H), 1.68-1.77 (m, 1H), 1.54-1.65 (m, 1H), 1.16-1.28 (m, 1H)	--	--
370	500MHz d ₆ -DMSO	7.89 (br d, <i>J</i> =8.04 Hz, 2H), 7.44 (br d, <i>J</i> =7.53 Hz, 1H), 7.39 (br d, <i>J</i> =8.04 Hz, 2H), 7.15 (br d, <i>J</i> =7.79 Hz, 1H), 7.09 (br t, <i>J</i> =7.14 Hz, 1H), 6.99-7.05 (m, 1H), 5.41 (s, 2H), 3.40 (br d, <i>J</i> =10.38 Hz, 1H), 3.25-3.30 (m, 1H), 2.83-2.92 (m, 2H), 2.63-2.71 (m, 1H), 1.82 (br dd, <i>J</i> =3.37, 8.04 Hz, 1H), 1.71 (br dd, <i>J</i> =4.54, 8.69 Hz, 1H), 1.52-1.65 (m, 1H), 1.15-1.27 (m, 1H)	--	--
371	500MHz d ₆ -DMSO	9.23 (s, 1H), 8.21 (s, 1H), 7.81 (br d, <i>J</i> =8.56 Hz, 2H), 7.43 (br d, <i>J</i> =7.27 Hz, 1H), 7.33 (br d, <i>J</i> =8.56 Hz, 2H), 7.19 (br d, <i>J</i> =7.53 Hz, 1H), 6.99-7.12 (m, 2H), 5.35 (s, 2H), 3.43 (br d, <i>J</i> =9.86 Hz, 1H), 2.83-2.95 (m, 2H), 2.61-2.71 (m, 1H), 1.81-1.91 (m, 1H), 1.72 (br dd, <i>J</i> =3.63, 9.08 Hz, 1H), 1.56-1.65 (m, 1H), 1.15-1.30 (m, 1H)	--	--

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
372	500MHz d6-DMSO	7.90 (br d, <i>J</i> =7.01 Hz, 1H), 7.62 (br t, <i>J</i> =7.27 Hz, 1H), 7.42-7.53 (m, 2H), 7.10 (br dd, <i>J</i> =4.80, 7.14 Hz, 2H), 7.00-7.06 (m, 1H), 6.97 (br d, <i>J</i> =7.78 Hz, 1H), 5.48 (s, 2H), 3.30-3.43 (m, 2H), 2.76-2.91 (m, 3H), 2.61 (br dd, <i>J</i> =9.08, 11.68 Hz, 1H), 1.77-1.87 (m, 1H), 1.65-1.74 (m, 1H), 1.52-1.62 (m, 1H)	--	--
373	500MHz d6-DMSO	7.48 (br d, <i>J</i> =8.04 Hz, 2H), 7.38 (br d, <i>J</i> =8.04 Hz, 2H), 6.98 (br t, <i>J</i> =7.27 Hz, 1H), 6.86 (br t, <i>J</i> =7.40 Hz, 1H), 6.75 (br d, <i>J</i> =8.04 Hz, 1H), 5.44-5.54 (m, 2H), 3.41 (br d, <i>J</i> =8.82 Hz, 2H), 2.80-2.94 (m, 2H), 2.61-2.69 (m, 1H), 1.86 (br dd, <i>J</i> =3.76, 8.43 Hz, 1H), 1.74-1.81 (m, 1H), 1.58-1.70 (m, 1H), 1.14-1.30 (m, 1H)	--	--
374	500MHz d6-DMSO	7.52 (br d, <i>J</i> =7.01 Hz, 1H), 7.45 (br d, <i>J</i> =7.79 Hz, 1H), 7.32 (br t, <i>J</i> =7.01 Hz, 1H), 7.22-7.28 (m, 1H), 6.96-7.13 (m, 3H), 6.79 (br d, <i>J</i> =6.75 Hz, 1H), 5.32 (s, 2H), 2.75-2.90 (m, 3H), 2.61 (br dd, <i>J</i> =9.08, 11.68 Hz, 1H), 1.77-1.87 (m, 1H), 1.67 (br dd, <i>J</i> =3.76, 9.21 Hz, 1H), 1.47-1.61 (m, 1H), 1.10-1.26 (m, 1H)	--	--
375	500MHz d6-DMSO	7.70 (br d, <i>J</i> =7.79 Hz, 2H), 7.43 (br d, <i>J</i> =7.79 Hz, 1H), 7.34 (br d, <i>J</i> =8.04 Hz, 2H), 7.14 (br d, <i>J</i> =7.79 Hz, 1H), 7.08 (br t, <i>J</i> =7.14 Hz, 1H), 6.99-7.05 (m, 1H), 5.39 (s, 2H), 3.39 (br d, <i>J</i> =9.60 Hz, 2H), 2.78-2.91 (m, 3H), 2.63 (br dd, <i>J</i> =9.34, 11.68 Hz, 1H), 1.81 (br dd, <i>J</i> =3.89, 8.04 Hz, 1H), 1.66-1.76 (m, 1H), 1.52-1.64 (m, 1H), 1.12-1.26 (m, 1H)	--	--
376	500MHz d6-DMSO	7.40-7.47 (m, 1H), 7.23-7.37 (m, 4H), 7.17 (br d, <i>J</i> =8.04 Hz, 1H), 6.96-7.12 (m, 2H), 5.25-5.41 (m, 2H), 3.39 (br d, <i>J</i> =10.90 Hz, 2H), 2.77-2.89 (m, 2H), 2.62 (br dd, <i>J</i> =9.21, 11.81 Hz, 1H), 1.78-1.88 (m, 1H), 1.54-1.75 (m, 2H), 1.12-1.23 (m, 1H)	--	--
377	500MHz d6-DMSO	7.34-7.46 (m, 3H), 7.12-7.21 (m, 3H), 6.96-7.11 (m, 2H), 5.23-5.31 (m, 2H), 3.35-3.42 (m, 2H), 2.78-2.90 (m, 3H), 2.57-2.68 (m, 1H), 1.79-1.88 (m, 1H), 1.66-1.77 (m, 1H), 1.53-1.64 (m, 1H), 1.11-1.24 (m, 1H)	--	--
378	500MHz d6-DMSO	7.43 (br d, <i>J</i> =7.79 Hz, 1H), 7.30-7.37 (m, 2H), 7.25 (s, 1H), 7.19 (br d, <i>J</i> =7.79 Hz, 1H), 6.99-7.12 (m, 3H), 5.24-5.36 (m, 2H), 3.39 (br d, <i>J</i> =10.12 Hz, 2H), 2.78-2.92 (m, 2H), 2.62 (br dd, <i>J</i> =9.08, 11.68 Hz, 1H), 1.79-1.89 (m, 1H), 1.70 (br d, <i>J</i> =3.63 Hz, 1H), 1.53-1.66 (m, 1H), 1.18 (br d, <i>J</i> =10.38 Hz, 1H)	--	--

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
379	500MHz d6-DMSO	7.52 (br d, J=8.30 Hz, 1H), 7.47-7.59 (m, 1H), 7.42 (br d, J=7.79 Hz, 1H), 7.25 (br d, J=7.78 Hz, 2H), 6.95-7.18 (m, 3H), 5.25-5.40 (m, 2H), 3.40 (br d, J=11.68 Hz, 2H), 2.79-2.90 (m, 2H), 2.64 (br dd, J=9.21, 11.55 Hz, 1H), 1.92 (br t, J=18.81 Hz, 3H), 1.82 (br dd, J=3.37, 9.08 Hz, 1H), 1.71 (br dd, J=4.02, 9.21 Hz, 1H), 1.60 (br s, 1H), 1.09-1.24 (m, 1H)	--	--
380	500MHz d6-DMSO	7.39-7.49 (m, 3H), 7.22 (br d, J=8.30 Hz, 2H), 7.15 (br d, J=7.79 Hz, 1H), 6.97-7.10 (m, 2H), 5.23-5.34 (m, 2H), 3.41 (br d, J=11.68 Hz, 2H), 2.78-2.91 (m, 2H), 2.59-2.69 (m, 1H), 1.79-1.86 (m, 1H), 1.68-1.76 (m, 1H), 1.59-1.68 (m, 6H), 1.12-1.24 (m, 1H)	--	--
381	500MHz d6-DMSO	7.53 (br d, J=7.78 Hz, 2H), 7.43 (br d, J=7.53 Hz, 1H), 7.27 (br d, J=7.79 Hz, 2H), 6.96-7.16 (m, 4H), 5.28-5.39 (m, 2H), 3.40 (br d, J=9.86 Hz, 2H), 2.76-2.91 (m, 3H), 2.59-2.68 (m, 1H), 1.83 (br dd, J=3.76, 8.17 Hz, 1H), 1.70 (br dd, J=4.41, 9.34 Hz, 1H), 1.51-1.62 (m, 1H), 1.11-1.25 (m, 1H)	--	--
382	500MHz d6-DMSO	8.37 (br d, J=4.41 Hz, 1H), 7.76 (br d, J=8.30 Hz, 2H), 7.39-7.47 (m, 1H), 7.21 (br d, J=8.04 Hz, 2H), 6.97-7.17 (m, 3H), 5.33 (s, 2H), 3.40 (br d, J=9.08 Hz, 2H), 2.78-2.91 (m, 2H), 2.63 (br dd, J=9.47, 11.29 Hz, 1H), 1.53-1.92 (m, 3H), 1.09-1.24 (m, 1H)	--	--
383	500MHz d6-DMSO	7.86-7.94 (m, 1H), 7.57-7.66 (m, 1H), 7.36-7.50 (m, 1H), 6.93-7.23 (m, 5H), 5.41 (s, 2H), 2.72-2.93 (m, 3H), 2.57-2.66 (m, 1H), 1.81 (br dd, J=3.11, 4.93 Hz, 1H), 1.65-1.74 (m, 1H), 1.51-1.63 (m, 1H), 1.10-1.26 (m, 1H)	--	--
384	500MHz d6-DMSO	7.41 (br d, J=7.53 Hz, 1H), 7.13-7.20 (m, 3H), 6.96-7.08 (m, 4H), 5.20-5.27 (m, 2H), 5.11 (s, 2H), 3.41 (br d, J=12.20 Hz, 2H), 2.81-2.89 (m, 2H), 2.63 (br dd, J=9.08, 11.68 Hz, 1H), 1.79-1.88 (m, 1H), 1.72 (br dd, J=3.89, 8.56 Hz, 1H), 1.61 (br dd, J=3.89, 10.90 Hz, 1H), 1.18 (br d, J=10.38 Hz, 1H)	--	--
385	500MHz d6-DMSO	7.71 (br d, J=8.30 Hz, 2H), 7.44 (br d, J=7.78 Hz, 1H), 7.38 (br d, J=8.04 Hz, 2H), 7.18 (br d, J=7.79 Hz, 1H), 6.99-7.12 (m, 2H), 5.36-5.45 (m, 2H), 3.37 (br d, J=11.68 Hz, 2H), 2.71-2.89 (m, 2H), 1.76-1.84 (m, 1H), 1.65-1.73 (m, 1H), 1.48-1.61 (m, 2H), 1.11-1.22 (m, 1H)	--	--
386	500MHz d6-DMSO	7.41 (br d, J=7.79 Hz, 1H), 6.96-7.16 (m, 5H), 7.16 (br s, 1H), 5.15-5.29 (m, 2H), 3.40 (br d, J=11.42 Hz, 2H), 2.79-2.89 (m, 2H), 2.58-2.67 (m, 1H), 2.24 (s, 3H), 1.79-1.87 (m, 1H), 1.69 (br d, J=3.63 Hz, 1H), 1.54-1.65 (m, 1H), 1.13-1.22 (m, 1H)	--	--

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
387	500MHz d6-DMSO	7.41 (br d, J=7.53 Hz, 1H), 7.11-7.27 (m, 5H), 6.97-7.09 (m, 2H), 5.21-5.35 (m, 2H), 3.39 (br d, J=11.94 Hz, 2H), 2.79-2.89 (m, 2H), 2.62 (br dd, J=9.21, 11.55 Hz, 1H), 1.78-1.88 (m, 1H), 1.71 (br dd, J=3.63, 8.56 Hz, 1H), 1.54-1.65 (m, 1H), 1.08-1.25 (m, 1H)	--	--
388	500MHz d6-DMSO	8.05 (s, 1H), 7.64-7.71 (m, 1H), 7.46 (br d, J=7.79 Hz, 1H), 7.02-7.12 (m, 1H), 6.90-7.02 (m, 3H), 6.56-6.64 (m, 1H), 5.90 (br d, J=5.97 Hz, 2H), 4.32 (s, 3H), 3.40 (br d, J=10.90 Hz, 2H), 2.89-2.96 (m, 1H), 2.78-2.86 (m, 1H), 2.70 (br dd, J=8.69, 11.81 Hz, 1H), 1.74-1.82 (m, 1H), 1.64-1.70 (m, 1H), 1.50-1.60 (m, 1H), 1.11-1.26 (m, 1H)	--	--
389	500MHz d6-DMSO	7.40-7.45 (m, 1H), 7.24-7.32 (m, 1H), 7.16 (br d, J=7.79 Hz, 1H), 6.96-7.11 (m, 3H), 5.26-5.33 (m, 1H), 3.37 (br d, J=1.56 Hz, 2H), 2.77-2.91 (m, 2H), 2.58-2.65 (m, 1H), 1.80-1.87 (m, 1H), 1.67-1.76 (m, 1H), 1.52-1.64 (m, 1H), 1.09-1.24 (m, 1H)	--	--
390	500MHz d6-DMSO	7.33-7.45 (m, 2H), 7.16-7.30 (m, 2H), 7.00-7.11 (m, 2H), 6.95 (br s, 1H), 5.22-5.33 (m, 2H), 3.39 (br d, J=11.16 Hz, 2H), 2.85 (br d, J=9.60 Hz, 2H), 2.63 (br dd, J=9.34, 11.68 Hz, 1H), 1.78-1.88 (m, 1H), 1.71 (br d, J=3.63 Hz, 1H), 1.59 (br dd, J=2.47, 10.51 Hz, 1H), 1.12-1.24 (m, 1H)	--	--
391	500MHz d6-DMSO	7.53 (br t, J=7.91 Hz, 1H), 7.43 (br d, J=7.53 Hz, 1H), 7.23 (br d, J=8.82 Hz, 1H), 7.18 (br d, J=7.78 Hz, 1H), 6.99-7.12 (m, 2H), 6.94 (br d, J=7.78 Hz, 1H), 5.25-5.34 (m, 2H), 3.38 (br d, J=11.42 Hz, 2H), 2.80-2.91 (m, 2H), 2.63 (br dd, J=9.34, 11.68 Hz, 1H), 1.78-1.88 (m, 1H), 1.67-1.77 (m, 1H), 1.60 (br s, 1H), 1.12-1.24 (m, 1H)	--	--
392	500MHz d6-DMSO	7.92 (s, 1H), 7.84 (br d, J=7.53 Hz, 1H), 7.49-7.59 (m, 2H), 7.44 (br d, J=7.01 Hz, 1H), 7.35 (br d, J=7.01 Hz, 1H), 7.04-7.16 (m, 3H), 5.47-5.57 (m, 2H), 3.38-3.46 (m, 2H), 2.85-2.96 (m, 2H), 2.69 (br dd, J=9.08, 11.42 Hz, 1H), 1.81-1.90 (m, 1H), 1.77 (br dd, J=4.15, 8.82 Hz, 1H), 1.61-1.70 (m, 1H), 1.18-1.29 (m, 1H)	--	--
393	500MHz d6-DMSO	7.41 (br d, J=7.53 Hz, 1H), 7.29 (s, 1H), 7.20 (br d, J=7.53 Hz, 1H), 6.99-7.12 (m, 4H), 5.17-5.25 (m, 2H), 3.80 (s, 3H), 3.40 (br d, J=9.86 Hz, 2H), 2.79-2.91 (m, 2H), 2.62 (br dd, J=9.34, 11.68 Hz, 1H), 1.84 (br dd, J=4.02, 8.17 Hz, 1H), 1.72 (br d, J=3.37 Hz, 1H), 1.53-1.66 (m, 2H), 1.10-1.25 (m, 1H)	--	--

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
394	500MHz d ₆ -DMSO	8.15 (br d, J=1.30 Hz, 1H), 7.75 (br dd, J=1.17, 7.91 Hz, 1H), 7.46 (br d, J=8.04 Hz, 1H), 7.00-7.14 (m, 3H), 6.88 (br d, J=8.04 Hz, 1H), 5.33-5.44 (m, 2H), 3.15-3.24 (m, 2H), 2.74-2.89 (m, 2H), 2.60 (br dd, J=9.34, 11.42 Hz, 1H), 1.77-1.85 (m, 1H), 1.63-1.73 (m, 1H), 1.46-1.57 (m, 1H), 1.09-1.25 (m, 1H)	--	--
395	500MHz d ₆ -DMSO	7.66-7.74 (m, 1H), 7.42-7.48 (m, 1H), 7.31-7.38 (m, 1H), 7.00-7.16 (m, 3H), 6.79 (br d, J=8.30 Hz, 1H), 5.30 (s, 2H), 3.14-3.27 (m, 2H), 2.73-2.91 (m, 2H), 2.60 (br dd, J=9.21, 11.81 Hz, 1H), 1.77-1.86 (m, 1H), 1.67-1.74 (m, 1H), 1.50-1.61 (m, 1H), 1.09-1.20 (m, 1H)	--	--
396	500MHz d ₆ -DMSO	7.54-7.58 (m, 1H), 7.44 (br d, J=7.27 Hz, 1H), 7.33 (br d, J=8.04 Hz, 1H), 6.98-7.14 (m, 3H), 6.71-6.77 (m, 1H), 5.20-5.27 (m, 1H), 5.18-5.28 (m, 1H), 3.10-3.23 (m, 2H), 2.75-2.88 (m, 2H), 2.58-2.64 (m, 1H), 1.79-1.84 (m, 1H), 1.64-1.71 (m, 1H), 1.51-1.58 (m, 1H), 1.16 (br dd, J=8.04, 10.90 Hz, 1H)	--	--
397	500MHz d ₆ -DMSO	8.11 (br d, J=2.08 Hz, 1H), 7.67-7.74 (m, 1H), 7.46 (br d, J=8.30 Hz, 1H), 7.07-7.15 (m, 2H), 7.04 (br d, J=7.53 Hz, 1H), 6.95 (br d, J=8.56 Hz, 1H), 5.46 (s, 2H), 3.17-3.26 (m, 2H), 2.78-2.88 (m, 2H), 2.57-2.65 (m, 1H), 1.77-1.86 (m, 1H), 1.66-1.75 (m, 1H), 1.53-1.62 (m, 1H), 1.14-1.22 (m, 1H)	--	--
398	400MHz MeOD	7.69-7.76 (m, 2H), 7.50-7.56 (m, 1H), 7.46 (d, J=8.09 Hz, 2H), 7.11-7.19 (m, 1H), 6.95-7.07 (m, 2H), 5.91 (q, J=7.12 Hz, 1H), 3.43 (dd, J=3.73, 11.61 Hz, 1H), 3.27-3.31 (m, 1H), 2.95-3.08 (m, 2H), 2.87 (dd, J=8.91, 11.61 Hz, 1H), 1.96-2.00 (m, 2H), 1.95-2.01 (m, 1H), 1.86-1.94 (m, 1H), 1.69-1.83 (m, 1H), 1.33-1.47 (m, 1H)	--	--
399	400MHz MeOD	Mixture of diastereomers: 7.70-7.78 (m, 2H), 7.52 (d, J=7.88 Hz, 1H), 7.45 (dd, J=6.32, 7.98 Hz, 2H), 7.15 (dt, J=1.24, 7.57 Hz, 1H), 6.94-7.07 (m, 2H), 5.86-5.98 (m, 1H), 3.40-3.54 (m, 1H), 3.36 (s, 2H), 2.97-3.09 (m, 2H), 2.86 (ddd, J=8.91, 11.51, 16.27 Hz, 1H), 2.00 (dd, J=7.36, 8.19 Hz, 3H), 1.68-1.92 (m, 2H), 1.32-1.45 (m, 1H)	--	--
400	400MHz d ₅ -DMSO	8.03 (br s, 3H), 7.79 (d, J=7.67 Hz, 1H), 7.72 (s, 1H), 7.55-7.62 (m, 1H), 7.47-7.54 (m, 2H), 7.11-7.25 (m, 3H), 5.44 (s, 2H), 3.66 (br dd, J=3.01, 12.54 Hz, 1H), 3.47 (br d, J=2.90 Hz, 1H), 3.25-3.34 (m, 1H), 3.21 (dd, J=8.50, 12.23 Hz, 1H), 2.98-3.09 (m, 1H), 1.95-2.03 (m, 1H), 1.79-1.90 (m, 1H), 1.53-1.71 (m, 2H)	--	--

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
494	500MHz d ₄ -MeOH	8.77 (s, 2H), 7.39-7.45 (m, 1H), 6.98 (dd, J=2.34, 8.82 Hz, 1H), 6.85-6.93 (m, 1H), 5.50 (s, 2H), 3.90 (td, J=3.60, 7.07 Hz, 1H), 3.31-3.44 (m, 3H), 3.22-3.29 (m, 1H), 3.06-3.15 (m, 1H), 3.03 (td, J=3.50, 7.01 Hz, 1H), 1.77-1.93 (m, 2H)	B	Chiralpak ID, 25% IPA w/ 0.2% DEA, peak 1
495	500MHz d ₄ -MeOH	7.42-7.47 (m, 1H), 7.31 (d, J=1.82 Hz, 1H), 7.18 (dd, J=1.95, 8.43 Hz, 1H), 5.08 (s, 2H), 4.38-4.55 (m, 1H), 3.75-3.81 (m, 2H), 3.71-3.75 (m, 2H), 3.67-3.70 (m, 2H), 3.59-3.65 (m, 2H), 3.53 (br d, J=12.46 Hz, 1H), 3.38 (s, 1H), 3.16-3.22 (m, 1H), 3.07-3.15 (m, 1H), 2.97 (dd, J=8.56, 12.46 Hz, 1H), 2.18-2.29 (m, 1H), 1.89-2.01 (m, 1H)	B	Chiralpak IC, 35% MeOH, peak 1
496	500MHz d ₄ -MeOH	8.77 (s, 2H), 7.15-7.19 (m, 1H), 7.10-7.14 (m, 1H), 6.83-6.90 (m, 1H), 5.50 (s, 2H), 3.90 (td, J=3.44, 7.14 Hz, 1H), 3.24-3.45 (m, 4H), 3.11-3.18 (m, 1H), 2.99-3.05 (m, 1H), 1.79-1.95 (m, 2H)	B	Chiralpak ID, 25% IPA w/ 0.2% DEA, peak 2
497	500MHz d ₄ -MeOH	7.45-7.50 (m, 1H), 7.20-7.24 (m, 1H), 7.13-7.20 (m, 1H), 5.08 (s, 2H), 4.41-4.58 (m, 1H), 3.75-3.81 (m, 2H), 3.70 (td, J=4.57, 16.28 Hz, 4H), 3.60-3.66 (m, 2H), 3.56 (dtd, J=1.95, 4.23, 12.42 Hz, 1H), 3.41-3.48 (m, 1H), 3.18-3.26 (m, 1H), 3.10-3.16 (m, 1H), 2.99 (dd, J=8.69, 12.59 Hz, 1H), 2.18-2.30 (m, 1H), 1.89-2.02 (m, 1H)	B	Chiralpak IC, 35% MeOH, peak 2
498	600MHz DMSO – d ₆	8.97 (s, 2H), 7.50 (dd, J=7.59, 11.09 Hz, 1H), 7.13 (dd, J=7.36, 10.94 Hz, 1H), 5.93 (q, J=7.19 Hz, 1H), 4.36-4.57 (m, 1H), 3.38-3.56 (m, 1H), 3.22 (br d, J=7.24 Hz, 1H), 2.94-3.00 (m, 1H), 2.88 (dd, J=8.76, 12.34 Hz, 1H), 2.37-2.47 (m, 1H), 2.07-2.14 (m, 1H), 1.88 (d, J=7.16 Hz, 4H)	B	Chiralpak AD-H, 25% IPA, peak 1
499	600MHz DMSO – d ₆	8.92-8.95 (m, 1H), 8.53-8.56 (m, 1H), 8.35 (dd, J=2.10, 8.17 Hz, 1H), 8.01 (d, J=2.10 Hz, 1H), 7.60 (d, J=8.17 Hz, 1H), 5.69 (s, 2H), 4.33-4.44 (m, 1H), 3.51-3.70 (m, 1H), 3.14-3.19 (m, 1H), 2.81-2.91 (m, 1H), 2.51-2.55 (m, 1H), 2.37-2.47 (m, 1H), 2.02-2.09 (m, 1H), 1.62-1.76 (m, 1H)	B	Chiralpak AD-H, 25% IPA, peak 1
500	600MHz DMSO – d ₆	7.45-7.54 (m, 1H), 7.26-7.42 (m, 1H), 5.01-5.18 (m, 2H), 4.35-4.54 (m, 2H), 4.22 (q, J=9.60 Hz, 2H), 3.32-3.41 (m, 1H), 3.20-3.26 (m, 1H), 2.94-3.07 (m, 3H), 2.81 (dd, J=8.17, 12.59 Hz, 1H), 2.65-2.74 (m, 1H), 2.02-2.19 (m, 1H), 1.77 (br d, J=9.86 Hz, 1H)	--	--
501	600MHz DMSO – d ₆	7.57-7.62 (m, 2H), 7.51 (dd, J=7.40, 11.13 Hz, 1H), 7.32 (d, J=3.50 Hz, 1H), 5.37-5.43 (m, 2H), 4.36-4.48 (m, 1H), 3.83 (s, 3H), 3.51 (br d, J=13.00 Hz, 1H), 3.13-3.23 (m, 2H), 2.99-3.10 (m, 1H), 2.79-2.84 (m, 1H), 2.07-2.14 (m, 1H), 1.75-1.84 (m, 1H)	--	--

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
502	600MHz DMSO – d ₆	8.43 (br s, 2H), 7.44 (d, <i>J</i> =8.51 Hz, 1H), 7.41 (s, 1H), 7.14 (dd, <i>J</i> =2.06, 8.45 Hz, 2H), 4.98-5.07 (m, 2H), 4.73-4.92 (m, 1H), 3.65-3.72 (m, 2H), 3.34 (br s, 1H), 2.77-3.13 (m, 6H), 2.51-2.55 (m, 2H), 2.16-2.24 (m, 1H), 1.81-1.90 (m, 1H)	B	Chiralpak AD-H, 25% IPA, peak 1
503	600MHz DMSO – d ₆	¹ 7.41 (dd, <i>J</i> =4.87, 8.68 Hz, 1H), 7.15 (dd, <i>J</i> =2.49, 9.19 Hz, 1H), 6.94 (ddd, <i>J</i> =2.53, 8.64, 10.08 Hz, 1H), 4.67-4.80 (m, 2H), 4.50-4.65 (m, 1H), 4.22-4.33 (m, 2H), 3.94 (t, <i>J</i> =7.71 Hz, 2H), 3.39-3.57 (m, 1H), 3.23-3.39 (m, 1H), 2.96-3.10 (m, 1H), 2.88 (dd, <i>J</i> =8.99, 12.57 Hz, 1H), 2.52-2.55 (m, 1H), 2.29 (quin, <i>J</i> =7.69 Hz, 2H), 2.11-2.20 (m, 1H), 1.80-1.88 (m, 1H)	B	Chiralpak AD-H, 25% IPA, peak 1
504	600MHz DMSO – d ₆	7.35-7.48 (m, 2H), 4.99-5.12 (m, 2H), 4.40-4.47 (m, 1H), 4.30-4.39 (m, 1H), 3.90 (br d, <i>J</i> =13.23 Hz, 1H), 3.15-3.30 (m, 4H), 2.94-3.04 (m, 2H), 2.90 (br t, <i>J</i> =11.64 Hz, 1H), 2.69-2.84 (m, 2H), 2.04-2.16 (m, 1H), 1.91-2.03 (m, 1H), 1.71-1.89 (m, 1H), 1.54-1.67 (m, 2H)	--	--
505	600MHz DMSO – d ₆	7.40-7.52 (m, 3H), 6.92 (dd, <i>J</i> =5.14, 10.98 Hz, 1H), 5.14-5.18 (m, 1H), 5.08-5.12 (m, 1H), 4.75 (s, 1H), 4.57 (s, 1H), 3.78-3.89 (m, 2H), 3.20-3.29 (m, 2H), 2.93-3.03 (m, 2H), 2.75-2.83 (m, 2H), 2.37-2.46 (m, 1H), 1.92-2.11 (m, 2H), 1.70-1.79 (m, 1H)	--	--
506	600MHz DMSO – d ₆	7.45 (d, <i>J</i> =1.87 Hz, 1H), 7.20 (d, <i>J</i> =8.49 Hz, 1H), 7.08 (dd, <i>J</i> =2.02, 8.49 Hz, 1H), 4.94-5.04 (m, 2H), 4.33-4.48 (m, 1H), 3.28-3.38 (m, 1H), 2.96-3.13 (m, 6H), 2.88 (s, 3H), 2.76-2.85 (m, 1H), 1.99-2.16 (m, 1H), 1.74-1.87 (m, 1H)	B	Chiralpak AD-H, 25% IPA, peak 2
507	600MHz DMSO – d ₆	7.46 (dd, <i>J</i> =7.43, 11.17 Hz, 1H), 7.39 (t, <i>J</i> =8.84 Hz, 1H), 5.06-5.19 (m, 1H), 4.93 (br t, <i>J</i> =18.33 Hz, 1H), 4.06-4.13 (m, 1H), 3.80-3.93 (m, 2H), 3.49-3.60 (m, 1H), 3.36-3.48 (m, 1H), 3.28-3.30 (m, 1H), 3.20-3.28 (m, 2H), 3.17 (d, <i>J</i> =5.06 Hz, 1H), 2.88-3.05 (m, 2H), 2.73-2.83 (m, 1H), 2.42-2.48 (m, 1H), 2.00-2.16 (m, 1H), 1.92 (br s, 1H), 1.73-1.89 (m, 1H), 1.06-1.18 (m, 3H)	--	--
508	600MHz DMSO – d ₆	8.97 (s, 2H), 7.50 (dd, <i>J</i> =7.59, 11.09 Hz, 1H), 7.13 (dd, <i>J</i> =7.36, 10.94 Hz, 1H), 5.93 (q, <i>J</i> =7.19 Hz, 1H), 4.36-4.57 (m, 1H), 3.38-3.56 (m, 1H), 3.22 (br d, <i>J</i> =7.24 Hz, 1H), 2.94-3.00 (m, 1H), 2.88 (dd, <i>J</i> =8.76, 12.34 Hz, 1H), 2.37-2.47 (m, 1H), 2.07-2.14 (m, 1H), 1.88 (d, <i>J</i> =7.16 Hz, 4H)	B	Chiralpak AD-H, 25% IPA, peak 2
509	600MHz DMSO – d ₆	6.73 (dd, <i>J</i> =2.26, 8.95 Hz, 1H), 6.56-6.64 (m, 1H), 5.03-5.12 (m, 2H), 4.29-4.49 (m, 1H), 4.22 (q, <i>J</i> =9.58 Hz, 2H), 3.89 (s, 3H), 3.26 (s, 3H), 3.18 (br d, <i>J</i> =12.53 Hz, 1H), 2.89-3.00 (m, 3H), 2.68-2.77 (m, 1H), 2.07 (ddd, <i>J</i> =4.01, 8.91, 13.08 Hz, 1H), 1.70-1.86 (m, 1H)	B	SFC: Whelk-01, 25% methanol Peak 2

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
510	600MHz DMSO – d ₆	7.47 (dd, <i>J</i> =7.47, 11.13 Hz, 1H), 7.35 (dd, <i>J</i> =7.36, 10.70 Hz, 1H), 4.99 (s, 2H), 4.33-4.445 (m, 1H), 3.49-3.57 (m, 2H), 3.38-3.45 (m, 1H), 3.25-3.30 (m, 1H), 2.91-3.04 (m, 2H), 2.78 (dd, <i>J</i> =8.64, 12.53 Hz, 1H), 2.06-2.14 (m, 1H), 1.71-1.87 (m, 5H), 1.57-1.66 (m, 4H), 1.43-1.57 (m, 4H)	--	--
511	600MHz DMSO – d ₆	8.39 (d, <i>J</i> =1.32 Hz, 1H), 8.13 (dd, <i>J</i> =1.52, 2.61 Hz, 1H), 7.89 (d, <i>J</i> =2.57 Hz, 1H), 7.46 (t, <i>J</i> =9.08 Hz, 1H), 7.42 (t, <i>J</i> =8.88 Hz, 1H), 5.04-5.14 (m, 2H), 4.34-4.35 (m, 1H), 3.67-3.79 (m, 4H), 3.58-3.66 (m, 4H), 3.23-3.28 (m, 1H), 2.96-3.05 (m, 2H), 2.80 (dd, <i>J</i> =8.06, 12.57 Hz, 1H), 2.07-2.15 (m, 1H), 1.74-1.92 (m, 2H)	--	--
512	600MHz DMSO – d ₆	7.46 (t, <i>J</i> =9.16 Hz, 1H), 7.39 (t, <i>J</i> =9.02 Hz, 1H), 4.95-5.07 (m, 2H), 4.36-4.44 (m, 1H), 4.18 (br t, <i>J</i> =11.64 Hz, 1H), 3.83-3.97 (m, 1H), 3.63 (s, 2H), 3.13-3.26 (m, 3H), 2.93-3.05 (m, 2H), 2.73-2.89 (m, 2H), 2.68 (tt, <i>J</i> =3.97, 10.94 Hz, 1H), 2.51-2.56 (m, 1H), 2.09 (br d, <i>J</i> =13.16 Hz, 1H), 1.89-1.98 (m, 1H), 1.74-1.89 (m, 2H), 1.60-1.70 (m, 1H), 1.40-1.50 (m, 1H)	--	--
513	600MHz DMSO – d ₆	7.46 (dd, <i>J</i> =7.43, 11.02 Hz, 1H), 7.39 (dd, <i>J</i> =7.55, 10.35 Hz, 1H), 5.07-5.18 (m, 1H), 4.93 (dd, <i>J</i> =14.95, 17.28 Hz, 1H), 4.33-4.48 (m, 1H), 4.09-4.16 (br d, <i>J</i> =13.00 Hz, 1H), 3.82-3.93 (m, 2H), 3.53 (dt, <i>J</i> =2.37, 11.46 Hz, 1H), 3.19-3.30 (m, 2H), 2.90-3.05 (m, 2H), 2.69-2.84 (m, 2H), 2.44-2.48 (m, 1H), 2.06-2.16 (m, 1H), 1.72-1.90 (m, 2H), 1.39-1.52 (m, 2H), 0.85-0.97 (m, 3H)	--	--
514	600MHz DMSO – d ₆	7.20-7.26 (m, 2H), 6.95 (ddd, <i>J</i> =2.49, 8.74, 9.87 Hz, 1H), 4.71-4.77 (m, 2H), 4.63-4.55 (m, 1H), 4.23-4.29 (m, 2H), 3.94 (t, <i>J</i> =7.71 Hz, 2H), 3.45-3.63 (m, 1H), 3.39-3.45 (m, 1H), 3.14-3.35 (m, 1H), 2.98-3.12 (m, 1H), 2.93 (dd, <i>J</i> =9.19, 12.69 Hz, 1H), 2.28 (quin, <i>J</i> =7.69 Hz, 2H), 2.08-2.23 (m, 1H), 1.79-1.89 (m, 1H)	B	SFC: Chiralpak IC, 40% methanol peak 2
515	600MHz DMSO – d ₆	7.69 (d, <i>J</i> =8.32 Hz, 2H), 7.48-7.65 (m, 7H), 5.67-5.99 (m, 1H), 5.17-5.57 (m, 1H), 4.36-4.51 (m, 2H), 3.86 (br s, 1H), 3.49 (br d, <i>J</i> =11.99 Hz, 1H), 3.38-3.44 (m, 1H), 2.90-3.03 (m, 2H), 2.67-2.84 (m, 1H), 2.12 (br s, 1H), 1.68-1.84 (m, 1H)	--	--
516	600MHz DMSO – d ₆	7.46 (dd, <i>J</i> =7.47, 11.13 Hz, 1H), 7.37 (dd, <i>J</i> =7.32, 10.74 Hz, 1H), 4.94-5.04 (m, 2H), 4.28 (br d, <i>J</i> =12.85 Hz, 1H), 3.93 (br d, <i>J</i> =13.23 Hz, 1H), 3.21-3.29 (m, 2H), 3.09 (br t, <i>J</i> =11.91 Hz, 1H), 2.93-3.03 (m, 2H), 2.78 (dt, <i>J</i> =8.41, 12.53 Hz, 1H), 2.59-2.65 (m, 1H), 2.07-2.14 (m, 1H), 1.67-1.82 (m, 4H), 1.63 (br d, <i>J</i> =10.98 Hz, 2H), 1.10-1.18 (m, 1H), 0.90-1.00 (m, 3H)	--	--

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
517	600MHz DMSO – d ₆	8.47 (d, <i>J</i> =5.76 Hz, 1H), 7.41 (dd, <i>J</i> =4.87, 8.68 Hz, 1H), 7.13 (dd, <i>J</i> =2.49, 9.26 Hz, 1H), 6.91 (ddd, <i>J</i> =2.57, 8.68, 10.08 Hz, 1H), 6.85 (d, <i>J</i> =5.84 Hz, 1H), 5.36 (s, 2H), 4.27-4.43 (m, 1H), 3.74 (s, 3H), 3.37-3.48 (m, 2H), 2.98-3.06 (m, 1H), 2.91 (tdd, <i>J</i> =4.17, 7.93, 14.39 Hz, 1H), 2.80 (dd, <i>J</i> =8.64, 12.46 Hz, 1H), 1.93-2.09 (m, 1H), 1.65-1.79 (m, 1H)	B	SFC: Chiralpak OD analytical column, 15% isopropanol Peak 1
518	600MHz DMSO – d ₆	7.46 (t, <i>J</i> =8.90 Hz, 1H), 7.40 (t, <i>J</i> =9.01 Hz, 1H), 5.13 (dd, <i>J</i> =12.96, 17.56 Hz, 1H), 4.93 (br t, <i>J</i> =16.66 Hz, 1H), 4.32-4.49 (m, 1H), 4.02-4.21 (m, 1H), 3.82-3.93 (m, 2H), 3.36-3.43 (m, 1H), 3.19-3.28 (m, 3H), 2.90-3.06 (m, 3H), 2.72-2.83 (m, 2H), 2.00-2.15 (m, 1H), 1.79 (br s, 1H), 1.39-1.54 (m, 1H), 0.86-0.97 (m, 3H)	--	--
519	600MHz DMSO – d ₆	8.81-9.03 (m, 1H), 8.27-8.41 (m, 2H), 7.63-7.75 (m, 1H), 7.38-7.55 (m, 1H), 5.85-5.99 (m, 2H), 4.19-4.51 (m, 3H), 2.83-2.95 (m, 1H), 2.63-2.78 (m, 1H), 1.94-2.14 (m, 1H), 1.69-1.86 (m, 1H), 1.41-1.58 (m, 1H)	B	SFC: Regis Whelk-O analytical column, 35% isopropanol. Peak 2
520	600MHz DMSO – d ₆	8.63 (br s, 2H), 7.22-7.35 (m, 2H), 7.11-7.22 (m, 2H), 4.74-4.85 (m, 2H), 4.28 (t, <i>J</i> =7.63 Hz, 1H), 3.94 (br t, <i>J</i> =7.71 Hz, 1H), 3.43-3.78 (m, 6H), 3.04-3.20 (m, 1H), 2.38-2.59 (m, 3H), 2.21-2.32 (m, 1H), 1.81-1.98 (m, 1H)	--	--
521	600MHz DMSO – d ₆	7.34-7.51 (m, 4H), 7.24 (br s, 1H), 4.91-5.16 (m, 3H), 4.66 (br dd, <i>J</i> =2.65, 17.20 Hz, 1H), 4.32-4.48 (m, 1H), 3.84-3.90 (m, 1H), 3.17 (d, <i>J</i> =4.13 Hz, 1H), 2.93-3.05 (m, 2H), 2.61-2.74 (m, 1H), 2.07-2.22 (m, 1H), 1.74-1.89 (m, 2H), 1.64 (br d, <i>J</i> =12.77 Hz, 2H), 1.42-1.57 (m, 2H), 1.26-1.38 (m, 2H)	--	--
522	600MHz DMSO – d ₆	7.48 (dd, <i>J</i> =7.51, 10.78 Hz, 1H), 7.33-7.43 (m, 1H), 7.04 (d, <i>J</i> =2.73 Hz, 2H), 7.04 (m, 1H), 5.20-5.38 (m, 1H), 4.90-5.05 (m, 2H), 4.75-4.87 (m, 1H), 4.68 (dd, <i>J</i> =6.85, 15.88 Hz, 1H), 3.67 (dt, <i>J</i> =8.25, 13.04 Hz, 1H), 3.38-3.52 (m, 1H), 3.26 (br d, <i>J</i> =5.22 Hz, 1H), 3.09-3.23 (m, 3H), 2.88-3.05 (m, 1H), 2.79-2.86 (m, 1H), 2.57-2.70 (m, 1H), 2.51-2.57 (m, 1H), 2.31-2.47 (m, 2H), 1.95-2.11 (m, 1H), 1.71-1.87 (m, 1H).	--	--
523	600MHz DMSO – d ₆	7.44-7.63 (m, 1H), 7.32-7.40 (m, 1H), 4.96-5.13 (m, 2H), 4.24-4.50 (m, 1H), 3.41 (br s, 1H), 3.21 (br s, 1H), 2.96-3.03 (m, 2H), 2.33-2.46 (m, 2H), 2.17-2.32 (m, 1H), 2.10 (br d, <i>J</i> =10.20 Hz, 1H), 1.88 (br d, <i>J</i> =6.85 Hz, 1H), 1.77 (br d, <i>J</i> =8.49 Hz, 1H), 1.67 (br d, <i>J</i> =9.81 Hz, 1H), 1.62 (br s, 1H), 1.56 (br s, 2H), 1.43-1.53 (m, 1H), 1.30-1.42 (m, 3H), 1.21-1.30 (m, 2H), 1.07-1.21 (m, 2H), 0.90-1.06 (m, 1H).	--	--

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
524	600MHz DMSO – d ₆	8.47 (d, <i>J</i> =5.84 Hz, 1H), 7.23 (d, <i>J</i> =9.56 Hz, 1H), 7.18-7.21 (m, 1H), 6.83-6.89 (m, 2H), 5.32-5.40 (m, 2H), 4.37-4.44 (m, 1H), 4.28-4.35 (m, 1H), 3.75 (s, 3H), 3.45-3.54 (m, 2H), 3.03-3.10 (m, 1H), 2.83 (dd, <i>J</i> =8.68, 12.50 Hz, 1H), 2.03-2.10 (m, 1H), 1.65-1.80 (m, 1H)	B	SFC: Chiralpak OD analytical column, 15% isopropanol peak 2
525	600MHz DMSO – d ₆	7.36-7.49 (m, 2H), 5.09-5.19 (m, 2H), 4.93-5.05 (m, 2H), 4.36-4.44 (m, 1H), 3.61 (td, <i>J</i> =8.79, 13.18 Hz, 1H), 3.37-3.49 (m, 1H), 3.24-3.30 (m, 1H), 3.10-3.24 (m, 3H), 3.07 (s, 3H), 2.93-3.05 (m, 3H), 2.74-2.83 (m, 3H), 2.18-2.34 (m, 1H), 2.05-2.15 (m, 1H), 1.73-1.91 (m, 1H)	--	--
526	600MHz DMSO – d ₆	7.45-7.58 (m, 2H), 5.02-5.14 (m, 2H), 4.40-4.49 (m, 1H), 4.33-4.40 (m, 1H), 3.36-3.51 (m, 1H), 3.22-3.29 (m, 3H), 3.17 (s, 1H), 2.93-3.12 (m, 4H), 2.77 (ddd, <i>J</i> =4.17, 8.31, 12.59 Hz, 1H), 2.34-2.47 (m, 2H), 2.08-2.17 (m, 1H), 1.74-1.92 (m, 1H), 1.06 (br d, <i>J</i> =8.33 Hz, 2H), 0.94-1.03 (m, 2H)	--	--
527	600MHz DMSO – d ₆	7.36-7.51 (m, 2H), 4.95-5.24 (m, 2H), 4.71-4.86 (m, 1H), 4.45-4.54 (m, 1H), 4.32-4.38 (m, 1H), 3.45-3.55 (m, 1H), 3.35-3.44 (m, 2H), 3.24-3.31 (m, 2H), 3.09-3.22 (m, 2H), 2.92-3.04 (m, 2H), 2.73-2.81 (m, 1H), 2.23-2.39 (m, 2H), 2.04-2.15 (m, 1H), 1.65-1.92 (m, 3H), 1.25 (t, <i>J</i> =7.05 Hz, 2H), 1.05 (br t, <i>J</i> =6.77 Hz, 1H)	--	--
528	600MHz DMSO – d ₆	7.46-7.54 (m, 2H), 5.00-5.15 (m, 2H), 4.68-4.86 (m, 1H), 4.23 (s, 1H), 3.91-4.00 (m, 1H), 3.75 (br t, <i>J</i> =5.29 Hz, 1H), 3.57-3.68 (m, 3H), 3.20-3.26 (m, 2H), 2.95-3.06 (m, 2H), 2.51-2.65 (m, 1H), 2.15-2.22 (m, 1H), 1.82-1.92 (m, 1H)	--	--
529	600MHz DMSO – d ₆	7.46 (dd, <i>J</i> =7.51, 11.09 Hz, 1H), 7.38 (dd, <i>J</i> =7.32, 10.74 Hz, 1H), 4.95-5.08 (m, 2H), 4.28-4.38 (m, 1H), 3.99 (br d, <i>J</i> =13.31 Hz, 1H), 3.46-3.55 (m, 2H), 3.24-3.30 (m, 4H), 3.11-3.23 (m, 1H), 2.93-3.10 (m, 2H), 2.68-2.82 (m, 3H), 2.11 (ddd, <i>J</i> =4.48, 8.31, 12.59 Hz, 1H), 1.89 (quin, <i>J</i> =6.79 Hz, 2H), 1.68-1.82 (m, 5H), 1.64 (dt, <i>J</i> =3.43, 12.26 Hz, 1H), 1.35-1.45 (m, 1H)	--	--
530	600MHz DMSO – d ₆	7.40-7.48 (m, 1H), 7.31-7.40 (m, 1H), 4.94-5.09 (m, 2H), 3.73-3.91 (m, 2H), 3.42-3.57 (m, 1H), 3.08-3.22 (m, 3H), 2.97-3.05 (m, 3H), 2.79 (tt, <i>J</i> =8.44, 12.15 Hz, 2H), 2.33-2.48 (m, 1H), 2.01-2.16 (m, 1H), 1.86-1.98 (m, 1H), 1.68-1.84 (m, 2H), 1.58-1.66 (m, 1H)	--	--

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
531	600MHz DMSO – d ₆	7.46 (t, <i>J</i> =9.14 Hz, 1H), 7.41 (t, <i>J</i> =8.98 Hz, 1H), 5.00-5.12 (m, 2H), 4.35-4.46 (m, 1H), 3.82 (br s, 1H), 3.49 – 3.82 (m, 7H), 3.23-3.30 (m, 1H), 2.94-3.11 (m, 2H), 2.79 (dd, <i>J</i> =8.06, 12.57 Hz, 1H), 2.06-2.17 (m, 1H), 2.00 (br s, 1H), 1.73-1.92 (m, 2H), 0.71-0.80 (m, 4H)	--	--
532	600MHz DMSO – d ₆	7.46 (dd, <i>J</i> =7.47, 11.13 Hz, 1H), 7.37 (dd, <i>J</i> =7.40, 10.74 Hz, 1H), 7.30 (br d, <i>J</i> =5.37 Hz, 1H), 6.82 (br s, 1H), 4.95-5.06 (m, 2H), 4.31-4.45 (m, 1H), 4.22-4.30 (m, 1H), 3.97 (br d, <i>J</i> =13.16 Hz, 1H), 3.10-3.22 (m, 2H), 2.91-3.09 (m, 3H), 2.66-2.82 (m, 2H), 2.35-2.47 (m, 1H), 2.00-2.16 (m, 1H), 1.77-1.85 (m, 2H), 1.71-1.77 (m, 1H), 1.56-1.68 (m, 1H), 1.36-1.44 (m, 1H)	--	--
533	600MHz DMSO – d ₆	7.36 (t, <i>J</i> =9.19 Hz, 1H), 6.93 (s, 1H), 6.89 (s, 1H), 6.80 (dt, <i>J</i> =7.32, 10.20 Hz, 1H), 4.27-4.45 (m, 1H), 3.63-3.75 (m, 2H), 3.59 (br d, <i>J</i> =11.83 Hz, 1H), 3.11-3.25 (m, 1H), 2.98-2.74-2.92 (m, 3H), 1.90-2.05 (m, 1H), 1.58-1.72 (m, 2H), 1.44 (d, <i>J</i> =7.08 Hz, 3H), 1.36 (d, <i>J</i> =7.24 Hz, 3H)	--	--
534	600MHz DMSO – d ₆	7.77 (br dd, <i>J</i> =4.44, 7.32 Hz, 1H), 7.46 (dd, <i>J</i> =7.43, 11.09 Hz, 1H), 7.37 (dd, <i>J</i> =7.36, 10.70 Hz, 1H), 4.94-5.07 (m, 2H), 4.32-4.44 (m, 1H), 4.24-4.31 (m, 1H), 3.98 (br d, <i>J</i> =13.23 Hz, 1H), 3.26 (br s, 1H), 3.09-3.21 (m, 1H), 2.92-3.07 (m, 2H), 2.66-2.81 (m, 2H), 2.58 (d, <i>J</i> =4.59 Hz, 3H), 2.32-2.47 (m, 2H), 2.10 (br dd, <i>J</i> =3.54, 13.20 Hz, 1H), 1.57-1.86 (m, 4H), 1.33-1.46 (m, 1H)	--	--
535	600MHz DMSO – d ₆	7.32-7.49 (m, 2H), 4.89-5.05 (m, 2H), 4.34-4.45 (m, 1H), 3.69-3.85 (m, 2H), 3.16-3.27 (m, 1H), 2.95-3.12 (m, 4H), 2.72-2.88 (m, 1H), 1.98-2.16 (m, 2H), 1.86 (br d, <i>J</i> =1.71 Hz, 4H), 1.70-1.84 (m, 3H), 1.40-1.59 (m, 2H)	--	--
536	600MHz DMSO – d ₆	7.46 (dd, <i>J</i> =7.47, 11.13 Hz, 1H), 7.38 (dd, <i>J</i> =7.36, 10.70 Hz, 1H), 4.95-5.08 (m, 2H), 4.35-4.44 (m, 3H), 3.98 (br d, <i>J</i> =13.31 Hz, 1H), 3.49 (br s, 2H), 3.38-3.45 (m, 3H), 3.16-3.28 (m, 2H), 2.91-3.04 (m, 3H), 2.71-2.83 (m, 2H), 1.97-2.15 (m, 1H), 1.73-1.91 (m, 1H), 1.57-1.70 (m, 4H), 1.51 (br s, 2H), 1.36-1.46 (m, 3H)	--	--
537	600MHz DMSO – d ₆	7.46 (dd, <i>J</i> =7.43, 11.09 Hz, 1H), 7.38 (dd, <i>J</i> =7.40, 10.74 Hz, 1H), 4.95-5.08 (m, 2H), 4.28-4.39 (m, 1H), 3.99 (br d, <i>J</i> =13.39 Hz, 1H), 3.52 (br t, <i>J</i> =5.99 Hz, 2H), 3.37-3.44 (m, 2H), 3.25-3.30 (m, 1H), 3.13-3.25 (m, 2H), 2.94-3.05 (m, 2H), 2.85-2.93 (m, 1H), 2.70-2.85 (m, 2H), 2.11 (ddd, <i>J</i> =4.44, 8.19, 12.51 Hz, 1H), 1.74-1.84 (m, 2H), 1.63-1.72 (m, 5H), 1.58 (quin, <i>J</i> =5.90 Hz, 2H), 1.40-1.53 (m, 5H)	--	--

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
538	600MHz DMSO – d ₆	7.47 (dd, <i>J</i> =7.43, 11.17 Hz, 1H), 7.31 (dd, <i>J</i> =7.28, 10.70 Hz, 1H), 5.03 (br s, 2H), 4.31-4.46 (m, 2H), 3.55-3.71 (m, 4H), 3.34-3.42 (m, 4H), 3.21-3.28 (m, 3H), 3.04-3.20 (m, 2H), 2.92-3.03 (m, 2H), 2.69-2.81 (m, 1H), 2.26-2.40 (m, 2H), 1.99-2.14 (m, 1H), 1.70-1.86 (m, 1H)	--	--
539	600MHz DMSO – d ₆	7.46 (dd, <i>J</i> =7.47, 11.13 Hz, 1H), 7.38 (dd, <i>J</i> =7.40, 10.74 Hz, 1H), 5.01 (dq, <i>J</i> =9.61, 17.43 Hz, 2H), 4.43 (td, <i>J</i> =4.02, 7.61 Hz, 1H), 4.31-4.38 (m, 1H), 4.29 (br s, 1H), 3.98 (br d, <i>J</i> =13.23 Hz, 1H), 3.83-3.92 (m, 1H), 3.15-3.29 (m, 2H), 2.92-3.04 (m, 4H), 2.73-2.81 (m, 2H), 2.51-2.62 (m, 1H), 2.06-2.15 (m, 1H), 1.71-1.88 (m, 4H), 1.59-1.71 (m, 4H), 1.39 (br s, 2H), 1.09-1.17 (m, 1H), 0.90 (br d, <i>J</i> =6.38 Hz, 2H), 0.85 (br d, <i>J</i> =6.46 Hz, 2H)	--	--
540	600MHz DMSO – d ₆	7.46 (t, <i>J</i> =9.12 Hz, 1H), 7.40 (t, <i>J</i> =9.00 Hz, 1H), 5.00-5.11 (m, 2H), 4.33-4.44 (m, 1H), 3.51-3.63 (m, 5H), 3.43-3.49 (m, 3H), 3.23-3.30 (m, 1H), 2.94-3.06 (m, 2H), 2.79 (dd, <i>J</i> =8.06, 12.57 Hz, 1H), 2.02-2.17 (m, 4H), 1.75-1.93 (m, 2H)	--	--
541	600MHz DMSO – d ₆	7.47 (t, <i>J</i> =9.15 Hz, 1H), 7.30-7.41 (m, 1H), 4.99-5.17 (m, 2H), 4.30-4.44 (m, 1H), 4.06-4.15 (m, 1H), 3.85-3.93 (m, 1H), 3.71-3.79 (m, 1H), 3.45-3.64 (m, 2H), 3.35-3.42 (m, 1H), 3.17 (d, <i>J</i> =4.98 Hz, 1H), 3.05-3.13 (m, 1H), 2.93-3.04 (m, 2H), 2.69-2.80 (m, 1H), 2.30-2.47 (m, 2H), 2.02-2.13 (m, 2H), 1.91-1.96 (m, 1H), 1.74-1.90 (m, 4H), 1.46-1.54 (m, 1H)	--	--
542	600MHz DMSO – d ₆	7.46 (dd, <i>J</i> =7.47, 11.13 Hz, 1H), 7.38 (dd, <i>J</i> =7.32, 10.74 Hz, 1H), 4.95-5.07 (m, 2H), 4.67 (spt, <i>J</i> =6.76 Hz, 1H), 4.29-4.37 (m, 1H), 4.25 (td, <i>J</i> =3.24, 6.52 Hz, 1H), 3.99 (br d, <i>J</i> =13.47 Hz, 1H), 3.17-3.35 (m, 1H), 2.92-3.05 (m, 3H), 2.86 (s, 2H), 2.69-2.83 (m, 2H), 2.66 (s, 1H), 2.06-2.16 (m, 1H), 1.74-1.91 (m, 3H), 1.59-1.70 (m, 3H), 1.35-1.47 (m, 1H), 1.16 (dd, <i>J</i> =2.57, 6.31 Hz, 3H), 1.02 (dd, <i>J</i> =3.58, 6.62 Hz, 3H)	--	--
543	600MHz DMSO – d ₆	7.47-7.55 (m, 1H), 7.26-7.33 (m, 1H), 5.06-5.14 (m, 2H), 4.38-4.56 (m, 2H), 4.11-4.27 (m, 1H), 3.36-3.46 (m, 1H), 3.11-3.28 (m, 3H), 2.93-3.09 (m, 2H), 2.79 (br s, 1H), 1.99-2.16 (m, 2H), 1.74 (br t, <i>J</i> =9.42 Hz, 1H), 0.98 (d, <i>J</i> =6.54 Hz, 3H), 0.83 (dd, <i>J</i> =2.34, 6.62 Hz, 3H)	--	--
544	600MHz DMSO – d ₆	6.80-6.88 (m, 1H), 6.56-6.63 (m, 1H), 5.03-5.14 (m, 2H), 4.38-4.53 (m, 1H), 4.30-4.37 (m, 1H), 4.23 (q, <i>J</i> =9.52 Hz, 2H), 3.73-3.77 (m, 3H), 3.24 (s, 3H), 2.92-3.04 (m, 3H), 2.72-2.82 (m, 1H), 2.03-2.13 (m, 1H), 1.73-1.90 (m, 1H)	B	SFC: Chiralpak IC, 20% methanol. Peak 1

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
545	600MHz DMSO – d ₆	6.83 (dd, <i>J</i> =2.18, 9.42 Hz, 1H), 6.61 (dd, <i>J</i> =2.18, 11.99 Hz, 1H), 4.96-5.07 (m, 2H), 4.34-4.44(m, 1H), 3.80 (s, 3H), 3.63-3.70 (m, 2H), 3.59 (br d, <i>J</i> =4.83 Hz, 4H), 3.40-3.52 (m, 3H), 3.22-3.28 (m, 1H), 2.94-3.11 (m, 2H), 2.77 (dd, <i>J</i> =8.49, 12.53 Hz, 1H), 2.02-2.19 (m, 1H), 1.75-1.84 (m, 1H)	B	SFC: Chiralpak IC, 35% methanol Peak 1
546	600MHz DMSO – d ₆	6.74 (dd, <i>J</i> =2.26, 8.95 Hz, 1H), 6.57 (dd, <i>J</i> =2.22, 12.18 Hz, 1H), 4.94-5.02 (m, 2H), 4.35-4.43 (m, 1H), 3.89 (s, 3H), 3.61-3.70 (m, 2H), 3.59 (br s, 3H), 3.36-3.53 (m, 3H), 3.16-3.28 (m, 2H), 2.92-3.02 (m, 2H), 2.74 (dd, <i>J</i> =8.17, 12.46 Hz, 1H), 1.98-2.14 (m, 1H), 1.74-1.86 (m, 1H)	B	SFC: Chiralpak IC, 35% methanol Peak 2
547	500 MHz, METHA NOL-d ₄	7.35 (dd, <i>J</i> =7.53, 10.64 Hz, 1H), 7.01 (dd, <i>J</i> =6.88, 10.25 Hz, 1H), 5.38 (t, <i>J</i> =10.12 Hz, 1H), 4.34-4.52 (m, 1H), 3.59-3.69 (m, 1H), 3.55 (dt, <i>J</i> =7.40, 9.67 Hz, 1H), 3.41-3.51 (m, 2H), 3.05-3.22 (m, 2H), 2.94 (dd, <i>J</i> =8.82, 12.46 Hz, 1H), 2.79-2.87 (m, 1H), 2.61-2.70 (m, 1H), 2.37-2.48 (m, 1H), 2.18-2.30 (m, 1H), 1.91-2.03 (m, 1H), 0.80-0.94 (m, 4H)	B	SC: Regis Whelk-O, 30% IPA, Peak 1
548	500 MHz, CHLOR OFORM-d	7.39 (dd, <i>J</i> =7.27, 10.64 Hz, 1H), 6.69 (dd, <i>J</i> =7.01, 9.86 Hz, 1H), 5.21 (t, <i>J</i> =9.99 Hz, 1H), 4.27-4.46 (m, 2H), 4.04-4.16 (m, 2H), 3.48-3.70 (m, 6H), 3.14-3.24 (m, 1H), 2.96-3.11 (m, 2H), 2.53-2.63 (m, 1H), 2.41 (qd, <i>J</i> =9.54, 13.43 Hz, 1H), 2.18-2.26 (m, 1H), 1.92-2.08 (m, 2H), 1.69-1.91 (m, 3H)	B	SC: Chiralpak IC, 20% methanol, Peak 1
549	500 MHz, METHA NOL-d ₄	7.36 (dd, <i>J</i> =7.27, 10.64 Hz, 1H), 7.02 (dd, <i>J</i> =7.01, 10.38 Hz, 1H), 5.39 (t, <i>J</i> =10.12 Hz, 1H), 4.35-4.53 (m, 1H), 3.64 (dt, <i>J</i> =1.04, 9.73 Hz, 1H), 3.50-3.60 (m, 2H), 3.41 (br dd, <i>J</i> =5.19, 7.27 Hz, 1H), 3.11-3.21 (m, 2H), 2.93 (dd, <i>J</i> =8.56, 12.46 Hz, 1H), 2.79-2.87 (m, 1H), 2.57-2.67 (m, 1H), 2.42 (qd, <i>J</i> =9.87, 12.94 Hz, 1H), 2.17-2.30 (m, 1H), 1.94-2.04 (m, 1H), 0.78-0.94 (m, 4H)	B	SC: Regis Whelk-O, 30% IPA, Peak 2
550	500 MHz, CHLOR OFORM-d	7.39 (dd, <i>J</i> =7.40, 10.51 Hz, 1H), 6.69 (dd, <i>J</i> =6.75, 9.86 Hz, 1H), 5.19 (t, <i>J</i> =9.86 Hz, 1H), 4.35-4.47 (m, 2H), 4.02-4.19 (m, 2H), 3.40-3.71 (m, 6H), 3.16-3.38 (m, 2H), 2.89 (dd, <i>J</i> =8.69, 12.59 Hz, 1H), 2.58 (dddd, <i>J</i> =1.30, 7.72, 9.34, 13.30 Hz, 1H), 2.40 (qd, <i>J</i> =9.68, 13.27 Hz, 1H), 2.16-2.32 (m, 1H), 1.90-2.04 (m, 2H), 1.72-1.90 (m, 3H)	B	SC: Chiralpak IC, 20% methanol, Peak 2
551	600 MHz, DMSO-d ₆	7.46-7.56 (m, 2H), 7.38-7.45 (m, 1H), 5.56 (s, 2H), 4.32-4.50 (m, 1H), 3.37-3.51 (m, 2H), 3.04-3.12 (m, 1H), 2.94-3.04 (m, 1H), 2.80-2.90 (m, 1H), 2.07-2.17 (m, 1H), 1.73-1.85 (m, 1H)	-	-
552	500 MHz, METHA NOL-d ₄	7.06-7.14 (m, 1H), 6.80-6.91 (m, 1H), 5.76 (s, 2H), 4.54-4.72 (m, 1H), 3.66-3.79 (m, 1H), 3.52-3.61 (m, 1H), 3.41-3.52 (m, 1H), 3.32 (t, <i>J</i> =1.62 Hz, 3H), 3.15-3.24 (m, 1H), 3.07-3.15 (m, 1H), 2.22-2.34 (m, 1H), 1.93-2.09 (m, 1H)	B	Regis Whelk-O s.s, 25% MeOH, peak 2

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
553	600 MHz, DMSO-d ₆	7.46-7.63 (m, 2H), 5.68-5.79 (m, 2H), 4.32-4.52 (m, 1H), 3.37-3.47 (m, 2H), 2.98-3.11 (m, 2H), 2.79-2.88 (m, 1H), 2.62-2.69 (m, 3H), 2.07-2.17 (m, 1H), 1.75-1.85 (m, 1H)	-	-
554	500 MHz, METHA NOL-d ₄	7.54-7.67 (m, 2H), 7.43-7.53 (m, 1H), 5.21 (s, 2H), 4.10-4.57 (m, 3H), 3.52-3.62 (m, 1H), 3.39-3.47 (m, 1H), 3.35 (s, 3H), 3.13 (m, 2H), 2.92-3.06 (m, 1H), 2.12-2.28 (m, 1H), 1.86-2.03 (m, 1H)	F	Chiralpak AD-H, 15% MeOH/DEA, peak 1
555	500 MHz, METHA NOL-d ₄	8.81 (s, 2H), 8.16 (t, <i>J</i> =2.34 Hz, 1H), 7.58 (dd, <i>J</i> =2.59, 8.43 Hz, 1H), 5.54 (s, 2H), 4.36-4.56 (m, 1H), 3.68-3.79 (m, 1H), 3.58-3.68 (m, 1H), 3.10-3.25 (m, 2H), 2.96-3.10 (m, 1H), 2.10-2.27 (m, 1H), 1.81-1.97 (m, 1H)	F	Chiralpak IC, 40% MeOH with 0.2% DEA, peak 2
556	600 MHz, DMSO-d ₆	8.98 (d, <i>J</i> =1.79 Hz, 1H), 8.29-8.34 (m, 1H), 7.53 (d, <i>J</i> =8.25 Hz, 1H), 7.01-7.06 (m, 1H), 6.97 (td, <i>J</i> =10.59, 2.18 Hz, 1H), 5.57 (s, 2H), 4.32-4.40 (m, 1H), 3.36-3.51 (m, 2H), 3.31 (s, 3H), 2.98-3.09 (m, 1H), 2.86-2.95 (m, 1H), 2.80 (dd, <i>J</i> =12.46, 8.49 Hz, 1H), 2.01-2.09 (m, 1H), 1.68-1.76 (m, 1H)	B	Lux Cellulose-2, 30% MeOH, peak 2
557	500 MHz, METHA NOL-d ₄	7.21-7.40 (m, 1H), 7.07-7.17 (m, 1H), 6.81-6.93 (m, 1H), 5.83-5.96 (m, 2H), 4.63-4.80 (m, 1H), 3.73-3.86 (m, 1H), 3.54-3.72 (m, 2H), 3.12-3.25 (m, 2H), 2.24-2.36 (m, 1H), 1.98-2.10 (m, 1H)	B	Regis Whelk-O s,s, 10% MeOH, peak 2
558	500 MHz, METHA NOL-d ₄	7.00-7.08 (m, 1H), 6.74-6.84 (m, 1H), 5.19 (s, 2H), 4.38-4.56 (m, 1H), 4.06-4.28 (m, 3H), 3.48-3.58 (m, 1H), 3.38-3.46 (m, 1H), 3.33 (s, 3H), 3.14-3.20 (m, 1H), 2.88-3.02 (m, 1H), 2.14-2.27 (m, 1H), 1.88-2.00 (m, 1H)	F	Regis Whelk-O s,s, 15% MeOH, peak 1
559	500 MHz, METHA NOL-d ₄	7.39-7.50 (m, 1H), 7.22-7.34 (m, 1H), 7.09-7.23 (m, 1H), 5.10 (s, 2H), 4.11-4.53 (m, 3H), 3.44-3.55 (m, 1H), 3.34-3.41 (m, 1H), 3.34 (s, 3H), 3.05-3.16 (m, 2H), 2.87-2.98 (m, 1H), 2.12-2.25 (m, 1H), 1.82-2.00 (m, 1H)	F	Chiralpak AD-H, 25% MeOH/DEA, peak 1
560	600 MHz, DMSO-d ₆	7.42-7.68 (m, 3H), 5.84-5.98 (m, 2H), 4.30-4.51 (m, 1H), 3.34-3.49 (m, 2H), 3.04-3.13 (m, 1H), 2.93-3.02 (m, 1H), 2.79-2.90 (m, 1H), 2.08-2.18 (m, 1H), 1.73-1.86 (m, 1H)	-	-
561	500 MHz, METHA NOL-d ₄	7.43-7.54 (m, 1H), 7.16-7.27 (m, 1H), 6.94-7.04 (m, 1H), 5.75 (s, 2H), 4.54-4.74 (m, 1H), 3.66-3.75 (m, 1H), 3.51-3.59 (m, 1H), 3.43-3.49 (m, 1H), 3.28-3.36 (m, 3H), 3.06-3.24 (m, 2H), 2.22-2.39 (m, 1H), 1.96-2.14 (m, 1H)	B	Chiralpak AZ-H, 30% MeOH, peak 2
562	600 MHz, DMSO-d ₆	8.92-9.00 (m, 1H), 8.26-8.35 (m, 1H), 7.44-7.57 (m, 2H), 7.32-7.42 (m, 1H), 5.55 (s, 2H), 4.29-4.48 (m, 1H), 3.38-3.47 (m, 2H), 3.31 (s, 3H), 2.99-3.09 (m, 1H), 2.89-2.98 (m, 1H), 2.75-2.84 (m, 1H), 2.00-2.11 (m, 1H), 1.65-1.78 (m, 1H)	-	-

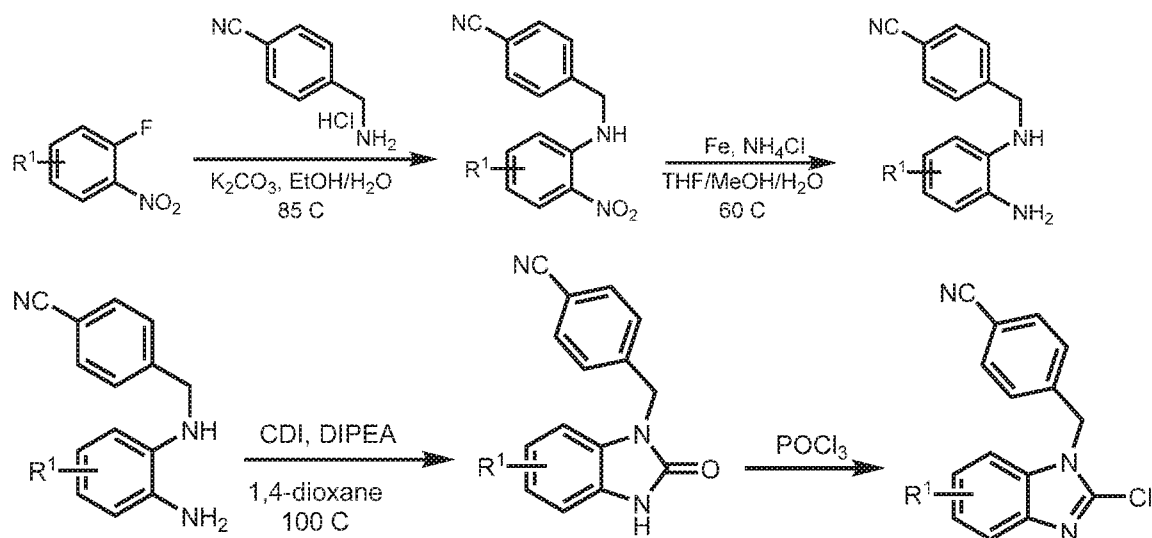
Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
563	600 MHz, DMSO-d ₆	7.64 (s, 1H), 7.56 (d, <i>J</i> =8.33 Hz, 1H), 7.40 (dd, <i>J</i> =8.33, 1.25 Hz, 1H), 5.06-5.15 (m, 2H), 4.38-4.46 (m, 1H), 3.39-3.41 (m, 2H), 3.07-3.15 (m, 4H), 2.99 (m, 1H), 2.90 (s, 3H), 2.84 (dd, <i>J</i> =12.69, 8.17 Hz, 1H), 2.01-2.17 (m, 1H), 1.74-1.85 (m, 1H)	B	Chiralpak IC, 15% MeOH, peak 1
564	600 MHz, DMSO-d ₆	7.47-7.52 (m, 1H), 7.42-7.46 (m, 1H), 6.07-6.14 (m, 1H), 5.34 (s, 2H), 4.31-4.55 (m, 1H), 3.40-3.51 (m, 2H), 2.98-3.12 (m, 2H), 2.79-2.89 (m, 1H), 2.36 (s, 3H), 2.07-2.18 (m, 1H), 1.75-1.85 (m, 1H)	-	-
565	600 MHz, DMSO-d ₆	7.02-7.09 (m, 1H), 6.90-6.98 (m, 1H), 4.94-5.05 (m, 2H), 4.31-4.49 (m, 1H), 3.32 (s, 2H), 3.12 (s, 3H), 2.93-3.07 (m, 2H), 2.88 (s, 3H), 2.75-2.82 (m, 1H), 2.04-2.18 (m, 1H), 1.77-1.83 (m, 1H)	B	Phenomenex CEL 2, 25% MeOH, peak 1
566	600 MHz, DMSO-d ₆	7.35-7.44 (m, 1H), 7.07-7.13 (m, 1H), 6.84-6.95 (m, 1H), 4.90-5.04 (m, 2H), 4.31-4.49 (m, 1H), 3.24-3.25 (m, 2H), 3.12 (s, 3H), 2.93-3.03 (m, 2H), 2.89 (s, 3H), 2.72-2.81 (m, 1H), 2.03-2.17 (m, 1H), 1.73-1.86 (m, 1H)	B	Phenomenex CEL 2, 25% MeOH, peak 1
567	600 MHz, DMSO-d ₆	7.49-7.54 (m, 1H), 7.40-7.46 (m, 1H), 6.77-6.87 (m, 1H), 5.40 (s, 2H), 4.30-4.48 (m, 1H), 3.37-3.50 (m, 2H), 3.03-3.13 (m, 1H), 2.91-3.00 (m, 1H), 2.80-2.88 (m, 1H), 2.26 (d, <i>J</i> =1.09 Hz, 3H), 2.06-2.15 (m, 1H), 1.72-1.81 (m, 1H)	-	-
568	600 MHz, DMSO-d ₆	7.47-7.57 (m, 2H), 7.18-7.28 (m, 1H), 5.59 (s, 2H), 4.31-4.48 (m, 1H), 3.38-3.51 (m, 2H), 3.03-3.12 (m, 1H), 2.92-3.01 (m, 1H), 2.79-2.88 (m, 1H), 2.32 (s, 3H), 2.04-2.17 (m, 1H), 1.73-1.81 (m, 1H)	-	-
569	600 MHz, DMSO-d ₆	7.45-7.53 (m, 1H), 7.35-7.42 (m, 1H), 6.96-7.06 (m, 1H), 5.89 (s, 2H), 4.28-4.47 (m, 1H), 3.32 (m, 2H), 2.97-3.06 (m, 1H), 2.87-2.95 (m, 1H), 2.73-2.82 (m, 1H), 2.04-2.14 (m, 1H), 1.67-1.77 (m, 1H)	B	Chiralcel OD-H, 15% isopropanol, peak 1
570	500 MHz, METHA NOL-d ₄	7.42-7.52 (m, 1H), 7.09-7.21 (m, 2H), 5.11 (s, 2H), 4.09-4.53 (m, 3H), 3.46-3.56 (m, 1H), 3.35-3.45 (m, 1H), 3.34 (s, 3H), 3.05-3.15 (m, 2H), 2.87-2.98 (m, 1H), 2.13-2.26 (m, 1H), 1.85-1.97 (m, 1H)	F	Chiralpak AD-H, 25% MeOH/DEA, peak 2
571	600 MHz, DMSO-d ₆	7.48-7.57 (m, 2H), 5.59 (s, 2H), 4.32-4.50 (m, 1H), 3.39-3.46 (m, 2H), 3.02-3.10 (m, 1H), 2.94-3.02 (m, 1H), 2.76-2.88 (m, 1H), 2.47 (s, 3H), 2.06-2.17 (m, 1H), 1.73-1.82 (m, 1H)	-	-
572	600 MHz, DMSO-d ₆	7.48-7.56 (m, 1H), 7.39-7.47 (m, 1H), 5.44 (s, 2H), 4.31-4.50 (m, 1H), 3.35-3.48 (m, 2H), 3.02-3.13 (m, 1H), 2.91-3.01 (m, 1H), 2.78-2.89 (m, 1H), 2.57 (s, 3H), 2.06-2.16 (m, 1H), 1.72-1.80 (m, 1H)	-	-
573	500 MHz, METHA NOL-d ₄	7.47-7.56 (m, 1H), 7.10-7.37 (m, 2H), 6.99-7.07 (m, 1H), 5.90 (s, 2H), 4.65-4.84 (m, 1H), 3.75-3.84 (m, 1H), 3.53-3.70 (m, 2H), 3.13-3.23 (m, 2H), 2.26-2.37 (m, 1H), 2.00-2.11 (m, 1H)	B	Chiralcel OD-H, 15% isopropanol, peak 1

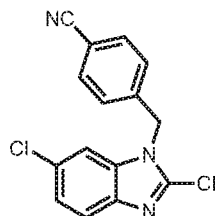
Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
574	500 MHz, METHA NOL-d ₄	8.18-8.24 (m, 1H), 7.68-7.75 (m, 1H), 5.73-5.82 (m, 2H), 4.54-4.74 (m, 1H), 3.77-3.88 (m, 1H), 3.41-3.77 (m, 2H), 3.32 (td, <i>J</i> =1.62, 3.24 Hz, 1H), 3.06-3.22 (m, 1H), 2.68-2.79 (m, 3H), 2.21 (s, 1H), 1.90-2.05 (m, 1H)	B	Chiralpak IC, 35% MeOH, peak 1
575	600 MHz, DMSO-d ₆	7.47-7.55 (m, 1H), 7.36-7.46 (m, 1H), 5.35 (s, 2H), 4.32-4.48 (m, 1H), 3.39-3.49 (m, 2H), 3.03-3.12 (m, 1H), 2.93-3.02 (m, 1H), 2.79-2.89 (m, 1H), 2.18 (s, 3H), 2.05-2.14 (m, 1H), 1.97 (s, 3H), 1.70-1.82 (m, 1H)	-	-
576	600 MHz, DMSO-d ₆	7.20-7.24 (m, 1H), 7.12-7.19 (m, 1H), 6.86-6.95 (m, 1H), 4.91-5.05 (m, 2H), 4.31-4.48 (m, 1H), 3.33-3.39 (m, 2H), 3.12 (s, 3H), 2.93-3.06 (m, 2H), 2.89 (s, 3H), 2.74-2.82 (m, 1H), 2.05-2.15 (m, 1H), 1.74-1.82 (m, 1H)	B	Chiralpak IC, 15% MeOH, peak 2
577	600 MHz, DMSO-d ₆	7.42-7.54 (m, 2H), 5.45 (s, 2H), 4.29-4.49 (m, 1H), 3.37-3.50 (m, 2H), 3.03-3.13 (m, 1H), 2.92 (m, 3H), 2.77-2.87 (m, 1H), 2.06-2.17 (m, 1H), 1.71-1.80 (m, 1H), 1.24 (t, <i>J</i> =7.55 Hz, 3H)	-	-
578	600 MHz, DMSO-d ₆	7.43-7.56 (m, 2H), 5.37-5.45 (m, 2H), 4.31-4.49 (m, 1H), 3.36-3.47 (m, 2H), 3.03-3.11 (m, 1H), 2.90-2.99 (m, 1H), 2.75-2.86 (m, 1H), 2.29-2.37 (m, 1H), 2.05-2.17 (m, 1H), 1.69-1.82 (m, 1H), 1.20-1.27 (m, 3H), 1.03-1.10 (m, 3H)	-	-
579	600 MHz, DMSO-d ₆	7.45-7.58 (m, 2H), 6.28-6.36 (m, 1H), 5.45 (s, 2H), 4.32-4.51 (m, 1H), 3.39-3.47 (m, 1H), 3.35-3.39 (m, 1H), 3.04-3.13 (m, 1H), 2.94-3.03 (m, 1H), 2.79-2.89 (m, 1H), 2.19 (s, 3H), 2.08-2.16 (m, 1H), 1.78-1.84 (m, 1H)	-	-
580	500 MHz, METHA NOL-d ₄	7.70-7.83 (m, 1H), 7.42-7.53 (m, 1H), 7.27-7.41 (m, 1H), 5.21 (s, 2H), 4.13-4.56 (m, 3H), 3.51-3.62 (m, 1H), 3.40-3.48 (m, 1H), 3.37 (s, 3H), 3.12 (s, 2H), 2.93-3.05 (m, 1H), 2.14-2.30 (m, 1H), 1.88-2.03 (m, 1H)	F	Chiralpak AD-H, 15% MeOH/DEA, peak 2
581	600 MHz, DMSO-d ₆	7.47-7.61 (m, 2H), 5.48-5.60 (m, 2H), 4.30-4.49 (m, 1H), 3.37-3.46 (m, 2H), 2.99-3.08 (m, 1H), 2.90-2.98 (m, 1H), 2.78-2.86 (m, 1H), 2.18-2.25 (m, 1H), 2.06-2.16 (m, 1H), 1.72-1.81 (m, 1H), 1.08-1.15 (m, 2H), 0.91-0.99 (m, 2H)	-	-
582	500 MHz, METHA NOL-d ₄	7.33-7.40 (m, 1H), 7.16-7.25 (m, 1H), 6.92-7.01 (m, 1H), 5.70-5.80 (m, 2H), 4.48-4.68 (m, 1H), 3.65-3.75 (m, 1H), 3.50-3.59 (m, 1H), 3.36 (s, 3H), 3.30-3.34 (m, 1H), 3.14-3.25 (m, 1H), 3.02-3.12 (m, 1H), 2.22-2.34 (m, 1H), 1.93-2.07 (m, 1H)	B	Chiralpak AZ-H, 30% MeOH, peak 1
583	500 MHz, METHA NOL-d ₄	8.70-8.80 (m, 2H), 7.94-8.04 (m, 1H), 7.56-7.66 (m, 1H), 5.62 (s, 2H), 4.39-4.61 (m, 1H), 3.63-3.87 (m, 2H), 3.13-3.25 (m, 2H), 2.95-3.09 (m, 1H), 2.12-2.26 (m, 1H), 1.74-1.92 (m, 1H)	F	Chiralpak IC, 40% MeOH with 0.2% DEA, peak 2

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
584	600 MHz, DMSO-d ₆	7.37-7.45 (m, 1H), 7.26-7.35 (m, 1H), 6.95-7.06 (m, 1H), 5.89 (s, 2H), 4.30-4.49 (m, 1H), 3.32-3.44 (m, 2H), 3.00-3.11 (m, 1H), 2.86-2.97 (m, 1H), 2.75-2.84 (m, 1H), 2.06-2.17 (m, 1H), 1.67-1.77 (m, 1H)	B	Chiralcel OD-H, 15% isopropanol, peak 2
585	600 MHz, DMSO-d ₆	7.77-7.84 (m, 2H), 7.39-7.47 (m, 4H), 7.30 (dd, <i>J</i> =9.23, 2.45 Hz, 1H), 6.95 (ddd, <i>J</i> =10.02, 8.66, 2.57 Hz, 1H), 5.48-5.55 (m, 2H), 4.34-4.48 (m, 1H), 3.37-3.51 (m, 2H), 3.03-3.12 (m, 2H), 2.84 (dd, <i>J</i> =12.42, 8.91 Hz, 1H), 2.52 (s, 3H), 2.12-2.21 (m, 1H), 1.79 - 1.97 (m, 1H)	B	Chiralcel OJ-H, 30% MeOH, peak 1
586	600 MHz, DMSO-d ₆	7.46-7.55 (m, 1H), 7.26-7.35 (m, 1H), 5.45 (s, 2H), 4.30-4.49 (m, 1H), 3.39 (s, 5H), 2.96-3.11 (m, 2H), 2.78-2.88 (m, 1H), 2.26-2.32 (m, 3H), 2.06-2.18 (m, 1H), 1.77-1.86 (m, 1H)	-	-
587	500 MHz, METHA NOL-d ₄	7.35-7.42 (m, 1H), 7.23 (s, 2H), 6.95-7.03 (m, 1H), 5.90 (s, 2H), 4.50-4.70 (m, 1H), 3.67-3.77 (m, 1H), 3.54-3.63 (m, 1H), 3.37-3.49 (m, 1H), 3.15-3.25 (m, 1H), 3.02-3.13 (m, 1H), 2.21-2.33 (m, 1H), 1.94-2.08 (m, 1H)	B	Chiralcel OD-H, 15% isopropanol, peak 2
588	500 MHz, METHA NOL-d ₄	7.43-7.52 (m, 1H), 7.17-7.25 (m, 1H), 6.95-7.04 (m, 1H), 5.77 (d, <i>J</i> =1.95 Hz, 2H), 3.50-3.61 (m, 1H), 3.40-3.49 (m, 1H), 3.29-3.35 (m, 2H), 3.14-3.25 (m, 1H), 2.73 (s, 3H), 2.29-2.45 (m, 1H), 2.14-2.30 (m, 1H)	B	Chiralcel OD-H, 10% isopropanol, peak 1
589	600 MHz, DMSO-d ₆	7.37-7.44 (m, 1H), 7.19-7.27 (m, 1H), 6.89-6.97 (m, 1H), 5.34-5.44 (m, 2H), 4.30-4.49 (m, 1H), 3.37-3.47 (m, 2H), 2.97-3.11 (m, 2H), 2.75-2.85 (m, 1H), 2.46-2.48 (m, 3H), 2.39 (s, 3H), 2.09-2.19 (m, 1H), 1.81-1.91 (m, 1H)	B	Chiralcel OJ-H, 10% isopropanol, peak 1
590	500 MHz, METHA NOL-d ₄	7.86-7.98 (m, 1H), 7.34-7.49 (m, 1H), 6.05 (s, 2H), 4.65-4.85 (m, 2H), 4.48-4.63 (m, 1H), 3.13-3.48 (m, 3H), 2.75 (s, 3H), 2.25-2.38 (m, 1H), 1.77-1.94 (m, 1H)	B	Chiralpak IC, 35% MeOH, peak 2
591	500 MHz, METHA NOL-d ₄	6.87-6.95 (m, 1H), 6.74-6.86 (m, 1H), 5.07-5.21 (m, 2H), 4.12-4.56 (m, 3H), 3.45-3.59 (m, 1H), 3.36 (s, 3H), 2.89-3.23 (m, 4H), 2.11-2.28 (m, 1H), 1.84-1.99 (m, 1H)	F	Regis Whelk-O s,s, 15% MeOH, peak 2
592	600 MHz, DMSO-d ₆	7.73 (s, 1H), 7.39 (s, 2H), 5.03-5.12 (m, 2H), 4.37-4.46 (m, 1H), 3.36-3.44 (m, 2H), 3.14 (s, 3H), 2.96-3.12 (m, 2H), 2.89 (s, 3H), 2.84 (dd, <i>J</i> =12.57, 8.29 Hz, 1H), 2.08-2.17 (m, 1H), 1.81-1.92 (m, 1H)	B	Chiralpak IC, 15% MeOH, peak 2
593	600 MHz, DMSO-d ₆	7.76-7.83 (m, 2H), 7.39-7.46 (m, 3H), 7.36 (dd, <i>J</i> =8.76, 4.71 Hz, 1H), 7.25 (dd, <i>J</i> =9.73, 2.49 Hz, 1H), 6.95 (ddd, <i>J</i> =9.85, 8.80, 2.53 Hz, 1H), 5.52 (s, 2H), 4.35-4.49 (m, 1H), 3.39-3.54 (m, 2H), 3.03-3.15 (m, 2H), 2.87 (dd, <i>J</i> =12.42, 8.91 Hz, 1H), 2.47 (s, 3H), 2.12-2.22 (m, 1H), 1.78 - 1.94 (m, 1H)	B	Chiralcel OJ-H, 30% MeOH, peak 2

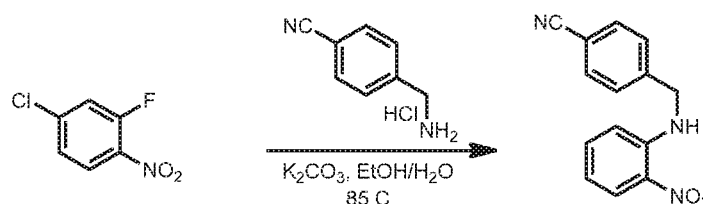
Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
594	600 MHz, DMSO-d ₆	7.09-7.17 (m, 1H), 6.86-6.96 (m, 1H), 4.96-5.09 (m, 2H), 4.32-4.50 (m, 1H), 3.22-3.43 (m, 2H), 3.10 (s, 3H), 2.96-3.07 (m, 2H), 2.89 (s, 3H), 2.77-2.85 (m, 1H), 2.07-2.18 (m, 1H), 1.74-1.87 (m, 1H)	B	Phenomenex CEL 2, 25% MeOH, peak 2
595	600 MHz, DMSO-d ₆	8.97 (d, <i>J</i> =1.79 Hz, 1H), 8.32 (dd, <i>J</i> =8.25, 2.34 Hz, 1H), 7.55 (d, <i>J</i> =8.33 Hz, 1H), 7.17 (dd, <i>J</i> =9.26, 2.18 Hz, 1H), 6.88 (t, <i>J</i> =10.33 Hz, 1H), 5.54 - 5.61 (m, 2H), 4.31-4.45 (m, 1H), 3.39-3.45 (m, 2H), 3.04-3.14 (m, 1H), 2.92-3.03 (m, 1H), 2.85 (dd, <i>J</i> =12.61, 8.49 Hz, 1H), 2.03-2.20 (m, 1H), 1.73-1.82 (m, 1H)	B	Lux Cellulose-2, 30% MeOH, peak 1
596	600 MHz, DMSO-d ₆	7.28-7.34 (m, 1H), 7.20-7.26 (m, 1H), 6.90-6.98 (m, 1H), 5.40 (s, 2H), 4.33-4.49 (m, 1H), 3.40-3.53 (m, 2H), 3.01-3.14 (m, 2H), 2.80-2.89 (m, 1H), 2.45-2.48 (m, 3H), 2.39 (s, 3H), 2.10-2.21 (m, 1H), 1.80-1.89 (m, 1H)	B	Chiralcel OJ-H, 10% isopropanol, peak 2
597	500 MHz, METHA NOL-d ₄	7.33-7.40 (m, 1H), 7.16-7.26 (m, 1H), 6.93-7.04 (m, 1H), 5.77 (d, <i>J</i> =1.56 Hz, 2H), 3.54-3.63 (m, 1H), 3.44-3.52 (m, 1H), 3.37-3.43 (m, 1H), 3.32 (s, 1H), 3.18-3.27 (m, 1H), 2.68-2.77 (m, 3H), 2.31-2.44 (m, 1H), 2.14-2.30 (m, 1H)	B	Chiralcel OD-H, 10% isopropanol, peak 2
598	500 MHz, METHA NOL-d ₄	7.24 (t, <i>J</i> =55 Hz, 1H), 7.08-7.16 (m, 1H), 6.83-6.92 (m, 1H), 5.94 (s, 2H), 4.70-4.86 (m, 1H), 3.85-3.93 (m, 1H), 3.73-3.83 (m, 1H), 3.64-3.72 (m, 1H), 3.24 (dd, <i>J</i> =10.45, 12.65 Hz, 2H), 2.25-2.38 (m, 1H), 2.08 (br dd, <i>J</i> =1.36, 2.92 Hz, 1H)	B	Regis Whelk-O s,s, 10% MeOH, peak 1
599	500 MHz, METHA NOL-d ₄	7.04-7.11 (m, 1H), 6.80-6.92 (m, 1H), 5.79 (s, 2H), 4.58-4.79 (m, 1H), 3.74-3.84 (m, 1H), 3.52-3.68 (m, 2H), 3.12-3.27 (m, 2H), 2.74 (s, 3H), 2.24-2.36 (m, 1H), 1.99-2.10 (m, 1H)	B	Regis Whelk-O s,s, 25% MeOH, peak 1

Scheme 11. Accessing chlorobenzimidazoles selectively



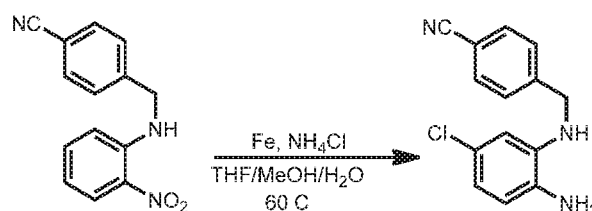


Intermediate 86: 4-((2,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile



Step 1. 4-(((5-chloro-2-nitrophenyl)amino)methyl)benzonitrile

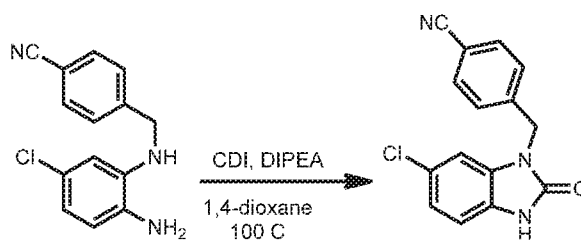
To a stirred solution of 4-chloro-2-fluoro-1-nitrobenzene (8.0 g, 45.6 mmol, 1 equiv) in ethanol (104.0 mL) and water (80.0 mL) was added 4-(aminomethyl)benzonitrile hydrochloride (8.45 g, 50.1 mmol, 1.1 equiv) followed by addition of potassium carbonate (11.34 g, 82.0 mmol, 1.8 equiv). The reaction mixture was heated to 85 °C for 10 h then stirred for 8 h at ambient temperature. After completion (monitored by TLC), the reaction mixture was diluted with water (100 mL) and solids were filtered. The obtained solid was dried under high vacuum to provide 4-(((5-chloro-2-nitrophenyl)amino)methyl)benzonitrile (9 g, 68.6 % yield) as yellow solid. ¹H NMR (400 MHz, DMSO-*d*₆): δ 8.85 (t, *J* = 6.3 Hz, 1H), 8.08 – 8.13 (m, 1H), 7.86 – 7.79 (m, 2H), 7.56 (d, *J* = 8.0 Hz, 2H), 6.90 (t, *J* = 2.4 Hz, 1H), 6.77 – 6.66 (m, 1H), 4.76 (d, *J* = 6.3 Hz, 2H).



Step 2. 4-(((2-amino-5-chlorophenyl)amino)methyl)benzonitrile

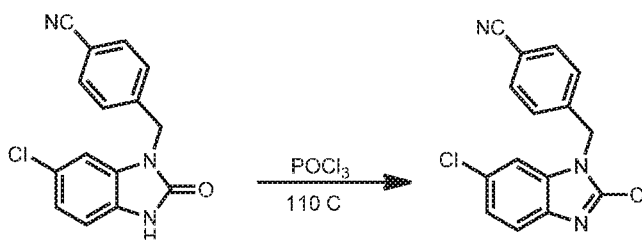
To a stirred solution of 4-(((5-chloro-2-nitrophenyl)amino)methyl)benzonitrile (9.0 g, 31.3 mmol, 1.0 equiv) in mixture of tetrahydrofuran (90.0 mL), methanol (90.0 mL) and water (60.0 mL) was added iron powder (7.51 g, 135.0 mmol, 4.3 equiv) followed by ammonium chloride (7.53 g, 141.0 mmol, 4.5 equiv). The resulting reaction mixture was heated to 60 °C for 2 h. After completion (monitored by TLC), the reaction mixture was filtered through celite pad and was washed with ethyl acetate (100 mL). The filtrate was diluted with water (100 mL) and layers were separated, aqueous layer was washed with ethyl acetate (2 x 200 mL). The combined organic layers were washed with water (2 x 200 mL), brine (2 x 200 mL), dried over sodium sulphate, filtered and concentrate under reduced pressure to provide 4-(((2-amino-5-

chlorophenyl)amino)methyl)benzonitrile (7.5 g, 93 % yield) as light yellow solid which was sufficiently pure to use in the next step. ¹H NMR (400 MHz, DMSO-d₆): δ 7.81 (dd, J = 8.3, 2.3 Hz, 2H), 7.65 – 7.45 (m, 2H), 6.53 (dd, J = 8.2, 2.2 Hz, 1H), 6.40 (dt, J = 8.1, 2.4 Hz, 1H), 6.19 (d, J = 2.4 Hz, 1H), 5.58 (t, J = 7.2 Hz, 1H), 4.75 (s, 2H), 4.54 – 4.28 (m, 2H).



Step 3. 4-(((6-chloro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile

To a stirred solution of 4-(((2-amino-5-chlorophenyl)amino)methyl)benzonitrile (7.5 g, 29.1 mmol, 1.0 equiv) in 1,4-dioxane (120.0 mL) was added DIPEA (7.62 mL, 43.7 mmol, 1.5 equiv) and CDI (11.80 g, 72.8 mmol, 2.5 equiv) portion wise. The resulting reaction mixture was heated to 100 °C for 1 h. After completion (monitored by TLC), the reaction mixture was cooled to ambient temperature and slowly quenched with ice cold water (100 mL). The reaction mixture was extracted with ethyl acetate (2 x 150 mL). The combined organic layers were washed with water (2 x 150 mL) and brine solution (2 x 100 mL), dried over sodium sulphate, filtered and concentrate under reduced pressure to provide 4-(((6-chloro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile (6 g, 72.7 % yield) as light brown solid which was sufficiently pure to use in next step as such. ¹H NMR (400 MHz, DMSO-d₆): δ 11.21 (s, 1H), 7.86 – 7.79 (m, 2H), 7.54 – 7.40 (m, 2H), 7.23 (d, J = 1.7 Hz, 1H), 7.06 – 6.97 (m, 2H), 5.12 (s, 2H). MS: (ESI neg. ion) *m/z*: 282 [M-1]



Step 4. 4-(((2,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile

To a stirred solution of 4-(((6-chloro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile (6.0 g, 21.15 mmol, 1.0 equiv) in POCl₃ (60.0 mL) was heated to 110 °C for 5 h. After completion (monitored by TLC), the reaction mixture was concentrated under high vacuum pressure. The obtained residue was diluted with DCM and slowly neutralized with 10 % aqueous sodium bicarbonate solution at 0 °C. The layers were separated and aqueous layer was extracted with DCM (2 x 150 mL). The combined organic layers were washed with water (200 mL), brine (200 mL), dried over sodium sulphate, filtered and concentrated under reduced pressure. The obtained crude was purified on silica gel 230-400 mesh using

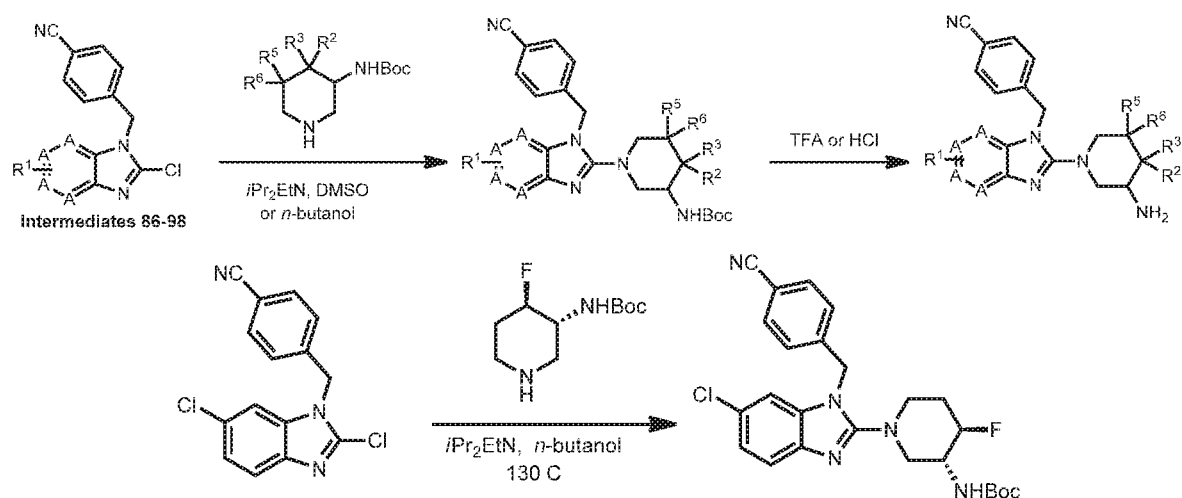
petroleum ether and ethyl acetate as an eluent (15-20 %) to afford 4-((2,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile (2.5 g, 39.1 % yield) as an off white solid. ^1H NMR (400 MHz, DMSO- d_6): δ 7.91 – 7.79 (m, 3H), 7.68 (d, J = 8.7 Hz, 1H), 7.39 – 7.28 (m, 3H), 5.67 (s, 2H). MS: (ESI pos. ion) m/z : 302.0 $[\text{M}+1]$

5 **Table 7.** Intermediates accessed using the sequence outlines in Scheme 11

Int #	Structure	Compound Name	^1H NMR	MS MH+
86		4-((2,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	^1H NMR (400 MHz, DMSO- d_6): δ 7.91 – 7.79 (m, 3H), 7.68 (d, J = 8.7 Hz, 1H), 7.39 – 7.28 (m, 3H), 5.67 (s, 2H)	302.0
87		4-((2-chloro-6-ethoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	^1H NMR (400 MHz, DMSO- d_6): δ 7.84 (dq, J = 8.5, 1.9 Hz, 2H), 7.52 (dd, J = 8.8, 1.2 Hz, 1H), 7.34 (d, J = 8.2 Hz, 2H), 7.22 (d, J = 2.3 Hz, 1H), 6.88 (dt, J = 8.8, 1.8 Hz, 1H), 5.62 (s, 2H), 4.02 (q, J = 7.0 Hz, 2H), 1.32 (t, J = 7.0 Hz, 3H)	312.0
88		4-((2-chloro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)benzonitrile	^1H NMR (400 MHz, DMSO- d_6): δ 11.74 (s, 1H), 7.93 (d, J = 5.1 Hz, 1H), 7.82 (d, J = 7.9 Hz, 2H), 7.49 (d, J = 7.8 Hz, 2H), 7.38 (d, J = 7.5 Hz, 1H), 6.99 (dd, J = 7.7, 5.1 Hz, 1H), 5.14 (s, 2H)	251.2
89		4-((2-chloro-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	^1H NMR (400 MHz, DMSO- d_6): δ 7.87 – 7.81 (m, 2H), 7.71 – 7.59 (m, 2H), 7.39 – 7.33 (m, 2H), 7.15 (ddd, J = 10.0, 8.9, 2.5 Hz, 1H), 5.64 (s, 2H)	286.0
90		4-((2-chloro-1H-imidazo[4,5-c]pyridin-1-yl)methyl)benzonitrile	--	269.2
91		4-((2-chloro-3H-imidazo[4,5-c]pyridin-3-yl)methyl)benzonitrile	--	269.2
92		4-((2,4-dichloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	^1H NMR (400 MHz, DMSO- d_6): δ 7.87 – 7.80 (m, 2H), 7.65 – 7.58 (m, 1H), 7.42 – 7.27 (m, 4H), 5.70 (d, J = 2.8 Hz, 2H)	302.1
93		4-((2-chloro-3H-imidazo[4,5-b]pyridin-3-yl)methyl)benzonitrile	^1H NMR (400 MHz, DMSO- d_6): δ 8.41 (dd, J = 4.7, 2.0 Hz, 1H), 8.13 (dt, J = 8.1, 1.7 Hz, 1H), 7.83 (dd, J = 8.3, 2.3 Hz, 2H), 7.46 – 7.34 (m, 3H), 5.64 (d, J = 2.2 Hz, 2H)	269.0

Int #	Structure	Compound Name	¹ H NMR	MS MH+
94		4-((2,7-dichloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	¹ H NMR (400 MHz, DMSO-d ₆): δ 7.84 (d, J = 8.1 Hz, 2H), 7.69 (dd, J = 7.8, 1.1 Hz, 1H), 7.36 (dd, J = 7.9, 1.2 Hz, 1H), 7.32 (d, J = 7.8 Hz, 1H), 7.25 (d, J = 8.1 Hz, 2H), 5.89 (s, 2H)	302.1
95		4-((2-chloro-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	--	298.2
96		4-((2-chloro-5-methoxy-3H-imidazo[4,5-b]pyridin-3-yl)methyl)benzonitrile	--	299.2
97		4-((2-chloro-4-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	¹ H NMR (400 MHz, DMSO-d ₆): δ 7.87 – 7.80 (m, 2H), 7.36 – 7.27 (m, 2H), 7.26 – 7.14 (m, 2H), 6.81 (dd, J = 7.7, 1.3 Hz, 1H), 5.62 (s, 2H), 3.93 (s, 3H)	298.2
98		4-((2,5-dichloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	--	302.2

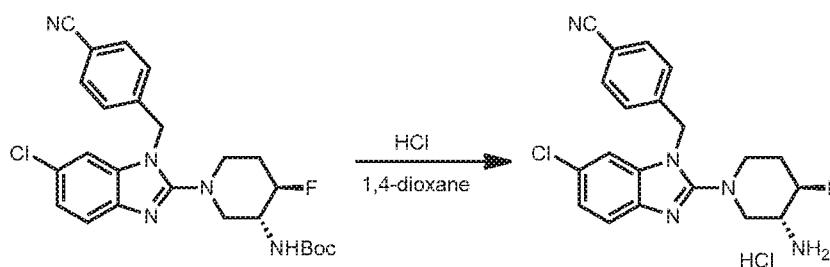
Scheme 12. Advancement of benzylated intermediates to final products



5 Step 1. 4-((2,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile

To a suspension of 4-((2,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile (50 mg, 0.165 mmol, 1 equiv) and tert-butyl ((3R,4R)-4-fluoropiperidin-3-yl)carbamate (72.2 mg, 0.331 mmol, 2 equiv) in 1-

butanol (662 μ l, 0.25 M) in a microwave vial was added DIEA (43.4 μ l, 0.248 mmol, 1.5 equiv). The vial was heated to 130 $^{\circ}$ C for 12 hours. The reaction mixture was cooled to room temperature, concentrated, and loaded onto a 12 g RediSep ISCO cartridge, eluting with 20-80% ethyl acetate in heptane, to provide tert-butyl ((3R,4R)-1-(6-chloro-1-(4-cyanobenzyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl)carbamate (40 mg, 49.9 % yield) as a white solid. MS (ESI pos. ion) m/z : 484.0 (M+H).

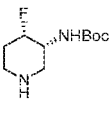
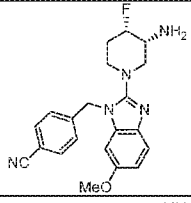
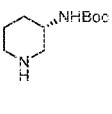
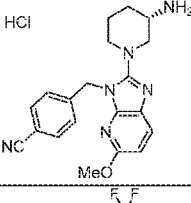
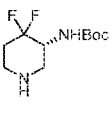
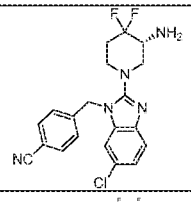
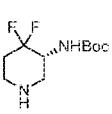
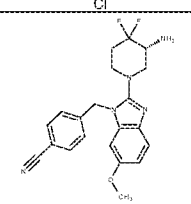
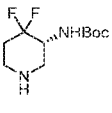
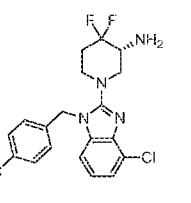
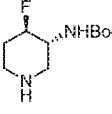
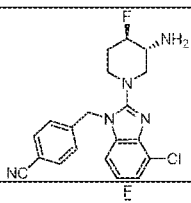
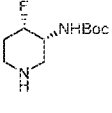
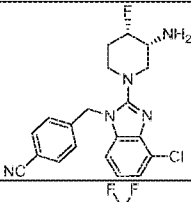
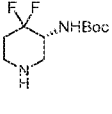
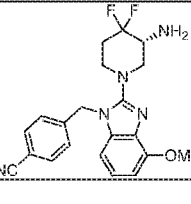


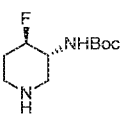
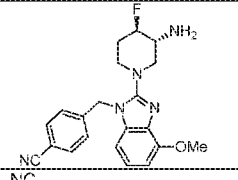
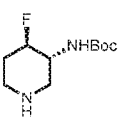
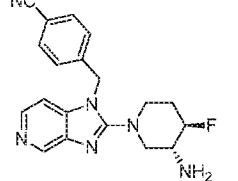
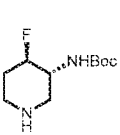
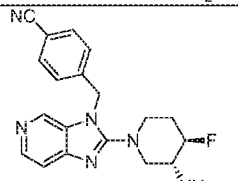
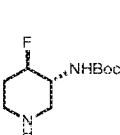
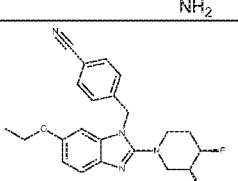
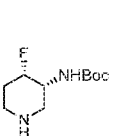
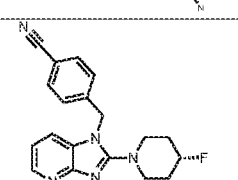
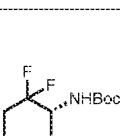
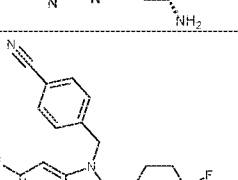
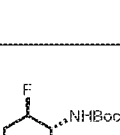
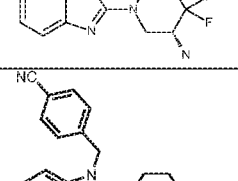
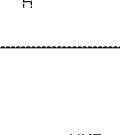
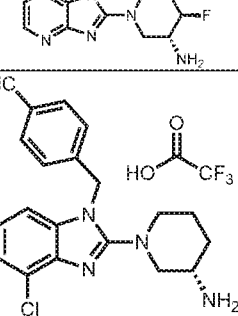
Step 2. 4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile

To a solution of tert-butyl ((3R,4R)-1-(6-chloro-1-(4-cyanobenzyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl)carbamate (40 mg, 0.083 mmol, 1 equiv) in 1,4-dioxane (1 mL) was added 4 N HCl in dioxane (0.517 mL, 2.066 mmol, 25 equiv). The reaction was stirred at ambient temperature for 6 hours at which time the reaction mixture was concentrated to provide 4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile hydrochloride as a white solid. NMR (400 MHz, DMSO- d_6) δ 8.78 (br s, 2H), 7.87 - 7.80 (m, 2H), 7.55 (d, J =8.5 Hz, 1H), 7.49 - 7.35 (m, 3H), 7.31 - 7.21 (m, 1H), 5.65 - 5.49 (m, 2H), 5.05 - 4.91 (m, 1H), 3.95 (br d, J =12.3 Hz, 1H), 3.79 - 3.61 (m, 1H), 3.52 - 3.44 (m, 1H), 3.35 - 3.22 (m, 1H), 3.12 (br t, J =11.5 Hz, 1H), 2.32 - 2.15 (m, 1H), 1.99 - 1.79 (m, 1H). MS (ESI pos. ion) m/z : 384.0 (M+H).

Table 8. Examples prepared in a manner analogous to Schemes 11-12

Ex. #	Benzimidazole Intermediate	Amine	Structure	Compound Name	MS MH+
401	86			4-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile hydrochloride	384.0
402	95			(S)-4-((2-(3-aminopiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile hydrochloride	362.0

Ex. #	Benzimidazole Intermediate	Amine	Structure	Compound Name	MS MH+
403	95			4-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	380.0
404	95			(S)-4-((2-(3-aminopiperidin-1-yl)-5-methoxy-3H-imidazo[4,5-b]pyridin-3-yl)methyl)benzonitrile hydrochloride	363.0
405	86			(R)-4-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	402.0
406	95			(R)-4-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	398.0
407	92			(R)-4-((2-(3-amino-4,4-difluoropiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	402.0
408	92			4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	384.0
409	92			4-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	384.0
410	97			(R)-4-((2-(3-amino-4,4-difluoropiperidin-1-yl)-4-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	398.0

Ex. #	Benzimidazole Intermediate	Amine	Structure	Compound Name	MS MH+
411	97			4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	380.2
412	90			4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-imidazo[4,5-c]pyridin-1-yl)methyl)benzonitrile	351.2
413	91			4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-3H-imidazo[4,5-c]pyridin-3-yl)methyl)benzonitrile	351.2
414	87			4-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-6-ethoxy-1H-benzimidazol-1-yl)methyl)benzonitrile	394.2
415	88			4-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1H-imidazo[4,5-b]pyridin-1-yl)methyl)benzonitrile	351.2
416	89			4-((2-((3R)-3-amino-4,4-difluoro-1-piperidinyl)-6-fluoro-1H-benzimidazol-1-yl)methyl)benzonitrile	386.2
417	88			4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-imidazo[4,5-b]pyridin-1-yl)methyl)benzonitrile	351.2
418	92			(S)-4-((2-(3-aminopiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile 2,2,2-trifluoroacetate	366.0

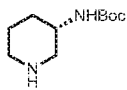
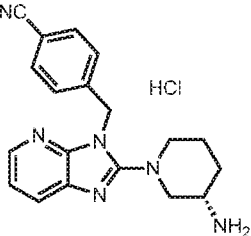
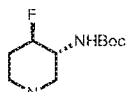
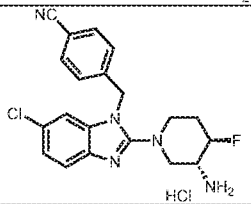
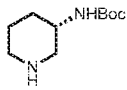
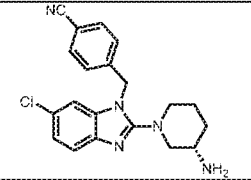
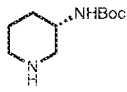
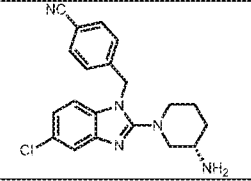
Ex. #	Benzimidazole Intermediate	Amine	Structure	Compound Name	MS MH+
419	93			(S)-4-((2-(3-aminopiperidin-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)methyl)benzonitrile hydrochloride	333.2
420	86			4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile hydrochloride	384.2
421	86			(S)-4-((2-(3-aminopiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	366.2
422	98			(S)-4-((2-(3-aminopiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile	366.2

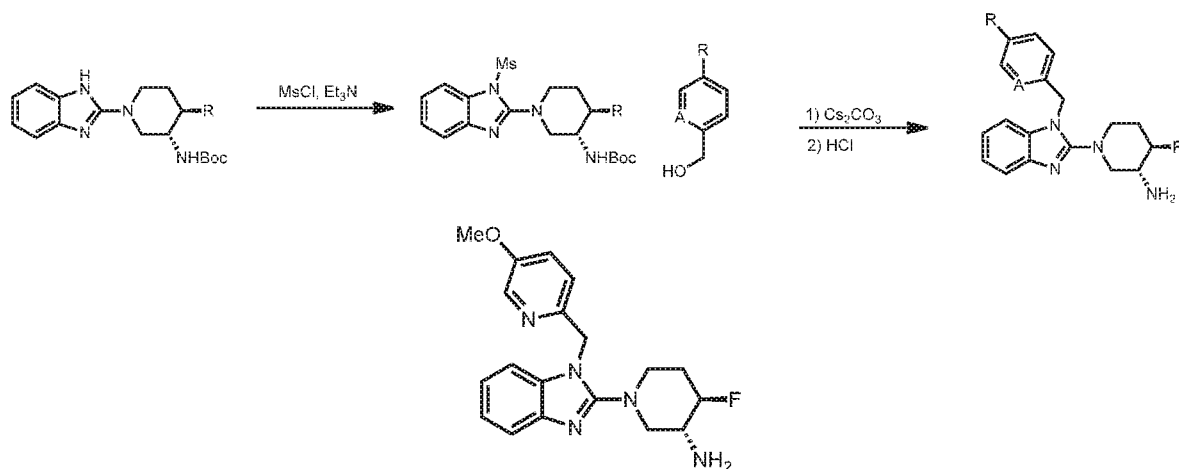
Table 9. Characterization data for compounds following Schemes 11-12.

Ex. #	Freq., Solvent	¹ H NMR Data (δ ppm)
401	400MHz d ₆ -DMSO	8.57 (br s, 2H), 7.81-7.86 (m, 1H), 7.83 (d, <i>J</i> =7.30 Hz, 1H), 7.50-7.55 (m, 1H), 7.40-7.43 (m, 1H), 7.34-7.39 (m, 2H), 7.23 (dd, <i>J</i> =1.92, 8.34 Hz, 1H), 5.49-5.60 (m, 2H), 5.22-5.04 (m, 1H), 3.61-3.69 (m, 4H), 3.34-3.44 (m, 1H), 3.22-3.31 (m, 1H), 3.08-3.22 (m, 1H), 2.05-2.16 (m, 1H), 1.93-2.05 (m, 1H)
402	400MHz d ₆ -DMSO	8.45 (br s, 3H), 7.87 (d, <i>J</i> =8.29 Hz, 2H), 7.49 (t, <i>J</i> =8.91 Hz, 3H), 6.95-7.02 (m, 2H), 5.56-5.72 (m, 2H), 3.72 (s, 3H), 3.37 (br d, <i>J</i> =7.67 Hz, 4H), 3.12 (br t, <i>J</i> =10.05 Hz, 1H), 1.97 (br d, <i>J</i> =8.40 Hz, 1H), 1.88 (br dd, <i>J</i> =3.63, 9.64 Hz, 1H), 1.62-1.70 (m, 1H), 1.56 (br dd, <i>J</i> =4.09, 9.38 Hz, 1H)
403	400MHz d ₆ -DMSO	7.80 (d, <i>J</i> =8.29 Hz, 2H), 7.27-7.37 (m, 3H), 6.81 (d, <i>J</i> =2.38 Hz, 1H), 6.73 (dd, <i>J</i> =2.44, 8.66 Hz, 1H), 5.40 (s, 2H), 4.66-4.87 (m, 1H), 3.68 (s, 3H), 3.14-3.21 (m, 2H), 3.00-3.10 (m, 3H), 2.90-2.99 (m, 2H), 1.81-2.05 (m, 2H)
404	400MHz d ₆ -DMSO	8.40 (br s, 3H), 7.79-7.89 (m, 3H), 7.52 (d, <i>J</i> =7.98 Hz, 2H), 6.75 (d, <i>J</i> =8.60 Hz, 1H), 5.45-5.59 (m, 2H), 3.79 (s, 3H), 3.64-3.76 (m, 1H), 3.48 (br dd, <i>J</i> =4.25, 11.30 Hz, 2H), 3.21-3.31 (m, 1H), 3.00 (br t, <i>J</i> =10.21 Hz, 1H), 1.93-2.02 (m, 1H), 1.80-1.93 (m, 1H), 1.46-1.69 (m, 2H)
405	400MHz d ₆ -DMSO	7.82 (d, <i>J</i> =7.88 Hz, 2H), 7.47 (d, <i>J</i> =8.40 Hz, 1H), 7.29-7.35 (m, 3H), 7.14 (d, <i>J</i> =8.50 Hz, 1H), 5.49 (s, 2H), 3.26-3.40 (m, 2H), 3.08-3.24 (m, 2H), 2.93-3.05 (m, 1H), 2.18-2.32 (m, 1H), 1.90-2.15 (m, 1H), 1.77 (br s, 2H)

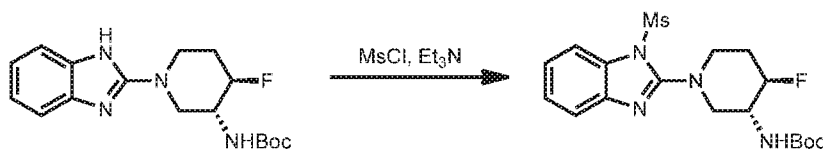
Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)
406	400MHz d ₆ -DMSO	7.80 (d, <i>J</i> =7.67 Hz, 2H), 7.28-7.39 (m, 3H), 6.82 (s, 1H), 6.74 (br d, <i>J</i> =8.71 Hz, 1H), 5.44 (s, 2H), 3.68 (s, 3H), 3.19-3.29 (m, 2H), 3.08-3.18 (m, 2H), 2.86-3.01 (m, 1H), 2.17-2.31 (m, 1H), 1.92-2.14 (m, 1H), 1.76 (br s, 2H)
407	400MHz d ₆ -DMSO	7.78-7.83 (m, <i>J</i> =8.29 Hz, 2H), 7.31-7.36 (m, <i>J</i> =8.40 Hz, 2H), 7.16 (dd, <i>J</i> =0.83, 13.06 Hz, 1H), 7.18 (br dd, <i>J</i> =0.83, 12.85 Hz, 1H), 7.02-7.09 (m, 1H), 5.50 (s, 2H), 3.34-3.46 (m, 2H), 3.00-3.26 (m, 3H), 2.21-2.35 (m, 1H), 1.98-2.16 (m, 1H), 1.78 (br s, 2H)
408	400MHz d ₆ -DMSO	7.78-7.83 (m, <i>J</i> =8.29 Hz, 2H), 7.28-7.34 (m, <i>J</i> =8.29 Hz, 2H), 7.17 (t, <i>J</i> =6.59 Hz, 2H), 6.99-7.08 (m, 1H), 5.46 (s, 2H), 4.39-4.51 (m, 1H), 4.29-4.36 (m, 1H), 4.25-4.54 (m, 1H), 3.34-3.53 (m, 3H), 3.02-3.10 (m, 1H), 2.91-3.02 (m, 1H), 2.80-2.90 (m, 1H), 2.02-2.16 (m, 2H), 1.76-1.85 (m, 1H)
409	400MHz d ₆ -DMSO	7.77-7.83 (m, <i>J</i> =8.40 Hz, 2H), 7.26-7.36 (m, <i>J</i> =8.40 Hz, 2H), 7.16 (t, <i>J</i> =8.41 Hz, 2H), 7.00-7.07 (m, 1H), 5.46 (s, 2H), 4.80-4.88 (m, 1H), 4.69-4.75 (m, 1H), 4.68-4.89 (m, 1H), 3.26-3.41 (m, 3H), 3.10-3.25 (m, 2H), 2.95-3.07 (m, 2H), 1.84-2.12 (m, 2H)
410	400MHz d ₆ -DMSO	7.77-7.82 (m, <i>J</i> =8.40 Hz, 2H), 7.27-7.33 (m, <i>J</i> =8.29 Hz, 2H), 7.00 (t, <i>J</i> =8.03 Hz, 1H), 6.78 (d, <i>J</i> =7.57 Hz, 1H), 6.69 (d, <i>J</i> =7.77 Hz, 1H), 5.44 (s, 2H), 3.89 (s, 3H), 3.38-3.59 (m, 3H), 3.31-3.21 (m, 2H), 3.02-3.20 (m, 2H), 2.08-2.36 (m, 2H)
411	400MHz d ₆ -DMSO	7.75-7.83 (m, 2H), 7.22-7.33 (m, <i>J</i> =8.40 Hz, 2H), 6.97 (t, <i>J</i> =7.85 Hz, 1H), 6.78 (d, <i>J</i> =7.46 Hz, 1H), 6.67 (d, <i>J</i> =7.98 Hz, 1H), 5.40 (s, 2H), 4.24-4.47 (m, 1H), 3.89 (s, 3H), 3.11-3.41 (m, 4H), 2.88-3.08 (m, 2H), 2.77 (dd, <i>J</i> =8.71, 12.44 Hz, 1H), 1.92-2.15 (m, 1H), 1.61-1.87 (m, 2H)
412	500MHz d ₄ -MeOH	8.69 (s, 1H), 8.20 (d, <i>J</i> =5.45 Hz, 1H), 7.72 (d, <i>J</i> =8.30 Hz, 2H), 7.33 (d, <i>J</i> =8.04 Hz, 2H), 7.24 (d, <i>J</i> =5.71 Hz, 1H), 5.51 (s, 2H), 4.34-4.55 (m, 1H), 3.61-3.69 (m, 1H), 3.47-3.54 (m, 1H), 3.07-3.22 (m, 2H), 3.01 (br dd, <i>J</i> =9.08, 12.46 Hz, 1H), 2.05-2.28 (m, 1H), 1.80-1.95 (m, 1H)
413	500MHz d ₄ -MeOH	8.34 (d, <i>J</i> =0.78 Hz, 1H), 8.26 (d, <i>J</i> =5.45 Hz, 1H), 7.74 (d, <i>J</i> =8.56 Hz, 2H), 7.50 (dd, <i>J</i> =0.91, 5.58 Hz, 1H), 7.36 (d, <i>J</i> =8.56 Hz, 2H), 5.53 (s, 2H), 4.33-4.50 (m, 1H), 3.66-3.75 (m, 1H), 3.54-3.64 (m, 1H), 3.17-3.26 (m, 1H), 2.99-3.12 (m, 2H), 2.11-2.22 (m, 1H), 1.80-1.94 (m, 1H)
414	600MHz DMSO-d ₆	7.81 (d, <i>J</i> =8.33 Hz, 2H), 7.28-7.34 (m, 3H), 6.81 (d, <i>J</i> =2.34 Hz, 1H), 6.71 (d, <i>J</i> =8.92 Hz, 1H), 5.35-5.43 (m, 2H), 4.25-4.43 (m, 1H), 3.89-3.95 (m, 2H), 3.29-3.32 (m, 1H), 3.21-3.29 (m, 1H), 2.90-3.00 (m, 2H), 2.74 (dd, <i>J</i> =8.68, 12.42 Hz, 1H), 1.97-2.10 (m, 1H), 1.71-1.89 (m, 2H), 1.23-1.29 (m, 3H)
415	600MHz DMSO-d ₆	8.07 (dd, <i>J</i> =1.40, 4.90 Hz, 1H), 7.77-7.83 (m, 3H), 7.38 (d, <i>J</i> =8.49 Hz, 2H), 7.17 (dd, <i>J</i> =4.90, 7.86 Hz, 1H), 5.46 (s, 2H), 4.76-4.83 (m, 0.5H), 4.68-4.73 (m, 0.5H), 3.21-3.29 (m, 2H), 3.08-3.20 (m, 1H), 2.89-3.02 (m, 2H), 1.80-2.00 (m, 2H)
416	600MHz DMSO-d ₆	7.78-7.83 (m, <i>J</i> =8.43 Hz, 2H), 7.46 (dd, <i>J</i> =4.93, 8.69 Hz, 1H), 7.30-7.35 (m, <i>J</i> =8.30 Hz, 2H), 7.14 (dd, <i>J</i> =2.47, 9.21 Hz, 1H), 6.96 (ddd, <i>J</i> =2.53, 8.69, 10.06 Hz, 1H), 5.46 (s, 2H), 3.28 (br d, <i>J</i> =6.36 Hz, 1H), 3.10-3.21 (m, 2H), 2.93-3.01 (m, 1H), 2.19-2.35 (m, 1H), 1.91-2.13 (m, 1H), 1.80 (br s, 2H)
417	500MHz d ₄ -MeOH	8.25 (d, <i>J</i> =4.93 Hz, 1H), 7.74 (d, <i>J</i> =8.04 Hz, 2H), 7.54 (d, <i>J</i> =7.79 Hz, 1H), 7.36 (d, <i>J</i> =8.30 Hz, 2H), 7.13 (dd, <i>J</i> =5.06, 7.91 Hz, 1H), 5.50 (s, 2H), 4.36-4.54 (m, 1H), 3.69-3.78 (m, 1H), 3.51-3.64 (m, 1H), 3.18-3.26 (m, 1H), 3.09-3.17 (m, 1H), 3.05 (dd, <i>J</i> =9.08, 12.72 Hz, 1H), 2.12-2.23 (m, 1H), 1.81-1.96 (m, 1H)
418	400MHz d ₆ -DMSO	8.02 (br s, 3H), 7.82 (d, <i>J</i> =7.98 Hz, 2H), 7.31 (d, <i>J</i> =7.98 Hz, 2H), 7.20 (d, <i>J</i> =7.77 Hz, 1H), 7.15 (d, <i>J</i> =7.98 Hz, 1H), 7.00-7.10 (m, 1H), 5.38-5.55 (m, 2H), 3.64 (br d, <i>J</i> =12.02 Hz, 1H), 3.07-3.27 (m, 2H), 2.85-2.97 (m, 1H), 1.98 (br d, <i>J</i> =9.23 Hz, 1H), 1.75-1.87 (m, 1H), 1.49-1.67 (m, 2H)

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)
419	400MHz d ₆ -DMSO	8.39 (br s, 3H), 8.20 (d, <i>J</i> =4.98 Hz, 1H), 7.90 (d, <i>J</i> =7.87 Hz, 1H), 7.84 (d, <i>J</i> =7.89 Hz, 2H), 7.47 (d, <i>J</i> =7.91 Hz, 2H), 7.31 (dd, <i>J</i> =4.99, 7.85 Hz, 1H), 5.48-5.68 (m, 2H), 3.84 (br d, <i>J</i> =11.72 Hz, 1H), 3.28-3.42 (m, 2H), 3.01-3.10 (m, 1H), 1.93-2.06 (m, 1H), 1.78-1.90 (m, 1H), 1.48-1.72 (m, 2H)
420	400MHz d ₆ -DMSO	8.78 (br s, 2H), 7.87 - 7.80 (m, 2H), 7.55 (d, <i>J</i> =8.5 Hz, 1H), 7.49 - 7.35 (m, 3H), 7.31 - 7.21 (m, 1H), 5.65 - 5.49 (m, 2H), 5.05 - 4.91 (m, 1H), 3.95 (br d, <i>J</i> =12.3 Hz, 1H), 3.79 - 3.61 (m, 1H), 3.52 - 3.44 (m, 1H), 3.35 - 3.22 (m, 1H), 3.12 (br t, <i>J</i> =11.5 Hz, 1H), 2.32 - 2.15 (m, 1H), 1.99 - 1.79 (m, 1H)
421	400MHz d ₆ -DMSO	7.82 (d, <i>J</i> =8.09 Hz, 2H), 7.46 (d, <i>J</i> =8.50 Hz, 1H), 7.25-7.35 (m, 3H), 7.13 (dd, <i>J</i> =1.66, 8.29 Hz, 1H), 5.39-5.51 (m, 2H), 4.04-4.14 (m, 1H), 3.48-3.57 (m, 1H), 3.20-3.26 (m, 1H), 2.81-3.02 (m, 2H), 1.86-1.98 (m, 1H), 1.69-1.83 (m, 1H), 1.37-1.62 (m, 2H)
422	400MHz d ₆ -DMSO	8.34 (br d, <i>J</i> =1.04 Hz, 3H), 7.82 (d, <i>J</i> =8.29 Hz, 2H), 7.51 (d, <i>J</i> =7.88 Hz, 1H), 7.34 (d, <i>J</i> =8.29 Hz, 2H), 7.05-7.23 (m, 3H), 5.44-5.52 (m, 2H), 5.06 (br d, <i>J</i> =2.90 Hz, 1H), 3.78-3.88 (m, 1H), 3.73-3.92 (m, 1H), 3.52-3.61 (m, 1H), 3.33-3.43 (m, 1H), 3.12-3.26 (m, 2H), 1.96-2.16 (m, 2H)

Scheme 13. Mesylate Transfer Chemistry



- 5 **Example 425:** (3R,4R)-4-fluoro-1-(1-((5-methoxypyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine

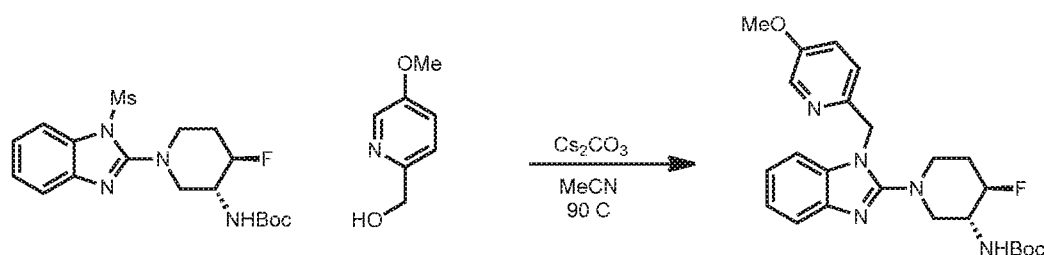


Step 1. **tert-Butyl ((3R,4R)-4-fluoro-1-(1-((methanesulfonyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-yl)carbamate**

10

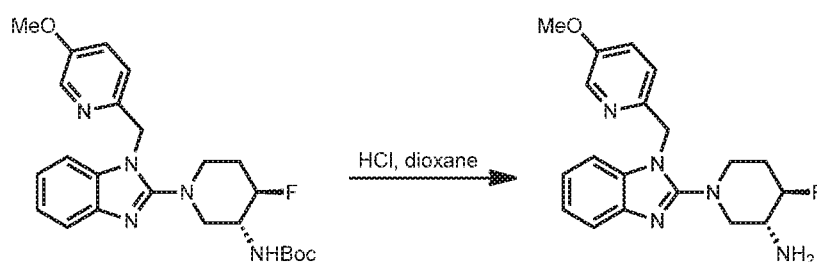
tert-Butyl ((3R,4R)-1-(1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl)carbamate (**Intermediate 54**, 156 mg, 0.467 mmol) was dissolved in DCM (2.3 mL). The mixture was treated with methanesulfonyl

chloride (100 μ l, 0.700 mmol, 2 equiv) and triethylamine, anhydrous (197 μ l, 1.400 mmol). The resulting yellow solution was left to stir overnight. The reaction was quenched with NH_4Cl (aq), diluted with DCM, extracted into DCM, dried over MgSO_4 , filtered, concentrated to give the crude as an oil. The oil was purified on column chromatography (25g SiO_2 , 0-45% ethyl acetate in heptane), to give tert-butyl ((3R,4R)-4-fluoro-1-(1-(methylsulfonyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-yl)carbamate as a colorless solid. (ESI, pos. ion) m/z: 413.2 [M+1].



Step 2. Tert-butyl ((3R,4R)-4-fluoro-1-(1-((5-methoxypyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-yl)carbamate

A vial was charged with (S)-1-(1-(methylsulfonyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine (150 mg, 0.38 mmol), 1-hydroxy-2,3-dihydro-1H-indene-5-carbonitrile (67 mg, 1.1 equiv), and Cs_2CO_3 (150 mg, 1.2 equiv). The vial was fitted with a stirring bar, capped, and MeCN (1.3 ml) was added. The mixture was placed into a heating block set at 90°C for 18h. The reaction was diluted with EtOAc and $\text{NH}_4\text{Cl}_{(\text{aq})}$, the mixture was extracted into EtOAc. The combined organic extracts were dried over MgSO_4 , filtered, and concentrated to give the reaction crude. Crude material was purified on column chromatography (4g SiO_2 , 0-30% EtOAc in heptane) to afford tert-butyl ((3R,4R)-4-fluoro-1-(1-((5-methoxypyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-yl)carbamate as a colorless oil. (ESI, pos. ion) m/z: 456.2 [M+1].



Step 3. (3R,4R)-4-fluoro-1-(1-((5-methoxypyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine (Example 425)

tert-butyl ((3R,4R)-4-fluoro-1-(1-((5-methoxypyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-yl)carbamate (32 mg, 1 equiv) was dissolved in DCM (5 mL). HCl in dioxane (10 equiv) was added, and the mixture was allowed to stir overnight. The solution was concentrated, then purified using reverse phase HPLC to provide the title compound. ^1H NMR (600 MHz, d_6 -DMSO) δ 7.79 (s, 1H), 7.50 (t, $J=7.53$ Hz, 2H), 7.11 (t, $J=7.66$ Hz, 1H), 6.96 (d, $J=7.79$ Hz, 1H), 6.88-6.94 (m, 1H), 6.39-6.49 (m, 1H), 6.19 (t, $J=8.95$ Hz, 1H), 3.54-3.62 (m, 1H), 3.36-3.43 (m, 1H), 3.18-3.24 (m, 3H), 3.00-3.13 (m, 2H), 2.74-2.87 (m, 1H),

2.52-2.63 (m, 1H), 1.91-2.12 (m, 2H), 1.77-1.89 (m, 1H), 1.47-1.56 (m, 1H). (ESI, pos. ion) m/z: 356.2 [M+1].

Table 10. Compounds made following Scheme 13 and analogous to preparation of Example 425

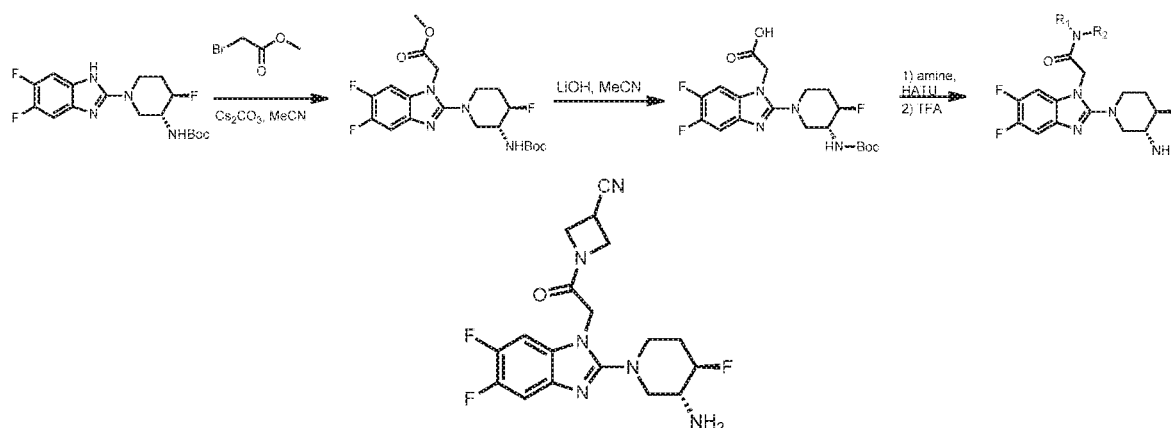
Ex. #	Alcohol	Structure	Compound Name	MS MH+
423			(R)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)-2,3-dihydro-1H-indene-5-carbonitrile	358.2
424			(S)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)-2,3-dihydro-1H-indene-5-carbonitrile	358.2
425			(3R,4R)-4-fluoro-1-(1-((5-methoxypyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine	356.2

5 **Table 11.** Characterization data for compounds made following scheme 13

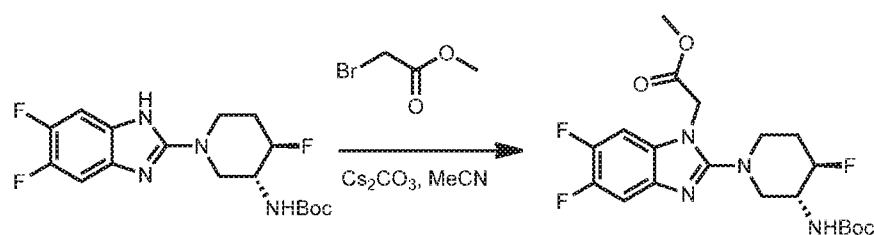
Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
423	500MH z d ₄ - MeOH	7.79 (s, 1H), 7.50 (t, J=7.53 Hz, 2H), 7.11 (t, J=7.66 Hz, 1H), 6.96 (d, J=7.79 Hz, 1H), 6.88-6.94 (m, 1H), 6.39-6.49 (m, 1H), 6.19 (t, J=8.95 Hz, 1H), 3.54-3.62 (m, 1H), 3.36-3.43 (m, 1H), 3.18-3.24 (m, 3H), 3.00-3.13 (m, 2H), 2.74-2.87 (m, 1H), 2.52-2.63 (m, 1H), 1.91-2.12 (m, 2H), 1.77-1.89 (m, 1H), 1.47-1.56 (m, 1H)	B	Phenomenex Lux Cellulose- 2, 30% MeOH, Chiralcel OD, 25% MeOH Peak 1
424	500MH z d ₄ - MeOH	7.79 (s, 1H), 7.49 (dd, J=7.91, 11.03 Hz, 2H), 7.06-7.14 (m, 1H), 6.86-6.96 (m, 2H), 6.45 (br d, J=5.71 Hz, 1H), 6.19 (br t, J=8.95 Hz, 1H), 3.53-3.62 (m, 1H), 3.35-3.44 (m, 2H), 3.11-3.24 (m, 3H), 2.81-2.96 (m, 2H), 2.51-2.65 (m, 1H), 1.90-2.10 (m, 2H), 1.73-1.88 (m, 1H), 1.42-1.53 (m, 1H)	B	Phenomenex Lux Cellulose- 2, 30% MeOH Peak 3

Ex. #	Freq., Solvent	¹ H NMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
425	600MHz Z d ₆ -DMSO	8.22 (d, <i>J</i> =2.80 Hz, 1H), 7.42 (d, <i>J</i> =7.79 Hz, 1H), 7.37 (dd, <i>J</i> =3.11, 8.72 Hz, 1H), 7.17 (d, <i>J</i> =8.72 Hz, 1H), 7.11 (d, <i>J</i> =7.79 Hz, 1H), 7.04-7.09 (m, 1H), 6.98-7.03 (m, 1H), 5.31 (s, 2H), 4.32-4.47 (m, 1H), 3.79 (s, 3H), 3.40-3.52 (m, 2H), 2.96-3.09 (m, 2H), 2.84 (dd, <i>J</i> =8.72, 12.46 Hz, 1H), 2.04-2.14 (m, 1H), 1.73-1.84 (m, 1H)	--	--

Scheme 14. Compounds made through peptide coupling



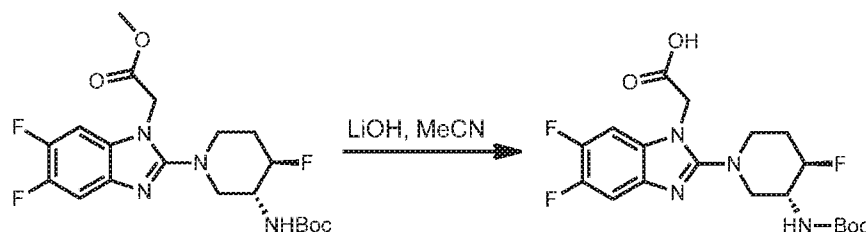
- 5 **Example 426:** 1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)azetidine-3-carbonitrile



Step 1. methyl 2-(2-((3R,4R)-3-((tert-butoxycarbonyl)amino)-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetate

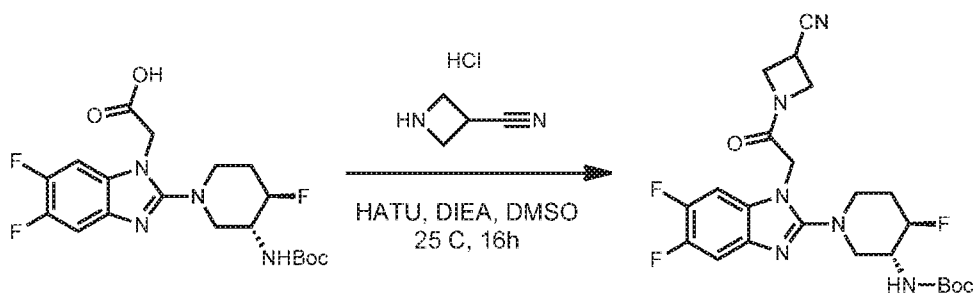
- 10 A vial was charged with tert-butyl ((3R,4R)-1-(5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl)carbamate (0.3 g, 0.810 mmol) Cs₂CO₃ (0.792 g, 2.430 mmol) in acetonitrile (2.70 ml), and methyl 2-bromoacetate (0.149 g, 0.972 mmol) and shaken on J-Kem block for 16h. Reaction mixture was filtered through Celite® brand filter agent plug and purified by reverse phase HPLC to obtain methyl 2-(2-((3R,4R)-3-((tert-butoxycarbonyl)amino)-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetate.
- 15 ¹H NMR (600 MHz, DMSO-d₆) δ 7.56 (t, *J*=9.06 Hz, 1H), 7.51 (t, *J*=8.85 Hz, 1H), 7.19 (br d, *J*=8.25 Hz, 1H), 4.94-5.03 (m, 2H), 4.51-4.59 (dt, *J*=4.63, 9.01 Hz, 1H), 3.68-3.77 (m, 3H), 3.35-3.46 (m, 2H), 3.24-

3.30 (m, 1H), 2.95 (br t, $J=10.63$ Hz, 1H), 2.73-2.89 (m, 1H), 2.13-2.21 (m, 1H), 1.79-1.89 (m, 1H), 1.39 (s, 9H). MS: (ESI pos. ion) m/z : 443.2 [M+1].



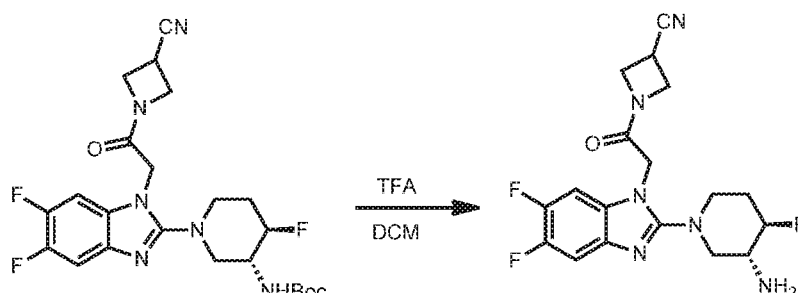
5 Step 2. **2-(2-((3R,4R)-3-((tert-butoxycarbonyl)amino)-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetic acid**

Methyl 2-(2-((3R,4R)-3-((tert-butoxycarbonyl)amino)-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetate was saponified using LiOH (0.097 g, 4.05 mmol) in dioxane (1 mL) and water (1 mL). Reaction mixture was stirred at ambient temperature for 1h. Reaction mixture was acidified using acetic acid and the resulting off white precipitate was filtered to obtain 2-(2-((3R,4R)-3-((tert-butoxycarbonyl)amino)-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetic acid. MS: (ESI pos. ion) m/z : 429.2 [M+1].



15 Step 3. **tert-butyl ((3R,4R)-1-(1-(2-(3-cyanoazetidin-1-yl)-2-oxoethyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl)carbamate**

A solution of 2-(2-((3R,4R)-3-((tert-butoxycarbonyl)amino)-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetic acid (0.015 g, 0.035 mmol), 3-cyanoazetidine hydrochloride (4.15 mg, 0.035 mmol) and 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (0.013 g, 0.035 mmol) in dimethyl sulfoxide (0.117 mL) and DIPEA (0.024 mL, 0.140 mmol) was shaken at ambient temperature. The reaction mixture was purified by reverse phase HPLC to obtain tert-butyl ((3R,4R)-1-(1-(2-(3-cyanoazetidin-1-yl)-2-oxoethyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl)carbamate. MS: (ESI pos. ion) m/z : 493.2 [M+1].



Step 4. **1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)azetidine-3-carbonitrile (Example 426)**

tert-Butyl ((3R,4R)-1-(1-(2-(3-cyanoazetidin-1-yl)-2-oxoethyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl)carbamate was treated with TFA (0.5 mL) in DCM (0.5 mL). Mixture was concentrated and purified using reverse phase HPLC to obtain the title compound. ¹H NMR (600 MHz, DMSO-d₆) δ 7.34-7.60 (m, 2H), 4.73-4.80 (m, 2H), 4.48-4.60 (m, 2H), 4.31-4.48 (m, 1H), 4.17-4.28 (m, 1H), 4.06-4.15 (m, 1H), 3.82-3.94 (m, 1H), 2.96-3.06 (m, 2H), 2.74-2.84 (m, 1H), 2.06-2.17 (m, 1H), 1.64-1.88 (m, 3H). MS: (ESI pos. ion) m/z: 393.2 [M+1].

The following compounds were made following an analogous procedure to that described for Example 426 and general Scheme 14 above:

Table 12. Compounds made following Scheme 14

Ex. #	Amine	Structure	Compound Name	MS MH+
426			1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)azetidine-3-carbonitrile	393.2
427			2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(3-(tert-butoxy)azetidin-1-yl)ethan-1-one	440.2
428			2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(3,3-difluoroazetidin-1-yl)ethanone	404.2

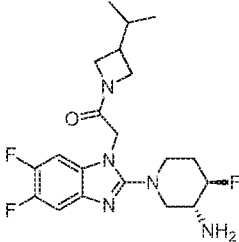
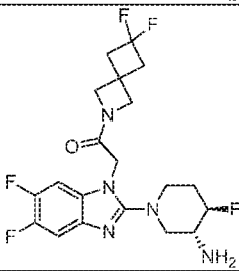
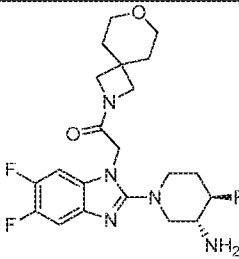
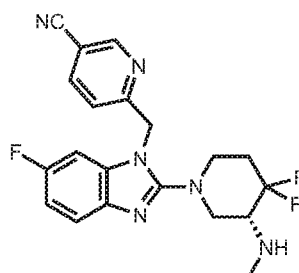
429			2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl-1-(3-isopropylazetidin-1-yl)ethanone	410.2
430			2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl-1-(6,6-difluoro-2-azaspiro[3.3]heptan-2-yl)ethanone	444.2
431			2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl-1-(7-oxa-2-azaspiro[3.5]nonan-2-yl)ethanone	438.2

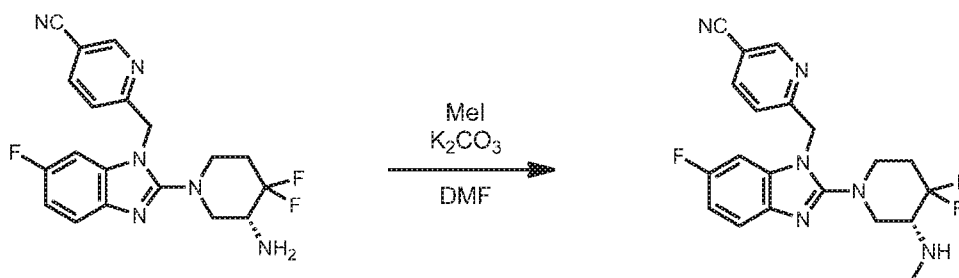
Table 13. Characterization data for compounds made following scheme 14

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
426	600MHz DMSO-d ₆	7.34-7.60 (m, 2H), 4.73-4.80 (m, 2H), 4.48-4.60 (m, 2H), 4.31-4.48 (m, 1H), 4.17-4.28 (m, 1H), 4.06-4.15 (m, 1H), 3.82-3.94 (m, 1H), 2.96-3.06 (m, 2H), 2.74-2.84 (m, 1H), 2.06-2.17 (m, 1H), 1.64-1.88 (m, 3H).	--	--
427	600MHz DMSO-d ₆	7.46 (dd, <i>J</i> =7.43, 11.17 Hz, 1H), 7.40 (dd, <i>J</i> =7.36, 10.39 Hz, 1H), 4.72-4.79 (m, 2H), 4.56-4.64 (m, 1H), 4.41-4.49 (m, 2H), 4.36 (br s, 1H), 4.16 (dd, <i>J</i> =7.20, 9.77 Hz, 1H), 4.08 (dt, <i>J</i> =4.98, 8.25 Hz, 1H), 3.70 (dd, <i>J</i> =4.71, 10.00 Hz, 1H), 2.95-3.06 (m, 2H), 2.78 (ddd, <i>J</i> =5.02, 8.10, 12.73 Hz, 1H), 2.02-2.16 (m, 1H), 1.89 (br s, 1H), 1.72-1.87 (m, 1H), 1.15 (s, 9H).	--	--
428	600MHz DMSO-d ₆	7.37-7.50 (m, 2H), 4.87 (s, 1H), 4.76-4.85 (m, 2H), 4.34-4.47 (m, 2H), 3.20-3.27 (m, 1H), 3.14-3.19 (m, 1H), 2.98-3.11 (m, 2H), 2.87-2.97 (m, 1H), 2.79 (dd, <i>J</i> =8.37, 12.57 Hz, 1H), 2.03-2.18 (m, 1H), 1.96 (dt, <i>J</i> =4.67, 9.19 Hz, 1H), 1.78-1.91 (m, 1H).	--	--
429	600MHz DMSO-d ₆	7.46 (dd, <i>J</i> =7.47, 11.13 Hz, 1H), 7.38 (dd, <i>J</i> =7.32, 10.67 Hz, 1H), 4.70-4.79 (m, 2H), 4.32-4.47 (m, 1H), 4.25-4.30 (m, 1H), 3.92-3.99 (m, 2H), 3.62 (dd, <i>J</i> =5.92, 9.65 Hz, 1H), 3.34-3.43 (m, 1H), 2.96-3.05 (m, 2H), 2.76-2.82 (m, 1H), 2.31-2.47 (m, 1H), 2.08-2.16 (m, 1H), 1.74-1.91 (m, 3H), 0.86 (t, <i>J</i> =5.57 Hz, 6H).	--	--

Ex. #	Freq., Solvent	¹ H NMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
430	600MHz DMSO-d ₆	7.47 (t, <i>J</i> =9.20 Hz, 1H), 7.39 (dd, <i>J</i> =7.36, 10.70 Hz, 1H), 4.74 (d, <i>J</i> =1.79 Hz, 2H), 4.32-4.46 (m, 3H), 4.03-4.10 (m, 2H), 3.37-3.54 (m, 1H), 2.92-3.05 (m, 3H), 2.88 (t, <i>J</i> =12.38 Hz, 4H), 2.74-2.83 (m, 1H), 2.11 (ddd, <i>J</i> =3.97, 8.10, 17.13 Hz, 1H), 1.74-1.93 (m, 1H).	--	--
431	600MHz DMSO-d ₆	7.47 (dd, <i>J</i> =7.43, 11.17 Hz, 1H), 7.39 (dd, <i>J</i> =7.36, 10.70 Hz, 1H), 4.72-4.80 (m, 2H), 4.34-4.47 (m, 1H), 4.02 (q, <i>J</i> =8.33 Hz, 2H), 3.69 (s, 2H), 3.46-3.59 (m, 4H), 3.34-3.36 (m, 1H), 2.96-3.06 (m, 2H), 2.80 (dd, <i>J</i> =8.21, 12.50 Hz, 1H), 2.08-2.16 (m, 1H), 1.70-1.88 (m, 6H)	--	--

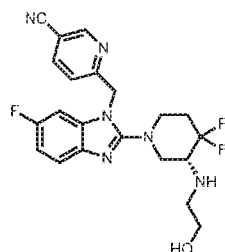


Example 432: (R)-6-((2-(4,4-difluoro-3-(methylamino)piperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile

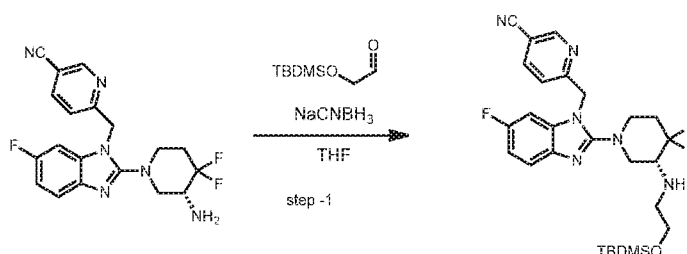


A vial was charged with (R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile (100 mg, 0.259 mmol). The vial was fitted with a stirring bar and DMF (1.3 mL) was added. Potassium carbonate (53.7 mg, 0.388 mmol) was added, followed by iodomethane (40.4 mg, 0.285 mmol). The mixture was left to stir at room temperature for 2 hours. Formation of the mono and bis-methylated amine was observed by LCMS. The reaction was worked up by diluting with EtOAc and NH₄Cl (aq). The mixture was extracted with EtOAc, the organic extracts were combined, dried over MgSO₄, filtered and concentrated to give the crude mixture. The crude was purified on HPLC to afford the title compound. MS: (ESI pos. ion) *m/z*: 401.2 [M+1]; ¹H NMR (600 MHz, d₆-DMSO) δ 8.95 (dd, *J*=0.62, 2.18 Hz, 1H), 8.33 (dd, *J*=2.18, 8.10 Hz, 1H), 7.51 (d, *J*=8.10 Hz, 1H), 7.46 (dd, *J*=4.98, 8.72 Hz, 1H), 7.11 (dd, *J*=2.49, 9.03 Hz, 1H), 6.95 (ddd, *J*=2.49, 8.72, 9.96 Hz, 1H), 5.54 (s, 2H), 3.35-3.41 (m, 1H), 3.28-3.32 (m,

1H), 3.10-3.16 (m, 1H), 2.91-2.96 (m, 1H), 2.88 (td, $J=3.66, 13.23$ Hz, 1H), 2.25 (s, 3H), 2.13-2.23 (m, 1H), 2.01-2.13 (m, 1H).

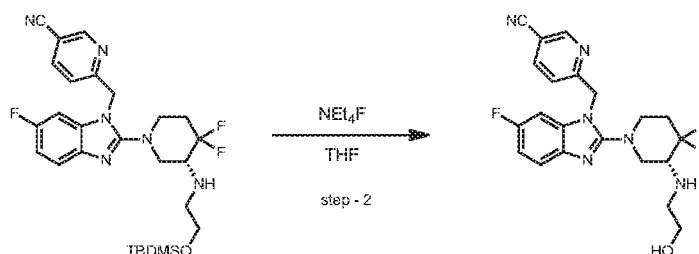


Example 433: (R)-6-((2-(4,4-difluoro-3-((2-hydroxyethyl)amino)piperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile



Step 1. (R)-6-((2-(3-((tert-butyldimethylsilyloxy)ethyl)amino)-4,4-difluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile

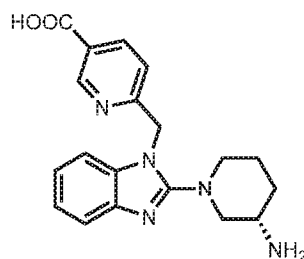
(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile (89.4 mg, 0.231 mmol) was combined with (tert-butyldimethylsilyloxy)acetaldehyde (63.7 μ l, 0.301 mmol) in a vial. Tetrahydrofuran (2.3 mL) and sodium cyanoborohydride (24.2 μ l, 0.463 mmol) were added. The mixture was allowed to stir at room temperature for 2 hours, at which time starting material was fully consumed. The reaction was quenched with $\text{NH}_4\text{Cl(aq)}$, extracted into EtOAc, washed with brine, dried over MgSO_4 , filtered and concentrated to give (R)-6-((2-(3-((tert-butyldimethylsilyloxy)ethyl)amino)-4,4-difluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile, which was used in the next step without further purification.



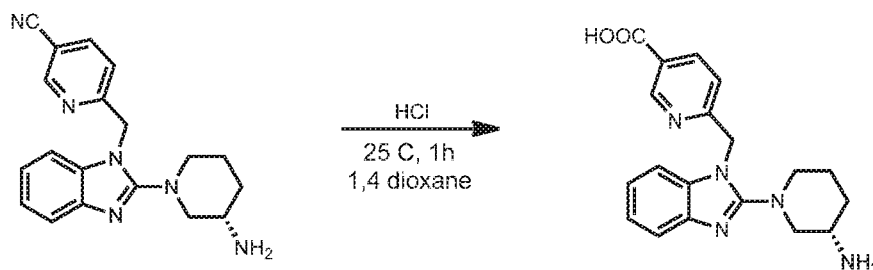
Step 2. (R)-6-((2-(4,4-difluoro-3-((2-hydroxyethyl)amino)piperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile (Example 433)

(R)-6-((2-(3-((tert-butyldimethylsilyloxy)ethyl)amino)-4,4-difluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile was dissolved in THF (2.3 mL), and tetrabutylammonium

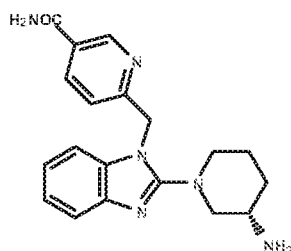
fluoride (1.0 M solution in THF, 301 μ l, 0.301 mmol) was added. The mixture was left to stir at rt for 16 h. Clean deprotection was observed by LCMS. The resulting mixture was worked up by diluting with water and EtOAc, extracting into EtOAc, drying over $MgSO_4$, filtering and concentrating. The crude was purified by column chromatography (4g SiO_2 , 0-70% EtOAc in heptane) to furnish the title compound. MS: (ESI pos. ion) m/z : 431.2 $[M+1]$. ^1H NMR (500 MHz, d_4 -MeOH) δ 8.82 (br s, 1H), 8.13-8.25 (m, 1H), 7.59 (d, $J=8.30$ Hz, 1H), 7.55 (dd, $J=4.67, 8.30$ Hz, 1H), 6.98-7.06 (m, 2H), 5.58 (s, 2H), 4.17 (dtd, $J=4.80, 8.63, 12.98$ Hz, 1H), 4.06 (br d, $J=13.23$ Hz, 1H), 3.84-3.95 (m, 2H), 3.53-3.66 (m, 2H), 3.38-3.47 (m, 1H), 3.32-3.37 (m, 2H), 2.25-2.42 (m, 2H).



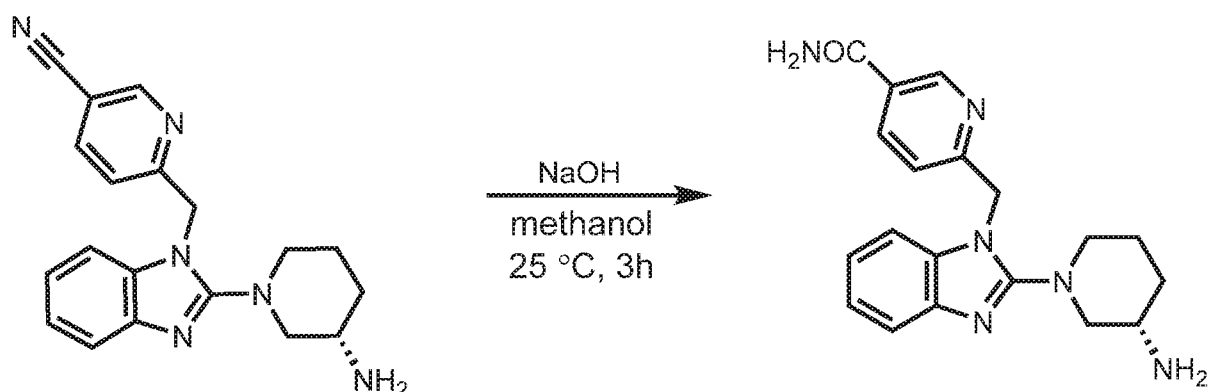
Example 434: (S)-6-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinic acid



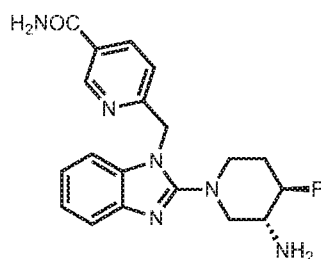
A vial was charged with (S)-6-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile (0.03 g, 0.09 mmol) and 3.99 N aqueous hydrochloric acid (0.075 ml, 0.451 mmol) in 1,4-dioxane (0.301 ml), and shaken at ambient temperature for 1h. The reaction mixture was concentrated and purified by reverse phase HPLC. ^1H NMR (600 MHz, $DMSO-d_6$) δ 13.23-13.65 (br s, 1H), 8.98 (d, $J=1.40$ Hz, 1H), 8.29 (br d, $J=6.85$ Hz, 1H), 8.12-8.19 (m, 1H), 8.11 (br s, 1H), 7.51 (br d, $J=7.71$ Hz, 1H), 7.21 (br s, 1H), 7.15 (br s, 1H), 5.57-5.61 (br s, 2H), 3.58-3.76 (m, 1H), 3.44-3.57 (m, 1H), 3.16-3.29 (m, 2H), 3.06 (br s, 1H), 2.52-2.55 (m, 1H), 1.95 (br s, 1H), 1.83 (br s, 1H), 1.53-1.64 (m, 1H). MS: (ESI pos. ion) m/z : 352.2 $[M+1]$.



Example 435: (S)-6-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinamide

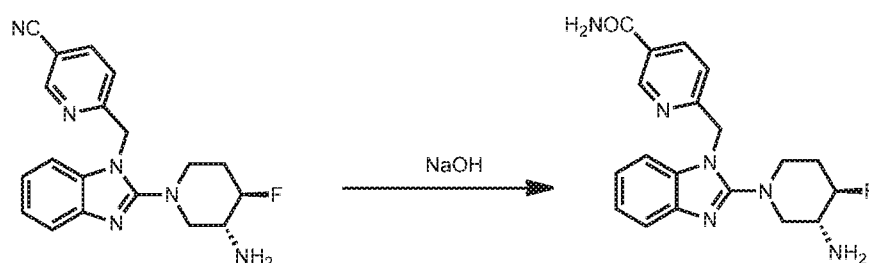


A vial containing (S)-6-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile (0.03 g, 0.090 mmol) and NaOH (1 M in water) (0.271 ml, 0.271 mmol) in methanol (0.30 mL) was shaken at rt for 3h. The reaction mixture was diluted with EtOAc, filtered, concentrated, and purified by reverse phase HPLC to afford the title compound. ¹H NMR (600 MHz, DMSO-d₆) δ 8.94 (s, 1H), 8.16 (dd, *J*=2.22, 8.14 Hz, 1H), 8.11 (br s, 1H), 7.56 (br s, 1H), 7.43 (d, *J*=7.79 Hz, 1H), 7.18 (d, *J*=8.17 Hz, 1H), 6.98-7.11 (m, 3H), 5.38-5.44 (m, 2H), 3.37-3.43 (m, 1H), 2.76-2.89 (m, 2H), 2.57-2.66 (m, 1H), 2.52-2.56 (m, 1H), 1.78-1.84 (m, 1H), 1.65-1.74 (m, 1H), 1.50-1.58 (m, 1H), 1.14-1.28 (m, 1H). MS: (ESI pos. ion) *m/z*: 351.2 [M+1].



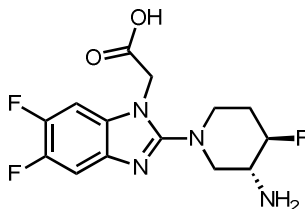
Example 436:
6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinamide

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinamide

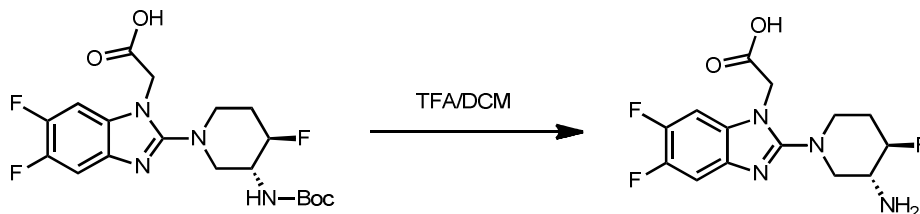


A vial containing 6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile (0.03 g, 0.090 mmol) and NaOH (1 M in water) (0.271 ml, 0.271 mmol) in methanol (0.301 ml) was shaken at ambient temperature for 3h. The reaction mixture was diluted with EtOAc, filtered concentrated and purified by reverse phase HPLC to afford the title compound. ¹H NMR

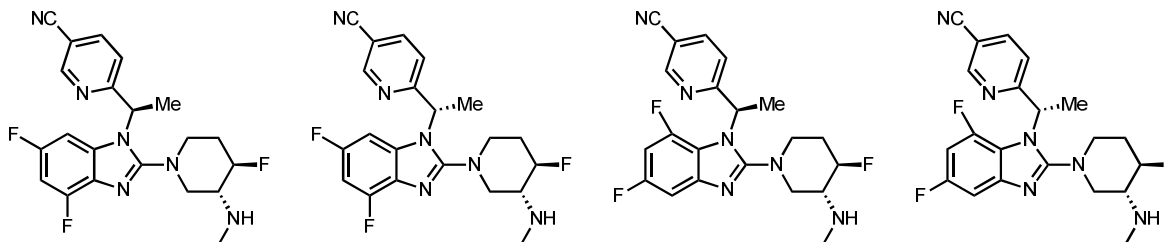
(500 MHz, MeOH-d₄) δ 8.84-9.04 (m, 1H), 8.08-8.27 (m, 1H), 7.48-7.58 (m, 1H), 7.06-7.34 (m, 4H), 5.51 (br d, J=6.75 Hz, 3H), 4.29-4.50 (m, 1H), 3.61 (br dd, J=3.89, 7.79 Hz, 1H), 3.39-3.50 (m, 1H), 2.87-3.19 (m, 3H), 2.10-2.27 (m, 1H), 1.78-1.97 (m, 1H), 0.79-0.98 (m, 1H). MS: (ESI pos. ion) m/z : 369.2 [M+1].



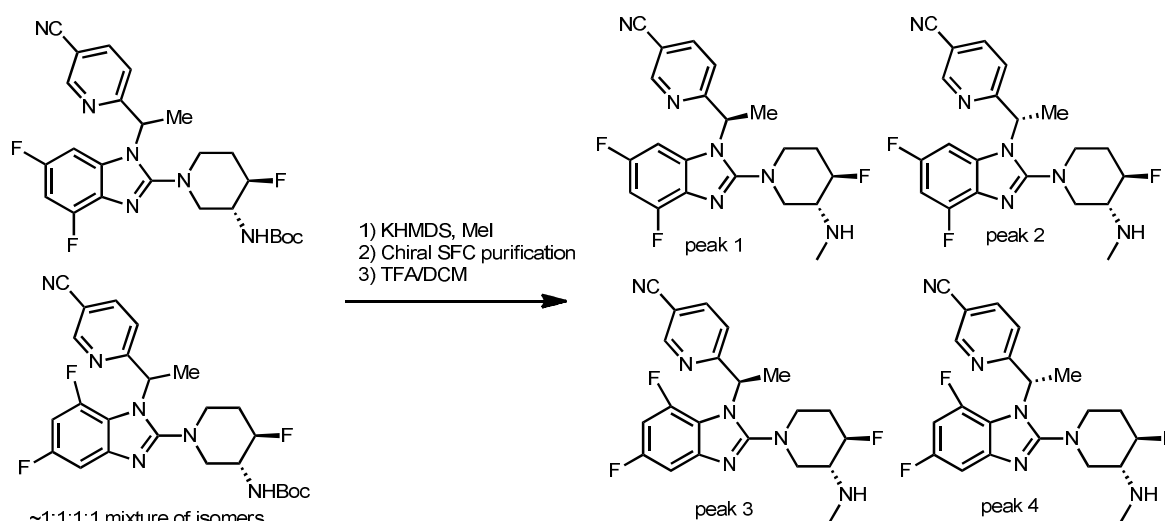
Example 437: 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetic acid



2-(2-((3R,4R)-3-((tert-butoxycarbonyl)amino)-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetic acid was treated with TFA (0.5 mL) in DCM (1 mL) and stirred at rt for 1h. Reaction mixture was concentrated and purified via reverse phase HPLC to obtain the title compound. ¹H NMR (600 MHz, DMSO-d₆) δ 7.47-7.60 (m, 2H), 4.82-4.92 (m, 2H), 4.51-4.59 (dt, J=4.63, 9.01 Hz, 1H), 3.35-3.46 (m, 2H), 3.24-3.30 (m, 1H), 2.95 (br t, J=10.63 Hz, 1H), 2.73-2.89 (m, 1H), 2.13-2.21 (m, 1H), 1.79-1.89 (m, 1H). MS: (ESI pos. ion) m/z : 329.0 [M+1].



Examples 438-441: 6-((R)-1-(4,6-difluoro-2-((3R,4R)-4-fluoro-3-(methylamino)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile (Example 438) and 6-((S)-1-(4,6-difluoro-2-((3R,4R)-4-fluoro-3-(methylamino)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile (Example 439) and 6-((R)-1-(5,7-difluoro-2-((3R,4R)-4-fluoro-3-(methylamino)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile (Example 440) and 6-((S)-1-(5,7-difluoro-2-((3R,4R)-4-fluoro-3-(methylamino)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile (Example 441)



Step 1. tert-butyl ((3R,4R)-1-(1-(1-(5-cyanopyridin-2-yl)ethyl)-4,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl)carbamate (1.05 g, 2.098 mmol, mixture of 4 isomers) and methyl iodide (0.144 ml, 2.308 mmol) were dissolved in THF and cooled to 0 C. potassium bis(trimethylsilyl)amide solution, 1M in tetrahydrofuran (2.203 ml, 2.203 mmol) was added slowly and the reaction stirred for 1 hour. Conversion stalled, so the reaction was quenched with ammonium chloride, then extracted with DCM (3X). The organics were combined, dried over Na₂SO₄, filtered, and concentrated to provide a mixture of methylated and N-H products.

Step 2. Isomers were separated using chiral SFC: Chiralpak Cel2, 15% MeOH, 0.2% DEA.

Step 3. Each individual isomer (100 mg, 1 equiv), was dissolved in DCM (5 mL), then TFA (0.5 mL) was added. After 1 hour, the solutions were poured onto pre-wetted SCX columns and flushed with methanol. The products were eluted with methanolic ammonia.

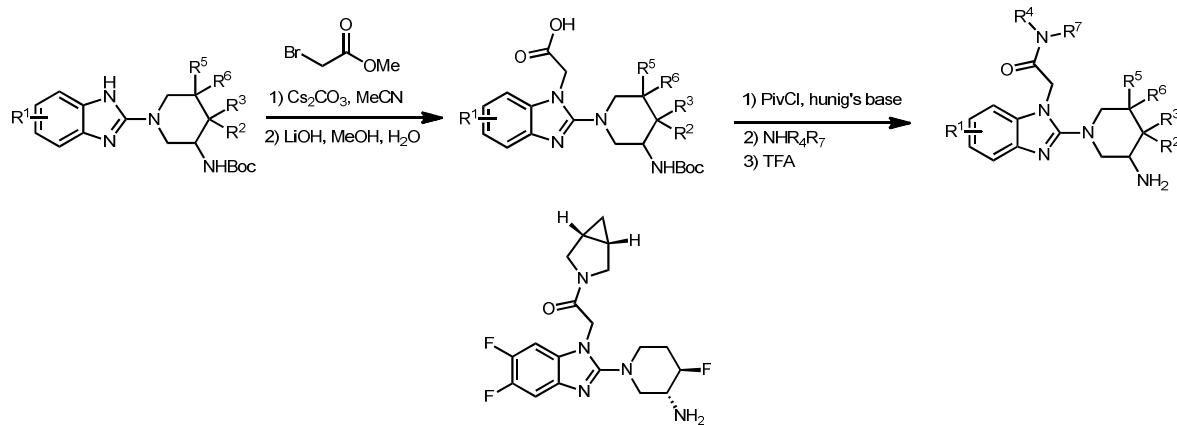
Peak 1: **6-((R)-1-(4,6-difluoro-2-((3R,4R)-4-fluoro-3-(methylamino)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile (Example 438):** ¹H NMR (500 MHz, METHANOL-d₄) δ ppm 1.88 - 2.08 (m, 4 H) 2.22 - 2.33 (m, 1 H) 2.41 - 2.50 (m, 3 H) 2.99 (dd, J=12.72, 9.34 Hz, 1 H) 3.16 - 3.30 (m, 2 H) 3.50 - 3.64 (m, 1 H) 3.77 - 3.95 (m, 1 H) 4.53 - 4.76 (m, 1 H) 5.97 (q, J=7.01 Hz, 1 H) 6.63 - 6.78 (m, 1 H) 7.04 - 7.16 (m, 1 H) 7.62 (d, J=8.30 Hz, 1 H) 8.19 (dd, J=8.30, 2.08 Hz, 1 H) 8.84 (d, J=1.56 Hz, 1 H). MS: (ESI pos. ion) m/z: 415.2 [M+1].

Peak 2: **6-((S)-1-(4,6-difluoro-2-((3R,4R)-4-fluoro-3-(methylamino)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile (Example 439):** ¹H NMR (500 MHz, METHANOL-d₄) δ ppm 1.97 (d, J=7.01 Hz, 3 H) 2.03 - 2.28 (m, 2 H) 2.52 (s, 3 H) 2.99 - 3.21 (m, 3 H) 3.59 (br d, J=12.98 Hz, 1 H) 3.71 - 3.80 (m, 1 H) 4.54 - 4.75 (m, 1 H) 5.97 (q, J=7.01 Hz, 1 H) 6.64 - 6.75 (m, 1 H) 7.10 (dd, J=8.82, 2.08 Hz, 1 H) 7.58 (d, J=8.30 Hz, 1 H) 8.18 (dd, J=8.30, 2.08 Hz, 1 H) 8.76 - 8.87 (m, 1 H). MS: (ESI pos. ion) m/z: 415.2 [M+1].

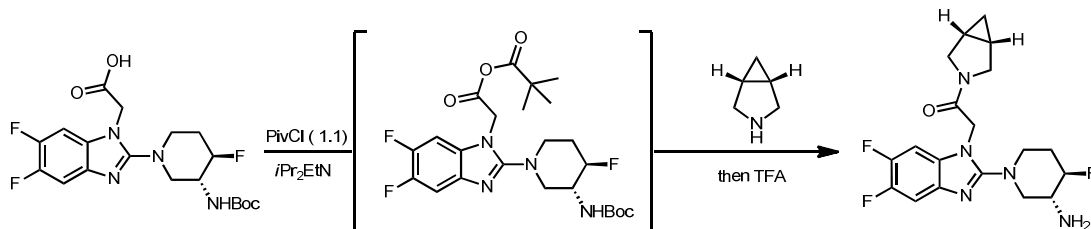
Peak 3: **6-((R)-1-(5,7-difluoro-2-((3R,4R)-4-fluoro-3-(methylamino)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile (Example 440):** ¹H NMR (500 MHz, METHANOL-d₄) δ ppm 2.01 (d, J=7.27 Hz, 4 H) 2.18 - 2.33 (m, 1 H) 2.49 (s, 3 H) 2.98 (dd, J=12.46, 9.34 Hz, 1 H) 3.14 - 3.28 (m, 2 H) 3.47 (br dd, J=12.85, 1.95 Hz, 1 H) 3.79 (dtd, J=8.40, 4.04, 4.04, 2.47 Hz, 1 H) 4.57 - 4.76 (m, 1 H) 5.91 - 6.04 (m, 1 H) 6.67 - 6.85 (m, 2 H) 7.63 (d, J=8.30 Hz, 1 H) 8.13 - 8.25 (m, 1 H) 8.84 - 8.96 (m, 1 H). MS: (ESI pos. ion) *m/z*: 415.2 [M+1].

Peak 4: **6-((S)-1-(5,7-difluoro-2-((3R,4R)-4-fluoro-3-(methylamino)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile (Example 441):** ¹H NMR (500 MHz, METHANOL-d₄) δ ppm 2.02 (d, J=7.01 Hz, 3 H) 2.16 - 2.35 (m, 1 H) 2.51 - 2.68 (m, 3 H) 2.98 - 3.20 (m, 3 H) 3.46 - 3.60 (m, 1 H) 3.65 - 3.78 (m, 1 H) 4.54 - 4.78 (m, 1 H) 5.99 (q, J=7.27 Hz, 1 H) 6.64 - 6.85 (m, 2 H) 7.58 (d, J=8.30 Hz, 1 H) 8.19 (dd, J=8.17, 2.21 Hz, 1 H) 8.83 - 8.96 (m, 1 H). MS: (ESI pos. ion) *m/z*: 415.2 [M+1].

Scheme 15. Compounds made through mixed anhydride



Example 607: 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-((1R,5S)-3-azabicyclo[3.1.0]hexan-3-yl)ethanone



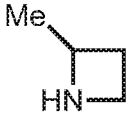
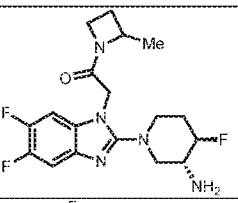
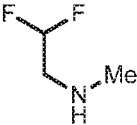
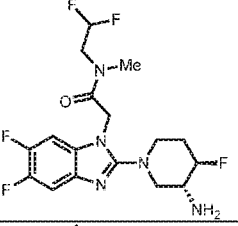
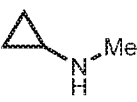
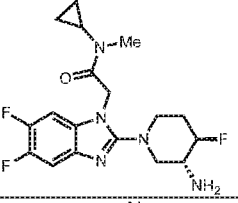
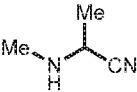
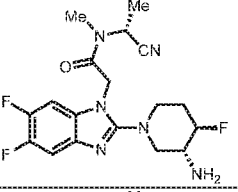
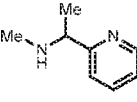
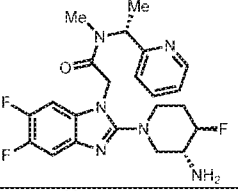
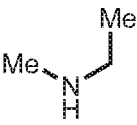
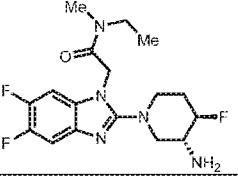
Step 1. 2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-((1R,5S)-3-azabicyclo[3.1.0]hexan-3-yl)ethanone

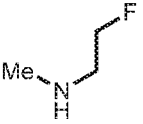
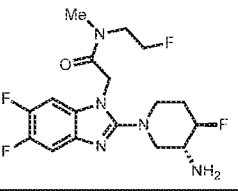
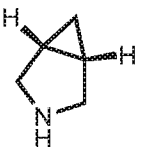
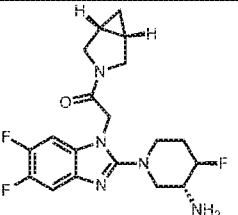
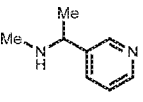
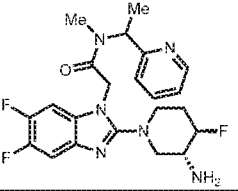
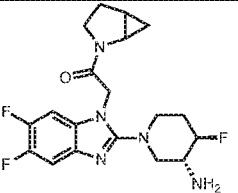
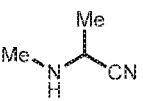
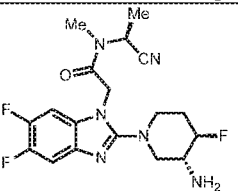
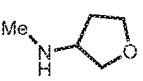
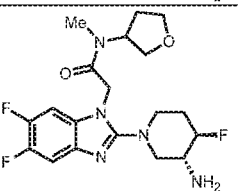
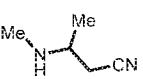
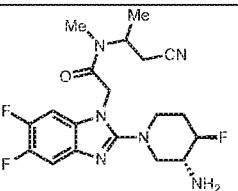
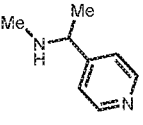
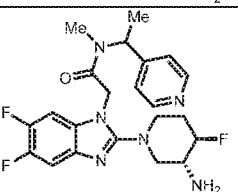
2-(2-((3R,4R)-3-((tert-butoxycarbonyl)amino)-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetic acid (110 mg, 0.257 mmol), 1,1'-dimethyltriethylamine (135 μ l, 0.770 mmol), and tetrahydrofuran (1284 μ l) were combined in a vial and cooled to 0°C. trimethyl acetyl chloride (24.12 μ l, 0.282 mmol) was added dropwise and the mixture stirred for 15 minutes. LCMS showed full conversion to

mixed anhydride (appears as methyl ester by LCMS from MeOH displacement). 3-azabicyclo[3.1.0]hexane (1.5 equiv) was added and allowed to stir for 1 hour. The mixture was concentrated down, then redissolved in DCM/TFA (1:1) and allowed to stir for 1 hour. The mixture was reconcentrated, then redissolved in 1 mL DMSO, filtered, and purified by reverse phase HPLC to provide the desired product.

5

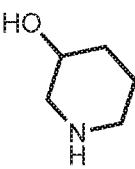
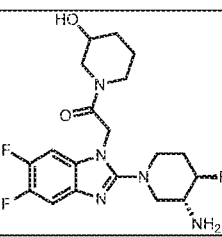
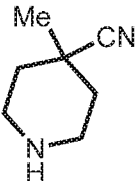
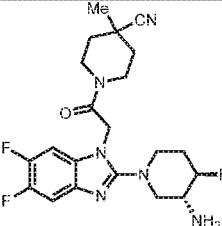
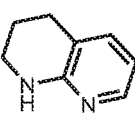
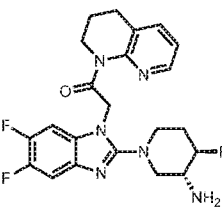
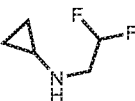
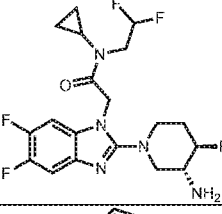
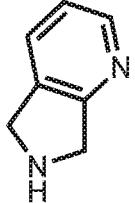
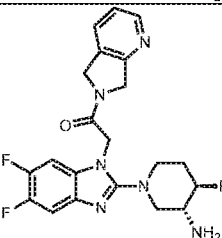
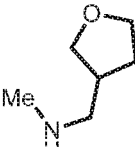
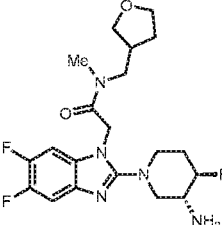
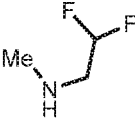
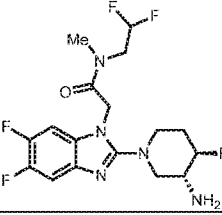
Table 14. The following compounds were made following an analogous procedure to that described for Example 607 and general Scheme 15 above:

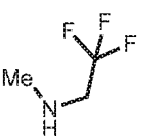
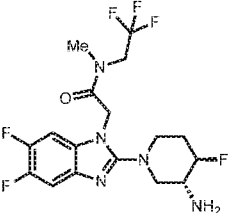
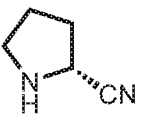
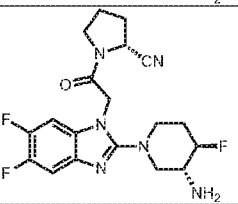
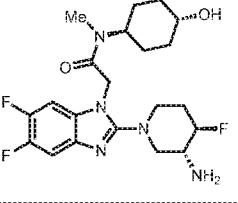
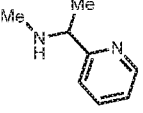
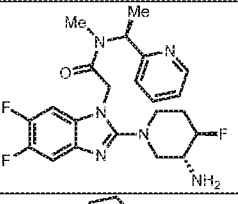
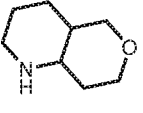
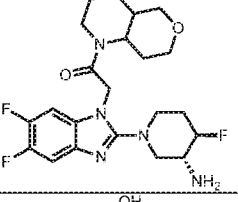
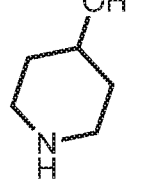
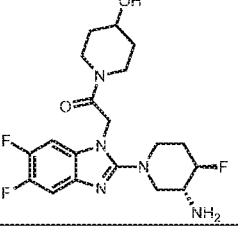
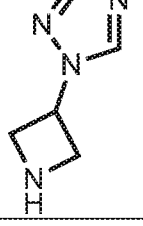
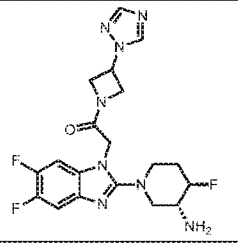
Ex. #	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
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601		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(2,2-difluoroethyl)-N-methylacetamide	406.2
602		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-cyclopropyl-N-methylacetamide	382.2
603		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-((R)-1-cyanoethyl)-N-methylacetamide	395.2
604		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-((R)-1-(pyridin-2-yl)ethyl)acetamide	447.0
605		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-ethyl-N-methylacetamide	370.2

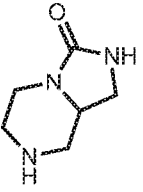
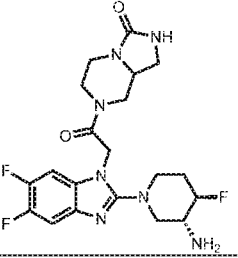
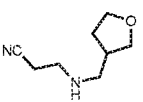
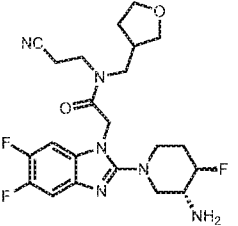
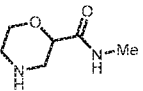
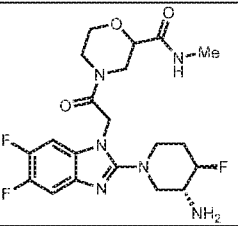
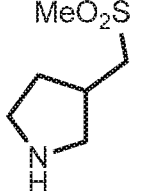
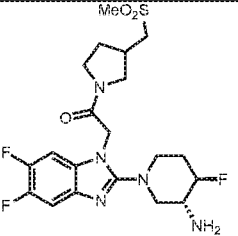
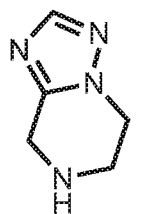
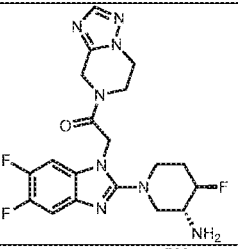
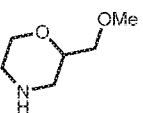
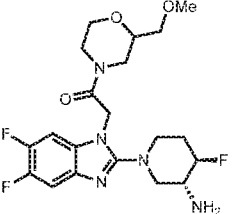
Ex. #	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
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607		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-((1R,5S)-3-azabicyclo[3.1.0]hexan-3-yl)ethanone	394.0
608		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(1-(pyridin-2-yl)ethyl)acetamide	447.2
609		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-((1R,5S)-3-azabicyclo[3.1.0]hexan-2-yl)ethanone	394.2
610		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-((S)-1-cyanoethyl)acetamide	395.4
611		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(tetrahydrofuran-3-yl)acetamide	412.2
612		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(1-cyanopropan-2-yl)acetamide	409.2
613		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(1-(pyridin-4-yl)ethyl)acetamide	447.2

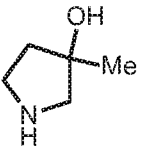
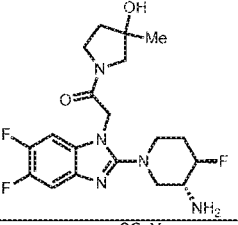
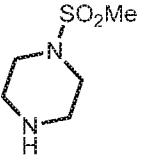
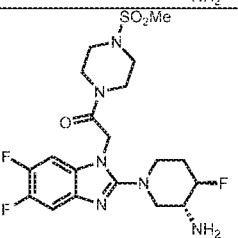
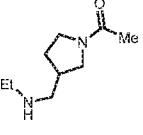
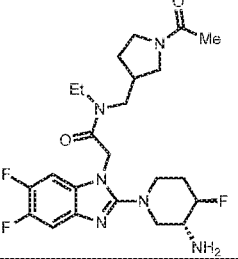
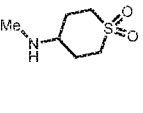
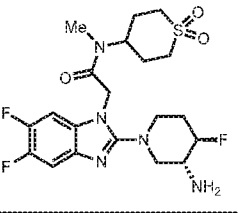
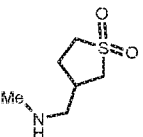
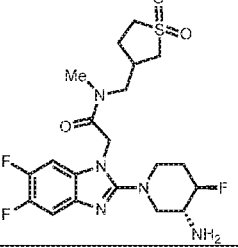
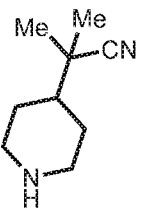
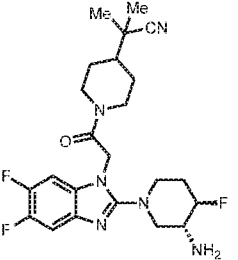
Ex. #	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
614		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(1,1,1-trifluoropropan-2-yl)acetamide	438.2
615		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(cyanomethyl)-N-methylacetamide	381.2
616		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-propylacetamide	384.2
617		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-cyclopropyl-N-(2-hydroxyethyl)acetamide	412.0
618		B		1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)-3-fluoropyrrolidine-3-carbonitrile	425.2
619		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)ethanone	410.0
620		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(hexahydropyrano[4,3-b][1,4]oxazin-4(7H)-yl)ethanone	454.2

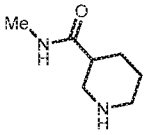
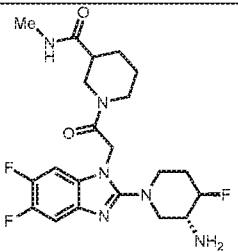
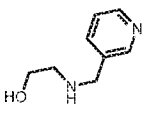
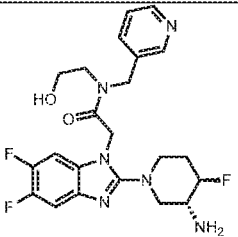
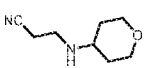
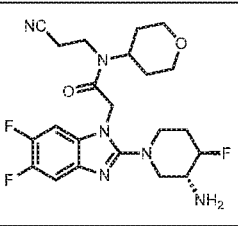
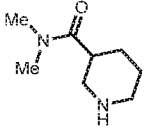
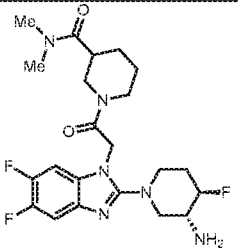
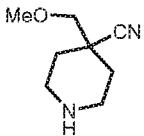
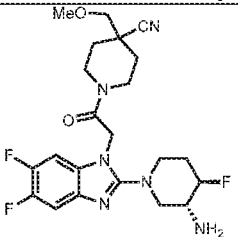
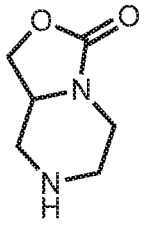
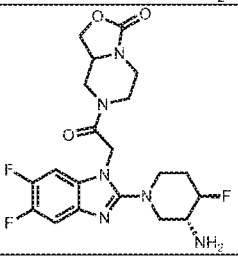
Ex. #	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
621		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(2-cyanopropyl)-N-methylacetamide	409.2
622		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(3,3,3-trifluoropropyl)acetamide	438.2
623		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-((1R,5S)-6,6-difluoro-3-azabicyclo[3.1.0]hexan-3-yl)ethanone	430.2
624		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-(pyrimidin-2-yl)piperazin-1-yl)ethanone	475.0
625		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(2-isopropylazetidin-1-yl)ethanone	410.2
626		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(3-(difluoromethoxy)pyrrolidin-1-yl)ethanone	448.2
627		B		4-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)morpholine-2-carbonitrile	423.0

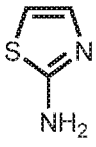
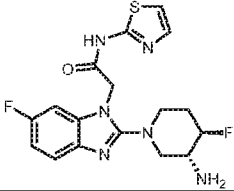
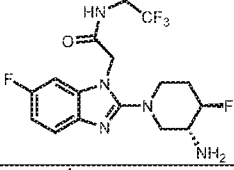
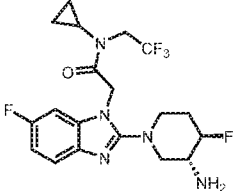
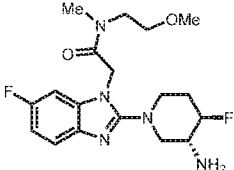
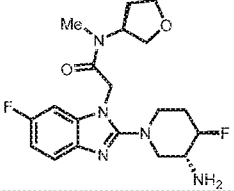
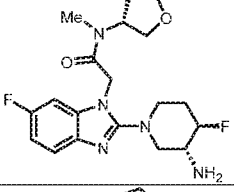
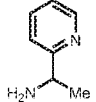
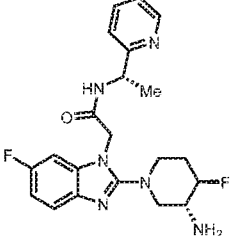
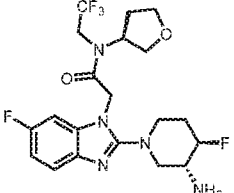
Ex. #	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
628		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(3-hydroxypiperidin-1-yl)ethanone	412.2
629		B		1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)-4-methylpiperidine-4-carbonitrile	435.2
630		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(3,4-dihydro-1,8-naphthyridin-1(2H)-yl)ethanone	445.0
631		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-cyclopropyl-N-(2,2-difluoroethyl)acetamide	432.2
632		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(5H-pyrrolo[3,4-b]pyridin-6(7H)-yl)ethanone	431.2
633		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(tetrahydrofuran-3-yl)methylacetamide	426.0
634		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(2,2-difluoroethyl)-N-methylacetamide	406.2

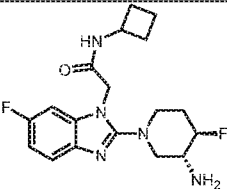
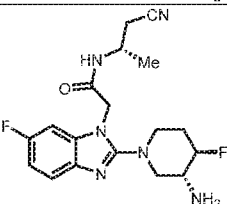
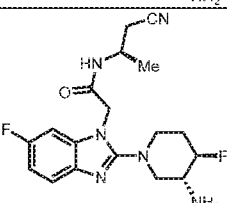
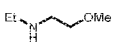
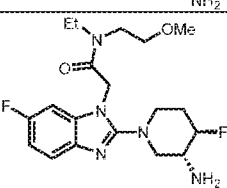
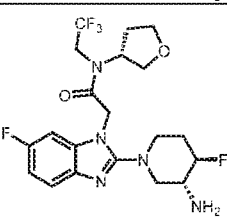
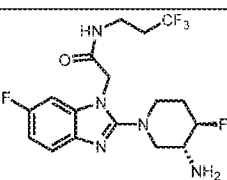
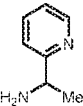
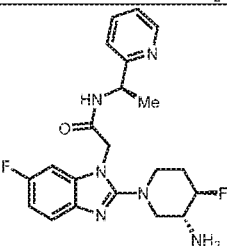
Ex. #	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
635		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-(2,2,2-trifluoroethyl)acetamide	424.2
636		B		(R)-1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)pyrrolidine-2-carbonitrile	407.0
637		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-((1R,4R)-4-hydroxycyclohexyl)-N-methylacetamide	440.0
638		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-((S)-1-(pyridin-2-yl)ethyl)acetamide	447.2
639		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(octahydro-1H-pyrano[4,3-b]pyridin-1-yl)ethanone	452.2
640		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-hydroxypiperidin-1-yl)ethanone	412.2
641		B		1-(3-(1H-1,2,4-triazol-1-yl)azetidin-1-yl)-2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)ethanone	435.2

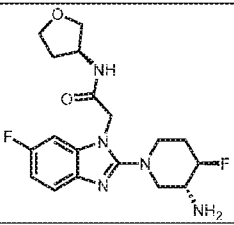
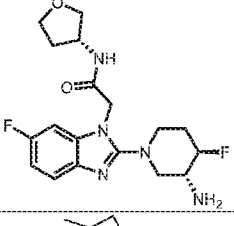
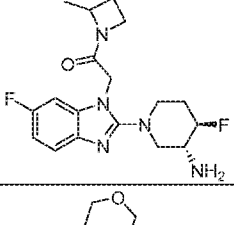
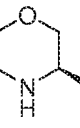
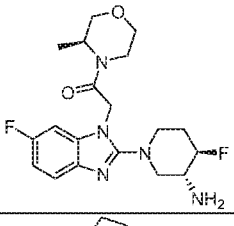
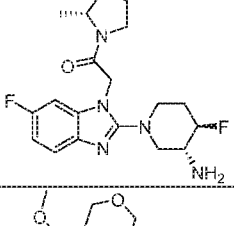
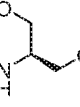
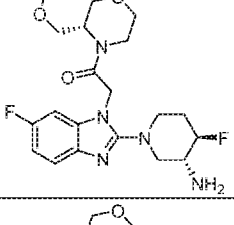
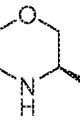
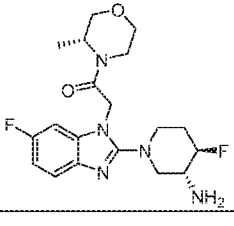
Ex. #	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
642		B		7-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)hexahydroimidazo[1,5-a]pyrazin-3(2H)-one	452.2
643		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(2-cyanoethyl)-N-((tetrahydrofuran-3-yl)methyl)acetamide	465.2
644		B		4-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)-N-methylmorpholine-2-carboxamide	455.2
645		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(3-((methylsulfonyl)methyl)pyrrolidin-1-yl)ethanone	474.2
646		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(5,6-dihydro[1,2,4]triazolo[1,5-a]pyrazin-7(8H)-yl)ethanone	435.2
647		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(2-(methoxymethyl)morpholino)ethanone	442.2

Ex. #	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
648		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(3-hydroxy-3-methylpyrrolidin-1-yl)ethanone	412.2
649		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-(methylsulfonyl)piperazin-1-yl)ethanone	475.2
650		B		N-((1-acetylpyrrolidin-3-yl)methyl)-2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-ethylacetamide	481.2
651		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(1,1-dioxido-2,2-dihydro-4H-thiopyran-4-yl)-N-methylacetamide	474.2
652		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-((1,1-dioxido-2,2-dihydro-4H-thiophen-3-yl)methyl)-N-methylacetamide	474.0
653		B		2-(1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)piperidin-4-yl)-2-methylpropanenitrile	463.0

Ex. #	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
654		B		1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)-N-methylpiperidine-3-carboxamide	453.2
655		B		2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(2-hydroxyethyl)-N-(pyridin-3-ylmethyl)acetamide	463.2
656		B		2-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(2-cyanoethyl)-N-(tetrahydro-2H-pyran-4-yl)acetamide	465.2
657		B		1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)-N,N-dimethylpiperidine-3-carboxamide	467.2
658		B		1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)-4-(methoxymethyl)piperidine-4-carbonitrile	465.2
659		B		7-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)tetrahydro-1H-oxazolo[3,4-a]pyrazin-3(5H)-one	453.2

Ex. #	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
660		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-(thiazol-2-yl)acetamide	393.0
661		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-(2,2,2-trifluoroethyl)acetamide	392.2
662		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-cyclopropyl-N-(2,2,2-trifluoroethyl)acetamide	432.2
663		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-(2-methoxyethyl)-N-methylacetamide	382.2
664		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-((S)-tetrahydrofuran-3-yl)acetamide	394.2
665		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-methyl-N-((R)-tetrahydrofuran-3-yl)acetamide	394.2
666		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-((S)-1-(pyridin-2-yl)ethyl)acetamide	415.2
667		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-((S)-2,2,2-trifluoroethyl)-N-(tetrahydrofuran-3-yl)acetamide	462.2

Ex. #	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
				(2,2,2-trifluoroethyl)acetamide	
668		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-cyclobutylacetamide	364.2
669		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-((S)-1-cyanopropan-2-yl)acetamide	377.2
670		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-((R)-1-cyanopropan-2-yl)acetamide	377.2
671		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-ethyl-N-(2-methoxyethyl)acetamide	396.2
672		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-((R)-tetrahydrofuran-3-yl)-N-(2,2,2-trifluoroethyl)acetamide	462.2
673		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-(3,3,3-trifluoropropyl)acetamide	406.2
674		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-((R)-1-(pyridin-2-yl)ethyl)acetamide	415.2

Ex. #	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
675		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-((S)-tetrahydrofuran-3-yl)acetamide	380.2
676		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-N-((R)-tetrahydrofuran-3-yl)acetamide	380.2
677		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-1-(2-methylazetidin-1-yl)ethan-1-one	464.2
678		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-1-((S)-3-methylmorpholino)ethan-1-one	394.2
679		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-1-((R)-2-methylpyrrolidin-1-yl)ethan-1-one	378.2
680		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-1-((R)-3-(methoxymethyl)morpholino)ethan-1-one	424.2
681		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-1-((R)-3-methylmorpholino)ethan-1-one	394.2

Ex. #	Amine	Boc Deprotection Procedure	Structure	Compound Name	MS MH+
682		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-1-((S)-2-methylpyrrolidin-1-yl)ethan-1-one	378.2
683		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-1-(3,5-dimethylmorpholino)ethan-1-one	408.2
684		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-1-(3-ethylmorpholino)ethan-1-one	408.2
685		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-1-((S)-3-cyclopropylmorpholino)ethan-1-one	420.2
686		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-1-((R)-3-(hydroxymethyl)morpholino)ethan-1-one	410.2
687		B		2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)-1-(3,3-dimethylmorpholino)ethan-1-one	408.2

Table 15. Characterization data for compounds tabulated in Table 14

The column “Separation Stage” indicates after which process step regioisomers formed due to asymmetric benzimidazole substitution at R^1 in Scheme 15 were separated during the preparation of the tabulated final compound (I = after preparation of the acetic acid intermediate (where at least one R^1 is not hydrogen); B = prior to boc deprotection; or F = final compound).

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
600	600 MHz, DMSO-d ₆	7.42-7.56 (m, 1H), 7.38 (dd, J=7.47, 10.59 Hz, 1H), 4.60-4.88 (m, 2H), 4.55-4.90 (m, 3H), 4.32-4.52 (m, 2H), 4.11-4.21 (m, 1H), 3.76-3.90 (m, 1H), 2.96-3.09 (m, 2H), 2.71-2.88 (m, 1H), 2.37-2.46 (m, 1H), 2.12 (dt, J=3.11, 13.08 Hz, 1H), 1.73-1.90 (m, 3H), 1.53 (d, J=6.23 Hz, 1H), 1.35 (dd, J=1.87, 6.23 Hz, 2H)	--	--
601	600 MHz, DMSO-d ₆	7.44-7.53 (m, 1H), 7.25-7.43 (m, 1H), 6.02-6.55 (m, 1H), 4.99-5.11 (m, 2H), 4.30-4.48 (m, 1H), 3.93-4.03 (m, 1H), 3.78 (dt, J=3.74, 15.41 Hz, 1H), 3.22 (s, 2H), 2.94-3.04 (m, 3H), 2.71-2.82 (m, 1H), 2.01-2.15 (m, 1H), 1.70-1.87 (m, 3H)	--	--
602	600 MHz, DMSO-d ₆	7.35-7.53 (m, 2H), 4.99-5.15 (m, 2H), 4.30-4.46 (m, 1H), 3.28 (br d, J=3.43 Hz, 1H), 2.95-3.10 (m, 3H), 2.86 (s, 3H), 2.79 (br dd, J=8.25, 12.61 Hz, 1H), 2.02-2.18 (m, 1H), 1.71-1.88 (m, 3H), 0.86-1.01 (m, 4H)	--	--
603	500MHz d ₄ -MeOH	7.31-7.40 (m, 1H), 7.18-7.30 (m, 1H), 5.58 (q, J=7.18 Hz, 1H), 5.02-5.19 (m, 2H), 4.42-4.61 (m, 1H), 3.53 (dtd, J=1.56, 4.18, 12.39 Hz, 1H), 3.39 (br d, J=12.98 Hz, 1H), 3.28 (s, 2H), 3.21-3.30 (m, 1H), 3.04-3.15 (m, 1H), 3.07 (br s, 1H), 2.98 (dd, J=8.82, 12.46 Hz, 1H), 2.17-2.29 (m, 1H), 1.89-2.03 (m, 1H), 1.56 (d, J=7.01 Hz, 3H)	B	Chiralpak OJ, 10% MeOH, peak 2
604	500MHz d ₄ -MeOH	mixture of rotamers: 8.68 (d, J=4.67 Hz, 1H), 8.53-8.62 (m, 1H), 7.90 (dt, J=1.82, 7.79 Hz, 1H), 7.83 (dt, J=1.82, 7.79 Hz, 1H), 7.54 (d, J=7.79 Hz, 1H), 7.27-7.46 (m, 3H), 5.83 (q, J=7.01 Hz, 1H), 5.20-5.48 (m, 1H), 5.09 (d, J=2.34 Hz, 1H), 4.37-4.57 (m, 1H), 3.48-3.57 (m, 1H), 3.34-3.46 (m, 1H), 3.05-3.21 (m, 2H), 3.03 (s, 2H), 2.90-3.01 (m, 1H), 2.77 (s, 1H), 2.12-2.27 (m, 1H), 1.88-2.01 (m, 1H), 1.80 (d, J=7.01 Hz, 1H), 1.64 (d, J=7.01 Hz, 2H)	B	Chiralpak AD, 20% MeOH, peak 2
605	600 MHz, DMSO-d ₆	Mixture of rotamers: 7.41-7.52 (m, 1H), 7.29-7.40 (m, 1H), 4.94-5.01 (m, 2H), 4.26-4.49 (m, 1H), 3.42-3.50 (m, 1H), 3.07-3.11 (m, 2H), 2.93-3.05 (m, 2H), 2.85 (s, 1H), 2.75-2.82 (m, 1H), 2.03-2.15 (m, 1H), 1.64-1.83 (m, 3H), 1.00-1.24 (m, 3H)	--	--
606	600 MHz, DMSO-d ₆	Mixture of rotamers: 7.43-7.50 (m, 1H), 7.23-7.41 (m, 1H), 4.98-5.05 (m, 2H), 4.66-4.77 (m, 1H), 4.49-4.61 (m, 1H), 4.30-4.47 (m, 1H), 3.75-3.86 (m, 1H), 3.60-3.69 (m, 1H), 3.18 (s, 2H), 2.94-3.04 (m, 2H), 2.93 (s, 1H), 2.77 (ddd, J=8.56, 12.61, 18.68 Hz, 1H), 1.97-2.14 (m, 1H), 1.71-1.85 (m, 3H)	--	--

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
607	600 MHz, DMSO-d ₆	7.34-7.50 (m, 2H), 4.91 (dd, J=14.95, 17.44 Hz, 1H), 4.71-4.83 (m, 1H), 4.32-4.48 (m, 1H), 3.76 (dd, J=8.25, 9.81 Hz, 1H), 3.56-3.70 (m, 2H), 3.20-3.30 (m, 2H), 2.91-3.06 (m, 2H), 2.73-2.83 (m, 1H), 2.06-2.16 (m, 1H), 1.82-1.96 (m, 1H), 1.73-1.82 (m, 1H), 1.69 (br dd, J=3.74, 7.47 Hz, 1H), 1.57 (td, J=3.62, 7.40 Hz, 1H), 0.70-0.80 (m, 1H), 0.20 (d, J=4.36 Hz, 1H)	--	--
608	600 MHz, DMSO-d ₆	Mixture of diastereomers: 8.46-8.53 (m, 2H), 7.68-7.76 (m, 1H), 7.44-7.52 (m, 3H), 5.74-5.81 (m, 1H), 4.97-5.13 (m, 2H), 4.32-4.48 (m, 1H), 2.94-3.07 (m, 2H), 2.89 (d, J=3.43 Hz, 3H), 2.76-2.84 (m, 1H), 2.04-2.15 (m, 1H), 1.76-1.86 (m, 3H), 1.68 (br t, J=6.85 Hz, 1H), 1.53 (dd, J=2.49, 7.16 Hz, 3H)	--	--
609	600 MHz, DMSO-d ₆	Mixture of diastereomers: 7.43-7.53 (m, 1H), 7.38 (qd, J=7.06, 10.59 Hz, 1H), 5.18 (dd, J=7.63, 17.59 Hz, 1H), 4.88-5.03 (m, 1H), 4.27-4.49 (m, 1H), 3.69-3.78 (m, 1H), 3.62 (dtd, J=2.96, 5.98, 8.76 Hz, 1H), 3.10-3.20 (m, 1H), 2.94-3.08 (m, 3H), 2.75-2.86 (m, 1H), 2.08-2.20 (m, 2H), 1.90 (ddd, J=3.43, 8.88, 12.61 Hz, 1H), 1.71-1.83 (m, 4H), 0.81-0.90 (m, 1H)	--	--
610	500MHz d ₄ -MeOH	7.35 (dd, J=7.27, 10.64 Hz, 1H), 7.28 (dd, J=7.14, 10.25 Hz, 1H), 5.48-5.60 (m, 1H), 5.01-5.19 (m, 2H), 4.51-4.66 (m, 1H), 3.56-3.64 (m, 1H), 3.38-3.45 (m, 2H), 3.28 (s, 3H), 3.03-3.13 (m, 1H), 2.17-2.31 (m, 1H), 1.90-2.05 (m, 1H), 1.56 (d, J=7.27 Hz, 3H)	B	Chiralpak OJ, 10% MeOH, peak 1
611	600 MHz, DMSO-d ₆	7.25-7.58 (m, 2H), 4.90-5.18 (m, 3H), 4.28-4.49 (m, 1H), 3.93-4.00 (m, 1H), 3.54-3.79 (m, 3H), 2.89-3.08 (m, 4H), 2.71-2.84 (m, 2H), 2.07-2.23 (m, 2H), 1.71-1.89 (m, 2H), 1.66-2.00 (m, 1H)	--	--
612	600 MHz, DMSO-d ₆	Mixture of diastereomers: 7.43-7.51 (m, 1H), 7.28-7.41 (m, 1H), 4.93-5.20 (m, 2H), 4.74-4.85 (m, 1H), 4.30-4.55 (m, 1H), 3.21-3.29 (m, 2H), 3.01-3.05 (m, 3H), 2.96-3.00 (m, 1H), 2.75-2.90 (m, 4H), 2.75-2.88 (m, 3H), 2.04-2.20 (m, 1H), 1.70-1.87 (m, 3H), 1.14-1.35 (m, 3H)	--	--
613	600 MHz, DMSO-d ₆	8.53-8.60 (m, 2H), 7.43-7.51 (m, 2H), 7.31 (dd, J=5.45, 8.56 Hz, 2H), 5.69 (quin, J=6.54 Hz, 1H), 4.99-5.18 (m, 2H), 4.34-4.52 (m, 1H), 2.93-3.09 (m, 2H), 2.90 (d, J=4.67 Hz, 3H), 2.75-2.86 (m, 1H), 2.05-2.18 (m, 1H), 1.76-1.88 (m, 3H), 1.51 (dd, J=2.96, 7.01 Hz, 3H)	--	--

Ex. #	Freq., Solvent	¹ H NMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
614	600 MHz, DMSO-d ₆	Mixture of diastereomers: 7.45-7.53 (m, 1H), 7.30-7.43 (m, 1H), 5.17-5.30 (m, 1H), 5.02-5.17 (m, 2H), 4.30-4.48 (m, 1H), 3.20-3.26 (m, 1H), 3.11 (s, 3H), 2.91-3.04 (m, 2H), 2.73-2.82 (m, 1H), 2.03-2.15 (m, 1H), 1.80-1.86 (m, 1H), 1.68-1.79 (m, 1H), 1.33-1.53 (m, 3H)	--	--
615	600 MHz, DMSO-d ₆	7.40-7.55 (m, 2H), 5.02-5.15 (m, 2H), 4.46 (s, 2H), 4.31-4.44 (m, 1H), 3.27-3.30 (m, 2H), 3.23 (s, 3H), 2.97-3.06 (m, 1H), 2.93-3.05 (m, 1H), 2.78 (dd, J=8.10, 12.46 Hz, 1H), 2.06-2.18 (m, 1H), 1.71-1.82 (m, 1H)	--	--
616	600 MHz, DMSO-d ₆	7.41-7.52 (m, 1H), 7.29-7.40 (m, 1H), 4.94-5.01 (m, 2H), 4.26-4.49 (m, 1H), 3.42-3.50 (m, 1H), 3.07-3.11 (m, 2H), 2.93-3.05 (m, 2H), 2.85 (s, 1H), 2.75-2.82 (m, 1H), 2.03-2.15 (m, 1H), 1.64-1.83 (m, 3H), 1.00-1.24 (m, 3H)	--	--
617	600 MHz, DMSO-d ₆	7.45 (ddd, J=7.47, 10.98, 14.25 Hz, 2H), 5.00-5.14 (m, 2H), 4.31-4.50 (m, 1H), 3.49-3.54 (m, 2H), 3.38-3.48 (m, 4H), 3.19-3.24 (m, 1H), 2.93-3.06 (m, 3H), 2.77 (dd, J=8.41, 12.46 Hz, 1H), 2.03-2.21 (m, 1H), 1.73-1.88 (m, 1H), 0.88-1.03 (m, 4H)	--	--
618	600 MHz, DMSO-d ₆	7.45-7.51 (m, 1H), 7.33-7.44 (m, 1H), 4.82-5.09 (m, 2H), 4.42-4.54 (m, 1H), 4.26-4.39 (m, 1H), 3.91-4.21 (m, 2H), 3.71-3.86 (m, 2H), 3.43 (dt, J=7.32, 10.98 Hz, 1H), 3.16-3.26 (m, 1H), 2.97-3.07 (m, 2H), 2.75-2.86 (m, 2H), 2.52-2.73 (m, 2H), 2.05-2.14 (m, 1H), 1.74-1.85 (m, 1H)	--	--
619	600 MHz, DMSO-d ₆	7.44-7.50 (m, 1H), 7.32-7.43 (m, 1H), 4.84-5.14 (m, 2H), 4.61-4.79 (m, 2H), 4.33-4.49 (m, 1H), 3.74-3.86 (m, 1H), 3.71 (s, 1H), 3.60 (s, 1H), 3.25-3.30 (m, 2H), 3.23 (br d, J=11.52 Hz, 1H), 2.91-3.06 (m, 2H), 2.80 (dd, J=8.25, 12.61 Hz, 1H), 2.07-2.18 (m, 1H), 1.73-1.96 (m, 5H)	--	--
620	600 MHz, DMSO-d ₆	Mixture of isomers: 7.39-7.49 (m, 2H), 4.91-5.08 (m, 2H), 4.33-4.52 (m, 2H), 3.87-3.96 (m, 2H), 3.74-3.85 (m, 2H), 3.58-3.67 (m, 1H), 3.51 (t, J=11.05 Hz, 1H), 3.43 (dt, J=3.11, 9.65 Hz, 1H), 3.21-3.27 (m, 2H), 2.94-3.05 (m, 2H), 2.79 (td, J=8.10, 12.46 Hz, 1H), 2.07-2.17 (m, 1H), 1.73-1.85 (m, 3H), 1.52-1.61 (m, 1H)	--	--
621	600 MHz, DMSO-d ₆	Mixture of diastereomers: 7.42-7.51 (m, 1H), 7.38 (dd, J=7.47, 10.59 Hz, 1H), 4.93-5.13 (m, 2H), 4.29-4.47 (m, 1H), 3.65-3.88 (m, 1H), 3.40-3.57 (m, 1H), 3.19-3.23 (m, 3H), 2.95-3.07 (m, 2H), 2.67-2.86 (m, 1H), 2.04-2.17 (m, 1H), 1.71-1.85 (m, 3H)	--	--

Ex. #	Freq., Solvent	¹ H NMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
622	600 MHz, DMSO-d ₆	7.42-7.51 (m, 1H), 7.30-7.39 (m, 1H), 4.91-5.10 (m, 2H), 4.32-4.49 (m, 1H), 3.53-3.74 (m, 2H), 3.26 (br dd, J=5.14, 7.32 Hz, 1H), 3.15 (s, 1H), 3.11-3.21 (m, 1H), 2.93-3.05 (m, 2H), 2.78 (dd, J=8.25, 12.61 Hz, 1H), 2.52-2.57 (m, 1H), 2.04-2.15 (m, 1H), 1.71-1.82 (m, 3H)	--	--
623	600 MHz, DMSO-d ₆	7.43-7.52 (m, 1H), 7.33 (dd, J=7.16, 10.59 Hz, 1H), 4.93-5.01 (m, 1H), 4.81-4.90 (m, 1H), 4.31-4.48 (m, 1H), 4.02-4.12 (m, 1H), 3.91-4.01 (m, 1H), 3.80 (br d, J=12.46 Hz, 1H), 3.58-3.70 (m, 1H), 3.17-3.26 (m, 1H), 2.91-3.03 (m, 2H), 2.72-2.85 (m, 2H), 2.56-2.65 (m, 1H), 2.02-2.20 (m, 1H), 1.68-1.81 (m, 2H)	--	--
624	600 MHz, DMSO-d ₆	8.32-8.47 (m, 2H), 7.35-7.53 (m, 2H), 6.61-6.74 (m, 1H), 5.03-5.16 (m, 2H), 4.32-4.48 (m, 1H), 3.83-3.93 (m, 2H), 3.77 (br t, J=4.20 Hz, 2H), 3.67-3.73 (m, 4H), 3.60-3.64 (m, 2H), 2.95-3.06 (m, 2H), 2.81 (dd, J=7.94, 12.61 Hz, 1H), 2.05-2.19 (m, 1H), 1.75-1.86 (m, 1H)	--	--
625	600 MHz, DMSO-d ₆	Mixture of Rotamers: 7.44-7.53 (m, 1H), 7.36 (dd, J=7.32, 10.74 Hz, 1H), 4.66-4.90 (m, 2H), 4.50-4.65 (m, 1H), 4.31-4.48 (m, 1H), 4.10-4.28 (m, 2H), 3.99-4.09 (m, 1H), 2.91-3.09 (m, 2H), 2.79 (dt, J=8.56, 13.16 Hz, 1H), 2.20-2.32 (m, 1H), 2.08-2.16 (m, 2H), 2.00 (td, J=5.61, 15.26 Hz, 1H), 1.69-1.89 (m, 3H), 0.77-0.92 (m, 6H)	--	--
626	600 MHz, DMSO-d ₆	Mixture of Rotamers: 7.47 (dd, J=7.47, 11.21 Hz, 1H), 7.39 (dd, J=7.16, 10.59 Hz, 1H), 6.61-6.99 (m, 1H), 4.79-5.01 (m, 3H), 4.30-4.48 (m, 1H), 3.63-3.94 (m, 3H), 3.51-3.61 (m, 2H), 2.96-3.07 (m, 2H), 2.79 (ddd, J=1.25, 8.33, 12.53 Hz, 1H), 2.17-2.31 (m, 1H), 1.98-2.15 (m, 3H), 1.73-1.81 (m, 1H)	--	--
627	600 MHz, DMSO-d ₆	Mixture of diastereomers: 7.43-7.53 (m, 1H), 7.28-7.40 (m, 1H), 4.98-5.28 (m, 3H), 4.30-4.51 (m, 1H), 4.01-4.26 (m, 1H), 3.74-3.98 (m, 4H), 3.44-3.53 (m, 1H), 3.40-3.59 (m, 1H), 2.94-3.10 (m, 3H), 2.72-2.87 (m, 1H), 2.06-2.19 (m, 1H), 1.71-1.94 (m, 1H)	--	--
628	600 MHz, DMSO-d ₆	Mixture of diastereomers: 7.23-7.49 (m, 2H), 4.91-5.18 (m, 4H), 4.29-4.49 (m, 1H), 3.49-4.15 (m, 4H), 2.92-3.09 (m, 3H), 2.71-2.82 (m, 1H), 2.04-2.16 (m, 1H), 1.29-1.90 (m, 8H)	--	--

Ex. #	Freq., Solvent	¹ H NMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
629	600 MHz, DMSO-d ₆	7.44-7.52 (m, 1H), 7.41 (dd, J=7.32, 10.74 Hz, 1H), 4.94-5.14 (m, 2H), 4.34-4.49 (m, 1H), 4.23-4.32 (m, 1H), 3.97-4.06 (m, 1H), 3.21 (br d, J=1.25 Hz, 1H), 2.95-3.05 (m, 2H), 2.74-2.91 (m, 2H), 2.06-2.16 (m, 1H), 2.01 (td, J=2.76, 5.99 Hz, 1H), 1.88-1.96 (m, 2H), 1.72-1.85 (m, 2H), 1.60-1.72 (m, 1H), 1.43-1.51 (m, 1H), 1.40 (s, 3H)	--	--
630	600 MHz, DMSO-d ₆	8.35-8.57 (m, 1H), 7.59-7.69 (m, 1H), 7.26-7.53 (m, 2H), 7.24 (dd, J=4.83, 7.63 Hz, 1H), 5.02-5.21 (m, 2H), 4.66-4.93 (m, 1H), 4.60-4.95 (m, 1H), 4.25-4.48 (m, 1H), 3.92 (br t, J=5.92 Hz, 1H), 3.80-3.87 (m, 1H), 2.71-3.14 (m, 5H), 1.97-2.15 (m, 1H), 1.62-1.80 (m, 1H)	--	--
631	600 MHz, DMSO-d ₆	7.19-7.28 (m, 2H), 6.88-6.96 (m, 1H), 6.00-6.28 (m, 1H), 5.11-5.23 (m, 2H), 4.31-4.50 (m, 1H), 3.76 (dt, J=3.74, 15.26 Hz, 2H), 2.92-3.08 (m, 3H), 2.81 (dd, J=8.25, 12.61 Hz, 1H), 2.07-2.18 (m, 1H), 1.70-1.84 (m, 1H), 0.89-1.07 (m, 4H)	--	--
632	600 MHz, DMSO-d ₆	8.49-8.55 (m, 1H), 7.81-7.90 (m, 1H), 7.42-7.51 (m, 2H), 7.33-7.40 (m, 1H), 5.00-5.17 (m, 4H), 4.67-4.79 (m, 2H), 4.32-4.47 (m, 1H), 3.36-3.42 (m, 1H), 2.95-3.09 (m, 2H), 2.82 (dd, J=7.94, 12.61 Hz, 1H), 2.05-2.16 (m, 1H), 1.76-1.87 (m, 2H)	--	--
633	600 MHz, DMSO-d ₆	Mixture of diastereomers: 7.43-7.52 (m, 1H), 7.29-7.41 (m, 1H), 4.91-5.05 (m, 2H), 4.29-4.50 (m, 1H), 3.55-3.89 (m, 3H), 3.36-3.49 (m, 2H), 3.19-3.28 (m, 1H), 3.14 (s, 2H), 2.94-3.05 (m, 2H), 2.87 (s, 1H), 2.73-2.83 (m, 1H), 2.51-2.66 (m, 1H), 2.02-2.15 (m, 1H), 1.86-1.94 (m, 1H), 1.72-1.84 (m, 2H), 1.43-1.64 (m, 1H)	--	--
634	600 MHz, DMSO-d ₆	7.22-7.29 (m, 1H), 7.06-7.21 (m, 1H), 6.87-6.96 (m, 1H), 6.01-6.52 (m, 1H), 4.97-5.13 (m, 2H), 4.29-4.50 (m, 1H), 3.68-4.05 (m, 2H), 3.57 (q, J=7.16 Hz, 1H), 3.40 (br d, J=7.16 Hz, 1H), 2.93-3.06 (m, 2H), 2.71-2.89 (m, 1H), 2.06-2.15 (m, 1H), 1.78 (ddd, J=3.58, 6.46, 9.58 Hz, 1H), 1.24 (t, J=7.16 Hz, 2H), 1.06 (t, J=7.01 Hz, 1H)	--	--
635	600 MHz, DMSO-d ₆	7.21-7.27 (m, 1H), 7.16 (dd, J=4.67, 8.72 Hz, 1H), 7.08 (dd, J=4.67, 8.72 Hz, 1H), 6.88-6.98 (m, 1H), 4.98-5.20 (m, 2H), 4.15-4.52 (m, 1H), 4.21 (q, J=9.65 Hz, 1H), 3.63 (q, J=7.06 Hz, 2H), 3.42 (br d, J=6.85 Hz, 1H), 2.89-3.07 (m, 2H), 2.69-2.85 (m, 1H), 2.03-2.13 (m, 1H), 1.69-1.81 (m, 1H), 1.28 (t, J=7.16 Hz, 2H), 1.07 (t, J=7.01 Hz, 1H)	--	--

Ex. #	Freq., Solvent	¹ H NMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
636	600 MHz, DMSO-d ₆	7.39-7.56 (m, 2H), 4.92 (br d, J=3.43 Hz, 3H), 4.81 (dd, J=3.43, 7.47 Hz, 1H), 4.34-4.49 (m, 1H), 3.81 (ddd, J=3.89, 7.71, 9.58 Hz, 1H), 3.56-3.71 (m, 1H), 2.98-3.09 (m, 3H), 2.80 (dd, J=8.10, 12.77 Hz, 1H), 2.05-2.30 (m, 8H)	--	--
637	600 MHz, DMSO-d ₆	7.43-7.50 (m, 1H), 7.37 (dd, J=7.16, 10.59 Hz, 1H), 4.99-5.11 (m, 1H), 4.88-4.99 (m, 1H), 4.53-4.62 (m, 1H), 4.30-4.48 (m, 1H), 4.15 (tt, J=3.89, 11.99 Hz, 1H), 2.98-3.05 (m, 1H), 2.91-2.98 (m, 3H), 2.78 (td, J=7.43, 12.53 Hz, 1H), 2.72 (s, 1H), 2.07-2.14 (m, 1H), 1.86 (br d, J=11.21 Hz, 3H), 1.73-1.80 (m, 1H), 1.66 (br d, J=8.41 Hz, 2H), 1.52-1.60 (m, 1H), 1.48 (br dd, J=3.11, 9.34 Hz, 1H), 1.29-1.37 (m, 1H), 1.13-1.26 (m, 2H)	--	--
638	600 MHz, DMSO-d ₆	Mixture of rotamers: 8.68 (dd, J=0.78, 4.67 Hz, 1H), 8.58 (dd, J=0.78, 4.93 Hz, 1H), 7.79-7.95 (m, 1H), 7.54 (d, J=7.79 Hz, 1H), 7.26-7.46 (m, 3H), 5.83 (q, J=7.18 Hz, 1H), 5.41 (d, J=6.75 Hz, 1H), 5.22-5.37 (m, 1H), 5.04-5.14 (m, 1H), 4.35-4.61 (m, 1H), 3.50-3.61 (m, 1H), 3.35-3.47 (m, 1H), 3.05-3.20 (m, 2H), 3.02 (s, 1H), 2.89-2.98 (m, 1H), 2.76 (s, 1H), 2.12-2.28 (m, 1H), 1.86-2.01 (m, 1H), 1.80 (d, J=6.75 Hz, 1H), 1.63 (d, J=7.27 Hz, 1H)	B	Chiralpak AD, 20% MeOH, peak 1
639	600 MHz, DMSO-d ₆	7.42-7.52 (m, 1H), 7.32-7.41 (m, 1H), 5.04-5.26 (m, 1H), 4.83-5.02 (m, 1H), 4.55-4.65 (m, 1H), 4.31-4.48 (m, 1H), 4.10-4.26 (m, 1H), 3.85-3.95 (m, 1H), 3.77 (br d, J=11.21 Hz, 1H), 3.58-3.68 (m, 1H), 3.46-3.56 (m, 1H), 3.13-3.21 (m, 1H), 2.92-3.07 (m, 2H), 2.76-2.87 (m, 1H), 2.59-2.71 (m, 1H), 2.02-2.26 (m, 2H), 1.86-1.93 (m, 1H), 1.66-1.82 (m, 3H), 1.50-1.60 (m, 2H), 1.21-1.35 (m, 1H)	--	--
640	600 MHz, DMSO-d ₆	7.46 (dd, J=7.47, 10.90 Hz, 1H), 7.37 (dd, J=7.47, 10.90 Hz, 1H), 4.91-5.08 (m, 3H), 4.30-4.49 (m, 1H), 3.69-3.94 (m, 4H), 3.05-3.15 (m, 1H), 2.93-3.05 (m, 3H), 2.79 (dd, J=8.25, 12.61 Hz, 1H), 2.04-2.17 (m, 2H), 1.67-1.86 (m, 4H), 1.41-1.50 (m, 1H), 1.24-1.33 (m, 1H)	--	--
641	600 MHz, DMSO-d ₆	8.66-8.70 (m, 1H), 8.13 (s, 1H), 7.42-7.51 (m, 2H), 5.44-5.53 (m, 1H), 4.81-4.90 (m, 2H), 4.77 (q, J=9.03 Hz, 1H), 4.55 (dt, J=5.29, 8.88 Hz, 1H), 4.33-4.49 (m, 2H), 4.24 (dd, J=5.29, 10.28 Hz, 1H), 3.15-3.28 (m, 1H), 3.01-3.08 (m, 2H), 2.82 (dd, J=8.41, 12.46 Hz, 1H), 2.10-2.17 (m, 1H), 1.90-2.07 (m, 1H), 1.79-1.87 (m, 1H)	--	--

Ex. #	Freq., Solvent	¹ H NMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
642	600 MHz, DMSO-d ₆	7.45-7.50 (m, 1H), 7.41 (br t, J=8.25 Hz, 1H), 6.50-6.64 (m, 1H), 5.07-5.19 (m, 1H), 4.94-5.03 (m, 1H), 4.21-4.50 (m, 2H), 3.91-4.05 (m, 1H), 3.73-3.85 (m, 1H), 3.53-3.69 (m, 2H), 2.91-3.10 (m, 5H), 2.71-2.86 (m, 2H), 2.56-2.65 (m, 1H), 2.11-2.18 (m, 1H), 1.74-1.82 (m, 1H)	--	--
643	600 MHz, DMSO-d ₆	7.48 (dd, J=7.47, 11.21 Hz, 1H), 7.35 (ddd, J=5.61, 7.08, 10.67 Hz, 1H), 4.92-5.18 (m, 2H), 4.30-4.47 (m, 1H), 3.74-3.92 (m, 2H), 3.57-3.73 (m, 3H), 3.47-3.53 (m, 1H), 3.32-3.44 (m, 6H), 3.22-3.27 (m, 1H), 2.93-3.05 (m, 3H), 2.74-2.80 (m, 2H), 2.01-2.16 (m, 2H), 1.73-1.91 (m, 3H), 1.47-1.67 (m, 1H)	--	--
644	600 MHz, DMSO-d ₆	7.81-8.03 (m, 1H), 7.44-7.50 (m, 1H), 7.40 (dd, J=7.47, 10.59 Hz, 1H), 4.92-5.22 (m, 2H), 4.10-4.47 (m, 2H), 3.77-4.02 (m, 3H), 3.47-3.60 (m, 1H), 3.44-3.71 (m, 1H), 3.13-3.25 (m, 2H), 2.99-3.09 (m, 2H), 2.73-2.86 (m, 2H), 2.59-2.69 (m, 3H), 2.05-2.19 (m, 1H), 1.70-1.85 (m, 1H)	--	--
645	600 MHz, DMSO-d ₆	7.42-7.52 (m, 1H), 7.31-7.42 (m, 1H), 4.72-5.01 (m, 2H), 4.32-4.53 (m, 1H), 3.89-4.17 (m, 1H), 3.71-3.85 (m, 1H), 3.53-3.67 (m, 1H), 3.43 (br dd, J=5.92, 14.01 Hz, 1H), 3.36-3.40 (m, 2H), 3.17 (d, J=4.98 Hz, 1H), 3.11-3.22 (m, 1H), 2.97-3.08 (m, 5H), 2.75-2.83 (m, 1H), 2.59-2.71 (m, 1H), 2.09-2.31 (m, 2H), 1.74-1.88 (m, 2H)	--	--
646	600 MHz, DMSO-d ₆	7.96-8.09 (m, 1H), 7.41-7.53 (m, 2H), 5.08-5.27 (m, 2H), 5.03 (s, 1H), 4.75-4.86 (m, 1H), 4.33-4.49 (m, 2H), 4.13-4.22 (m, 2H), 3.96-4.07 (m, 1H), 3.24-3.28 (m, 1H), 2.94-3.05 (m, 2H), 2.75-2.83 (m, 1H), 2.01-2.15 (m, 1H), 1.72-1.84 (m, 2H)	--	--
647	600 MHz, DMSO-d ₆	Mixture of Diastereomers: 7.44-7.50 (m, 1H), 7.37-7.43 (m, 1H), 5.13 (dt, J=6.23, 18.22 Hz, 1H), 4.94 (br dd, J=13.86, 17.28 Hz, 1H), 4.31-4.50 (m, 1H), 4.06-4.21 (m, 1H), 3.80-3.94 (m, 2H), 3.48-3.69 (m, 2H), 3.39-3.46 (m, 3H), 3.25 (s, 3H), 3.07-3.11 (m, 1H), 2.94-3.03 (m, 2H), 2.74-2.86 (m, 2H), 2.58-2.64 (m, 1H), 2.06-2.15 (m, 1H), 1.71-1.87 (m, 1H)	--	--
648	600 MHz, DMSO-d ₆	7.46 (dd, J=7.47, 10.90 Hz, 1H), 7.36 (dd, J=7.32, 10.74 Hz, 1H), 4.76-5.01 (m, 3H), 4.29-4.47 (m, 1H), 3.67-3.77 (m, 1H), 3.42-3.55 (m, 2H), 2.95-3.18 (m, 3H), 2.74-2.84 (m, 1H), 2.04-2.15 (m, 1H), 1.73-1.98 (m, 4H), 1.28-1.37 (m, 3H)	--	--

Ex. #	Freq., Solvent	¹ H NMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
649	600 MHz, DMSO-d ₆	7.44-7.51 (m, 1H), 7.32-7.41 (m, 1H), 4.99-5.14 (m, 2H), 4.29-4.48 (m, 1H), 3.54-3.75 (m, 5H), 3.18-3.26 (m, 3H), 3.11-3.17 (m, 2H), 2.97-3.06 (m, 2H), 2.94 (s, 3H), 2.74-2.83 (m, 1H), 2.08-2.19 (m, 1H), 1.75-1.95 (m, 3H)	--	--
650	600 MHz, DMSO-d ₆	Mixture of Diastereomers: 7.31-7.51 (m, 2H), 4.93-5.22 (m, 2H), 4.49-4.64 (m, 1H), 4.31-4.46 (m, 1H), 3.73-3.82 (m, 1H), 3.44-3.69 (m, 5H), 2.94-3.06 (m, 3H), 2.72-2.85 (m, 1H), 2.05-2.30 (m, 4H), 1.97 (d, J=12.46 Hz, 3H), 1.86-1.92 (m, 2H), 1.25 (q, J=7.16 Hz, 2H), 1.03 (q, J=6.75 Hz, 2H)	--	--
651	600 MHz, DMSO-d ₆	7.43-7.51 (m, 1H), 7.35-7.43 (m, 1H), 5.04-5.19 (m, 1H), 4.90-5.03 (m, 1H), 4.57 (tt, J=3.35, 12.22 Hz, 1H), 4.33-4.48 (m, 1H), 3.35-3.45 (m, 3H), 3.17-3.28 (m, 3H), 3.06 (br d, J=11.52 Hz, 1H), 3.00 (s, 3H), 2.73-2.83 (m, 2H), 2.06-2.31 (m, 4H), 1.88 (br d, J=10.90 Hz, 2H), 1.71-1.83 (m, 1H)	--	--
652	600 MHz, DMSO-d ₆	Mixture of Diastereomers: 7.34-7.49 (m, 2H), 4.93-5.05 (m, 2H), 4.33-4.50 (m, 1H), 3.40-3.60 (m, 3H), 3.20-3.26 (m, 3H), 3.14-3.18 (m, 3H), 2.95-3.10 (m, 3H), 2.78 (ddd, J=7.32, 8.95, 12.69 Hz, 3H), 2.05-2.24 (m, 2H), 1.65-1.91 (m, 2H)	--	--
653	600 MHz, DMSO-d ₆	7.43-7.50 (m, 1H), 7.31-7.39 (m, 1H), 5.04-5.16 (m, 1H), 4.93-5.03 (m, 1H), 4.31-4.50 (m, 2H), 4.02-4.12 (m, 1H), 3.18-3.29 (m, 2H), 3.09 (br t, J=12.77 Hz, 1H), 2.91-3.04 (m, 2H), 2.80 (td, J=7.63, 12.77 Hz, 1H), 2.55-2.64 (m, 1H), 2.06-2.19 (m, 1H), 1.88 (br s, 1H), 1.75-1.84 (m, 3H), 1.62-1.72 (m, 1H), 1.31 (br d, J=4.67 Hz, 6H), 1.07-1.15 (m, 1H)	--	--
654	600 MHz, DMSO-d ₆	7.80-7.93 (m, 1H), 7.42-7.50 (m, 1H), 7.32-7.39 (m, 1H), 4.89-5.17 (m, 2H), 4.31-4.48 (m, 1H), 3.74-3.93 (m, 2H), 3.40 (br dd, J=9.34, 13.70 Hz, 1H), 3.11-3.19 (m, 1H), 2.94-3.04 (m, 3H), 2.72-2.87 (m, 2H), 2.53-2.65 (m, 3H), 2.05-2.24 (m, 2H), 1.77-1.90 (m, 4H), 1.59-1.74 (m, 2H)	--	--
655	600 MHz, DMSO-d ₆	Mixture of Rotamers: 8.43-8.56 (m, 2H), 7.69 (td, J=1.87, 7.79 Hz, 1H), 7.47 (dd, J=7.32, 11.05 Hz, 1H), 7.33-7.39 (m, 1H), 7.25-7.31 (m, 1H), 5.25 (s, 2H), 4.62 (s, 2H), 4.32-4.50 (m, 1H), 3.64-3.72 (m, 2H), 3.53 (br t, J=4.98 Hz, 2H), 3.36-3.42 (m, 2H), 2.93-3.06 (m, 2H), 2.71-2.82 (m, 1H), 2.01-2.13 (m, 1H), 1.72-1.89 (m, 1H)	--	--

Ex. #	Freq., Solvent	¹ H NMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
656	600 MHz, DMSO-d ₆	Mixture of Rotamers: 7.47 (dd, J=7.63, 11.06 Hz, 1H), 7.33-7.42 (m, 1H), 5.04-5.21 (m, 2H), 4.31-4.48 (m, 1H), 3.86-4.07 (m, 3H), 3.51 (t, J=6.85 Hz, 1H), 3.41-3.46 (m, 1H), 3.41 (br s, 1H), 3.20-3.28 (m, 1H), 2.94-3.07 (m, 2H), 2.77-2.84 (m, 1H), 2.72 (t, J=6.85 Hz, 1H), 2.04-2.17 (m, 1H), 1.69-1.87 (m, 5H)	--	--
657	600 MHz, DMSO-d ₆	Mixture of Roatmers: 7.36-7.50 (m, 2H), 4.92-5.14 (m, 2H), 4.30-4.50 (m, 1H), 4.03-4.24 (m, 1H), 3.76-3.96 (m, 1H), 3.12-3.24 (m, 1H), 2.98-3.08 (m, 4H), 2.77-2.89 (m, 5H), 2.61-2.73 (m, 1H), 2.09-2.21 (m, 1H), 1.76-1.94 (m, 4H), 1.48-1.67 (m, 2H)	--	--
658	600 MHz, DMSO-d ₆	7.44-7.50 (m, 1H), 7.34-7.42 (m, 1H), 4.95-5.13 (m, 2H), 4.29-4.47 (m, 2H), 4.00-4.11 (m, 1H), 3.48 (d, J=1.56 Hz, 2H), 3.36 (s, 3H), 3.22-3.28 (m, 2H), 2.93-3.07 (m, 2H), 2.54-2.87 (m, 2H), 2.08-2.19 (m, 1H), 1.98-2.05 (m, 1H), 1.94 (br d, J=13.39 Hz, 1H), 1.76-1.88 (m, 3H), 1.63-1.73 (m, 1H), 1.44-1.53 (m, 1H)	--	--
659	600 MHz, DMSO-d ₆	7.37-7.51 (m, 2H), 4.93-5.21 (m, 2H), 4.32-4.51 (m, 3H), 3.95-4.07 (m, 2H), 3.59-3.69 (m, 1H), 3.09-3.22 (m, 2H), 2.93-3.07 (m, 3H), 2.61-2.83 (m, 2H), 2.04-2.21 (m, 1H), 1.74-1.96 (m, 3H)	--	--
660	600 MHz, DMSO-d ₆	7.51 (d, J=3.58 Hz, 1H), 7.24-7.29 (m, 3H), 6.91-6.97 (m, 1H), 5.07 (s, 2H), 4.31-4.46 (m, 1H), 3.31-3.43 (m, 2H), 2.95-3.10 (m, 2H), 2.78-2.87 (m, 1H), 2.07-2.16 (m, 1H), 1.73-1.84 (m, 1H)	I	SFC: Chiralpak AY-H, 10% IPA Peak 1
661	600 MHz, DMSO-d ₆	9.04-9.14 (m, 1H), 7.21-7.27 (m, 1H), 7.13-7.20 (m, 1H), 6.89-6.97 (m, 1H), 4.80 (s, 2H), 4.30-4.51 (m, 1H), 3.93-4.06 (m, 2H), 3.37-3.47 (m, 2H), 2.97-3.08 (m, 2H), 2.77-2.87 (m, 1H), 2.04-2.16 (m, 1H), 1.72-1.88 (m, 1H)	I	SFC: Chiralpak AY-H, 10% IPA Peak 1
662	600 MHz, DMSO-d ₆	7.18-7.27 (m, 2H), 6.93 (ddd, J=9.85, 8.76, 2.49 Hz, 1H), 5.17-5.28 (m, 2H), 4.32-4.50 (m, 1H), 4.13-4.25 (m, 2H), 2.95-3.10 (m, 3H), 2.62-2.91 (m, 2H), 2.52-2.57 (m, 1H), 2.07-2.18 (m, 1H), 1.71-1.83 (m, 1H), 0.98-1.13 (m, 4H)	I	SFC: Chiralpak AY-H, 10% IPA Peak 1
663	600 MHz, DMSO-d ₆	7.15-7.25 (m, 1H), 7.06 (dd, J=8.68, 4.87 Hz, 1H), 6.91 (t, J=9.22 Hz, 1H), 4.95-5.03 (m, 2H), 4.38-4.49 (m, 1H), 3.60-3.67 (m, 1H), 3.54-3.60 (m, 1H), 3.47-3.53 (m, 1H), 3.39-3.47 (m, 2H), 3.34-3.39 (m, 3H), 3.21-3.27 (m, 3H), 2.96-3.09 (m, 2H), 2.81 (dt, J=12.53, 9.26 Hz, 2H), 2.06-2.15 (m, 1H), 1.74-1.83 (m, 1H)	I	SFC: Chiralpak AY-H, 10% IPA Peak 1

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
664	500 MHz, METHA NOL-d ₄	7.13-7.24 (m, 2H), 6.87-7.00 (m, 1H), 4.96-5.14 (m, 2H), 4.34-4.55 (m, 1H), 4.04-4.17 (m, 1H), 3.64-3.97 (m, 3H), 3.47-3.57 (m, 1H), 3.38-3.46 (m, 1H), 3.30-3.34 (m, 2H), 3.06-3.21 (m, 4H), 2.93 (m, 1H), 2.16-2.44 (m, 2H), 1.87-2.10 (m, 2H)	F	Chiralpak IF, 30% MeOH w/ 0.2% DEA, peak 2
665	500 MHz, METHA NOL-d ₄	7.13-7.23 (m, 2H), 6.89-6.99 (m, 1H), 5.03 (s, 2H), 4.35-4.54 (m, 1H), 4.05-4.16 (m, 1H), 3.65-3.98 (m, 3H), 3.48-3.58 (m, 1H), 3.35-3.49 (m, 1H), 3.32 (td, <i>J</i> =1.57, 3.21 Hz, 3H), 3.06-3.14 (m, 2H), 2.89-3.02 (m, 2H), 2.15-2.45 (m, 2H), 1.85-2.09 (m, 2H)	F	Chiralpak IF, 30% MeOH w/ 0.2% DEA, peak 1
666	600 MHz, DMSO-d ₆	8.90-9.00 (m, 1H), 8.49-8.58 (m, 1H), 7.73-7.81 (m, 1H), 7.36-7.42 (m, 1H), 7.26-7.31 (m, 1H), 7.16-7.24 (m, 2H), 6.86-6.97 (m, 1H), 4.95-5.09 (m, 1H), 4.70-4.84 (m, 2H), 4.27-4.47 (m, 1H), 3.38-3.48 (m, 1H), 3.33-3.38 (m, 1H), 2.94-3.07 (m, 2H), 2.76-2.84 (m, 1H), 2.03-2.16 (m, 1H), 1.74-1.81 (m, 1H), 1.38-1.49 (m, 3H)	B	Chiralpak IC, 30% MeOH, peak 2
667	500 MHz, METHA NOL-d ₄	7.07-7.25 (m, 2H), 6.90-7.01 (m, 1H), 5.16-5.32 (m, 1H), 5.01-5.16 (m, 1H), 4.32-4.55 (m, 2H), 4.06-4.32 (m, 2H), 3.67-4.04 (m, 4H), 3.45-3.55 (m, 1H), 3.36-3.45 (m, 1H), 3.04-3.19 (m, 2H), 2.88-3.02 (m, 1H), 2.00-2.61 (m, 3H), 1.81-1.98 (m, 1H)	F	Chiralpak AD-H, 15% MeOH with 0.2% DEA, peak 2
668	600 MHz, DMSO-d ₆	8.63-8.71 (m, 1H), 7.20-7.25 (m, 1H), 7.13-7.20 (m, 1H), 6.87-6.98 (m, 1H), 4.63 (s, 2H), 4.31-4.48 (m, 1H), 4.16-4.28 (m, 1H), 3.35-3.47 (m, 1H), 2.95-3.10 (m, 2H), 2.76-2.88 (m, 1H), 2.15-2.24 (m, 2H), 2.05-2.14 (m, 1H), 1.86-1.99 (m, 3H), 1.76-1.86 (m, 1H), 1.57-1.71 (m, 2H)	I	SFC: Chiralpak AY-H, 10% IPA Peak 1
669	600 MHz, DMSO-d ₆	8.61-8.72 (m, 1H), 7.15-7.29 (m, 2H), 6.85-6.97 (m, 1H), 4.69 (d, <i>J</i> =9.19 Hz, 2H), 4.31-4.50 (m, 1H), 4.04-4.15 (m, 1H), 3.36-3.49 (m, 2H), 2.96-3.13 (m, 2H), 2.73-2.88 (m, 2H), 2.63-2.73 (m, 1H), 2.07-2.19 (m, 1H), 1.76-1.86 (m, 1H), 1.21 (d, <i>J</i> =6.77 Hz, 3H)	I	SFC: Chiralpak AY-H, 10% IPA Peak 1
670	600 MHz, DMSO-d ₆	8.63-8.74 (m, 1H), 7.16-7.29 (m, 2H), 6.85-6.96 (m, 1H), 4.61-4.77 (m, 2H), 4.30-4.50 (m, 1H), 4.04-4.15 (m, 1H), 3.35-3.47 (m, 2H), 2.98-3.11 (m, 2H), 2.81-2.87 (m, 1H), 2.75-2.80 (m, 1H), 2.66-2.71 (m, 1H), 2.08-2.20 (m, 1H), 1.75-1.88 (m, 1H), 1.21 (d, <i>J</i> =6.77 Hz, 3H)	I	SFC: Chiralpak AY-H, 10% IPA Peak 1

Ex. #	Freq., Solvent	¹ H NMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
671	600 MHz, DMSO-d ₆	7.23-7.34 (m, 1H), 7.12-7.14 (m, 1H), 6.98 (t, <i>J</i> =9.31 Hz, 1H), 4.95-5.09 (m, 2H), 4.77-4.86 (m, 1H), 3.66-3.76 (m, 1H), 3.57-3.62 (m, 1H), 3.46-3.56 (m, 4H), 3.37 (s, 3H), 3.31-3.35 (m, 2H), 3.07-3.12 (m, 2H), 2.91-3.05 (m, 1H), 2.16-2.23 (m, 1H), 1.76-1.88 (m, 1H), 1.04 (t, <i>J</i> =7.01 Hz, 3H)	I	SFC: Chiralpak AY-H, 10% IPA Peak 1
672	500 MHz, METHA NOL-d ₄	7.08-7.23 (m, 2H), 6.89-7.00 (m, 1H), 5.15-5.32 (m, 1H), 5.02-5.14 (m, 1H), 4.30-4.55 (m, 2H), 4.07-4.28 (m, 2H), 3.69-4.05 (m, 4H), 3.47-3.57 (m, 1H), 3.35-3.44 (m, 1H), 3.03-3.19 (m, 2H), 2.88-2.99 (m, 1H), 1.99-2.61 (m, 3H), 1.82-1.99 (m, 1H)	F	Chiralpak AD-H, 15% MeOH with 0.2% DEA, peak 1
673	600 MHz, DMSO-d ₆	8.55-8.63 (m, 1H), 7.20-7.27 (m, 1H), 7.13-7.19 (m, 1H), 6.88-6.99 (m, 1H), 4.63-4.71 (m, 2H), 4.31-4.49 (m, 1H), 3.35-3.47 (m, 4H), 2.96-3.11 (m, 2H), 2.79-2.87 (m, 1H), 2.41-2.48 (m, 2H), 2.07-2.15 (m, 1H), 1.74-1.86 (m, 1H)	I	SFC: Chiralpak AY-H, 10% IPA Peak 1
674	600 MHz, DMSO-d ₆	8.86-9.01 (m, 1H), 8.49-8.62 (m, 1H), 7.71-7.82 (m, 1H), 7.34-7.43 (m, 1H), 7.26-7.32 (m, 1H), 7.14-7.24 (m, 2H), 6.86-6.96 (m, 1H), 4.97-5.07 (m, 1H), 4.68-4.86 (m, 2H), 4.30-4.48 (m, 1H), 3.35-3.47 (m, 2H), 2.95-3.08 (m, 2H), 2.76-2.86 (m, 1H), 2.03-2.15 (m, 1H), 1.72-1.83 (m, 1H), 1.43 (d, <i>J</i> =7.01 Hz, 3H)	I	SFC: Chiralpak AY-H, 10% IPA Peak 1
675	600 MHz, DMSO-d ₆	8.62-8.77 (m, 1H), 7.14-7.26 (m, 2H), 6.83-6.98 (m, 1H), 4.67 (d, <i>J</i> =5.29 Hz, 2H), 4.33-4.48 (m, 1H), 4.26-4.32 (m, 1H), 3.79-3.86 (m, 1H), 3.73-3.78 (m, 1H), 3.67-3.73 (m, 1H), 3.50-3.56 (m, 1H), 3.37-3.46 (m, 2H), 2.97-3.09 (m, 2H), 2.76-2.85 (m, 1H), 2.07-2.17 (m, 2H), 1.74-1.85 (m, 2H)	B	Chiralpak AZ-H, 35% MeOH, peak 1
676	600 MHz, DMSO-d ₆	8.65-8.73 (m, 1H), 7.16-7.27 (m, 2H), 6.89-6.97 (m, 1H), 4.67 (s, 2H), 4.33-4.47 (m, 1H), 4.25-4.32 (m, 1H), 3.80-3.88 (m, 1H), 3.73-3.79 (m, 1H), 3.66-3.73 (m, 1H), 3.49-3.57 (m, 1H), 3.37-3.46 (m, 2H), 2.96-3.10 (m, 2H), 2.77-2.87 (m, 1H), 2.07-2.18 (m, 2H), 1.74-1.86 (m, 2H)	B	Chiralpak AZ-H, 35% MeOH, peak 2
677	600MHz DMSO - d ₆	8.18 (s, 2H), 7.17-7.25 (m, 2H), 6.93 (t, <i>J</i> =9.30 Hz, 1H), 4.59-4.76 (m, 2H), 4.44-4.53 (m, 1H), 4.34-4.43 (m, 1H), 4.07-4.22 (m, 1H), 3.84 (br t, <i>J</i> =7.75 Hz, 1H), 3.28-3.47 (m, 2H), 3.01-3.21 (m, 4H), 2.79-2.95 (m, 1H), 2.52-2.57 (m, 1H), 2.40-2.48 (m, 1H), 2.09-2.17 (m, 1H), 1.77-1.90 (m, 2H), 1.53 (d, <i>J</i> =6.23 Hz, 1H), 1.35 (dd, <i>J</i> =1.40, 6.31 Hz, 1H)	I	SFC: Chiralpak AY-H, 10% IPA Peak 1

Ex. #	Freq., Solvent	¹ H NMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
678	600MHz DMSO – d ₆	7.16-7.25 (m, 2H), 6.91 (t, <i>J</i> =9.20 Hz, 1H), 5.08-5.23 (m, 1H), 4.81-4.95 (m, 1H), 4.45 (dt, <i>J</i> =4.17, 7.88 Hz, 1H), 4.30-4.39 (m, 1H), 4.13 (br s, 1H), 4.00 (br d, <i>J</i> =13.47 Hz, 1H), 3.82-3.93 (m, 1H), 3.60-3.73 (m, 2H), 3.41-3.53 (m, 2H), 2.96-3.07 (m, 2H), 2.77-2.86 (m, 1H), 2.12 (br s, 2H), 1.75-1.84 (m, 1H), 1.37 (br d, <i>J</i> =5.61 Hz, 1H), 1.14-1.20 (m, 2H)	I	SFC: Chiralpak AY-H, 10% IPA Peak 1
679	600MHz DMSO – d ₆	7.15-7.25 (m, 2H), 6.91 (t, <i>J</i> =9.32 Hz, 1H), 4.87 (s, 1H), 4.29-4.39 (m, 1H), 4.05 (dt, <i>J</i> =2.61, 6.60 Hz, 1H), 3.61-3.75 (m, 1H), 3.42-3.59 (m, 3H), 2.95-3.12 (m, 2H), 2.77-2.85 (m, 1H), 2.52-2.55 (m, 1H), 2.06-2.18 (m, 1H), 1.89-2.06 (m, 2H), 1.75-1.87 (m, 1H), 1.45-1.63 (m, 1H), 1.22-1.29 (m, 1H), 1.11 (d, <i>J</i> =6.31 Hz, 2H)	I	SFC: Chiralpak AY-H, 10% IPA Peak 1
680	600MHz DMSO – d ₆	7.15-7.27 (m, 1H), 7.08 (dd, <i>J</i> =4.79, 8.60 Hz, 1H), 6.92 (t, <i>J</i> =8.75 Hz, 1H), 5.11-5.20 (m, 1H), 4.86-4.94 (m, 1H), 4.41-4.53 (m, 1H), 4.28-4.41 (m, 1H), 4.09-4.25 (m, 1H), 4.01 (br d, <i>J</i> =11.83 Hz, 1H), 3.77-3.90 (m, 3H), 3.64 (br dd, <i>J</i> =3.31, 11.87 Hz, 1H), 3.44-3.60 (m, 2H), 3.34-3.43 (m, 3H), 3.32 (br s, 2H), 2.97-3.09 (m, 3H), 2.75-2.85 (m, 1H), 2.06-2.25 (m, 1H), 1.74-1.84 (m, 1H).	I	SFC: Chiralpak AY-H, 10% IPA Peak 1
681	600MHz DMSO – d ₆	7.22 (d, <i>J</i> =9.53 Hz, 1H), 7.18 (t, <i>J</i> =7.08 Hz, 1H), 6.91 (t, <i>J</i> =9.33 Hz, 1H), 5.11 (br d, <i>J</i> =17.36 Hz, 1H), 4.87 (br d, <i>J</i> =17.05 Hz, 1H), 4.28-4.40 (m, 1H), 3.78-3.92 (m, 1H), 3.61-3.76 (m, 2H), 3.38-3.53 (m, 2H), 3.26-3.34 (m, 3H), 2.95-3.08 (m, 2H), 2.80 (dd, <i>J</i> =8.29, 12.50 Hz, 1H), 2.02-2.20 (m, 2H), 1.75-1.85 (m, 1H), 1.36 (br d, <i>J</i> =5.76 Hz, 1H), 1.13-1.21 (m, 2H)	I	SFC: Chiralpak AY-H, 10% IPA Peak 1
682	600MHz DMSO – d ₆	7.14-7.25 (m, 2H), 6.91 (t, <i>J</i> =9.19 Hz, 1H), 4.87 (q, <i>J</i> =17.44 Hz, 2H), 4.28-4.40 (m, 1H), 3.97-4.13 (m, 1H), 3.61-3.71 (m, 1H), 3.47-3.60 (m, 1H), 3.37-3.46 (m, 3H), 2.95-3.11 (m, 2H), 2.75-2.89 (m, 1H), 2.52-1.91 (m, 4H), 1.49-1.60 (m, 1H), 1.23-1.29 (m, 1H), 1.11 (d, <i>J</i> =6.31 Hz, 2H)	I	SFC: Chiralpak AY-H, 10% IPA Peak 1
683	600MHz DMSO – d ₆	8.43 (br s, 2H), 7.20-7.30 (m, 2H), 6.94-7.05 (m, 1H), 4.78-5.18 (m, 2H), 3.95-4.11 (m, 2H), 3.82-3.93 (m, 1H), 3.68-3.81 (m, 1H), 3.56-3.68 (m, 2H), 3.32-3.48 (m, 2H), 2.99-3.17 (m, 1H), 1.98-2.21 (m, 1H), 1.40-1.51-2.0 (m, 1H), 1.13-1.30 (m, 7H)	I	SFC: Chiralpak AY-H, 10% IPA Peak 1

Ex. #	Freq., Solvent	¹ HNMR Data (δ ppm)	Separation Stage	SFC Isomer Separation Conditions
684	600MHz DMSO – d ₆	7.10-7.26 (m, 2H), 6.90-6.96 (m, 1H), 5.11-5.21 (m, 1H), 4.90-5.00 (m, 1H), 4.41-4.49 (m, 1H), 4.37 (br d, <i>J</i> =6.07 Hz, 1H), 4.17 (br s, 1H), 3.70-3.87 (m, 2H), 3.61 (dt, <i>J</i> =2.61, 11.50 Hz, 1H), 3.38-3.33 (m, 2H), 3.13-3.20 (m, 1H), 2.99-3.05 (m, 2H), 2.87-2.98 (m, 1H), 2.77-2.85 (m, 1H), 2.52-2.55 (m, 1H), 2.29-2.47 (m, 1H), 1.71-1.89 (m, 1H), 0.97 (t, <i>J</i> =7.40 Hz, 1H), 0.81 (dt, <i>J</i> =1.40, 7.40 Hz, 3H)	I	SFC: Chiralpak AY-H, 10% IPA Peak 1
685	600MHz DMSO – d ₆	7.22 (br d, <i>J</i> =9.42 Hz, 1H), 7.16 (br d, <i>J</i> =4.44 Hz, 1H), 6.92 (br t, <i>J</i> =9.19 Hz, 1H), 5.04-5.19 (m, 1H), 4.93 (br d, <i>J</i> =17.44 Hz, 1H), 4.36-4.38 (br m, 1H), 3.86-3.95 (m, 1H), 3.77-3.86 (m, 2H), 3.53-3.68 (m, 2H), 3.37-3.51 (m, 3H), 3.14-3.27 (m, 1H), 2.96-3.08 (m, 2H), 2.77-2.89 (m, 1H), 2.12 (br s, 1H), 1.99 (br s, 1H), 1.75-1.91 (m, 1H), 1.48 (br s, 1H), 0.62 (br s, 1H), 0.51 (br s, 1H), 0.42 (br s, 1H), 0.24-0.36 (m, 1H)	I	SFC: Chiralpak AY-H, 10% IPA Peak 1
686	600MHz DMSO – d ₆	7.14-7.24 (m, 1H), 7.11 (dd, <i>J</i> =4.79, 8.60 Hz, 1H), 6.85-6.94 (m, 1H), 5.15 (br d, <i>J</i> =17.52 Hz, 1H), 5.06 (d, <i>J</i> =17.44 Hz, 1H), 4.42-4.58 (m, 1H), 3.96-4.04 (m, 1H), 3.77-3.94 (m, 2H), 3.59-3.74 (m, 2H), 3.44 (br d, <i>J</i> =9.89 Hz, 1H), 3.24-3.41 (m, 2H), 2.97-3.23 (m, 1H), 2.65-2.94 (m, 2H), 2.52-2.56 (m, 1H), 2.07-2.16 (m, 1H), 1.74-1.84 (m, 1H), 1.07-1.19 (m, 2H)	I	SFC: Chiralpak AY-H, 10% IPA Peak 1
687	600MHz DMSO – d ₆	8.29-8.40 (br s, 2H), 7.21-7.30 (m, 1H), 6.99 (t, <i>J</i> =9.33 Hz, 1H), 4.92-5.06 (m, 1H), 3.70-3.88 (m, 2H), 3.52-3.70 (m, 6H), 3.33-3.39 (m, 2H), 3.05-3.18 (m, 2H), 3.01 (br t, <i>J</i> =11.99 Hz, 1H), 2.52-2.55 (m, 1H), 1.12-1.41 (m, 6H)	I	SFC: Chiralpak AY-H, 10% IPA Peak 1

Biological Example 1 TRPC6 Calcium flux assay

Potency of TRPC6 (Transient receptor potential channel family C6) inhibitors were measured by their inhibition of Calcium influx triggered by OAG (1-Oleoyl-2-acetyl-*sn*-glycerol, Millipore Sigma, O6754) stimulation on HEK293 cells stably transfected with human TRPC6 using a FLIPR tetra system. Cells were grown in a humidified environment at 37°C under 5% CO₂ using the growth medium with the following selective reagents (Dulbecco's Modified Eagle's Medium (DMEM) high glucose, 10% Fetal Bovine Serum, 1XPSGlu (penicillin-streptomycin glutamine), 1X NEAA (Non-essential amino acid), 1X Na Pyruvate and 200ug/ml Hygromycin). For general passage, cells were grown to 70-90% confluency; the media was removed, and the cells were gently washed 2 times with calcium and magnesium free PBS (phosphate-buffered saline). Trypsin (3mL) was applied for 5 minutes at 37°C. The cells were dislodged by rapping flask against base of a hand and 7 mL of growth medium was added to deactivate trypsin and re-suspend cells. The usual splitting schedule was 1:5 every 2-3 days.

Cells were plated the day before the assay, plating cell density is $1.0-1.5 \times 10^4/25\mu\text{l}/\text{well}$ in poly-D-lysine (PDL) coated 384-well plates using either multichannel pipettes or multidrop. These cells were first incubated with fluorescence dye at room temperature for 90-120 minutes after they were grown on PDL-coated 384-well black plates overnight (Dye loading buffer 10ml example: 9 mL assay buffer, 1 mL, 10X PBX signal enhancer, 10 μL Calcium indicator). The cells were incubated with a dose of compounds for 25 minutes before being stimulated with TRPC6 agonist OAG. The OAG solution was prepared by adding OAG into assay buffer (Ca ringer solution base: 10mM HEPES (4-(2-hydroxyethyl)-1-piperazine-ethanesulfonic acid), 4mM MgCl_2 , 120mM NaCl, 5mM KCl, pH=7.2 @25 °C) + 0.1%BSA + 2mM CaCl_2) to the concentration of 0.2mM/2% DMSO, which achieves a final on cell concentration of 50uM/0.5% DMSO. 12.5 uL OAG mixture was added and the activation of the TRPC6 channel was measured by the change of intracellular Calcium levels on FLIPR terra system.

Data was acquired by measuring the fluorescent peak signal subtracted from the background during the 180 second imaging frame. Each data point is further normalized to 100% of OAG triggered signal vs. buffer. Table 16 provides the IC_{50} for each compound, which data is obtained by plotting peak signal over the compound dose.

Table 16

Ex. #	hTRPC6 Potency (μM)	Ex. #	hTRPC6 Potency (μM)
1	0.000696	345	0.0015
2	0.0032	346	0.00139
3	0.00199	347	0.00107
4	0.00167	348	0.493
5	0.00292	349	0.215
6	0.0004002	350	0.351
7	0.0011733	351	0.0103
8	0.00028336	352	0.328
9	0.0016133	353	0.0308
10	0.00606	354	0.133
11	0.00179	355	0.037
12	0.000285	356	0.239
13	0.00687	357	0.0245
14	0.000377	358	0.00647
15	0.00439	359	0.238
16	0.224	360	0.0429
17	0.118	361	0.0668
18	0.00785	362	0.256
19	0.000956	363	0.0313
20	0.00192	364	1.02
21	0.0006585	365	2.96
22	0.00162	366	0.232
23	> 3.75	367	0.354

Ex. #	hTRPC6 Potency (μ M)		Ex. #	hTRPC6 Potency (μ M)
24	0.145		368	0.0992
25	0.23		369	0.00865
26	0.161		370	> 50.0
27	0.0735		371	6.83
28	> 3.75		372	14.1
29	0.0448		373	5.85
30	1.94		374	3.41
31	0.000476		375	2.77
32	0.0472		376	3.05
33	0.0004325		377	1.65
34	0.0689		378	3.08
35	0.000491		379	4.44
36	0.00613		380	17
37	0.00692		381	5.68
38	0.00071978		382	> 50.0
39	0.000867		383	0.319
40	0.00461		384	16
41	0.0184		385	> 50.0
42	1.94		386	4.26
43	0.000581		387	5.36
44	0.000952		388	9.75
45	0.00236		389	4.58
46	0.001785		390	3.57
47	0.000686		391	1.82
48	0.002205		392	2.24
49	0.001095		393	5.05
50	0.000759		394	0.732
51	0.00647		395	1.12
52	0.0242		396	18.2
53	0.00152		397	1.58
54	0.00552		398	0.0874
55	0.00397		399	0.0205
56	0.0135		400	16.5
57	0.000784		401	0.00045573
58	0.000469		402	0.00133
59	0.000256		403	0.000395
60	0.000261		404	0.00167
61	0.0027		405	0.000708
62	0.0603		406	0.000447
63	0.000389		407	0.00585
64	0.132		408	0.000924
65	0.000598		409	0.0010356
66	0.237		410	0.0105

Ex. #	hTRPC6 Potency (μ M)		Ex. #	hTRPC6 Potency (μ M)
67	0.272		411	0.00268
68	0.0018215		412	0.322
69	0.01471		413	0.221
70	0.002325		414	0.0015
71	0.005615		415	0.274
72	0.000448		416	0.00236
73	0.0010945		417	0.0127
74	0.38		418	0.000584
75	0.0814		419	0.128
76	0.971		420	0.0006
77	0.0109		421	0.0005404
78	0.0707		422	0.00235
79	0.00509		423	0.351
80	0.0793		424	0.000707
81	0.557		425	0.113
82	0.000504		426	0.933
83	0.000906		427	> 3.75
84	0.00127		428	0.0183
85	0.00755		429	> 3.75
86	0.00137		430	0.88
87	0.000931		431	> 3.75
88	0.0006428		432	0.00777
89	0.368		433	> 3.75
90	0.068		434	> 3.75
91	0.0329		435	1.16
92	0.0438		436	0.0524
93	0.0068533		437	> 3.75
94	0.615		438	0.476
95	> 3.75		439	0.0367
96	0.134		440	1.34
97	> 3.75		441	0.002235
98	> 3.75		442	0.000319
99	> 3.75		443	0.000471
100	0.06		444	0.00442
101	> 3.75		445	0.0208
102	> 3.75		446	0.034
103	> 3.75		447	0.119
104	0.0618		448	0.123
105	2.48		449	1.16
106	0.0004496		450	> 3.75
107	0.00788		451	0.000613
108	0.000433		452	0.00117
109	0.0438		453	0.00151

Ex. #	hTRPC6 Potency (μ M)		Ex. #	hTRPC6 Potency (μ M)
110	0.001232		454	0.00152
111	0.0007875		455	0.00656
112	0.00028147		456	0.00844
113	0.0002855		457	0.0133
114	0.000382		458	0.0163
115	0.000446		459	0.0164
116	0.00779		460	0.0242
117	> 3.75		461	0.0289
118	0.000855		462	0.0294
119	0.00194		463	0.0339
120	0.00321		464	0.0631
121	0.00559		465	0.0867
122	0.0299		466	0.103
123	0.252		467	0.123
124	0.000741		468	0.178
125	0.000389		469	0.19
126	0.00048		470	0.219
127	0.000492		471	0.36
128	0.04935		472	0.383
129	> 3.75		473	0.398
130	0.269		474	0.411
131	0.08255		475	0.62
132	0.042		476	0.763
133	0.00698		477	1.03
134	0.00471		478	1.05
135	> 3.75 [2]		479	1.2
136	0.013945		480	1.2
137	0.0362		481	2.4
138	0.00052		482	2.74
139	0.001905		483	2.74
140	0.132		484	> 3.75
141	0.0135		485	> 3.75
142	0.0138		486	> 3.75
143	0.0068625		487	> 3.75
144	0.000462		488	> 3.75
145	0.014		489	> 3.75
146	0.000631		490	> 3.75
147	0.000433		491	> 3.75
148	0.0118		492	> 3.75
149	0.00109		493	> 3.75
150	0.00902		494	0.0126
151	0.00606		495	0.0127
152	0.0677		496	0.0611

Ex. #	hTRPC6 Potency (μ M)		Ex. #	hTRPC6 Potency (μ M)
153	0.072		497	0.094
154	0.00306		498	0.00188
155	0.0162		499	0.00258
156	0.0617		500	0.005145
157	0.000501		501	0.00621
158	0.00471		502	0.009095
159	0.0164		503	0.0256
160	0.0142		504	0.0393
161	0.133		505	0.0432
162	0.257		506	0.0766
163	2.84		507	0.102
164	0.253		508	0.112
165	2.06		509	0.131
166	0.56		510	0.139
167	0.0019657		511	0.158
168	1.6		512	0.162
169	0.0142		513	0.183
170	0.0259		514	0.185
171	0.544		515	0.186
172	0.00222		516	0.197
173	0.00138		517	0.319
174	0.564		518	0.4
175	1.7		519	0.476
176	2.33		520	0.686
177	1.54		521	0.757
178	0.0471		522	0.762
179	0.326		523	0.988
180	0.0149		524	1.49
181	0.000907		525	1.78
182	0.314		526	2.85
183	0.655		527	3.01
184	0.143		528	> 3.75
185	0.003585		529	> 3.75
186	0.278		530	> 3.75
187	0.0015905		531	> 3.75
188	0.013025		532	> 3.75
189	0.0035867		533	> 3.75
190	0.004015		534	> 3.75
191	0.13985		535	> 3.75
192	0.001725		536	> 3.75
193	0.0485		537	> 3.75
194	0.0142		538	> 3.75
195	0.000664		539	> 3.75

Ex. #	hTRPC6 Potency (μ M)		Ex. #	hTRPC6 Potency (μ M)
196	0.00647		540	> 3.75
197	0.2555		541	> 3.75
198	0.07125		542	> 3.75
199	0.0281		543	> 3.75
200	0.00218		544	> 3.75
201	0.0439		545	> 3.75
202	0.002137		546	> 3.75
203	0.598		547	0.0437
204	0.00492		548	0.382
205	0.003		549	0.41
206	0.0123		550	> 3.75
207	0.0496		551	0.0061
208	0.0477		552	0.00651
209	0.0038675		553	0.00669
210	0.0691		554	0.0109
211	0.001095		555	0.0116
212	0.0034975		556	0.0119
213	0.00993		557	0.0128
214	0.00042		558	0.0161
215	0.593		559	0.0166
216	0.0114		560	0.0187
217	0.0687		561	0.0198
218	0.00082		562	0.0208
219	0.0159		563	0.0216
220	0.0009855		564	0.0292
221	0.0549		565	0.0322
222	0.002045		566	0.0352
223	0.0515		567	0.0398
224	0.158		568	0.04805
225	0.00281		569	0.0784
226	0.0137		570	0.0854
227	0.00032823		571	0.0932
228	0.00032		572	0.106
229	0.0422		573	0.117
230	0.00049		574	0.153
231	0.737		575	0.155
232	0.00216		576	0.169
233	0.00147		577	0.184
234	0.0269		578	0.251
235	0.15		579	0.312
236	0.0238		580	0.365
237	0.223		581	0.368
238	0.185		582	0.376

Ex. #	hTRPC6 Potency (μ M)		Ex. #	hTRPC6 Potency (μ M)
239	0.562		583	0.42
240	0.0107		584	0.546
241	> 3.75		585	0.579
242	0.0735		586	0.742
243	1.97		587	0.765
244	> 3.75		588	0.811
245	0.0625		589	1.01
246	2.92		590	1.44
247	0.0754		591	1.59
248	0.00507		592	1.73
249	0.00765		593	2.12
250	0.0785		594	> 3.75
251	0.0172		595	> 3.75
252	0.00876		596	> 3.75
253	0.406		597	> 3.75
254	0.0739		598	> 3.75
255	0.10145		599	> 3.75
256	0.0194		600	0.00538
257	0.0524		601	0.00556
258	0.0002881		602	0.00575
259	1.43		603	0.00673
260	0.376		604	0.00778
261	> 3.75		605	0.0079
262	0.28		606	0.00806
263	0.765		607	0.0143
264	0.217		608	0.0183
265	2.86		609	0.0203
266	15.8		610	0.0212
267	> 3.75, > 50.0		611	0.0224
268	> 3.75, > 50.0		612	0.0224
269	0.002045		613	0.0242
270	0.0515		614	0.0248
271	0.158		615	0.0285
272	0.00281		616	0.0323
273	0.0137		617	0.0332
274	0.00032823		618	0.0483
275	0.00032		619	0.0574
276	0.0422		620	0.0604
277	0.00049		621	0.0753
278	0.737		622	0.0789
279	0.00216		623	0.089
280	0.00147		624	0.102
281	0.0269		625	0.105

Ex. #	hTRPC6 Potency (μ M)		Ex. #	hTRPC6 Potency (μ M)
282	0.15		626	0.117
283	0.0238		627	0.122
284	0.223		628	0.132
285	0.185		629	0.158
286	0.562		630	0.174
287	0.0107		631	0.225
288	> 3.75		632	0.23
289	0.0735		633	0.24
290	1.97		634	0.26
291	> 3.75		635	0.304
292	0.0625		636	0.326
293	2.92		637	0.341
294	0.0754		638	0.425
295	0.00507		639	0.657
296	0.00765		640	0.809
297	0.0785		641	1.28
298	0.0172		642	1.65
299	0.00876		643	1.82
300	0.406		644	1.91
301	0.0739		645	2.3
302	0.10145		646	2.31
303	0.0194		647	3.17
304	0.0524		648	3.35
305	0.0002881		649	> 3.75
306	1.43		650	> 3.75
307	0.376		651	> 3.75
308	> 3.75		652	> 3.75
309	0.28		653	> 3.75
310	0.765		654	> 3.75
311	0.217		655	> 3.75
312	2.86		656	> 3.75
313	15.8		657	> 3.75
314	> 3.75, > 50.0		658	> 3.75
315	> 3.75, > 50.0		659	> 3.75
316	0.002045		660	0.005037
317	1.36		661	0.279
318	0.0377		662	0.283
319	0.456		663	0.294
320	0.01205		664	0.555
321	0.00407		665	0.584
322	1.45		666	0.687
323	> 3.75		667	0.745
324	> 3.75		668	0.778

Ex. #	hTRPC6 Potency (μ M)		Ex. #	hTRPC6 Potency (μ M)
325	0.743		669	0.901
326	2.93		670	1.12
327	1.37		671	1.43
328	> 3.75		672	1.66
329	> 3.75		673	> 3.75
330	0.669		674	> 3.75
331	0.204		675	> 3.75
332	3.2		676	> 3.75
333	3.25		677	0.0881
334	3.54		678	0.0983
335	> 3.75		679	0.15
336	> 3.75		680	0.153
337	> 3.75		681	0.168
338	> 3.75		682	0.259
339	0.00323		683	0.29
340	0.000704		684	0.524
341	0.0258		685	1.16
342	0.0121		686	1.57
343	0.804		687	2.08
344	0.0853			

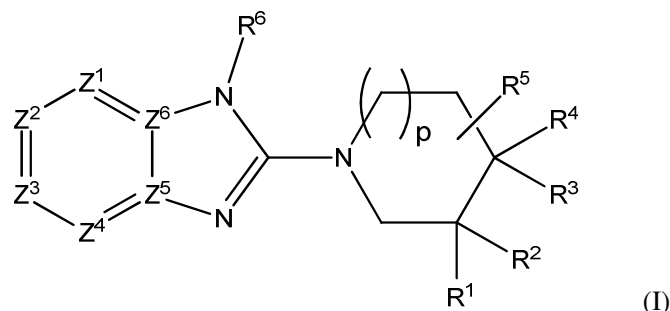
The foregoing is merely illustrative of the invention and is not intended to limit the invention to the disclosed compounds. Variations and changes which are obvious to one skilled in the art are intended to be within the scope and nature of the invention which are defined in the appended claims.

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From the foregoing description, one skilled in the art can easily ascertain the essential characteristics of this invention, and without departing from the spirit and scope thereof, can make various changes and modifications of the invention to adapt it to various usages and conditions.

What is claimed is

1. A compound or pharmaceutically acceptable salt thereof, according to Formula I:



Wherein

p is 0 or 1;

when p is 0, then R¹ is hydrogen, C₁-C₆alkyl, halogen or hydroxy; R² is amino or aminoC₁-C₄alkyl; R³ is hydrogen; and R⁴ is C₁-C₆alkyl or phenyl; or

when p is 0, then R¹ and R³, taken in combination, form a fused C₃-C₆cycloalkyl ring or a fused 4 to 6 member heterocycle ring having 1 or 2 ring heteroatoms independently selected from N, O or S, which cycloalkyl or heterocycle is optionally substituted with amino; R² is hydrogen, C₁-C₆alkyl or aminoC₁-C₄alkyl; and R⁴ is hydrogen; or

when p is 1, then R¹ is NHR^{1a}; R^{1a} is hydrogen, C₁-C₄alkyl, C₃-C₇cycloalkyl, hydroxyC₁-C₄alkyl, or 4 to 6 member heterocycloalkyl having one ring heteroatom selected from N, O or S; R² is hydrogen, C₁-C₄alkyl, hydroxyC₁-C₄alkyl or C(O)NH₂; R³ is halogen, C₁-C₄alkyl, C₁-C₄alkoxy or hydroxy; and R⁴ is hydrogen, C₁-C₄alkyl or halogen; or

when p is 0 or 1, then CR¹R², taken in combination, form a spirocyclic 4 to 6 member heterocycloalkyl; R³ is hydrogen, halogen, C₁-C₄alkyl, C₁-C₄alkoxy, or hydroxy; and R⁴ is hydrogen or halogen; or

when p is 1, then R¹ and R³, taken in combination, form a fused 4 to 6 member heterocycle or a fused 3 to 7 member carbocycle, which heterocycle comprises a ring nitrogen atom and optionally 0 or 1 additional ring heteroatoms selected from N, O and S, and which carbocycle is substituted with amino; and R² is hydrogen; and R⁴ is hydrogen, halogen or hydroxy;

R⁵ represents 1 or 2 substituents independently selected from hydrogen, halogen, hydroxy, amino, C₁-C₆alkyl or C₁-C₆alkoxy;

R⁶ is -(CR⁷R⁸)-A; or

R⁶ is a 4 to 7 member lactam which is optionally substituted with one or two substituents independently selected from the group consisting of hydroxy, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, C₃-C₆cycloalkyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, hydroxyC₁-C₆alkyl, C₁-C₆alkoxyC₁-C₆alkyl, phenyl, 4 to 7 member heterocycle having 1 ring atoms selected from N, O or S and 0 or 1 additional ring N atoms or 5 or 6 member heteroaryl having one ring heteroatom selected from N, O or S and 0 or 1

additional ring nitrogen atom, wherein the heteroaryl, heterocycle or phenyl group is optionally substituted with 0, 1 or 2 C₁-C₆alkyl or halogen; or

R⁶ is a partially unsaturated 9 or 10 member bicyclic carbocycle, which is optionally substituted with 1 or 2 substituents independently selected from halogen, cyano, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, C(O)NH₂ and C(O)NHC₁-C₆alkyl;

A is 5 or 6 member heteroaryl, which heteroaryl comprises one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms, which heteroaryl is optionally substituted with 0, 1, 2, 3 or 4 groups independently selected from halogen, cyano, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, C₃-C₆cycloalkyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, C(O)N(R^A)₂, S(O)₂C₁-C₆alkyl, phenyl or 5 or 6 member heteroaryl having one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms, wherein the optional heteroaryl or phenyl substituent is further substituted with 0, 1 or 2 C₁-C₆alkyl; or

A is phenyl substituted with 1, 2 or 3 substituents independently selected from halogen, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, haloC₁-C₆alkyl, cyanoC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, cyanoC₁-C₆alkoxy, S(O)_qC₁-C₆alkyl, S(O)₂NH₂, S(O)₂NHC₁-C₆alkyl, S(O)₂N(C₁-C₆alkyl)₂, C(O)NH₂, C(O)NHC₁-C₆alkyl, C(O)N(C₁-C₆alkyl)₂, hydroxy, cyano, or 5 or 6 member heteroaryl having one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms which heteroaryl is further substituted with 0, 1 or 2 C₁-C₆alkyl; or

A is C(O)OR⁹ or C(O)NR⁹R¹⁰; or

A is optionally substituted 9 or 10 member aromatic or partially unsaturated bicycyl having 0, 1 or 2 ring nitrogen atoms and 0 or 1 additional ring heteroatoms selected from N, O or S, which bicycyl is substituted with 0, 1 or 2 substituents independently selected from the group consisting of halogen, cyano, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, C(O)NH₂, C(O)OH or C(O)NHC₁-C₆alkyl;

R^A is independently selected at each occurrence from hydrogen or C₁-C₄alkyl; or

N(R^A)₂, taken in combination, forms a 4 to 7 member azacycle which is optionally substituted with 0, 1, or 2 C₁-C₄alkyl;

R⁷ is hydrogen, C₁-C₄alkyl or amino;

R⁸ is hydrogen or C₁-C₄alkyl; or

CR⁷R⁸, taken in combination form a 3 to 6 member cycloalkandiyl group;

R⁹ is hydrogen, C₁-C₆alkyl, C₃-C₆cycloalkyl, hydroxyC₁-C₆alkyl, C₁-C₄alkoxyC₁-C₆alkyl, haloC₁-C₆alkyl, cyano C₁-C₆alkyl or -(CH₂)_rR^{9A} wherein r is 0 or 1 and R^{9A} is phenyl, 4 to 7 member heterocycle having one ring heteroatoms selected from N, O or S, which ring sulfur may be optionally oxidized, and 0 or 1 additional ring N atoms or 5 or 6 member heteroaryl having one ring heteroatom selected from N, O or S and 0, 1, or 2 additional ring N atoms, which phenyl, heterocycle or heteroaryl is optionally substituted with 0, 1 or 2 halogen, C₁-C₄alkyl or C(O)C₁-C₄alkyl;

R^{10} is hydrogen, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, halo C_1 - C_6 alkyl, C_3 - C_7 cycloalkyl or saturated, partially unsaturated or aromatic 5 or 6 member heterocycle having 1 or 2 ring heteroatoms independently selected from N, O and S, which sulfur is optionally oxidized, and which heterocycle is optionally substituted with 1 or 2 substituents independently selected from C_1 - C_6 alkyl and halogen, which heterocycle has 1 or 2 ring hetero atoms selected from N, O or S, which sulfur may be optionally oxidized, and wherein each alkyl or cycloalkyl is optionally substituted with cyano, halogen, hydroxy, C_1 - C_6 alkoxy, $S(O)_qC_1$ - C_6 alkyl, 4 to 6 member heterocycle having 1 or 2 ring heteroatoms selected from N, O or S or 5 or 6 member heteroaryl having 1 ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms and where each heterocycle or heteroaryl is optionally substituted with 0, 1, or 2 C_1 - C_4 alkyl; or

NR^9R^{10} , taken in combination, form a monocyclic or bicyclic 4 to 10 member saturated or partially unsaturated heterocycle having one or two ring nitrogen atoms and 0 or 1 additional ring heteroatom selected from N, O or S, which ring sulfur may be optionally oxidized, which heterocycle is optionally substituted with 0, 1 or 2 substituents selected from halogen, oxo, hydroxy, cyano, C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, halo C_1 - C_6 alkyl, hydroxy C_1 - C_6 alkyl, cyano C_1 - C_6 alkyl, C_1 - C_6 alkoxy, halo C_1 - C_6 alkoxy, C_1 - C_6 alkoxy C_1 - C_4 alkyl, $S(O)_qC_1$ - C_6 alkyl, C_1 - C_6 alkyl $S(O)_qC_1$ - C_6 alkyl CO_2H , $C(O)C_1$ - C_6 alkyl, $C(O)OC_1$ - C_6 alkyl, $C(O)C_3$ - C_6 cycloalkyl, $N(R^{15})C(O)C_1$ - C_6 alkyl or $C(O)N(R^{15})_2$, phenyl, 4 to 6 member heterocycle having 1 or 2 ring heteroatoms selected from N, O or S or a 5 or 6 member heteroaryl having 1 ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms and where each heterocycle or heteroaryl is optionally substituted with 0, 1, or 2 C_1 - C_4 alkyl;

q is 0, 1 or 2;

Z^1 is N or CR^{11} ;

Z^2 is N or CR^{12} ;

Z^3 is N or CR^{13} ;

Z^4 is N or CR^{14} ,

Z^5 and Z^6 are each independently N or C;

wherein 0, 1 or 2 of Z^1 , Z^2 , Z^3 , Z^4 , Z^5 and Z^6 are N;

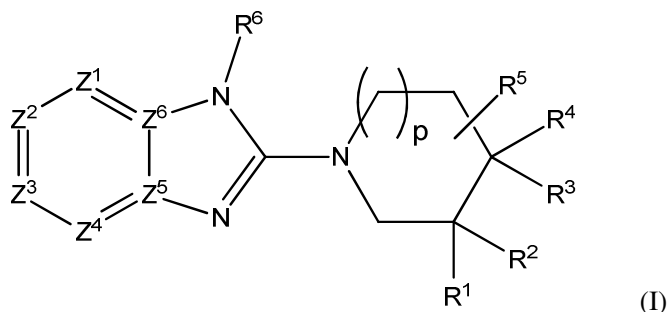
each of R^{11} , R^{12} , R^{13} and R^{14} is independently selected from the group consisting of hydrogen, halogen, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_1 - C_6 alkoxy, halo C_1 - C_6 alkyl, halo C_1 - C_6 alkoxy, C_3 - C_7 cycloalkyl, cyano, SO_2C_1 - C_6 alkyl, phenyl, and saturated, partially unsaturated or aromatic 5 or 6 member heterocycle having 1 or 2 ring heteroatoms independently selected from N, O and S, which heterocycle is optionally substituted with 1 or 2 substituents independently selected from C_1 - C_6 alkyl and halogen; and

R^{15} is selected at each occurrence from hydrogen or C_1 - C_4 alkyl, or

$N(R^{15})_2$, taken in combination, form a 4 to 7 member azacycle optionally substituted with 0, 1 or 2 C_1 - C_4 alkyl;

with the proviso that compounds of Formula I do not include 1- [7-fluoro-6-methoxy-1-[[2-(trifluoromethyl)phenyl]methyl]-1*H*-benzimidazol-2-yl]-3-piperidinamine.

2. A compound or pharmaceutically acceptable salt thereof, according to Formula I:



Wherein

p is 0 or 1;

when p is 0, then R¹ is hydrogen, C₁-C₆alkyl, halogen or hydroxy; R² is amino or aminoC₁-C₄alkyl; R³ is hydrogen; and R⁴ is C₁-C₆alkyl or phenyl; or

when p is 0, then R¹ and R³, taken in combination, form a fused C₃-C₆cycloalkyl ring or a fused 4 to 6 member heterocycle ring having 1 or 2 ring heteroatoms independently selected from N, O or S, which cycloalkyl or heterocycle is optionally substituted with amino; R² is hydrogen, C₁-C₆alkyl or aminoC₁-C₄alkyl; and R⁴ is hydrogen; or

when p is 1, then R¹ is NHR^{1a}; R^{1a} is hydrogen, C₁-C₄alkyl, C₃-C₇cycloalkyl, hydroxyC₁-C₄alkyl, or 4 to 6 member heterocycloalkyl having one ring heteroatom selected from N, O or S; R² is hydrogen, C₁-C₄alkyl, hydroxyC₁-C₄alkyl or C(O)NH₂; R³ is halogen, C₁-C₄alkyl, C₁-C₄alkoxy or hydroxy; and R⁴ is hydrogen, C₁-C₄alkyl or halogen; or

when p is 0 or 1, then C(NHR^{1a})R², taken in combination, form a spirocyclic 4 to 6 member heterocycloalkyl; R³ is hydrogen, halogen C₁-C₄alkyl, C₁-C₄alkoxy, or hydroxy; and R⁴ is hydrogen or halogen; or

when p is 1, then R¹ and R³, taken in combination, form a fused 4 to 6 member heterocycle or a fused 3 to 7 member carbocycle, which heterocycle comprises a ring nitrogen atom and optionally 0 or 1 additional ring heteroatoms selected from N, O and S, and which carbocycle is substituted with amino; and R² is hydrogen; and R⁴ is hydrogen, halogen or hydroxy;

R⁵ represents 1 or 2 substituents independently selected from hydrogen, halogen, hydroxy, amino, C₁-C₆alkyl or C₁-C₆alkoxy;

R⁶ is -(CR⁷R⁸)-A; or

R⁶ is a 4 to 7 member lactam which is optionally substituted with one or two substituents independently selected from the group consisting of hydroxy, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, hydroxyC₁-C₆alkyl, C₁-C₆alkoxyC₁-C₆alkyl, phenyl or 5 or 6 member heteroaryl having one ring heteroatom selected from N, O or S and 0 or 1 additional ring

nitrogen atom, wherein the heteroaryl or phenyl group is optionally substituted with 0, 1 or 2 C₁-C₆alkyl or halogen; or

R⁶ is a partially unsaturated 9 or 10 member bicyclic carbocycle, which is optionally substituted with 1 or 2 substituents independently selected from halogen, cyano, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, C(O)NH₂ and C(O)NHC₁-C₆alkyl;

A is 5 or 6 member heteroaryl, which heteroaryl comprises one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms, which heteroaryl is optionally substituted with 0, 1, 2, 3 or 4 groups independently selected from halogen, cyano, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, C(O)NH₂, C(O)NHC₁-C₆alkyl, phenyl or 5 or 6 member heteroaryl having one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms, wherein the optional heteroaryl or phenyl substituent is further substituted with 0, 1 or 2 C₁-C₆alkyl; or

A is phenyl substituted with 1, 2 or 3 substituents independently selected from halogen, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, haloC₁-C₆alkyl, cyanoC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, cyanoC₁-C₆alkoxy, S(O)_qC₁-C₆alkyl, S(O)₂NH₂, S(O)₂NHC₁-C₆alkyl, S(O)₂N(C₁-C₆alkyl)₂, C(O)NH₂, C(O)NHC₁-C₆alkyl, C(O)N(C₁-C₆alkyl)₂, hydroxy, cyano, or 5 or 6 member heteroaryl having one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms which heteroaryl is further substituted with 0, 1 or 2 C₁-C₆alkyl; or

A is C(O)OR⁹ or C(O)NR⁹R¹⁰; or

A is optionally substituted 9 or 10 member aromatic or partially unsaturated bicycyl having 0, 1 or 2 ring nitrogen atoms and 0 or 1 additional ring heteroatoms selected from N, O or S, which bicycyl is substituted with 0, 1 or 2 substituents independently selected from the group consisting of halogen, cyano, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, C(O)NH₂, C(O)OH or C(O)NHC₁-C₆alkyl;

R⁷ is hydrogen, C₁-C₄alkyl or amino;

R⁸ is hydrogen or C₁-C₄alkyl; or

CR⁷R⁸, taken in combination form a 3 to 6 member cycloalkandiyl group;

R⁹ is hydrogen, C₁-C₆alkyl, hydroxyC₁-C₆alkyl, haloC₁-C₆alkyl or cyano C₁-C₆alkyl;

R¹⁰ is hydrogen, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, halo C₁-C₆alkyl, C₃-C₇cycloalkyl or 4 to 7 member heterocycle, which heterocycle has 1 or 2 ring hetero atoms selected from N, O or S, which sulfur may be optionally oxidized, and wherein each alkyl or cycloalkyl is optionally substituted with cyano, halogen, hydroxy, C₁-C₆alkoxy, S(O)_qC₁-C₆alkyl, 4 to 6 member heterocycle having 1 or 2 ring heteroatoms selected from N, O or S or 5 or 6 member heteroaryl having 1 ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms; or

NR⁹R¹⁰, taken in combination, form a monocyclic or bicyclic 4 to 9 member heterocycle having one ring nitrogen atom and 0 or 1 additional ring heteroatom selected from N, O or S, which ring sulfur may be optionally oxidized, which heterocycle is optionally substituted with 0, 1 or 2 substituents

selected from halogen, oxo, hydroxy, cyano, C₁-C₆alkyl, halo C₁-C₆alkyl, hydroxyC₁-C₆alkyl, C₁-C₆alkoxy, S(O)_qC₁-C₆alkyl, CO₂H, C(O)C₁-C₆alkyl, or C(O)NH₂;

q is 0, 1 or 2;

Z¹ is N or CR¹¹;

Z² is N or CR¹²;

Z³ is N or CR¹³;

Z⁴ is N or CR¹⁴;

Z⁵ and Z⁶ are each independently N or C;

wherein 0, 1 or 2 of Z¹, Z², Z³, Z⁴, Z⁵ and Z⁶ are N;

each of R¹¹, R¹², R¹³ and R¹⁴ is independently selected from the group consisting of hydrogen, halogen, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, C₁-C₆alkoxy, haloC₁-C₆alkyl, haloC₁-C₆alkoxy, C₃-C₇cycloalkyl, cyano, SO₂C₁-C₆alkyl, phenyl, and saturated, partially unsaturated or aromatic 5 or 6 member heterocycle having 1 or 2 ring heteroatoms independently selected from N, O and S, which heterocycle is optionally substituted with 1 or 2 substituents independently selected from C₁-C₆alkyl and halogen; and with the proviso that compounds of Formula I do not include 1- [7-fluoro-6-methoxy-1-[[2-(trifluoromethyl)phenyl]methyl]-1*H*-benzimidazol-2-yl]-3-piperidinamine.

3. The compound of claim 1 or claim 2, wherein p is 0; R¹ and R³, taken in combination, form a fused C₃-C₆cycloalkyl ring or a fused 4 to 6 member azacycle ring, which cycloalkyl or azacycle is optionally substituted with amino; and R² and R⁴ are hydrogen.
4. The compound of claim 1 or claim 2, wherein p is 1, R¹ is NHR^{1a}; R^{1a} is hydrogen, C₁-C₄alkyl, C₃-C₇cycloalkyl or 4 to 6 member heterocycloalkyl having one ring heteroatom selected from N, O or S; R² is hydrogen or C₁-C₄alkyl; R³ is halogen, C₁-C₄alkyl, C₁-C₄alkoxy, or hydroxy; and R⁴ is hydrogen, halogen or C₁-C₄alkyl
5. The compound of claim 4, wherein R¹ is NHR^{1a}; R^{1a} is hydrogen, methyl, ethyl, propyl, isopropyl or cyclopropyl; R² is hydrogen or methyl; R³ is halogen, methyl, ethyl, methoxy, ethoxy, or hydroxy; and R⁴ is hydrogen, halogen, methyl or ethyl.
6. The compound of claim 4 or claim 5, wherein R¹ is NH₂; R² is hydrogen; R³ is fluorine, methyl, or hydroxy; and R⁴ is hydrogen, fluorine or methyl.
7. The compound of any one of claims 1 to 6, wherein R⁶ is -(CR⁷R⁸)-A.
8. The compound of either claim 7, wherein R⁷ is hydrogen or methyl; and R⁸ is hydrogen.
9. The compound of claim 7 or claim 8, wherein A is 5 or 6 member heteroaryl, which heteroaryl comprises one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms, which heteroaryl is optionally substituted with 0, 1, or 2 groups independently selected from halogen, cyano, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, C(O)NH₂, C(O)NHC₁-C₆alkyl, phenyl or 5 or 6 member heteroaryl having one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms, wherein the optional heteroaryl or phenyl substituent is further substituted with 0, 1 or 2 C₁-C₆alkyl.

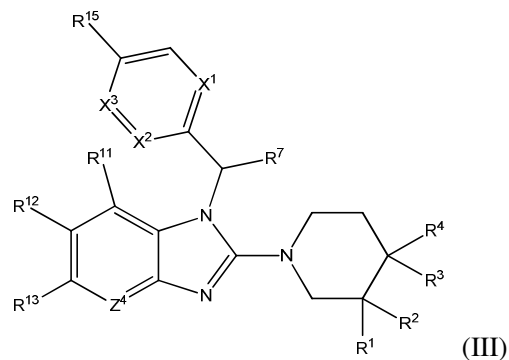
10. The compound of claim 9, wherein A is pyridin-2-yl, pyridin-3-yl, pyrimidin-2-yl, or pyrazin-2-yl, each of which is substituted with 1 to 3 groups independently selected from the group consisting of halogen, cyano, C₁-C₄alkyl, haloC₁-C₄alkyl, C₁-C₄alkoxy, haloC₁-C₄alkoxy, C(O)NH₂, C(O)NHC₁-C₄alkyl, phenyl or 5 member heteroaryl having one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms, wherein the optional heteroaryl or phenyl substituent is further substituted with 0, 1 or 2 C₁-C₆alkyl.
11. The compound of claim 7 or claim 8, wherein A is phenyl substituted with one substituent selected from the group consisting of halogen, C₁-C₄alkyl, haloC₁-C₄alkyl, C₁-C₄alkoxy, haloC₁-C₄alkoxy, hydroxy, cyano, or 5 member heteroaryl having one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms, and wherein the phenyl group is further optionally substituted with halogen, C₁-C₄alkyl, C₁-C₄alkoxy, haloC₁-C₄alkyl or haloC₁-C₄alkoxy.
12. The compound of claim 7 or claim 8, wherein A is C(O)NR⁹R¹⁰;
R⁹ is hydrogen, or C₁-C₄alkyl;
R¹⁰ is C₁-C₄alkyl, haloC₁-C₄alkyl, C₃-C₇cycloalkyl or 4 to 7 member heterocycle, which heterocycle has 1 or 2 ring hetero atoms selected from N, O or S, which sulfur may be optionally oxidized, and wherein each alkyl or cycloalkyl is optionally substituted with cyano, halogen, hydroxy, C₁-C₆alkoxy, S(O)_qC₁-C₆alkyl; or
NR⁹R¹⁰, taken in combination, form a monocyclic or bicyclic 4 to 9 member azacycle having one ring nitrogen atom and 0 or 1 additional ring heteroatom selected from N, O or S, which ring sulfur may be optionally oxidized, which azacycle is optionally substituted with 0, 1 or 2 substituents selected from halogen, oxo, hydroxy, cyano, C₁-C₆alkyl, halo C₁-C₆alkyl, hydroxyC₁-C₆alkyl, C₁-C₆alkoxy, S(O)₂C₁-C₆alkyl, CO₂H, C(O)C₁-C₆alkyl, or C(O)NH₂.
13. The compound of claim 12, wherein R⁹ is hydrogen, methyl or ethyl; and
R¹⁰ is C₁-C₄alkyl or haloC₁-C₄alkyl wherein each alkyl is optionally substituted with cyano, halogen, hydroxy, C₁-C₆alkoxy or S(O)_qC₁-C₆alkyl.
14. The compound of claim 12, wherein NR⁹R¹⁰, taken in combination, form a 4 to 6 member monocyclic azacycle or a 7 to 9 member bicyclic azacycle, each of which having one ring nitrogen atom and 0 or 1 additional ring heteroatom selected from N, O or S, which ring sulfur may be optionally oxidized, wherein each azacycle is optionally substituted with 0, 1 or 2 substituents selected from halogen, oxo, hydroxy, cyano, C₁-C₆alkyl, halo C₁-C₆alkyl, hydroxyC₁-C₆alkyl, C₁-C₆alkoxy, S(O)₂C₁-C₆alkyl, CO₂H, C(O)C₁-C₆alkyl, or C(O)NH₂.
15. The compound of any one of claims 1 to 14, wherein
Z¹ is CR¹¹;
Z² is CR¹²;
Z³ is CR¹³;
Z⁴ is N or CR¹⁴,
Z⁵ and Z⁶ are each C;

R¹¹ is hydrogen, halogen, cyano or C₁-C₄alkyl;

R¹² and R¹³ are each independently selected from the group consisting of hydrogen, halogen, cyano, C₁-C₄alkyl, haloC₁-C₄alkyl, C₁-C₄alkoxy, haloC₁-C₄alkoxy C₃-C₆cycloalkyl or 5 member saturated, partially unsaturated or aromatic 5 or 6 member heterocycle having 1 or 2 ring heteroatoms independently selected from N, O and S; and

R¹⁴ is hydrogen, halogen, cyano or C₁-C₄alkyl.

16. A compound of Formula III:



Wherein

X¹ is CR¹⁶ or N;

X² is CR¹⁷ or N;

X³ is CR¹⁸ or N;

Z⁴ is N or CR¹⁴;

R¹ is NHR^{1a};

R^{1a} is hydrogen or C₁-C₄alkyl;

R² is hydrogen or C₁-C₄alkyl;

R³ is hydrogen or halogen;

R⁴ is hydrogen or halogen;

R⁵ is hydrogen, methyl or ethyl;

R¹¹ is hydrogen, halogen, cyano or C₁-C₄alkyl;

R¹² and R¹³ are each independently selected from the group consisting of hydrogen, halogen, cyano, C₁-C₄alkyl, haloC₁-C₄alkyl, C₁-C₄alkoxy, or haloC₁-C₄alkoxy;

R¹⁴ is hydrogen, halogen, cyano or C₁-C₄alkyl;

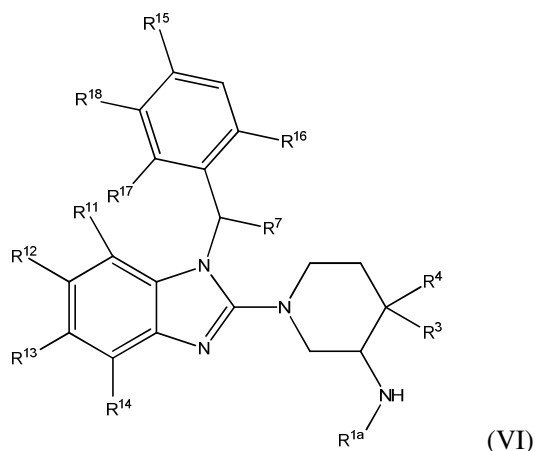
R¹⁵ is hydrogen, halogen, cyano, C₁-C₄alkyl, C₁-C₄alkoxy, haloC₁-C₄alkyl, haloC₁-C₄alkoxy, C(O)NH₂, C(O)NH(C₁-C₄alkyl) or 5 member heteroaryl having one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms;

R¹⁶ is hydrogen, halogen, cyano, C₁-C₄alkyl, C₁-C₄alkoxy, haloC₁-C₄alkyl or haloC₁-C₄alkoxy;

R¹⁷ is hydrogen or halogen; and

R¹⁸ is hydrogen, halogen, cyano, C₁-C₄alkyl, C₁-C₄alkoxy, haloC₁-C₄alkyl or haloC₁-C₄alkoxy, wherein at least one of R¹⁵, R¹⁶, R¹⁷ or R¹⁸ is not hydrogen.

17. A compound of Formula VI:



Wherein

R^{1a} is hydrogen or C_1 - C_4 alkyl;

R^3 is hydrogen or halogen;

R^4 is hydrogen or halogen;

R^7 is hydrogen, methyl or ethyl;

R^{11} is hydrogen, halogen, cyano or C_1 - C_4 alkyl;

R^{12} and R^{13} are each independently selected from the group consisting of hydrogen, halogen, cyano, C_1 - C_4 alkyl, halo C_1 - C_4 alkyl, C_1 - C_4 alkoxy, or halo C_1 - C_4 alkoxy;

R^{14} is hydrogen, halogen, cyano or C_1 - C_4 alkyl;

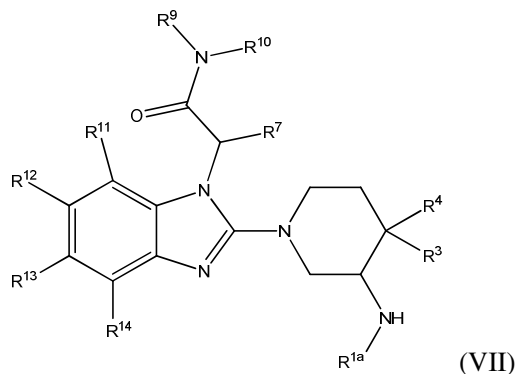
R^{15} is hydrogen, halogen, cyano, C_1 - C_4 alkyl, C_1 - C_4 alkoxy, halo C_1 - C_4 alkyl, halo C_1 - C_4 alkoxy, $C(O)NH_2$, $C(O)NH(C_1-C_4alkyl)$ or 5 member heteroaryl having one ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms;

R^{16} is hydrogen, halogen, cyano, C_1 - C_4 alkyl, C_1 - C_4 alkoxy, halo C_1 - C_4 alkyl or halo C_1 - C_4 alkoxy;

R^{17} is hydrogen or halogen; and

R^{18} is hydrogen, halogen, cyano, C_1 - C_4 alkyl, C_1 - C_4 alkoxy, halo C_1 - C_4 alkyl or halo C_1 - C_4 alkoxy, wherein at least one of R^{15} , R^{16} , R^{17} or R^{18} is not hydrogen.

18. A compound of Formula VII:



Wherein

R^{1a} is hydrogen or C₁-C₄alkyl;

R³ is hydrogen or halogen;

R⁴ is hydrogen or halogen;

R⁷ is hydrogen, methyl or ethyl;

R⁹ is hydrogen, methyl or ethyl;

R¹⁰ is C₁-C₄alkyl or haloC₁-C₄alkyl wherein each alkyl is optionally substituted with cyano, halogen, hydroxy, C₁-C₆alkoxy or S(O)_qC₁-C₆alkyl; or

NR⁹R¹⁰, taken in combination, form a 4 to 6 member monocyclic azacycle or a 7 to 9 member bicyclic azacycle, each of which having one ring nitrogen atom and 0 or 1 additional ring heteroatom selected from N, O or S, which ring sulfur may be optionally oxidized, wherein each azacycle is optionally substituted with 0, 1 or 2 substituents selected from halogen, oxo, hydroxy, cyano, C₁-C₆alkyl, halo C₁-C₆alkyl, hydroxyC₁-C₆alkyl, C₁-C₆alkoxy, S(O)₂C₁-C₆alkyl, CO₂H, C(O)C₁-C₆alkyl, or C(O)NH₂;

R¹¹ is hydrogen, halogen, cyano or C₁-C₄alkyl;

R¹² and R¹³ are each independently selected from the group consisting of hydrogen, halogen, cyano, C₁-C₄alkyl, haloC₁-C₄alkyl, C₁-C₄alkoxy, or haloC₁-C₄alkoxy; and

R¹⁴ is hydrogen, halogen, cyano or C₁-C₄alkyl.

19. The compound of any one of claims 16 to 18, wherein R¹¹ is hydrogen.

20. The compound of any one of claims 16 to 19, wherein R^{1a} is hydrogen or methyl; R³ is hydrogen or fluorine; and R⁴ is hydrogen or fluorine.

21. A compound, selected from:

(S)-6-((2-(3-aminopiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(S)-6-((2-(3-aminopiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(S)-6-((2-(3-aminopiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-4-carbonitrile;

(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3S,4S)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(S)-6-((2-(5-amino-3,3-difluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazole-4-carbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-(trifluoromethoxy)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-(trifluoromethoxy)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-5-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-6-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3aR,7aR)-hexahydro-1H-pyrrolo[2,3-c]pyridin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3aR,7aS)-hexahydro-1H-pyrrolo[2,3-c]pyridin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3aS,7aS)-hexahydro-1H-pyrrolo[2,3-c]pyridin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3aS,7aR)-hexahydro-1H-pyrrolo[2,3-c]pyridin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(R)-6-((2-(1,6-diazaspiro[3.5]nonan-6-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(S)-6-((2-(1,6-diazaspiro[3.5]nonan-6-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(3R,4R)-1-(1-((5-chloropyridin-2-yl)methyl)-6-(methylsulfonyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4R)-1-(1-((5-chloropyridin-2-yl)methyl)-5-(methylsulfonyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazole-4-carbonitrile;

(3R,4R)-1-(5,7-difluoro-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4R)-1-(4,6-difluoro-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4R)-1-(5,7-difluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4R)-1-(4,6-difluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-4-carbonitrile;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-4-carbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(3R,4S)-1-(1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4S)-1-(1-((5-chloropyrimidin-2-yl)methyl)-5-fluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(R)-2-(3-amino-4,4-difluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

(R)-2-(3-amino-4,4-difluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

tert-butyl ((3R,4R)-1-(1-((5-cyanopyridin-2-yl)methyl)-5,6-dimethyl-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-yl)carbamate;

(S)-6-((2-(3-aminopiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

(S)-6-((2-(3-aminopiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

(S)-2-(3-aminopiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

(S)-2-(3-aminopiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;

(R)-2-(3-amino-4,4-difluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

(R)-2-(3-amino-4,4-difluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;

(S)-6-((2-(3-aminopiperidin-1-yl)-4,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-4,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-4,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(S)-6-((2-(3-aminopiperidin-1-yl)-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(S)-6-((2-(3-aminopiperidin-1-yl)-5,7-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,7-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5,7-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-5,7-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;

(S)-6-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((1R,5S)-1-(aminomethyl)-3-azabicyclo[3.1.0]hexan-3-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((1S,5R)-1-(aminomethyl)-3-azabicyclo[3.1.0]hexan-3-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3aR,4R,6aS)-4-aminohexahydrocyclopenta[c]pyrrol-2(1H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3aS,4S,6aR)-4-aminohexahydrocyclopenta[c]pyrrol-2(1H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3aR,4S,6aS)-4-aminohexahydrocyclopenta[c]pyrrol-2(1H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3aS,4R,6aR)-4-aminohexahydrocyclopenta[c]pyrrol-2(1H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

(R)-6-((2-(3-(aminomethyl)pyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

(S)-6-((2-(3-(aminomethyl)pyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5,6-dichloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

(R)-1-(1-((5-chloropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4,4-difluoropiperidin-3-amine hydrochloride;

(3R,4S)-1-(1-((5-chloropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-4-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-4-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-3H-imidazo[4,5-b]pyridin-3-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-imidazo[4,5-b]pyridin-1-yl)methyl)-N-(tert-butyl)nicotinamide;

6-((2-((3R,4R)-3-amino-4-hydroxypiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3S,4S)-3-amino-4-hydroxypiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-(2,6-diazaspiro[3.4]octan-6-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((4aR,7aS)-hexahydropyrrolo[3,4-b][1,4]oxazin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((4aS,7aR)-hexahydropyrrolo[3,4-b][1,4]oxazin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((4aR,7aR)-hexahydropyrrolo[3,4-b][1,4]oxazin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((4aS,7aS)-hexahydropyrrolo[3,4-b][1,4]oxazin-6(2H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(S)-3-amino-1-(1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidine-3-carboxamide;

(R)-3-amino-1-(1-((5-cyanopyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidine-3-carboxamide;

(S)-6-((2-(3-amino-3-(hydroxymethyl)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(R)-6-((2-(3-amino-3-(hydroxymethyl)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4S)-3-amino-4-fluoro-1-piperidinyl)-6-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4S)-3-amino-4-fluoro-1-piperidinyl)-5-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R)-3-amino-4,4-difluoro-1-piperidinyl)-6-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R)-3-amino-4,4-difluoro-1-piperidinyl)-5-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5-methyl-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-6-methyl-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-6-chloro-5-methyl-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5-chloro-6-methyl-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-6-fluoro-5-methyl-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5-fluoro-6-methyl-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3S)-3-(methylamino)-1-piperidinyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R)-3-(methylamino)-1-piperidinyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-6-(difluoromethoxy)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5-(difluoromethoxy)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-4-methoxy-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-4-methyl-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

5-((2-((3R,4S)-3-amino-4-fluoro-1-piperidinyl)-6-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-2-pyrazinecarboxamide;

5-((2-((3R,4S)-3-amino-4-fluoro-1-piperidinyl)-5-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-2-pyrazinecarboxamide;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-6-chloro-5-(trifluoromethoxy)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5-chloro-6-(trifluoromethoxy)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-6-chloro-5-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5-chloro-6-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((5R)-1,7-diazaspiro[4.5]decan-7-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile, 6-((2-((5S)-1,7-diazaspiro[4.5]decan-7-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((6R)-1,8-diazaspiro[5.5]undecan-8-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((6S)-1,8-diazaspiro[5.5]undecan-8-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((4aR,8aR)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((4aS,8aS)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

5-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)-2-pyrazinecarboxamide;

5-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-6-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-2-pyrazinecarboxamide;

6-((2-((5R)-1,7-diazaspiro[4.5]decan-7-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((5S)-1,7-diazaspiro[4.5]decan-7-yl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R)-3-amino-4,4-difluoro-1-piperidinyl)-5-methoxy-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3R)-3-amino-4,4-difluoro-1-piperidinyl)-6-methoxy-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3S)-3-(methylamino)-1-piperidinyl)-6-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3S)-3-(methylamino)-1-piperidinyl)-5-(trifluoromethyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

6-((2-((3S)-3-amino-3-methyl-1-piperidinyl)-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

(S)-6-((2-(3-aminopiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile 2,2,2-trifluoroacetate;

(S)-6-((2-(3-aminopiperidin-1-yl)-5-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile 2,2,2-trifluoroacetate;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4-chloro-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile 2,2,2-trifluoroacetate;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5-methoxy-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazole-4-carbonitrile;

(R)-2-(3-amino-4,4-difluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-5-fluoro-1H-benzo[d]imidazole-7-carbonitrile;

(R)-2-(3-amino-4,4-difluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazole-4-carbonitrile;

6-((2-((3R,4R)-3-amino-4-hydroxypiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4S)-3-amino-4-hydroxypiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(R)-4-((2-(3-amino-4,4-difluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

4-((2-((3R,4R)-3-amino-4-hydroxypiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile compound with 4-((2-((3S,4S)-3-amino-4-hydroxypiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile (1:1) dihydrochloride;

4-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,7-difluoro-1H-benzimidazol-1-yl)methyl)benzonitrile;

4-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-4,6-difluoro-1H-benzimidazol-1-yl)methyl)benzonitrile;

2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-1-(4-cyanobenzyl)-1H-benzimidazole-6-carbonitrile;

2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-1-(4-cyanobenzyl)-1H-benzimidazole-5-carbonitrile;

2-((3R)-3-amino-4,4-difluoro-1-piperidinyl)-1-(4-cyanobenzyl)-1H-benzimidazole-6-carbonitrile;

2-((3R)-3-amino-4,4-difluoro-1-piperidinyl)-1-(4-cyanobenzyl)-1H-benzimidazole-5-carbonitrile;

(R)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

4-((2-((3R,4R)-3-amino-4-methylpiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

4-((2-(3-(aminomethyl)-3-methylpyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

4-((2-((3S,4R)-3-amino-4-phenylpyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile & 4-((2-((3R,4S)-3-amino-4-phenylpyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

(S)-4-((2-(3-aminopyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

(S)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

4-((2-(6-amino-2-azaspiro[4.4]nonan-2-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;
4-((2-(4-amino-4-hydroxycyclopenta[c]pyrrol-2(1H)-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;
4-((2-((3S,4S)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;
4-((2-((3S,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;
4-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;
4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;
(R)-4-((2-(3-(aminomethyl)-3-fluoropyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile 2,2,2-trifluoroacetate;
(S)-4-((2-(3-(aminomethyl)-3-fluoropyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile 2,2,2-trifluoroacetate;
(R)-4-((2-(3-(aminomethyl)-3-hydroxypyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile 2,2,2-trifluoroacetate;
(S)-4-((2-(3-(aminomethyl)-3-hydroxypyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile 2,2,2-trifluoroacetate;
(S)-4-((2-(3-(aminomethyl)pyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;
(R)-4-((2-(3-(aminomethyl)pyrrolidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;
4-((2-((3S,4S)-3-amino-4-methylpiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile 2,2,2-trifluoroacetate;
4-((2-((3S,4R)-3-amino-4-methylpiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile 2,2,2-trifluoroacetate;
4-((2-((3R,4S)-3-amino-4-methylpiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile 2,2,2-trifluoroacetate;
4-((2-((1S,5R)-1-(aminomethyl)-3-azabicyclo[3.1.0]hexan-3-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;
4-((2-((1R,5S)-1-(aminomethyl)-3-azabicyclo[3.1.0]hexan-3-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;
(R)-4-((2-(3-aminopiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;
(R)-4-((2-(3-aminopiperidin-1-yl)-5-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;
2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;
(3R,4R)-4-fluoro-1-(1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
(3R,4R)-4-fluoro-1-(1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;

(3R,4R)-1-(1-((5-bromopyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4R)-4-fluoro-1-(1-((5-(trifluoromethyl)pyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(3R,4R)-4-fluoro-1-(1-((5-methoxypyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(3R,4R)-1-(1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-cyanopyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-bromopyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-bromopyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;

5-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)pyrazine-2-carbonitrile;

2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile;

(3R,4R)-3-amino-1-(1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)piperidin-4-ol;

(3R,4R)-3-amino-1-(1-((5-chloropyrimidin-2-yl)methyl)-5-fluoro-1H-benzo[d]imidazol-2-yl)piperidin-4-ol;

6-((2-((3R,4R)-3-amino-4-hydroxypiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-hydroxypiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(S)-1-(1-((5-chloropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(S)-5-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)picolinonitrile;

(3R,4R)-1-(1-((5-chloropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyridin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile hydrochloride;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyridin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile hydrochloride;

(3R,4R)-1-(1-((R)-1-(5-chloropyridin-2-yl)ethyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

(3R,4R)-1-(1-((S)-1-(5-chloropyridin-2-yl)ethyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

(3R,4R)-1-(1-((R)-1-(5-chloropyridin-2-yl)ethyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

(3R,4R)-1-(1-((S)-1-(5-chloropyridin-2-yl)ethyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

(3R,4R)-1-(5-chloro-1-((R)-1-(5-chloropyridin-2-yl)ethyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

(3R,4R)-1-(5-chloro-1-((S)-1-(5-chloropyridin-2-yl)ethyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

(3R,4R)-1-(6-chloro-1-((R)-1-(5-chloropyridin-2-yl)ethyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

(3R,4R)-1-(6-chloro-1-((S)-1-(5-chloropyridin-2-yl)ethyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((R)-1-(5-cyanopyridin-2-yl)ethyl)-1H-benzo[d]imidazole-6-carbonitrile hydrochloride;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((R)-1-(5-cyanopyridin-2-yl)ethyl)-1H-benzo[d]imidazole-5-carbonitrile hydrochloride;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((S)-1-(5-cyanopyridin-2-yl)ethyl)-1H-benzo[d]imidazole-6-carbonitrile hydrochloride;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((S)-1-(5-cyanopyridin-2-yl)ethyl)-1H-benzo[d]imidazole-5-carbonitrile hydrochloride;

(3R,4R)-1-(1-((5-chloropyridin-2-yl)methyl)-5,6-difluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

(3R,4R)-1-(5,6-difluoro-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine hydrochloride;

(R)-1-(1-((5-chloropyridin-2-yl)methyl)-5,7-difluoro-1H-benzo[d]imidazol-2-yl)-4,4-difluoropiperidin-3-amine hydrochloride;

(R)-1-(1-((5-chloropyridin-2-yl)methyl)-4,6-difluoro-1H-benzo[d]imidazol-2-yl)-4,4-difluoropiperidin-3-amine hydrochloride;

(R)-1-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)-2,3-dihydro-1H-indene-5-carbonitrile hydrochloride;

(S)-1-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)-2,3-dihydro-1H-indene-5-carbonitrile hydrochloride;

(R)-5-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)pyrazine-2-carbonitrile;

(R)-5-((2-(3-amino-4,4-difluoropiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)methyl)pyrazine-2-carbonitrile;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-isopropylacetamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(azetidin-1-yl)ethanone;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-N-(2-cyanopropyl)-N-ethylacetamide;

3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-methylpyrrolidin-2-one;

3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-phenylpiperidin-2-one;

3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-chlorophenyl)pyrrolidin-2-one;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-methoxypyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile hydrochloride;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-methoxypyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile hydrochloride;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((6-(trifluoromethyl)pyridin-3-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile hydrochloride;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((6-(trifluoromethyl)pyridin-3-yl)methyl)-1H-benzo[d]imidazole-5-carbonitrile hydrochloride;

(S)-3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-methylpyrrolidin-2-one;

(R)-3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-methylpyrrolidin-2-one;

(S)-3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-chlorophenyl)pyrrolidin-2-one;

(R)-3-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(4-chlorophenyl)pyrrolidin-2-one;

2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-1-((5-cyano-2-pyrazinyl)methyl)-1H-benzimidazole-6-carbonitrile;

2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-1-((5-cyano-2-pyrazinyl)methyl)-1H-benzimidazole-5-carbonitrile;

5-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-4,6-difluoro-1H-benzimidazol-1-yl)methyl)-2-pyrazinecarbonitrile;

5-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,7-difluoro-1H-benzimidazol-1-yl)methyl)-2-pyrazinecarbonitrile;

(3S)-1-(1-((5-fluoro-2-pyridinyl)methyl)-1H-benzimidazol-2-yl)-N-methyl-3-piperidinamine;

(3S)-1-(1-((5-chloro-2-pyridinyl)methyl)-1H-benzimidazol-2-yl)-N-methyl-3-piperidinamine;

6-((1R)-1-(2-((3S)-3-(methylamino)-1-piperidinyl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile;

6-((1S)-1-(2-((3S)-3-(methylamino)-1-piperidinyl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile;

(3R,4R)-1-(1-((5-chloro-2-pyrimidinyl)methyl)-5,7-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((5-chloro-2-pyrimidinyl)methyl)-4,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(5,6-difluoro-1-((1-methyl-1H-indazol-4-yl)methyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(5,6-difluoro-1-(5-quinolinylmethyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(5,6-difluoro-1-((1R)-1-(8-quinolinyl)ethyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(5,6-difluoro-1-((1S)-1-(8-quinolinyl)ethyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((3-(3-chlorophenyl)-1,2-oxazol-5-yl)methyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(5,6-difluoro-1-((1-methyl-1H-indazol-7-yl)methyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-(2,6-dichlorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

1-(1-azetidiny)-2-(2-((3S)-3-(methylamino)-1-piperidinyl)-1H-benzimidazol-1-yl)ethanone;

6-((1R)-1-(4,6-difluoro-2-((4aR,8aR)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile;

6-((1R)-1-(4,6-difluoro-2-((4aS,8aS)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile;

6-((1S)-1-(4,6-difluoro-2-((4aS,8aS)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile;

6-((1S)-1-(4,6-difluoro-2-((4aR,8aR)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile;

6-((1R)-1-(5,7-difluoro-2-((4aR,8aR)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile;

6-((1R)-1-(5,7-difluoro-2-((4aS,8aS)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile;

6-((1S)-1-(5,7-difluoro-2-((4aS,8aS)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile;

6-((1S)-1-(5,7-difluoro-2-((4aR,8aR)-hexahydro-2H-pyrido[4,3-b][1,4]oxazin-6(5H)-yl)-1H-benzimidazol-1-yl)ethyl)-3-pyridinecarbonitrile;

2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-5,6-difluoro-1H-benzimidazol-1-yl)-N-methylacetamide;

2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-5,6-difluoro-1H-benzimidazol-1-yl)-1-(4-morpholinyl)ethanone;

2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-5,6-difluoro-1H-benzimidazol-1-yl)-1-(1-pyrrolidiny)ethanone;

2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-5,6-difluoro-1H-benzimidazol-1-yl)-N,N-dimethylacetamide;

(2R)-2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-5,6-difluoro-1H-benzimidazol-1-yl)-N,N-dimethylpropanamide;

(2S)-2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-5,6-difluoro-1H-benzimidazol-1-yl)-N,N-dimethylpropanamide;

2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-5,6-difluoro-1H-benzimidazol-1-yl)-1-(1-piperidiny)ethanone;

2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-5,6-difluoro-1H-benzimidazol-1-yl)-N-ethylacetamide;

1-((5-chloro-2-pyrimidinyl)methyl)-2-((3R,4R)-4-fluoro-3-(methylamino)-1-piperidiny)-1H-benzimidazole-6-carbonitrile;

1-((5-chloro-2-pyrimidinyl)methyl)-2-((3R,4R)-4-fluoro-3-(methylamino)-1-piperidiny)-1H-benzimidazole-5-carbonitrile;

2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-6-chloro-1H-benzimidazol-1-yl)-1-(1-azetidiny)ethanone;

2-(2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5-chloro-1H-benzimidazol-1-yl)-1-(1-azetidiny)ethanone;

2-((3R,4S)-3-amino-4-fluoro-1-piperidinyl)-1-(2-(1-azetidiny)-2-oxoethyl)-1H-benzimidazole-6-carbonitrile;

2-((3R,4S)-3-amino-4-fluoro-1-piperidinyl)-1-(2-(1-azetidiny)-2-oxoethyl)-1H-benzimidazole-5-carbonitrile;

(3R,4R)-1-(1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4R)-1-(1-((5-chloropyrimidin-2-yl)methyl)-5-fluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(R)-6-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(R)-5-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)picolinonitrile 2,2,2-trifluoroacetate;

(R)-1-(1-(isoquinolin-7-ylmethyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(R)-1-(1-((1-methyl-1H-indazol-7-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

6-((R)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile hydrochloride;

6-((S)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile hydrochloride;

6-((R)-1-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile hydrochloride;

6-((S)-1-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile hydrochloride;

6-((R)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)propyl)nicotinonitrile hydrochloride;

6-((S)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)propyl)nicotinonitrile hydrochloride;

(3R,4R)-1-(5,6-difluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

3-(1-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile;

(3R,4R)-1-(5,6-difluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4S)-1-(5,6-difluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

(3R,4S)-4-fluoro-1-(1-((5-fluoropyrimidin-2-yl)methyl)-6-(trifluoromethyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(3R,4S)-4-fluoro-1-(1-((5-fluoropyrimidin-2-yl)methyl)-5-(trifluoromethyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(R)-1-(5,6-difluoro-1-((5-fluoropyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4,4-difluoropiperidin-3-amine;

2-(2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)-1-(azetidin-1-yl)ethan-1-one;

2-(2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-5-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)-1-(azetidin-1-yl)ethan-1-one;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(2,2-dimethylpyrrolidin-1-yl)ethan-1-one;

6-((2-((3R,4S)-3-amino-4-hydroxypiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4S)-3-amino-4-hydroxypiperidin-1-yl)-5-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

4-((R)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile hydrochloride;

4-((S)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile hydrochloride;

(S)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-3-fluorobenzonitrile hydrochloride;

(S)-1-(1-(4-chlorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine hydrochloride;

4-((R)-1-(2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile hydrochloride;

4-((S)-1-(2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile hydrochloride;

4-((R)-1-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile hydrochloride;

4-((S)-1-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile hydrochloride;

(S)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-3-chlorobenzonitrile hydrochloride;

(3R,4R)-1-(1-((1R)-1-(2,4-dichlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((1S)-1-(2,4-dichlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((1R)-1-(2-chlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((1S)-1-(2-chlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((1R)-1-(3-chlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((1S)-1-(3-chlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((1R)-1-(2,5-dichlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((1S)-1-(2,5-dichlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((1R)-1-(2,4-difluorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((1S)-1-(2,4-difluorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((1R)-1-(3,4-dichlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((1S)-1-(3,4-dichlorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((1R)-1-(2,5-difluorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-((1S)-1-(2,5-difluorophenyl)ethyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(5,6-difluoro-1-((1R)-1-(4-(trifluoromethyl)phenyl)ethyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(5,6-difluoro-1-((1R)-1-(4-(trifluoromethoxy)phenyl)ethyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-(5-chloro-2-(trifluoromethoxy)benzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(5,6-difluoro-1-(4-(1H-1,2,4-triazol-1-yl)benzyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

2-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)-5-chlorobenzonitrile;

(3R,4R)-1-(1-(2,4-dichlorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

4-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)-3-(difluoromethoxy)benzonitrile;

(3R,4R)-1-(1-(2,5-dichlorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-(4-(1,1-difluoroethyl)benzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

4-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)-2-methylbenzonitrile;

4-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)-2-chlorobenzonitrile;

2-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)-4-chlorobenzonitrile;

(3R,4R)-1-(1-(2-(difluoromethoxy)benzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-(3-chloro-4-fluorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-(4-chloro-2-methoxybenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-(2,4-difluorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(5,6-difluoro-1-(2-(trifluoromethyl)benzyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

2-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)benzonitrile;

(3R,4R)-1-(1-(2-chlorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-(2-chloro-4-fluorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(5,6-difluoro-1-(4-fluoro-2-(trifluoromethyl)benzyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-(3,4-difluorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-(4-chloro-2-fluorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-(3,4-dichlorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-(4-chloro-3-fluorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(5,6-difluoro-1-(4-(trifluoromethyl)benzyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(5,6-difluoro-1-(4-(trifluoromethoxy)benzyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(1-(4-(difluoromethyl)benzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(5,6-difluoro-1-(3-(trifluoromethoxy)benzyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(3R,4R)-1-(5,6-difluoro-1-(3-(trifluoromethyl)benzyl)-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

3-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-5,6-difluoro-1H-benzimidazol-1-yl)methyl)benzonitrile;

(3R,4R)-1-(1-(3-chlorobenzyl)-5,6-difluoro-1H-benzimidazol-2-yl)-4-fluoro-3-piperidinamine;

(S)-1-(1-(4-fluorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(S)-1-(1-(4-(1,2,4-oxadiazol-3-yl)benzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(R)-1-(1-(4-(methylsulfonyl)benzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(R)-1-(1-(4-(1H-1,2,4-triazol-1-yl)benzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(R)-2-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

(R)-1-(1-(2,6-dichlorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(R)-1-(1-(2-chlorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(R)-1-(1-(4-(trifluoromethyl)benzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(R)-1-(1-(4-(trifluoromethoxy)benzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(R)-1-(1-(4-chlorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(R)-1-(1-(3-chlorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(R)-1-(1-(4-(1,1-difluoroethyl)benzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(R)-2-(4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)phenyl)-2-methylpropanenitrile;

(R)-1-(1-(4-(difluoromethyl)benzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(R)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-N-methylbenzamide;

(R)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-3-fluorobenzonitrile;

(R)-2-(4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)phenoxy)acetonitrile;

(R)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-N,N-dimethylbenzenesulfonamide;

(R)-1-(1-(4-methylbenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(R)-1-(1-(4-fluorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(R)-1-(1-((1-methyl-1H-indazol-7-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(R)-1-(1-(2,4-difluorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

(R)-1-(1-(3,4-difluorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
 (R)-1-(1-(4-chloro-3-fluorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
 (R)-1-(1-((3-(3-chlorophenyl)isoxazol-5-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
 (R)-1-(1-(3-chloro-4-methoxybenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
 (R)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-3-chlorobenzonitrile;
 (R)-1-(1-(2,4-dichlorobenzyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;
 (R)-4-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-3-methoxybenzonitrile;
 (R)-2-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)-5-chlorobenzonitrile;
 4-((R)-1-(2-((R)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile;
 4-(1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)benzonitrile;
 (R)-3-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;
 4-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile hydrochloride;
 (S)-4-((2-(3-aminopiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile hydrochloride;
 4-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;
 (S)-4-((2-(3-aminopiperidin-1-yl)-5-methoxy-3H-imidazo[4,5-b]pyridin-3-yl)methyl)benzonitrile hydrochloride;
 (R)-4-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;
 (R)-4-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;
 (R)-4-((2-(3-amino-4,4-difluoropiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;
 4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;
 4-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;
 (R)-4-((2-(3-amino-4,4-difluoropiperidin-1-yl)-4-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;
 4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-4-methoxy-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;
 4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-imidazo[4,5-c]pyridin-1-yl)methyl)benzonitrile;
 4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-3H-imidazo[4,5-c]pyridin-3-yl)methyl)benzonitrile;

4-((2-((3R,4R)-3-amino-4-fluoro-1-piperidinyl)-6-ethoxy-1H-benzimidazol-1-yl)methyl)benzonitrile;

4-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-1H-imidazo[4,5-b]pyridin-1-yl)methyl)benzonitrile;

4-((2-((3R)-3-amino-4,4-difluoro-1-piperidinyl)-6-fluoro-1H-benzimidazol-1-yl)methyl)benzonitrile;

4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-imidazo[4,5-b]pyridin-1-yl)methyl)benzonitrile;

(S)-4-((2-(3-aminopiperidin-1-yl)-4-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile 2,2,2-trifluoroacetate;

(S)-4-((2-(3-aminopiperidin-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)methyl)benzonitrile hydrochloride;

4-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile hydrochloride;

(S)-4-((2-(3-aminopiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

(S)-4-((2-(3-aminopiperidin-1-yl)-5-chloro-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile;

(R)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)-2,3-dihydro-1H-indene-5-carbonitrile;

(S)-1-(2-((S)-3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)-2,3-dihydro-1H-indene-5-carbonitrile;

(3R,4R)-4-fluoro-1-(1-((5-methoxypyridin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine;

1-(2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetyl)azetidine-3-carbonitrile;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(3-(tert-butoxy)azetidin-1-yl)ethan-1-one;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(3,3-difluoroazetidin-1-yl)ethanone;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(3-isopropylazetidin-1-yl)ethanone;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(6,6-difluoro-2-azaspiro[3.3]heptan-2-yl)ethanone;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)-1-(7-oxa-2-azaspiro[3.5]nonan-2-yl)ethanone;

(R)-6-((2-(4,4-difluoro-3-(methylamino)piperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(R)-6-((2-(4,4-difluoro-3-((2-hydroxyethyl)amino)piperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(S)-6-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinic acid;

(S)-6-((2-(3-aminopiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinamide;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinamide;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-5,6-difluoro-1H-benzo[d]imidazol-1-yl)acetic acid;

6-((R)-1-(4,6-difluoro-2-((3R,4R)-4-fluoro-3-(methylamino)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile;

6-((S)-1-(4,6-difluoro-2-((3R,4R)-4-fluoro-3-(methylamino)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile;

6-((R)-1-(5,7-difluoro-2-((3R,4R)-4-fluoro-3-(methylamino)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile; and

6-((S)-1-(5,7-difluoro-2-((3R,4R)-4-fluoro-3-(methylamino)piperidin-1-yl)-1H-benzo[d]imidazol-1-yl)ethyl)nicotinonitrile.

22. A compound, selected from:

6-((2-((3R,4S)-3-amino-4-fluoropiperidin-1-yl)-6-chloro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazole-4-carbonitrile;

(3R,4R)-1-(4,6-difluoro-1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine;

6-((2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-4,6-difluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile hydrochloride;

(R)-6-((2-(3-amino-4,4-difluoropiperidin-1-yl)-6-fluoro-1H-benzo[d]imidazol-1-yl)methyl)nicotinonitrile;

6-((2-((3R,4R)-3-amino-4-fluoro-1-piperidiny)-4-methoxy-1H-benzimidazol-1-yl)methyl)-3-pyridinecarbonitrile;

2-(2-((3R,4R)-3-amino-4-fluoropiperidin-1-yl)-1-((5-chloropyrimidin-2-yl)methyl)-1H-benzo[d]imidazole-6-carbonitrile;

(3R,4R)-4-fluoro-1-(1-((5-fluoropyrimidin-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)piperidin-3-amine; and

(3R,4R)-1-(1-((5-chloropyrimidin-2-yl)methyl)-6-fluoro-1H-benzo[d]imidazol-2-yl)-4-fluoropiperidin-3-amine.

23. The compound of any one of claims 1 to 22 in a form of a pharmaceutically acceptable salt.
24. A pharmaceutical composition comprising a pharmaceutically acceptable excipient, carrier or adjuvant and at least one compound of any one of claims 1 to 23.
25. Use of at least one compound of any one of claims 1 to 23, or a pharmaceutical salt thereof or a pharmaceutical composition thereof in the manufacture of a medicament for treating a disease or disorder mediated by TRPC6 in a mammal, wherein the disease or disorder mediated by TRPC6 is selected from the group consisting of nephrotic syndrome, minimal change disease, focal segmental glomerulosclerosis, collapsing glomerulopathy, membranous nephropathy, membranoproliferative glomerulonephritis, IGA nephropathy, acute renal failure, chronic renal failure, diabetic nephropathy, sepsis, pulmonary hypertension, acute lung disorder, acute respiratory distress syndrome (ARDS), heart failure, stroke, malignant tumor, and muscular dystrophy.
26. A compound of any one of claims 1 to 23 for use as a medicament.